E-Posters

All e-Posters will be available on the virtual congress platform during the entire congress until 3 months after the congress. In addition, Poster presenters that are registered to participate onsite in Milan were asked to print a Poster that will be available in the Poster area next to the exhibition. Poster presentations will not have a dedicated session time.

ID:1594

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

THE MACROPHAGE ACTIVATION AND THE CAROTID INTIMA-MEDIA THICKNESS IN UNTREATED RHEUMATOID ARTHRITIS PATIENTS (PRELIMINARY DATA).

POSTER VIEWING SESSION

Elena V. Gerasimova[1], Tatiana V. Kirichenko[2], Tatiana V. Popkova[1], Alexander M. Markin[2], Yulia V. Markina[2], Anastasia I. Bogatyreva[2]
[1]Laboratory Of Systemic Rheumatic Diseases, V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation, [2]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation

Background and Aims : To evaluate the macrophage activation, and the carotid intima-media thickness (IMT) in untreated rheumatoid arthritis patients (RApts).

Methods: Thirty six untreated RApts (30F/6M) were enrolled. RApts had median age of 39 years (range) (33-45), disease duration of 2.5 years (1-5), moderate clinical disease activity DAS 28 of 5.3(3.5;5.8). The value of monocyte activation was expressed as a ratio of the level of secretion of proinflammatory cytokines by monocytes cultured with and without LPS addition. Secretion levels were determined by ELISA. The belonging of the isolated cells to CD14 + monocytes was additionally confirmed by flow cytometry.

Results: In RApts, macrophage activation was 8.9 (range) (2.7;40.8)$ it was independent of age, sex, body mass index, CVR factors, DAS28, and RA-specific autoantibodies levels. In RApts, the carotid mean IMT (m-IMT) was 0.66±0.12mm, the maximum IMT (M-IMT) was 0.76±0.16mm. The prevalence of raised lesions (IMT>0.9 mm) were observed in 5 RApts (14%); the atherosclerotic plaques (IMT≥1.2 mm) **–** in 7 RApts (20%). There was a significant correlation between carotid m-IMT and age (R=0.76), level of total cholesterol (R=0.51), LDL cholesterol (R=0.27), systolic blood pressure (R=0.71), diastolic blood pressure (R=0.78), aMCV levels (R=0.79), p<0,05.

Conclusions: Macrophage activation in RApts was independent of CVR and RA-related factors. Subclinical carotid atherosclerotic lesions were observed in a every fifth untreated RApts. Carotid m-IMT correlated with traditional CVR factors and aMCV in RA pts. A study on a larger number of pts will clarify the link between macrophage activation, autoimmune disorders and carotid atherosclerotic lesions.

ID:931

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

INTERLABORATORY COMPARISON OF SERUM LIPOPROTEIN(A) ANALYTICAL RESULTS ACROSS CLINICAL ASSAYS – A STEP TOWARDS STANDARDIZATION

POSTER VIEWING SESSION

Alicia N. Lyle, Elias N. Flores, Clark C. Coffman, Alex H. Doty, Otoe Sugahara, Hubert W. Vesper
Division Of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, United States of America

Background and Aims : Lipoprotein(a) [Lp(a)] is an independent risk factor for atherosclerotic cardiovascular disease (CVD). The 2019 EAS and 2018 ACC/AHA clinical guidelines recommend measuring Lp(a); however, Lp(a) measurement variability across different assays persists. Standardization of Lp(a) clinical assays will minimize inter-assay variability, which will improve patient CVD risk assessment and future evaluations of Lp(a) therapeutic efficacy. Most individuals are heterozygous and have 2 Lp(a) sizes circulating. Lp(a) size heterogeneity stems from varying copies (1 – 40) of the kringle IV type 2 (KIV_2) domain. These factors may contribute to inter-assay measurement variability. The Centers for Disease Control and Prevention's Clinical Standardization Program (CDC-CSP) will launch an Lp(a) standardization program after the IFCC Working Group for Apolipoproteins by Mass Spectrometry establishes an SI-traceable Lp(a) LC-MS/MS Reference Measurement System. In preparation, the CDC-CSP conducted an Inter-Laboratory Comparison Study to evaluate the current status of accuracy and variability for serum Lp(a) measurements across assays.

Methods: Eight clinical laboratories measured Lp(a) in 40 individual clinical samples and 3 serum pool samples spanning the concentration range. Clinical samples were immunophenotyped by Western blot analysis to determine Lp(a) kringle sizes. Samples were measured in duplicate over 2 independent runs.

Results: Assay-specific Lp(a) measurements demonstrated good linear correlation compared to the all-assay mean concentration. Results showed that clinical sample deviations ranged from 3.3 – 69.1%, with higher deviations at higher Lp(a) concentrations, which were not correlated with kringle size.

Conclusions: This study provides new insights into Lp(a) inter-assay variability and assay performance in clinical laboratories that will guide future Lp(a) standardization efforts.

ID:1002

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

PREVALENCE OF PREMATURE ATHEROSCLEROTIC CORONARY ARTERY DISEASE (CAD) AMONG MEN AND WOMEN WITH FAMILIAL HYPERCHOLESTEROLAEMIA (FH) IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Žaneta Petrulionienė[1,2,3], Egle Skiauteryte[1], Dovile Gabartaite[1,3], Emilija Meskene[1,3], Juste Staigyte[1,3], Rimantė Čerkauskienė[3,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[1], Vilma Dzenkeviciute[1,2,3,5], Jolita Badariene[1,2,3], Sandra Kutkiene[1], Egidija Rinkuniene[1,2,3], Rasa Strupaite-Sileikiene[3,6,7], Rusne Jakaite[1], Goda Jackute[3]
[1]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [3]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Clinic Of Internal Diseases, Family Medicine And Oncology, Vilnius University, Faculty of Medicine, Vilnius, Lithuania, [6]Centre Of Eye Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [7]Center Of Eye Diseases, Clinic Of Ear, Nose, Throat, And Eye Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, vilnius, Lithuania

Background and Aims : According to various studies, coronary artery disease is the most prevalent type of cardiovascular disease amongFH patients. In our study we aimed to determine the distribution of premature CAD between men and women with clinical diagnosis of FH in Lithuania.

Methods: Prospective observational cohort study enrolled patients with clinically diagnosed FH according to Dutch Lipid Clinic Network(DLCN) criteria treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. Data of 119 study patients were included in the analysis. Premature CAD was defined as occuring in men younger than 55 years and women younger than 60 years. Obstructive Atherosclerotic CAD was defined as the presence of stenosis≥50% in at least one coronary vessel in Coronary Computed Tomography Angiography(CCTA) or coronary angiography, as well as performed percutaneous coronary intervention(PCI) or coronary arteries bypass grafting(CABG). The prevalence of premature CAD was compared by gender. Statistical analysis was performed using R(v. 4.0.4) program package.

Results: Of 119 examined patients 52,1%(n=62) were women and 47,9%(n=57) were men. In the study population, premature CAD was diagnosed for 26%(n=31) patients, 51,6%(n=16) men and 48,4%n=15) women. Comparing by gender, 24% of the women in the study and 28% of men had premature CAD(p=0,630).

Conclusions: PrematureCAD was diagnosed for one-fourth of the patients withFH. However, we found no significant differences by gender in the prevalence of CAD in the study population. As many cardiovascular events occur prematurely, our findings emphasize that among individuals with premature CAD there is an opportunity to detect an index case for initiation of cascade FH screening.

ID:1001

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

TANKYRASE INHIBITION ATTENUATES CARDIAC DILATATION AND DYSFUNCTION IN ISCHEMIC HEART FAILURE

POSTER VIEWING SESSION

Hong Wang[1], Heli Segersvärd[1], Juuso Siren[1], Sanni Perttunen[1], Katariina Immonen[1], Riikka Kosonen[1], Yu-Chia Chen[2], Johanna M. Tolva[3], Mirjami Laivuori[4], Mikko I. Mäyränpää[3], Petri T. Kovanen[5], Juha Sinisalo[6], Mika Laine[6], Ilkka Tikkanen[7], Päivi Lakkisto[8]
[1]Cardiovascular Research, Minerva Foundation Institute for Medical Research, Helsinki, Finland, [2]Anatomy And Neuroscience Centre, University of Helsinki, Helsinki, Finland, [3]Pathology, University of Helsinki, Helsinki, Finland, [4]Vascular Surgery, Helsinki University Hospital and University of Helsinki, Helsinki, Finland, [5]Atherosclerosis Unit, Wihuri Research Institute, Helsinki, Finland, [6]Heart And Lung Centre, Helsinki University Hospital and University of Helsinki, Helsinki, Finland, [7]Abdominal Centre Nephrology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland, [8]Clinical Chemistry, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

Background and Aims : Hyperactive poly(ADP-ribose) polymerases (PARP) promote ischemic heart failure (IHF) after myocardial infarction (MI). However, the role of Tankyrases (TNKSs), members of PARP family, in the progression of IHF remains unknown. We aimed to explore the role of TNKSs in pathophysiological process of IHF and the therapeutic potential of TNKS inhibition for IHF.

Methods: Cardiac samples from IHF patients and MI rats were employed to investigate the expression and activation of TNKSs. Isoproterenol-induced HF zebrafish model was utilized to explore a cardioprotective effect of TNKS inhibition.

Results: We demonstrate a significant augmentation of TNKS2 and DICER, and a concomitant upregulation of miR-34a-5p and miR-21-5p in the myocardium of IHF patients. We further reveal that MI augments TNKS1 and TNKS2 in infarct and border areas at 1 week and 4 weeks post-MI in rat. MI stimulates TNKS activity and triggers Wnt/β-catenin signalling in infarct area from 4 weeks onward. MI induces an abundant distribution of TNKS1 in a subset of non-cardiomyocytes with enhanced progenitor activity and TNKS2 in cardiomyocytes displaying cell shrinkage and sarcomere disorganization in infarct area in rat. Importantly, we show that TNKS inhibition with XAV939, a TNKS-specific inhibitor, protects against ventricular dilatation and cardiac dysfunction in isoproterenol-induced HF in zebrafish. Concomitantly, TNKS inhibition abrogates overactivation of Wnt/β-catenin signalling and dysregulation of miR-19b-3p, miR-181a-5p, and miR-34a-5p induced by isoproterenol.

Conclusions: Our study unravels a novel role of TNKSs in pathogenesis of IHF and a cardioprotective effect of TNKS inhibition via modulating miRNAs and Wnt/β-catenin signalling, highlighting the pharmacotherapeutic potential of TNKS inhibition.

ID:1000

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MYOCARDIAL FIBROSIS MARKERS CHANGES IN PATIENTS WITH HEART FAILURE WITH MID-RANGE EJECTION FRACTION OF ISCHEMIC GENESIS UNDER THERAPY

POSTER VIEWING SESSION

Olga Godlevska, Yana Samburg, Yuliya Rodionova, Tetiana Magdalits
Cardiology, Internal Medicine And Nephrology, Kharkiv Medical Academy Of Postgraduate Education, Kharkiv, Ukraine

Background and Aims : The aim of the study was to evaluate the therapy effectiveness by β-blockers bisoprolol or nebivolol in combination with eplerenone on myocardial fibrosis markers in patients with heart failure with mid-range ejection fraction (HFmrEF) and metabolic disorders.

Methods: We examined 120 patients with HFmrEF, and they were divided into groups depending on the therapy received: group 1 - bisoprolol (30 subjects), 2nd - bisoprolol and eplerenone (n=30), 3rd - nebivolol (n=30), 4th - nebivolol and eplerenone (n=30). Average doses of prescribed medications after 12 months were: nebivolol 8.55±1.75 mg, bisoprolol - 8.45±1.65 mg, eplerenone 48.25±2.25 mg. All patients underwent examination, including markers of myocardial fibrosis: MMP-1, MMP-9, TIMP-1.

Results: As a result of treatment, a decrease in the level of MMP-1 was noted in group 1 by 4% ($p>0.05$), in group 2 by 6% ($p>0.05$), in group 3 by 12%($p<0.05$) and in the 4th group by 19% ($p<0.01$). MMP-9 decreased by 4% ($p>0.05$) in group 1, by 6% ($p>0.05$) in 2nd, by 14% ($p<0.05$) in 3rd and 21% ($p<0.01$) in the 4th. There was also a decrease in TIMP-1 indicators in the first group by 3%($p>0.05$), in the 2nd by 5%($p>0.05$), in the 3rd by 12%($p<0.05$) and in the 4th by 18%($p<0.01$).

Conclusions: The results of our study showed a significant decrease in the indicators of collagen metabolism in patients who received nebivolol or a combination of nebivolol and eplerenone, in patients with HFmrEF of ischemic genesis with metabolic disorders. And the presented treatment options help to slow the progression of heart failure.

ID:997

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

ATHEROSCLEROSIS ASSOCIATED WITH HIV - IS IT A RESULT OF TREATMENT OR INFLAMMATION?

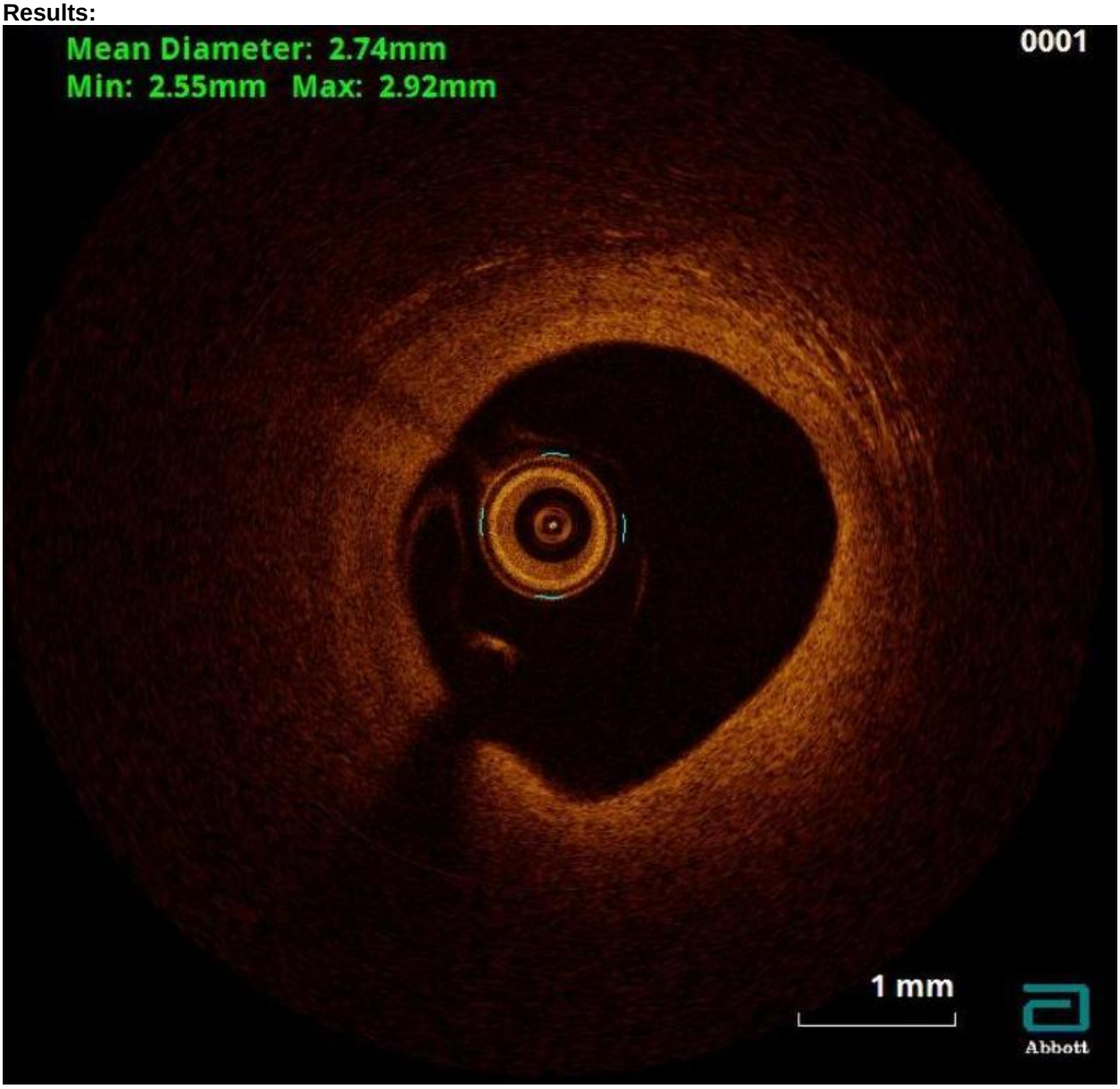
POSTER VIEWING SESSION

Nuriyat M. Efendieva, Oleg Shevchenko, Alexey Sozykine
Cardiology, Russian National Research Medical University, Moscow, Russian Federation

Background and Aims : Cardiovascular disease has emerged as an important cause of death in patients with HIV, as illustrated by clinical studies evaluating such hard endpoints as stroke or myocardial infarctions. Many studies have demonstrated an increased prevalence of subclinical atherosclerosis in individuals with HIV compared to those without. Such measurements include intima media thickness and intraluminal arterial plaque as assessed by ultrasound and evaluation of coronary artery calcification and plaque by computed tomography.

Methods: Fifty-two HIV-infected individuals had a mean age of 49.8 ± 11.4 years. There were 75% men, diabetes 30,8%, hypertension 30,8%, smokers 34,62% and 7,7 % with cholesterol levels ≥99 mg/dl. Control group included 120 non-HIV-infected controls with coronary heart disease. All the participants from HIV-group receive ART, 100% of participants had plasma HIV RNA <20 copies/mL and 78,85% of them have symptoms of coronary artery disease.

Results:



The average diffuse homogeneous thickening of the intima in patients with HIV was 0.67 ± 0.24 mm, and 0.34 ± 0.18 mm in control group, with normal values not exceeding 0.05 mm. There was impaired three-layer structure of coronary wall in 90,4% (47 of 52) HIV-infected participants and in 60% of control group, atherosclerotic plaque had only 34,62% of HIV group. All HIV-infected patients receive ART more than 5 years.

Conclusions: OCT demonstrated that the inflammatory process resulting from HIV-infection or HAART may be relevant in the changes of coronary arteries in HIV-positive patients. The changes are predominantly represented by thickening of the intima, impaired three-layer structure of arterial wall and accelerating atherosclerosis.

ID:994

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-11 Anti-inflammatory therapies*

A SYSTEMATIC REVIEW ON THE EFFECT OF UPADACITINIB ON LIPID PROFILE

POSTER VIEWING SESSION

Anastasios Makris, Aris P. Agouridis
School Of Medicine, European University Cyprus, Nicosia, Cyprus

Background and Aims : To systematically address the association between upadacitinib, an oral JAK-1 selective inhibitor, and its effect on lipid profile, as well as the role of this association in cardiovascular risk.

Methods: We searched PubMed, PubMed Central and ClinicalTrials.gov databases up to November 2021 for studies related to upadacitinib and lipid profile parameters. A qualitative synthesis of published randomized controlled trials (RCTs) for the role of upadacitinib in lipid profile changes was performed.

Results: Fifteen RCTs with a total of 10,318 patients were eligible for this systematic review. Ten of these studies were conducted in patients with rheumatoid arthritis, 2 in patients with psoriatic arthritis, while the remaining 3 studies included patients with Crohn's disease, ankylosing spondylitis and atopic dermatitis each, respectively. Significant increases in low density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were noted after the administration of upadacitinib (3-48 mg/day) in all fifteen studies, while the LDL-C:HDL-C ratio remained unchanged. Out of all patients who received upadacitinib, 22 developed a major adverse cardiovascular event, while 16 developed a venous thromboembolic event.

Conclusions: Treatment with upadacitinib increases LDL-C and HDL-C levels, without affecting their ratio. However, it seems that this increase does not affect cardiovascular risk.

ID:993

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

THE ASSOCIATION OF LIPOPROTEIN(A) AND LOW DENSITY LIPOPROTEIN CHOLESTEROL WITH AORTIC VALVE STENOSIS AND CORONARY HEART DISEASE.

POSTER VIEWING SESSION

Anna L. Burdeynaya[1], Olga I. Afanasieva[2], Elena A. Klesareva[2], Oksana A. Razova[2], Marat V. Ezhov[1], Sergey N. Pokrovsky[2]
[1]Laboratory Of Lipid Disorders, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation, [2]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Moscow, Russian Federation

Background and Aims : To assess the association of lipoprotein(a) [Lp(a)] and low density lipoprotein (LDL) concentration with calcific aortic valve stenosis (CAVS) in patients with and without CHD.

Methods: The study included 313 patients, they were divided into 4 groups: two groups with CAVS depending on presence (group 1, n=102) or absence of CHD (group 2, n=62), subjects with CHD and without CAVS, (group 3, n=105). Control group included patients without CHD or CAVS, (group 4, n=44). Lipids and Lp(a) level were determined in all patients.

Results: Patients with CAVS regardless of the presence of CHD were older than those from the control group ($p < 0.05$). Among patients with CHD the concentration of LDL cholesterol was significantly higher in group 1 compared to patients from group 3 (3.2±2.0 mmol/l and 2.6±0.9 mmol/l, respectively), $p<0.01$. In patients without CHD the concentration of LDL cholesterol did not differ depending on the presence of CAVS (3.4±1.4 mmol/l, 3.4±1.6 mmol/l, respectively). There was no difference in Lp(a) level in group 1 in comparison with group 3, median [25-75%] was 22.5 [14.8-31.5] and 19.4[14.9-24.7] mg/dl, respectively. Among patients without CHD Lp(a) concentration was significantly higher in patients with CAVS compare to subjects without CAVS, 14.9[11.1-27.0] mg/dl and 8.7[5.8-11.5] mg/dl, $p < 0.05$. The odds ratio for CAVS in the presence of Lp(a) ≥30 mg/dl was 3.9 (95%CI 1.3-11.4), $p < 0.05$ in patients without CHD, 1.2 (0.7-2.0) in patients with CHD, $p=0.6$.

Conclusions: Elevated Lp(a) associated with CAVS in patients without CHD and elevated LDL cholesterol associated with CAVS in patients with CHD.

ID:991

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-02 Smooth muscle cell biology*

ROLE OF LTA/TNFR AND LTA1B2/LTBR AXIS IN VASCULAR SMOOTH MUSCLE CELLS IN THE CONTEXT OF ATHEROSCLEROSIS

POSTER VIEWING SESSION

María Aguilar Ballester, Susana Martín-Vañó, Alejandra Abella Miralles, Gema Hurtado Genovés, Andrea Herrero-Cervera, Alida M. Taberner Cortés, Ángela Vinué, Sergio Martínez-Hervás, Herminia González-Navarro
Metabolic Diseases Research Group, INCLIVA, Valencia, Spain

Background and Aims : Several investigations indicate anti- and pro-atherogic effects of lymphotoxins in atherosclerosis development, including LTβR ligands as lymphotoxin β (LTβ) and heterotrimer LTα1β2 or lymphotoxin α (LTα), a ligand of the tumour necrosis factor receptor (TNFR). During atherosclerotic plaque development, vascular smooth muscle cells (VSMC) are recruited, whose phenotype-switching might be modulated by LTβR. Our aim was to dilucidate LTβR ligands role in VSMCs phenotype-switching.

Methods: Experiments were performed with cultured human (h)VSMCs stimulated for 72 hours with vehicle, LTα1β2, and LTα. Patients were classified in a control and metabolic syndrome (MetS) group. PBMCs were obtained from peripheral blood samples. Gene expression levels were analyzed by quantitative real-time PCR (qPCR).

Results: Analysis of the effect of LTα and LTα1β2 on hVSMCs phenotype-switching showed an important effect of these ligands. Treatment of hVSMCs with LTα decreased *Col1A1* and *TGFb1* and enhanced *MMP9* expression, suggesting LTα increases extracellular matrix degradation and diminishes atheroprotective secretor phenotype acquisirtion by hVSMCs. Decreased expression of pluripotency genes *SOX9*, *CKIT*, and *KLF4* were observed after LTα treatment. LTα and LTα1β2 modulated the expression of genes associated with LTo phenotype, such as lymphorganogenic cytokines, in VSMCs. Treatment with LTα augmented *CCL20* and *CXCL16* and with LTα1β2 decreased *CXCL13* and *CCL19* expression (Fig.1). Consistent with these results, PBMC analysis from patients with MetS showed increased LTβ and LTβR expression (Fig.2).

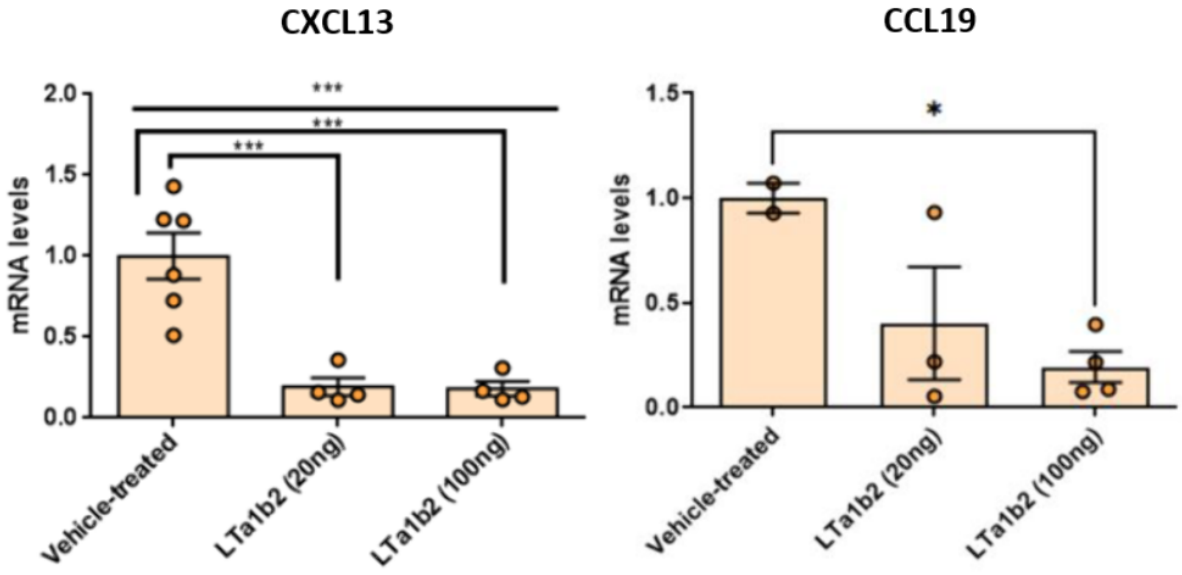


Figure 1: Cytokine gene expression analysis of LTα1β2 trimer-treated hVSMCs. mRNA expression levels of (a) CXCL13 and (b) CCL19, normalised to ciclophilin expression levels and relativised to vehicle-treated controls. Statistical analysis was performed with a t-Student. *p<0.05; **p<0.01; **p<0.001.

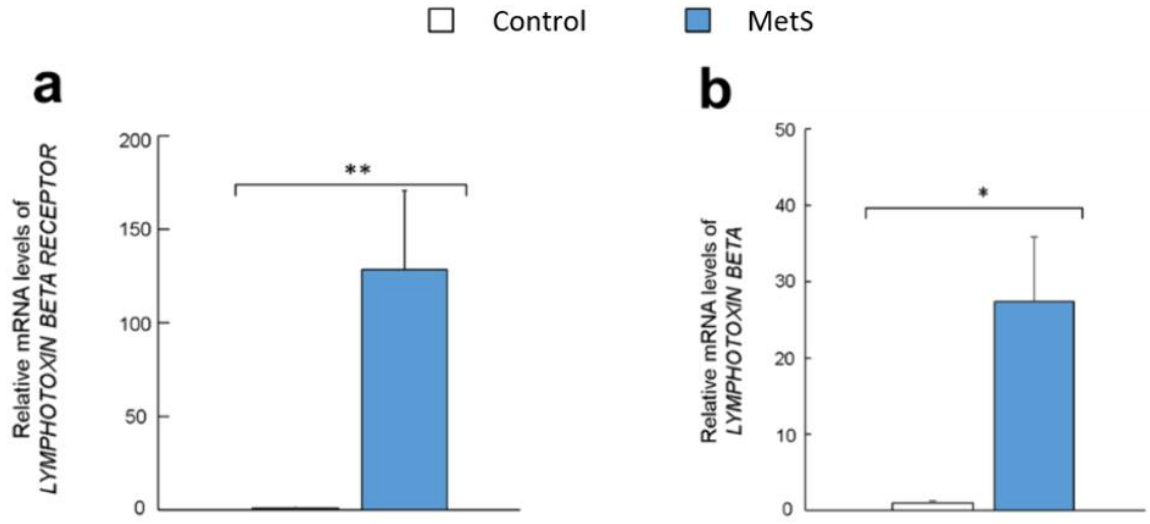


Figure 2: PBMC gene expression analysis of control and MetS groups. mRNA expression levels of (a) LTβc and (b) LTβRc, normalized to GAPDH expression levels and relativised to vehicle controls. Statistical analysis was performed with a t-Student. *p<0.05; **p<0.01.

Conclusions: Results suggest an LTα and LTα1β2-dependent signaling in VSMC phenotype detrimental effect during atheroma formation.The enhanced expression of LTβ and LTβR in patients displaying MetS suggest that modulation of LTβR signaling might prevent atherosclerosis.

Research funds: PI19/00169 from Carlos III Health Institute and FEDER funds.

ID:988

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

LIPID PROFILE OF PATIENTS WITH TYPE 1 DIABETES MELLITUS WITH LONG DURATION.

POSTER VIEWING SESSION

Tatyana Chalakova[1], Kaloyan Tsochev[2], Yana Bocheva[3], Gergana Chausheva[3], Georgi Valchev[4], Natalya Usheva[5], Violeta Iotova[2], Yoto Yotov[1]
[1]First Department Of Internal Diseases, Medical University of Varna, Varna, Bulgaria, [2]Pediatrics, Medical University of Varna, Varna, Bulgaria, [3]Clinical Laboratory, Medical University of Varna, Varna, Bulgaria, [4]Imaging, University Hospital St Marina, Varna, Bulgaria, [5]Social Medicine And Health Care Organization, Medical University of Varna, Varna, Bulgaria

Background and Aims : Type 1 diabetes mellitus (T1DM) has increasing survival implying the need to assess the cardiovascular risk factors. Dyslipidemia is such a factor and its evaluation in long-duration T1DM patients is important for successful prevention. Aim: to examine the lipid profile of patients with T1DM without CVD in comparison to healthy controls.

Methods: Overall, 183 participants were included – 124 patients with long-term T1DM (median 24 years), and 59 healthy controls, matched for age, sex and body mass index. Fasting blood samples were taken for analysis of lipids, blood glucose, and other parameters. Triglycerides/HDL ratio and Triglyceride/glucose index (TyG) were calculated. Dyslipidemia was defined according to guidelines. Computer tomography was performed for coronary artery calcium (CACS) and for epicardial fat tissue (EFT). Parametric t and ANOVA or non-parametric Mann-Whitney tests were used.

Results: Lipid levels are not significantly different between T1DM and controls. Dyslipidemia is equally highly prevalent in both T1DM and controls – 56.5% and 62.7%, p=0.52, while simultaneously high TG and low HDL-chol are present in only 3.2% and 3.4%, p=0.95. Patients with T1DM have significantly higher TyG index compared to controls – 4.87±0.39 vs 4.56±0.31, p<0.0001. All lipid parameters linearly and significantly change with tertiles of the EFT, irrespective of the diabetes status. The same association is not found with the CACS.

Conclusions: T1DM patients with a long duration and controls show similar lipid profile. Dyslipidemia is frequent in this relatively young population. The EFT, a marker of visceral adiposity, parallels the lipid profile of the study participants.

ID:980

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

THE GI-COUPLED P2Y13 RECEPTOR SIGNALING INHIBITS LIPOLYSIS AND PROTECTS FROM METABOLIC SYNDROME AND ASSOCIATED LIVER DISEASES

POSTER VIEWING SESSION

Laurent O. Martinez, Emilia Gore, Guillaume Combes, Cendrine Cabou, Thibaut Duparc
Inserm Umr1297, Institute of Cardiovascular and Metabolic Diseases (I2MC), TOULOUSE, France

Background and Aims : The G_i-coupled $P2Y_{13}$ receptor is a purinergic receptor that plays a role in lipid metabolism and protects from atherosclerosis. Given that $P2Y_{13}$ receptor is expressed in adipocytes, we aim to investigate its role in lipolysis and its effect on metabolic syndrome and associated liver diseases.

Methods: Wild-type (WT) and $P2Y_{13}$ KO mice were fed a Western-diet for 16- and 40-weeks. *In-vivo* lipolysis, glucose homeostasis and systemic inflammation were assessed. Lipolytic activity was measured in isolated adipocytes and explants from inguinal and epididymal white adipose tissue (iWAT and eWAT). Hepatic steatosis and fibrosis were assessed by histology and biochemical measurements, and lipidomic and transcriptomic analyses were performed.

Results: $P2Y_{13}$ KO mice displayed increased β-adrenergic lipolytic response, impaired glucose homeostasis and higher systemic inflammation. Adipocytes from $P2Y_{13}$ KO mice displayed higher intracellular cAMP, reflecting impaired G_i signaling. $P2Y_{13}$ deletion was associated to higher lipolysis in adipocytes and explants from iWAT and eWAT. In the liver, $P2Y_{13}$ KO mice displayed higher steatosis and fibrosis. Mechanistically, experiments on precision-cut liver slices (PCLS) exposed to adipose tissue conditioned medium indicate that $P2Y_{13}$ activity in WAT protects from hepatic steatosis. Moreover, lipidomic and microarray analyses in the liver concomitantly revealed a NASH-related lipid signature in $P2Y_{13}$ KO mice and activation of inflammatory pathways mediated by lipid mediators such as arachidonic and hydroxyeicosatetraenoic acids.

Conclusions: These results support a protective role of $P2Y_{13}$ against NAFLD/NASH development through a mechanism involving Gi-mediated inhibition of lipolysis. $P2Y_{13}$ activation may thus represents a potential pharmacological target to treat metabolic syndrome and NAFLD.

ID:963

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

THE RELATIONSHIP BETWEEN ENDOTHELIAL DYSFUNCTION AND CARDIOVASCULAR DISEASES AND RISK FACTORS IN THE ELDERLY POPULATION

POSTER VIEWING SESSION

Andrew Ryabikov[1,2], Maria Troshina[3], Maxim Ryabikov[1], Yuliia Palekhina[1], Olga Nikolaeva[2], Sofia Malyutina[1,2]
[1]Laboratory Of Internal Medicine, The Institute of Internal and Preventive Medicine - Branch of Institute of Cytology and Genetics SB RAS, Novosibirsk, Russian Federation, [2]Department Of Internal Medicine, Hematology & Transfusiology, Novosibirsk State Medical University, Novosibirsk, Russian Federation, [3]Laboratory Of Genetic And Environmental Determinants Of The Human Life Cycle, The Institute of Internal and Preventive Medicine – Branch of Institute of Cytology and Genetics SB RAS, Novosibirsk, Russian Federation

Background and Aims : Endothelial dysfunction (ED) is on the causal pathway for cardiovascular diseases (CVD) but most data originate from middle-age populations. We aimed to assess the association between flow-mediated dilation (FMD) and CVD and their risk factors (RFs) in the elderly population.

Methods: The study was carried out in a population sample aged 58-82 years (n=788 men/women, Novosibirsk, Russia). The ED was assessed with ultrasound reactive hyperemia test on brachial artery. ED was defined by FMD% <10%. Medical history of CVD and RFs were assessed by standard methods.

Results: The mean FMD was 2.7% in men (SD 7.32), and 3.2% in women (SD 7.19). The frequency of ED was 88.2% (men) and 85.8% (women). In men, ED was associated with higher triglycerides level (125.1 (SD 71.23) vs. 102.7 mg/dl (45.79), p=0.033), waist-hip ratio (0.94 (0.050) vs. 0.92 (0.076), p=0.009) and suggestively with body-mass index (27.7 (45.79) vs. 26.5 kg/m^2 (4.36), p=0.077). In women, there was borderline association between ED and smoking (p=0.067). In our sample, there were no associations between the FMD% and the presence of hypertension, diabetes mellitus, and CVD.

Conclusions: In a population sample aged 58-82 years ED was associated with metabolic factors in men and with smoking in women. We did not reveal association between FMD% and CVD due to high prevalence of ED, significant burden of cardiometabolic diseases and CVD in studied elderly population.
The study was supported by RSF #20-15-00371; RAS #AAAA-A17-117112850280-2.

ID:955

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

GENETIC RISK SCORE OF HYPERTIGLYCERIDEMIA AND ITS INTERACTION WITH CLINICAL VARIANTS

POSTER VIEWING SESSION

Virginia Esteve Luque[1,2], Marta Fanlo Maresma[1], Emili Corbella[1,2], Xavier Pintó[1,2,3,4]
[1]Internal Medicine, Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Spain, [2]Idibell, Institut de Recerca Biomedica, Hospitalet de Llobregat, Spain, [3]Ciberobn, Instituto Carlos III, Spain, Spain, [4]Facultat De Medicina, Universidad de Barcelona, Spain, Spain

Background and Aims : Numerous single nucleotide polymorphisms (SNPs) related to plasma TG have been identified and different genetic risk scores (GRS) have been developed to predict the risk of hypertriglyceridemia (HTG). However, there is a wide variability in TG concentration that is not explained by these scores, which may be due to a gene-environment interaction.

Methods: In this study, 276 Spanish individuals with primary HTG aged 18-80 years were selected. Six allelic variants related to TG concentrations, c.724C> G (ZPR1 gene), c.56C> G (APOA5 gene), c.1337T> C (GCKR gene), g.19986711A> G (LPL gene), c. 107 + 1647T> C (BAZ1B gene) and g.125478730A> T (TRIB gene) were studied. An unweighted GRS was created by summing the number of mutated alleles present in each individual for each of the six allelic variants. Multiple linear regression models were performed to analyze the effect of the GRS with the highest levels of TG and the interactions with other clinical variables such as BMI, diet, alcohol consumption physical activity and HbA1c were studied.

Results: A GRS ranging between 4-11 was observed in the individuals from this study. The GRS was associated with the concentration of TG and explained 7% of the variability of TG concentrations. Significant interactions between BMI and GRS were found regression coefficient 0.15 CI(0.03-0,28), p(0.02), and also with HbA1c RC 0.93 CI(0.13-1.74) p(0.02), whereas no evidence of such interactions with other clinical variables were found.

Conclusions: An interaction between GRS and BMI explains part of the variability of TG concentration in the individuals studied.

ID:953

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

TELMISARTAN IN PATIENTS WITH CHRONIC HEART FAILURE AND DIABETES MELLITUS TYPE 2

POSTER VIEWING SESSION

Nataliia Pavliukovych, Oleksandr Pavliukovych, Mariia Kozar
Department Of Internal Medicine, Clinical Pharmacology And Occupational Diseases, Bukovinian State Medical University, Chernivtsi, Ukraine

Background and Aims : Despite modern achievements in diagnosis and treatment of patients with chronic heart failure (CHF) and diabetes mellitus type 2 (DM), their incidence and unfavorable outcomes have been increased recently. The research aimed at the investigation of the possible clinical effectiveness of telmisartan in patients with CHF and comorbid DM.

Methods: 75 patients with CHF and DM were under investigation. They were randomized into 2 groups according to the prescribed treatment: I group – 40 patients who received statins, metformin and enalapril; II group – 35 patients for whom substitution of ACE inhibitor by telmisartan in daily dose of 40 mg was conducted. Clinical effectiveness of the prescribed treatment was estimated in 6 months by level of blood pressure (BP), fasting glucose (FG) and blood lipid spectrum (total cholesterol (TC), triacylglycerols (TG), HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C)).

Results: Comparison of BP in patients of both groups revealed no statistical difference. Valid decreasing of FG level for 33% was detected in I group (5,8±0,11 comparing with 8,6±0,23 mmol/L, $p<0,001$). In II group lower level of FG (4,6±0,18 comparing with 8,5±0,82 mmol/L, $p<0,001$) was observed. Patients of II group were also characterized by more pronounced changes in blood lipid spectrum, such as decreasing of TC in 1,89 times ($p<0,001$), TG – by 12,5% ($p<0,05$), LDL-C - approximately twice ($p<0,001$), increasing of HDL-C in 2,66 times ($p<0,001$).

Conclusions: So, advisability of telmisartan prescription in treatment of patients with CHF and DM opens new perspectives for its application in this category of patients.

ID:938

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

NUMBER OF LIPID-LOWERING MEDICATIONS AND ATTAINMENT OF LIPID GOALS IN FAMILIAL HYPERCHOLESTEROLEMIA PATIENTS: DATA FROM THE LATVIAN REGISTRY

POSTER VIEWING SESSION

Georgijs Nesterovics[1,2], Vita Saripo[1,2,3], Ruta Meiere[1,2,3], Elizabete Terauda[1,2,3], Gunda Skudrina[1,2,3], Dainus Gilis[1,2,3], Andrejs Erglis[1,2,3], Gustavs Latkovskis[1,2,3]
[1]Faculty Of Medicine, University of Latvia, Riga, Latvia, [2]Latvian Institute Of Cardiology And Regenerative Medicine, University of Latvia, Riga, Latvia, [3]Latvian Center Of Cardiology, Pauls Stradins Clinical University Hospital, Riga, Latvia

Background and Aims : Attainment of low-density lipoprotein cholesterol (LDL-C) goals remains a challenge in patients with heterozygous familial hypercholesterolemia (FH). Combinations of lipid lowering medications (LLM) are commonly required. National registries play a crucial role to monitor quality of care in FH patients. We aimed to provide contemporary data on the number of used LLM, achieved lipid levels and attainment of LDL-C goals in FH patients from the Latvian Registry of FH (LRFH).

Methods: Patients with clinical FH and at least one follow-up visit were included in this report. Clinical FH was defined as definite or probable FH according to the Dutch Lipid Clinic Network criteria for probands, or LDL-C levels >95th percentile or causal mutation in first-degree relatives. The goals were defined as <1.4 in primary and <1.8 mmol/L in secondary prevention.

Results: Among 1006 individuals included in the LRFH, 438 patients were diagnosed with clinical FH, and 211 had at least one follow-up visit. The main results are summarized in the Table. Maximal doses of rosuvastatin or atorvastatin were used by 39.5%, 56.0% and 84.6% users of one, two and three LLM, respectively. All patients using two LLM were on statin and ezetimibe except for one patient who was on a PCSK9 inhibitor and ezetimibe. The three-drug combination consisted of statin, ezetimibe and PCSK9 inhibitor in all
cases.

Number of LLM at the most recent visit	Highest documented LDL-C, mmol/L (mean, SD)	LDL-C upon inclusion in the LRFH, mmol/L (mean, SD)	LDL-C at the most recent visit, mmol/L (mean, SD)	Achieved LDL-C goal at the most recent visit (n, %)
No LLM (n=37)	6.69 ± 1.09	5.55 ± 1.46	5.93 ± 1.72	0 (0%)
One LLM (n=86)	7.15 ± 1.69	5.26 ± 2.31	3.13 ± 1.24	4 (4.7%)
Two LLM (n=75)	7.33 ± 1.61	5.32 ± 2.28	2.83 ± 1.92	10 (13.3%)
Three LLM (n=13)	8.58 ± 2.19	5.29 ± 3.00	1.68 ± 1.05	7 (53.9%)

Conclusions: Very few FH patients achieve LDL-C goals with one LLM or even two drug combinations. Use of three LLM has achieved the goals in about half of the patients.

ID:934

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

MALNUTRITION AND COMORBIDITY IN OLDER PATIENTS WITH CHRONIC KIDNEY DISEASE

POSTER VIEWING SESSION

Elena Efremova, Alexander Shutov, Ksenia Yafarkina, Alexey Semenov
Department Of Therapy And Occupational Diseases, Ulyanovsk State University, Ulyanovsk, Russian Federation

Background and Aims : Frailty syndrome, sarcopenia, cognitive impairments, comorbidity in older patients worsen quality of life and prognosis. Chronic kidney disease (CKD) is widespread in older patients with cardiovascular diseases.The aim of this study was to investigate features of malnutrition in older patients with CKD and cardiovascular comorbidity.

Methods: 472 older patients with stable cardiovascular diseases (231 males, mean age 69,6±7,3years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). Charlson comorbidity index was estimated. The presence and severity of malnutrition was assessed in high-risk patients according to the Global Leadership Initiative on Malnutrition (GLIM) criteria.Frailty syndrome and psychological status was studied using MMPI scale.

Results: CKD with GFR less than 60 ml/min/1.73 m^2 was observed in 277 (58.7%) patients: stage 3a - 185 (66.8%), 3b - 83 (29.9%), stage 4 - 9 (3.3%). Mild malnutrition was observed in 13 (4.7%) patients with CKD and in 6 (3.5%) patients without CKD ($p = 0.73$). All patients with malnutrition had frailty.GFR in older patients with CKD, depending on malnutrition, did not differ ($p = 0.65$). Patients with CKD and malnutrition had higher Charlson comorbidity index compared with patients with normal trophological status: 8 (7; 9) and 4.5 (4; 5) points, respectively, $p = 0.01$. Patients with malnutrition had higher hypochondria (scale of MMPI) (78.7 ± 11.3 and 67.6 ± 12.7 T-points, resp., $p = 0.01$) compared with patients without malnutrition.

Conclusions: Malnutrition is observed in 13 (4.7%) older patients with CKD and cardiovascular diseases and associated with frailty syndrome, high comorbidity, weakness and irritability.

ID:930

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

PLASMA ADIPONECTIN AS AN INDICATOR OF THE EFFECTIVENESS OF CHD THERAPY IN PATIENTS WITH METABOLIC SYNDROME

POSTER VIEWING SESSION

Dmitry Tanyanskiy, Elvira Firova, Alexander Denisenko
Department Of Biochemistry, Institute of Experimental Medicine, St-Petersburg, Russian Federation

Background and Aims : Adiponectin has a potential effect on atherogenesis. In this regard, adiponectin can be considered as a possible target of therapy. The objective is to check whether the initial concentration of adiponectin or its change during therapy is related to the effectiveness of treatment of coronary heart disease (CHD) in patients with metabolic syndrome (MS).

Methods: Thirty one patients with CHD and MS (aged 59.7+/-5.9 years, 21 females), receiving statins (27 patients) or fibrates (4 patients) for 2-3 years were selected for the study. The effectiveness of treatment was assessed by a changing in ECG, veloergometry (VEM), and plasma biochemical tests in this period of treatment.

Results: As expected, metabolic parameters (plasma lipoproteins, insulin concentration) have been improved during therapy, and plasma leptin and adiponectin concentrations were increased. Exercise tolerance performance has been enhanced as well. According to the VEM, change in the insulin, but not adiponectin concentration correlated with the improvement in the total amount of work performed (TAW) after therapy. At the same time, an initially higher level of adiponectin predicted an improved response to therapy (in particular, an increase in TAW), even after controlling for confounders (age, gender, anthropometry, lipoproteins, HOMA index, leptin).

Conclusions: Adiponectin has an impact on the course of CHD, possibly due to its anti-inflammatory effect on the endothelium, NO production, metabolic action, etc. It is possible that a higher increase in the concentration of adiponectin (by severe weight loss, medication by glitasons) could have a pronounced effect on CHD treatment.

ID:1006

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

THE ROLE OF SYSTEMIC INFLAMMATION IN REDUCING THE ELASTICITY OF THE MAIN ARTERIES IN PATIENTS WITH CHRONIC HEART FAILURE IN COMBINATION WITH OBESITY

POSTER VIEWING SESSION

Maria Derevyanchenko[1], Svetlana Fabritskaya[1], Mikhail Statsenko[1], Yulia Ryndina[1], Irina Starodubtseva[2]
[1]Internal Diseases, Volgograd State Medical University, Volgograd, Russian Federation, [2]Internal Diseases, NN Burdenko Voronezh State Medical University, Voronezh, Russian Federation

Background and Aims : Aim. To study the effect of systemic inflammation on the elasticity of the main arteries in patients with chronic heart failure (CHF) in combination with obesity.

Methods: Material and methods. 142 patients with CHF I-III functional class 45-65 years were divided into 3 groups. Group 1 is represented by patients with "isolated" CHF, 2 - patients with CHF and overweight, 3 - patients with CHF in combination with obesity. A standard examination was performed, the stiffness of the vascular wall was assessed by measuring the velocity of pulse wave propagation through the vessels of the muscular (PWVm) and elastic (PWVe) types, laboratory markers of systemic inflammation and endothelial dysfunction were determined.

Results: Results. PWVe and the percentage of occurrence of PWVe >10 m/s are significantly higher in patients of group 3 compared to patients of group 1 (10.8 [9.3;11.6] vs 9.2 [7.8;10.7] m/s and 74 vs 42%, respectively). The concentration of C-reactive protein (CRP) was significantly higher in group 3 patients compared to group 2 and 1 (8,31 [5,12; 15,41] vs 5,64 [4,92; 6,31], 8,31 [5,12; 15,41] vs 3.08 [1.57; 6.98] mg/l, respectively). The level of endothelin-1 (ET-1) in serum increased from group 1 to group 3. Significant correlations were revealed between the concentration of CRP and PWVe (r=0.48), PWVm (r=0.47), ET-1 level (0.56); between ET-1 and PWVe (r=0.52), PWVm (r=0.49).

Conclusions: Conclusion. Systemic inflammation has a negative effect on the elasticity of the main arteries, and also leads to the progression of endothelial dysfunction in patients with CHF in combination with obesity.

ID:926

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-10 Modified lipoproteins*

EFFECTS OF LONG COMPUTER GAMING SESSIONS ON LIPOPROTEIN LEVELS IN HEALTHY MALE ADULTS

POSTER VIEWING SESSION

Kasper B. Krarup[1], Henrik B. Krarup[2], Inge S. Pedersen[2], Morten Mørk[2], Søren R. Kristensen[3], Aase Handberg[3], Reinhard Wimmer[4], Hien T.T. Nguyen[2]
[1]Department Of Geriatric Medicine, Aalborg University Hospital, Aalborg Øst, Denmark, [2]Molecular Diagnostic, Aalborg University Hospital, Aalborg, Denmark, [3]Department Of Clinical Medicine, Aalborg University Hospital, Aalborg, Denmark, [4]Department Of Chemistry And Bioscience, Aalborg University, Aalborg, Denmark

Background and Aims : Long computer gaming sessions are an increasingly prevalent activity among young people. This behavior is known to influence several areas of emotional, cognitive, and behavioral functioning. Currently, there is insufficient experimental evidence concerning how long computer gaming sessions affect the physiological and biochemical processes of the body when combined with an ad libitum access to energy-dense foods and beverages. The aim of this study was to investigate the effects of long computer gaming sessions on macromolecule levels in healthy male adults.

Methods: We mimicked a “normal situation” around a local area network (LAN) party and analyzed serum metabolomics of nine adult male participants (mean age = 27.44 ± 2.60 years).

Results: Ten metabolites turned out to be most significantly affected during long gaming sessions. Nine out of ten metabolites were lipid carried by very low density lipoprotein (VLDL), three total lipids, five cholesterols (total cholesterol and free cholesterols), and one triglyceride. Overall, they increased after eating, depleted over time, and were exhausted at the end of each gaming session. This observation was also seen in twelve metabolites, that represent biomarkers of the healthy body. Several markers related to life expectancy, cardiovascular disease, obesity, and general health state did not return to baseline five days after the long gaming session.

Conclusions: Long gaming sessions cause shifts in macromolecule concentrations that are not quickly recovered even by healthy gamers. The skew towards pro-atherosclerotic macromolecules suggests that the risks of long gaming sessions should be researched more vigorously.

ID:920

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

TOWARDS SI-TRACEABILITY OF LIPOPROTEIN (A) MEASUREMENTS: COMPARISON OF A CANDIDATE LC-MRM-MS RMP METHOD WITH COMMERCIALLY AVAILABLE IMMUNOASSAYS FOR EVALUATING COMMUTABILITY OF CANDIDATE REFERENCE MATERIALS

POSTER VIEWING SESSION

Ioannis Dikaios[1], Liesbet Deprez[1], Harald Althaus[2], Eduardo Angles-Cano[3], Ilijana B. Brkovic[4], Timo Boesche[5], Uta Ceglarek[6], Stefan Coassin[7], Vincent Delatour[8], Benjamin Dieplinger[9], Julia Dittrich[4], Andrew Hoofnagle[10], Gerhard Kostner[11], Florian Kronenberg[12], Zsusanna Kuklenyik[13], Alycia N. Lyle[13], Urban Prinzing[5], Hubert Scharnagl[14], Hubert W. Vesper[13], Renee Ruhaak[15], Christa Cobbaert[15] [1]-, European Commission, Joint Research Centre (JRC), Geel, Belgium, [2]-, Siemens Healthcare Diagnostics Products, Marburg, Germany, [3]-, French Institute of Health and Medical Research (Inserm) Université de Paris, Paris, France, [4]. Institute Of Laboratory Medicine, Clinical Chemistry And Molecular Diagnostics, University Hospital Leipzig, Leipzig, Germany, [5]-, Roche Diagnostics GmbH, Penzberg, Germany, [6]Life-leipzig Research Center For Civilization Diseases, University of Leipzig, Leipzig, Germany, [7]Dept Of Genetics And Pharmacology, Medical University of Innsbruck, Innsbruck, Austria, [8]-, Laboratoire National de Métrologie et d'Essais, Paris, France, [9]Department Of Laboratory Medicine, Konventhospital Barmherzige Brueder Linz and Ordensklinikum Linz Barmherzige Schwestern, Linz, Austria, [10]Department Of Laboratory Medicine And Pathology, University of Washington, Seattle, United States of America, [11]Gottfried Schatz Research Center (for Cell Signaling, Metabolism And Aging) Division Of Molecular Biology And Biochemistry, Medical University of Graz, Graz, Austria, [12]Institute Of Genetic Epidemiology, Medical University of Innsbruck, Innsbruck, Austria, [13]Division Of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, United States of America, [14]Clinical Institute Of Medical And Chemical Laboratory Diagnostics, Medical University of Graz, Graz, Austria, [15]Clinical Chemistry And Laboratory Medicine, LUMC, Leiden, Netherlands

Background and Aims : Elevated concentrations of lipoprotein(a) (Lp(a)) are directly related to an increased risk of cardiovascular diseases, thus making its determination a crucial factor for clinical diagnosis. However, the lack of global standardisation of current immunoassay-based measuring procedures (MPs) for Lp(a) leads to inconsistent care of patients. The former Lp(a) reference method and the associated WHO-IFCC reference material are no longer available. Recently, it was decided to evolve to a next generation reference measurement system (RMS) with SI-traceability. To accomplish this an IFCC working group on quantitating apolipoproteins by mass spectrometry (MS) was formed. The SI-traceable RMS will consist of a MS-based, peptide-calibrated candidate reference measurement procedure (cRMP) and secondary serum-based reference materials (RMs) certified for their apolipoprotein(a) molar concentration.

Methods: A correlation study was performed between the cRMP and immunoassay-based MPs using a panel of 39 clinical samples (CS) that cover the whole Lp(a) concentration range. In addition, the commutability of 14 different candidate RMs was investigated to select a suitable RM format for the future development of the serum-based RM.

Results: Comparison of immunoassay-based MPs with the cRMP for measurements of CS in nmol/L demonstrated a good linear correlation, but showed significant measurement bias and sample specific differences.

Conclusions: The results of the commutability study show that RMs based on human serum pools with endogenous Lp(a) are good candidates for future matrix-based certified RM, whereas human pools - spiked with recombinant apo(a) show different behaviour compared to CS, making them unsuitable as RMs in most of the currently available routine assays.

ID:919

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

COLD-INDUCIBLE RNA-BINDING PROTEIN BUT NOT ITS ANTISENSE LNCRNA IS A DIRECT NEGATIVE REGULATOR OF ANGIOGENESIS VIA REGULATION OF THE 14Q32 ANGIO-MIRS—MICRORNA-329-3P AND MICRORNA-495-3P

POSTER VIEWING SESSION

Licheng Zhang[1,2], Eveline Goossens[1], Margreet R. De Vries[2], Wouter J. Jukema[1], Paul H.A. Quax[2], Yael Nossent[2]
[1]Cardiology, LUMC, Leiden, Netherlands, [2]Surgery, Leiden University Medical Center, Leiden, Netherlands

Background and Aims : Inhibition of the 14q32 microRNAs, miR-329-3p and miR-495-3p, improves post-ischemic neovascularization. Cold-inducible RNA-binding protein (CIRBP) facilitates maturation of these microRNAs. We hypothesized that CIRBP deficiency improves post-ischemic angiogenesis, including intraplaque angiogenesis, via downregulation of 14q32 microRNA expression.

Methods: We investigated these regulatory mechanisms both in vitro and in vivo.

Results: We induced hindlimb ischemia in $Cirp^{-/-}$ and C57Bl/6-J mice, monitored blood flow recovery with laser Doppler perfusion imaging, and assessed neovascularization via immunohistochemistry. Post-ischemic angiogenesis was enhanced in $Cirp^{-/-}$ mice by 34.3% with no effects on arteriogenesis. In vivo at day 7, miR-329-3p and miR-495-3p expression were down-regulated in $Cirp^{-/-}$ mice by 40.6% and 36.2%. In HUVECs, CIRBP expression was upregulated under hypothermia, while miR-329-3p and miR-495-3p expression remained unaffected. siRNA-mediated CIRBP knockdown led to the downregulation of CIRBP-splice-variant-1 (CIRBP-SV1), CIRBP antisense long noncoding RNA (lncRNA-CIRBP-AS1), and miR-495-3p with no effects on the expression of CIRBP-SV2-4 or miR-329-3p. siRNA-mediated CIRBP knockdown improved HUVEC migration and tube formation. SiRNA-mediated lncRNA-CIRBP-AS1 knock-down had similar long-term effects. After short incubation times, however, only CIRBP knock-down affected angiogenesis, indicating that the effects of lncRNA-CIRBP-AS1 knockdown were secondary to CIRBP-SV1 downregulation.

Conclusions: CIRBP is a negative regulator of angiogenesis in vitro and in vivo and acts, at least in part, through the regulation of miR-329-3p and miR-495-3p.

ID:918

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-10 Anti-thrombotic therapies*

ANTITHROMBOTIC THERAPY AND OUTCOMES OF CORONARY ARTERY BYPASS GRAFTING IN PATIENTS WITH CONCOMITANT CAROTID ATHEROSCLEROSIS (ACCORDING TO PROSPECTIVE REGISTER OF LONG-TERM ANTITHROMBOTIC THERAPY REGATA NCT04347200)

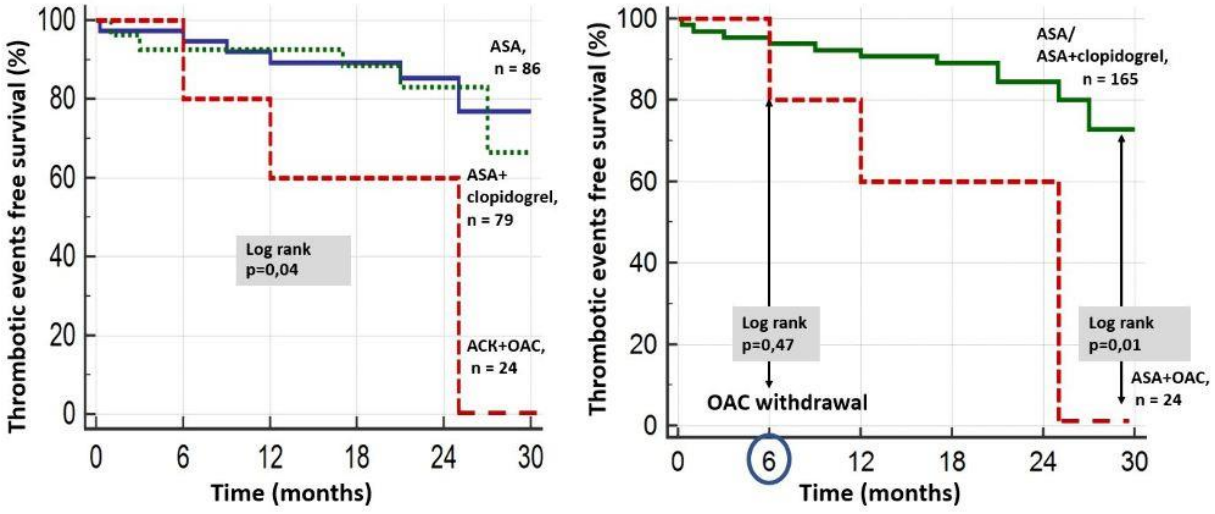
POSTER VIEWING SESSION

Elena Krivosheeva[1], Andrey Komarov[1], Damir M. Galyautdinov[2], Elina Vlasova[2], Olga Pogorelova[3], Renat Akchurin[2], Elizaveta Panchenko[1]
[1]Department Of Clinical Problems Of Atherothrombosis, NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation, [2]Department Of Cardiovascular Surgery, NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation, [3]Ultrasound Division, NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation

Background and Aims : We aimed to assess the impact of antithrombotic therapy on long-term prognosis in patients with coronary artery disease (CAD) and concomitant carotid atherosclerosis undergoing coronary artery bypass grafting (CABG).

Methods: 189 CAD patients (79.9% males, median age 65 [IQR 60; 71] years) after successful CABG with carotid artery stenosis≥ 50% were enrolled. Carotid endarterectomy was performed in 25.9% of patients. Patients with indications for chronic oral anticoagulation therapy were excluded. Antithrombotic therapy on discharge was chosen at the discretion of physician and include single (ASA) or dual (ASA+clopidogrel) antiplatelets (45.5% and 41.8%) or combination of ASA with oral anticoagulant (mostly warfarin) – dual antithrombotic therapy (DAT) in 12.7%. DAT was prescribed up to 6 months after CABG in patients with higher atherosclerotic burden.

Results: Frequency of thrombotic events (TE: cardiovascular death, acute coronary syndrome, ischemic stroke, urgent coronary or carotid arteries revascularization, acute limb ischemia) was similar in single or dual antiplatelet therapy groups. Kaplan-Meier curves demonstrated difference in TE free survival during median time of 3.2 years between antiplatelet and DAT groups (Log-Rank p=0.01). Increase of TE was observed after planned oral anticoagulant discontinuation. DAT was associated with higher incidence of BARC 2–5 bleeding: 16% vs 3% in antiplatelet therapy group, p=0.0165.



Conclusions: DAT is sufficient to prevent TE in high risk patients but increases the risk of bleeding. We supposed that long-term DAT, including ASA and a safer anticoagulant at a lower dose, possibly rivaroxaban 2.5 mg twice daily, may improve outcomes in this category of patients.

ID:913

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

THE PRESENCE OF MTDNA MUTATIONS IN THP1-BASED CYBRID CELLS AFFECTS THE EFFICIENTLY OF FCCP-INDUCED MITOPHAGY

POSTER VIEWING SESSION

Alexander D. Zhuravlev[1], Nikita Nikiforov[2,3], Svetlana Verkhova[2], Mihail Vysokikh[4], Maria Marey[4], Alexander N. Orekhov[3]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Centre Of Collective Usage, Institute of Gene Biology, Moscow, Russian Federation, [3]Laboratory Of Angiopathology, Institute Of General Pathology And Pathophysiology, Moscow, Russian Federation, [4]Mitochondrial Medicine Laboratory, National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I. Kulakov of Ministry of Healthcare of Russian Federation, Moscow, Russian Federation

Background and Aims : Mitophagy is an effective way to clearance of dysfunctional mitochondria. A disturbance in the clearance of dysfunctional organelles and their accumulation may indicate that mitophagy is defective. We hypothesize that mtDNA mutations may cause defective mitophagy.

Methods: Cybrids were created by fusion of mtDNA-free THP-1 cells with platelets isolated from patients with mtDNA mutations associated with progression of atherosclerosis. Cybrid lines differ from each other only in the mitochondrial genome. Mitophagy was assessed using confocal microscopy. FCCP was added to cells for 1.5 hours. Colocalization between mitochondria (MitoTracker Green) and lysosomes (LysoTracker Deep Red) was considered mitophagy.

Results: Cybrid lines HSMAM2 and TCN-521 demonstrate increased efficiently of mitophagy. Cybrid lines TCI-521 and HSM2 demonstrate reduced efficiently of mitophagy.

Conclusions: Lines that differ only in the mitochondrial genome have different levels of mitophagy. We assume that mtDNA mutations affect the efficiently of mitophagy. Supported by RSF (Grant №22-25-00650)

ID:909

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

EVALUATION OF THE ANTIDIABETIC TREATMENT IN DIABETIC PATIENTS HOSPITALIZED IN AN INTERNAL MEDICINE DEPARTMENT IN A COMMUNITY HOSPITAL

POSTER VIEWING SESSION

Miguel Angel Fernandez Verdú, Gustavo Calcaño, Angels Pedragosa, Rosa Borrallo, Carolina Guerrero
Internal Medicine, Consorci Sanitari de Terrassa, Terrassa, Spain

Background and Aims : Diabetes mellitus represents one of the diseases with the greatest social and health impact. The prevalence of diabetes in Spain is around 14% and increasing. A correct approach and optimization of the treatment is useful and necessary for the control of the pathology and consequently for the reduction of the derived complications.
Our aim was to describe the modifications of antidiabetic treatment in diabetic patients admitted to the hospital based on the HbA1c value.

Methods: Descriptive, retrospective, observational study. Diabetic patients admitted to internal medicine department for any reason of Hospital Terrassa, Spain, during the first quarter of 2021 were included.

Results: A total of 186 diabetics were analyzed, 55.91% men. Mean age 74.59 years. In 66.67% of patients HbA1c was determined during admission, with a mean value 7.59%. Three HbA1c ranges were established to assess chronic outpatient monitoring being <7% (42.47%), 7-8.5% (32.8%) and > 8.5% (23.66%). At discharge, treatment was optimized for 21% of the patients based on HbA1c, of which 82% intensified and 18% decreased. In 79% of the patients, no modifications were made at discharge. Treatment adjustment at discharge in the HbA1c range <7% was 20.51%, in the range 7-8.5% 41.03% and in the range> 8.5% 38.46%.

Conclusions: HbA1c is determined relatively frequently in patients admitted to the internal medicine department for any reason to assess diabetes chronic control.
However, it is not correlated with consequent treatment adjustment at discharge, mainly in those patients with worse controls. Hospital admission can be a key moment to detect and optimize diabetes control.

ID:900

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

ASYMMETRIC DIMETHYLARGININE (ADMA) MEDIATES THE EFFECT OF MIRNA-762 ON ALL-CAUSE MORTALITY IN PATIENTS WITH CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Natalia Jarzebska[1], Sergey Tselmin[2], Marcus E. Kleber[3], Winfried Maerz[4], Hong Jin[5], Stefan Bornstein[2], Arduino Mangoni[6], Norbert Weiss[1], Roman Rodionov[1]
[1]Angiology, Technische Universität Dresden, Dresden, Germany, [2]Department Of Medicine Iii, Technische Universität Dresden, Dresden, Germany, [3]Vth Department Of Medicine, Medical Faculty Mannheim, Heidelberg University, Heidelberg, Germany, [4]Mvz Humangenetik Mannheim, SYNLAB, Mannheim, Germany, [5]Molecular Medicine And Surgery, Karolinska Institutet, Solna, Sweden, [6]Department Of Clinical Pharmacology, Flinders University and Flinders Medical Center, Adelaide, Australia

Background and Aims : Background: Plasma concentrations of the endogenous L-arginine homologue asymmetric dimethylarginine (ADMA) independently predict cardiovascular and all-cause mortality. We sought to identify miRNAs that mediate the effects of ADMA on mortality or influence mortality through regulation of ADMA concentrations.

Methods: In 993 participants of the Ludwigshafen Risk and Cardiovascular Health study (age 63.0±10.5 years, 31.4% females and 74.7% with coronary artery disease (CAD)) we measured ADMA and miRNAs concentrations in citrate plasma and investigated associations between them and with all-cause mortality.

Results: miRNA-762 was positively and significantly correlated with ADMA concentrations (p=0.0013) and with all-cause mortality after adjusting for age and sex (HR (95%CI: 1.51(1.26-1.81); p=7.37E-06). The association remained significant after additionally adjusting for body mass index, CAD, arterial hypertension, diabetes, smoking, lipids, C-reactive protein, fibrinogen, renal function, homocysteine and medication (p=0.04). Mediation analyses showed that ADMA mediated 67% of the effect of miRNA-762 on mortality while miRNA-762 only mediated 8% of the effect of ADMA.

Conclusions: miRNA-762 is an independent predictor of all-cause mortality in patients with CAD. The effects of miRNA-762 on mortality might be at least partially mediated by ADMA. miRNA-762 has been recently shown to regulate apoptosis in cardiomyocytes in myocardial infarction. We are currently investigating the effects of miRNA-762 on ADMA metabolism and stress responses in cultured cardiomyocytes and endothelial cells.

ID:898

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

RELATIONSHIP BETWEEN SERUM LEVELS OF BDNF AND HDL-CHOLESTEROL IN WOMEN WITH METABOLIC SYNDROME

POSTER VIEWING SESSION

Daniela I. Koleva, Maria M. Orbetzova
Endocrinology, Medical University of Plovdiv, Plovdiv, Bulgaria

Background and Aims : Recently, a link between brain-derived neurotrophic factor (BDNF), glucose and lipid metabolism, inflammation and cardiovascular disease has been suggested. The aim of our study was to investigate the relationship between serum levels of BDNF and HDL-C in women with metabolic syndrome.

Methods: The present study comprised of 61 female patients with metabolic syndrome (MS) who were divided into 2 groups: 1. Women with MS and HDL-C<1.29 mmol/l (n=36) and 2.Women with MS and HDL-C≥1.3 mmol/l (n=25). The following measurement and laboratory tests were performed: weight, height, waist and hip circumferences; fasting levels of blood glucose and immunoreactive insulin; total cholesterol, HDL-C, LDL-C and triglycerides; basal concentrations of BDNF; systolic and diastolic blood pressure. Body mass index (BMI), waist-to-hip ratio (WHR), HOMA-IR, atherogenic index of plasma (AIP), Castelli's I and II risk indices were calculated. A comparative analysis of all the aforementioned parameters was carried out between the two groups of women with MS. Additionally, an investigation for the presence of correlations between BDNF and the other parameters was conducted.

Results: We found significantly lower levels of BDNF in the group of MS women with HDL-C<1.29 mmol/l. No significant differences concerning the other parameters, except LDL-C, AIP, Castelli's I and II, were observed. As it was expected, a significant positive correlation between serum BDNF and HDL-C was confirmed.

Conclusions: Our results revealed a possible role of BDNF in the occurrence of lipid disturbances and cardiovascular disease development, respectively, in women with diagnosed metabolic syndrome.

ID:896

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

A MOUSE MODEL OF ARTERIAL ENDOTHELIAL CELL-SPECIFIC INFLAMMATION REVEALS PATHWAYS OF ENDOTHELIAL DYSFUNCTION AND THE SIMULTANEOUS UPREGULATION OF ACE2, THE RECEPTOR OF SARS-COV2.

POSTER VIEWING SESSION

Johannes A. Schmid, Marion Mussbacher, José Basílio, Manuel Salzmann
Inst. Of Vascular Biology And Thrombosis Research, Medical Univ. of Vienna, Vienna, Austria

Background and Aims : Triggering chronic inflammation specifically in arterial endothelial cells of ApoE-deficient mice aggravates and accelerates atherosclerosis after feeding a cholesterol-rich high fat diet. Under these conditions, endothelial inflammation furthermore drives phenotypic transition of smooth muscle cells towards macrophage-like cells (Mussbacher M. et al, Atherosclerosis 2020, https://doi.org/10.1016/j.atherosclerosis.2020.06.005). Here, we wanted to study effects of persistent inflammatory activation of arterial endothelial cells under normal cholesterol levels.

Methods: Mice with arterial endothelial cell-specific expression of a tamoxifen-inducible Cre recombinase (via the BMX-promoter) were crossed with mice expressing constitutive active IKK2 (caIKK2), the main activator of the inflammatory NF-κB signaling pathway, downstream of a loxP-flanked stop cassette. Injection of tamoxifen thereby results in persistent inflammatory activation of arterial endothelial cells. Aortae of these mice were processed for RNA-sequencing, followed by bioinformatic analysis.

Results: Chronic inflammation of arterial endothelial cells led to a significant change of the transcriptome, with ACE2, the receptor of SARS-CoV2 being the highest upregulated gene, implying that a preexisting inflammatory state worsens the progression of COVID19. On the other hand, ribosomal proteins and elements of the protein synthesis machinery were significantly downregulated. Computational pathway analysis confirmed that and furthermore revealed a significant activation of death receptor signaling. It also predicted enhanced apoptosis, as well as necrosis of vascular endothelial cells. These findings suggest that persistent inflammation leads to endothelial dysfunction, exacerbating not only the progression of COVID-19, but also the erosion of atherosclerotic plaques.

Conclusions: Arterial endothelial inflammation leads to cellular dysfunction even under normal cholesterol levels.

ID:895

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-09 Epidemiology of socioeconomic and psychosocial risk factors*

ASSOCIATION OF SELF-REPORTED HEALTH AND WELLBEING INDICATORS WITH A POSITIVE DIAGNOSIS FOR COVID-19. CARTSESIAN-CY STUDY

POSTER VIEWING SESSION

Galatia Photiou[1], Nicos Middleton[2], Demosthenes B. Panagiotakos[3], Andrie Panayiotou[1]
[1]Cyprus International Institute For Environmental And Public Health, Cyprus University of Technology, Limassol, Cyprus, [2]Department Of Nursing, Cyprus University of Technology, Limassol, Cyprus, [3]Department Of Nutrition And Dietetics, Harokopio University, Athens, Greece, Kallithea, Greece

Background and Aims : Introduction: CARTESIAN-CY is part of a prospective, multicenter, international study on the medium- and long-term effects of COVID-19 on the cardiovascular system and arterial ageing, as well as social well-being and general health. **Objectives:** Investigate the association between self-reported health and well-being indicators and positive diagnosis of COVID-19.

Methods: Participants (18-80 years old of both sexes) provide information using the validated SF-12 questionnaire and have measurements of their arterial elasticity and central BP taken at 3-6 and 12-15 months following a positive or negative test result for COVID-19.

Results: include data from the first 89 participants (44.9% men; 27% with positive COVID-19). Age, gender, smoking and educational background did not differ statistically based on COVID-19 diagnosis and neither was self-reported health state overall (p for trend=0.6). Participants with a positive COVID -19 diagnosis reported more often that they "accomplished less than they would have liked at work/ regular daily activities" during the previous month, compared to those with a negative diagnosis (p for trend=0.02). The same was true for the question "how much pain interfered ordinary with your normal work (both their work outside the home and household chores)", with people who test positive for COVID-19 reporting a more frequent pain effect, while reporting less often "a lot of energy" (p for trend =0.045 and 0.014 respectively).

Conclusions: We report an association between positive diagnosis for COVID-19 at 3-6 months and the current general health of participants, mainly in terms of their daily activities

ID:892

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

SYSTOLIC BLOOD PRESSURE, MEDIATED BY ARTERIAL STIFFNESS, IS ASSOCIATED WITH CAROTID INTIMA-MEDIA THICKNESS IN WOMEN BUT NOT MEN WITH TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Ying Jie Chee, Rinkoo Dalan
Endocrinology, Tan Tock Seng Hospital, Singapore, Singapore

Background and Aims : There is a distinct sex disparity in cardiovascular diseases (CVD) among individuals with diabetes mellitus (DM). We aimed to study the impact of sex on cardiovascular risk factors, subclinical atherosclerosis and arterial stiffness in type 2 DM.

Methods: We recruited 398 individuals from a diabetes centre in Singapore. Carotid ultrasonography and applanation tonometry were performed to measure carotid intima-media thickness (CIMT) and arterial stiffness. Univariate and multivariate linear regression were used to evaluate associations between CVD risk factors, CIMT and arterial stiffness.

Results: There were 196 men and 202 women (mean age 54.2 and 54.5 years respectively). CIMT in men was higher despite having lower oxidative stress index and high-sensitivity C-reactive protein. Women had lower pulse wave velocity (pwv) but higher augmentation index than men (table 1). A significant association between systolic blood pressure (SBP) with standardized ln(CIMT) was observed only in women after adjusting for age, BMI, SBP, HbA1c and non-high-density lipoprotein cholesterol. Furthermore, increase in pwv was associated with significantly higher SBP in women than men (6.11mmHg in women vs 4.94mmHg in men; $p < 0.000$), while an association between augmentation index and SBP was only observed in

women.

Table 1: Baseline Characteristics

	Total (N = 398)	Male (N=196)	Female (N=202)	p-value
Age (years)	54.4 (10.4)	54.2 (10.2)	54.5 (10.7)	0.82
BMI	26.9 (24.1-30.2)	26.4 (24.0-29.5)	27.4 (24.5-30.5)	0.14
SBP (mmHg)	132 (122-141)	131.5 (122.3-140)	132 (122-142.5)	0.57
DBP (mmHg)	75 (70-80.5)	77 (71.5-82.5)	73.5 (68.5-78.5)	0.61
Total cholesterol (mmol/L)	4.2 (3.7-4.9)	4 (3.5-4.7)	4.4 (3.9-5.0)	0.38
LDL cholesterol (mmol/L)	2.4 (2.0-2.9)	2.3 (1.9-2.8)	2.4 (2.1-3.0)	0.013
HDL cholesterol (mmol/L)	1.1 (1.0-1.2)	1.0 (0.9-1.2)	1.1 (1.0-1.4)	0.000
Non-HDL cholesterol (mmol/L)	3.0 (2.6–3.7)	3.0 (2.5–3.7)	3.2 (2.6–3.8)	0.053
Triglyceride (mmol/L)	1.3 (1.0-2.0)	1.3 (1.0-2.0)	1.4 (1.0-2.0)	0.73
HbA1c (%)	8.4 (7.2-9.7)	8.6 (7.2-9.6)	8.3 (7.0-9.7)	0.55
Oxidative stress index	1.00 (0.85-1.15)	0.94 (0.80-1.07)	1.06 (0.91-1.23)	< 0.000
hsCRP (mmol/L)	1.8 (0.8-4.0)	1.2 (0.5-3)	2.4 (1.1-4.7)	< 0.000
Statin use	287 (76.7)	135 (73.8)	152 (80)	0.13
CIMT (mm)	0.617 (0.55-0.70)	0.650 (0.55-0.70)	0.617 (0.55-0.70)	0.004
Augmentation index	29 (23-36)	26 (20-32)	32 (26–39.5)	< 0.000
Pulse wave velocity (m/s)	8.1 (7-9.1)	8.3 (7.2 – 9.4)	7.8 (6.9 – 9)	0.02

Values are mean (SD) or median (IQR) or N (%). Chi-square (for categorical variables) and independent sample Student's/Mann-Whitney test (for continuous variables)

Conclusions: Increased SBP and arterial stiffness may modulate subclinical atherosclerosis to a larger extent among women with T2DM as compared to men. Greater emphasis on haemodynamic management may substantially impact CVD lowering among women. This sex dichotomy in the associations between arterial stiffness and blood pressure on subclinical atherosclerosis needs to be explored in larger population-based and mechanistic studies.

ID:887

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

ROLE OF THE INTEGRIN-LINKED KINASE/TGF-B/SMAD PATHWAY IN SITAGLIPTIN MEDIATED CARDIOPROTECTIVE EFFECTS IN A RAT MODEL OF DIABETIC CARDIOMYOPATHY

POSTER VIEWING SESSION

Nouf M. Alrasheed, Asma S. Alonazi, Nawal M. Alrasheed, Tahani K. Alshammari, Anfal F. Bin Dayel, Maha A. Alamin, Danah A. Albuaijan, Dareen N. Alassiri, Alanoud F. Aljarbua, Fatimah K. Almusaytir, Abeer O. Alharbi
Pharmacology And Toxicology, King Saud University, Riyadh, Saudi Arabia

Background and Aims : In this study, we investigate whether sitagliptin mediates cardioprotection via interference with transforming growth factor-beta (TGF-(β signaling through the SMAD and integrin-linked kinase (ILK) pathways in rats with streptozotocin-induced type 2 diabetes.

Methods: Twenty-four adult male Wistar rats were divided into four groups (6 rats/group). Two heathy control groups received 0.9% NaCl or sitagliptin orally (100 mg kg^{-1}) orally for six consecutive weeks. In the two other groups, diabetes was induced by a single intraperitoneal injection of streptozotocin (55mg kg^{-1}), and rats received the same saline or sitagliptin treatments as the healthy controls. The Heart\body weight ratio and circulating levels of the diabetic cardiomyopathy biomarkers, troponin-1 and creatine kinase-MB) were assessed. Protein levels of ILK, TGF-β1, tumor necrosis factor-alpha (TNF-α), phosphorylated SMAD 2/3 (p-SMAD 2/3), collagen I, and extracellular matrix (ECM) were detected by Western blot and immunohistochemistry.

Results: The Heart\body weight ratios in sitagliptin-treated diabetic rats were significantly reduced compared to those in the diabetic control group (3.10 ± 0.20 vs. 4.75 ± 0.49 mg g^{-1}, $p<0.01$), as were the circulating levels of troponin-I and creatine kinase-MB (216.0 ± 19.03 vs. 407.6 ± 29.83 ng ml^{-1}; 8.67 ± 0.71 vs. 22.62 ± 3.13 U ml^{-1}, $p<0.001$, respectively). Expression levels of the fibrotic biomarkers TGF-β1, TNF-α, ECM, collagen I, and p-SMAD 2\3 were markedly reduced in sitagliptin-treated diabetic group versus diabetic control group, while ILK expression was upregulated by sitagliptin treatment.

Conclusions: Our data indicate that sitagliptin may protect against diabetic cardiomyopathy through modulation of ILK-related TGF-β/SMAD signaling pathways.

ID:880

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

CONTENT AND EFFECTIVENESS OF COMMUNITY-BASED REHABILITATION ON QUALITY OF LIFE IN PEOPLE POST-STROKE: A SYSTEMATIC REVIEW WITH META-ANALYSIS.

POSTER VIEWING SESSION

Sènadé Inès Noukpo[1,2], Oyéné Kossi[1,2], Lisa Tedesco Triccas[1], Thierry Adoukonou[2], Peter Feys[1]
[1]Reval, UHasselt, Hasselt, Belgium, [2]Neurology, University of Parakou, Parakou, Benin

Background and Aims : Community based rehabilitation (CBR) aims to provide rehabilitative services to people with disabilities in their home or community. It was as an affordable way of offering rehabilitation to children with disabilities in the rural areas. After its adoption in 1978, it developed into more towards social inclusion of people with disability. Aims: To review the content and evaluate the effects of CBR on quality of life (QoL), balance, and walking capacity for people post-stroke compared to other rehabilitation protocols or no care.

Methods: We conducted a systematic search and meta-analysis of clinical trials of CBR interventions for stroke survivors. Five online electronic databases (PubMed, Web of sciences, Scopus, Hinari, and Pedro) were systematically searched for articles published in English and French languages from inception to September 2021. We included studies that reported on QoL as primary or secondary outcomes from CBR interventions involving adults post-stroke.

Results: Sixteen studies with 1755 people post-stroke were included. Different CBR interventions were used, grouped into three clusters: a) exercise programs, b) task-oriented training and c) educational and taking-charge program. CBR interventions were more effective than other rehabilitation protocols (SMD=0.16[0.02, 0.30], P=0.03, I2 =40%) on QoL for people with chronic stroke. The effects of interventions on walking capacity and balance demonstrated non-significant difference, SMD=0.31[-0.02, 0.64], P=0.06, I2 =88%) and (SMD= 0.20[-0.12, 0.53], P=0.22, I2 =68% respectively.

Conclusions: Current data indicates that CBR can benefit people with chronic stroke. Its benefits lie in improving the QoL which is a well-recognized goal for people after stroke.

ID:879

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

BURDEN OF FH IN ENGLAND

POSTER VIEWING SESSION

Raquel Lahoz[1], Adeline Durand[2], Christopher L. Morgan[3], Divyagiri Seshagiri[1]
[1]Rwe, Novartis Pharma AG, Basel, Switzerland, [2]Health Economics & Outcomes Research, Novartis Pharmaceuticals UK Ltd, London, United Kingdom, [3]Epidemiology, Pharmatelligence, Cardiff, United Kingdom

Background and Aims : This study describes the epidemiology (incidence and prevalence), healthcare resource utilization (HRU) and its associated costs in patients with familial hypercholesterolemia (FH) in England.

Methods: This retrospective non-interventional cohort study included patients with FH from the Clinical Practice Research Datalink (CPRD) Aurum database (January 2011 – December 2019). FH was defined as patients who had at-least one encounter of FH. Index-date was first FH encounter during Jan 2015 – Dec 2019. Incident and prevalent patients were identified, abstract presents data for incident patients.

Results: FH incidence and prevalence were evaluated for year 2019 and females had higher incidence rate; prevalence rate showed similar trend. From 2015 to 2018, 3,601 patients with incident FH and potential 12 months follow-up (66% females) with a mean (SD) age of 53.3 (12.2) were identified. More than 80% of patients were under 65 years of age and mean LDL-C at baseline was 4.99 mmol/L. Nearly 40% of FH patients were not taking statins at baseline, 45% were suffering from depression/anxiety and 27% had hypertension. For the total 10,093 patient-years of follow-up, nearly 32% of patients had inpatient admissions, 75% had out-patient appointments of which, 16% were cardiology appointments and almost all the patients (98.5%) had primary care appointments. Total cost for inpatient admissions was £3.16 million, for outpatient appointments was £3 million and for primary care was £1.8

million.

Table: Epidemiology in 2019, and healthcare resource use and costs for incident FH patients in 2015-2018

	Incidence rate (per 1,000 PY)		Prevalence rate (per 1,000 PY)	
Age groups	**Males**	**Females**	**Males**	**Females**
18-24 years	0.08	0.02	0.22	0.21
25-34 years	0.07	0.08	0.31	0.34
35-44 years	0.19	0.14	0.95	0.63
45-54 years	0.24	0.4	1.53	1.76
55-64 years	0.15	0.52	1.29	3.07
65-74 years	0.08	0.31	0.83	2.73
75+ years	0.02	0.07	0.24	0.79
18-64 years	0.16	0.28	0.88	1.19
65+ years	0.05	0.19	0.56	1.75
Overall	0.13	0.26	0.82	1.32
Healthcare resource utilization (N patients=3,601)	**N (patients)**	**%**		
Inpatient admissions, n (%)	1,138	31.6%		
ASCVD inpatient admissions, n (%)	70	1.9%		
Outpatient patients, n (%)	2,683	74.5%		
Cardiology outpatients, n (%)	420	11.7%		
Primary care patients, n (%)	3,546	98.5%		
Costs (N patients =3,601)	**N (contacts)**	**Total costs (10,029.8 PY)**	**Cost per person year**	
Inpatient admissions	2,639	£3,157,391	£314.8	
ASCVD inpatient admissions	98	£219,399	£21.9	
Outpatient appointments	26,848	£3,018,290	£300.9	
Cardiology outpatient appointments	1,489	£167,788	£16.7	
Primary care appointments	78,651	£1,838,614	£183.3	

Conclusions: Incidence and prevalence of FH was substantially higher in females; resource utilization was higher in primary care setting and cost was higher for inpatient admissions compared to outpatients.

ID:1005

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

THE INCIDENCE OF VISCERAL OBESITY IN PATIENTS WITH ARTERIAL HYPERTENSION AND NON-ALCOHOLIC FATTY LIVER DISEASE.

POSTER VIEWING SESSION

Maria Derevyanchenko[1], Anastasia Streltsova[1], Mikhail Statsenko[1], Irina Starodubtseva[2]
[1]Internal Diseases, Volgograd State Medical University, Volgograd, Russian Federation, [2]Internal Diseases, NN Burdenko Voronezh State Medical University, Voronezh, Russian Federation

Background and Aims : To determine the incidence of visceral obesity and the severity of adipose tissue dysfunction in patients with arterial hypertension (AH) and NAFLD.

Methods: A prospective controlled study involving 120 hypertensive patients with and without NAFLD was carried out.Anamnesiscollection,measurement of anthropometric parameters,body mass index (BMI), waist-to-hip ratio,and visceral obesity index (VOI) calculations (with the age norm for the studied group of patients being≤1.92 conventional units) and epicardial fat thickness were carried out.Also,the degree of adipose tissue dysfunction (ATD) and visceral fat percentage were determined using the bioelectrical impedance method.

Results: For a number of demographic and clinical parameters the comparison groups were comparable (p>0.05). When calculating the visceral obesity index,a significantly higher number of patients with VOI>1.92 was observed in patients with AH and NAFLD compared to patients with isolated AH (91.4% vs 40.9%,p=0.0000).As a result of assessing the degree of ATD in the main group, the following data were obtained:moderate ATD-20%,significant ATD-42.8%, severe ATD-28.5%(p=0.5361;p=0.1215;p=0.6281,respectively). At the same time,the percentage of visceral fat in the first group was significantly higher compared to the second group (12[11:14.5] vs 9[6:9],p=0.0000).94.2% of patients in the AH+NAFLD group had the waist-to-hip ration higher than the accepted norm,compared to 54.4% of patients in the AH group (p=0.0004).The epicardial fat thickness was also higher in patients with comorbid pathology (5,3[4,0-7,5] vs 3,0[2,5-3,5],p=0.0000).There is a significant increase in BMI in the first group compared to the second group (32[30.3:34.2] vs 27[24.5:28.7],p=0.0000).

Conclusions: Patients with AH and NAFLD have a significantly higher visceral obesity index compared to patients with isolated AH.

ID:1011

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EFFECTIVITY, SAFETY AND ADHERENCE WITH PCKS9 INHIBITORS

POSTER VIEWING SESSION

Meritxell Royuela[1], M. Pilar Alonso[2], Antònia Balet[2], Omar El Boutrouki[3], Mariona Bonet[3], Domingo Ruiz[3]
[1]Internal Medicine. Lipid Unit, ALTHAIA. Xarxa assistencial Universitària de Manresa, Manresa, Spain, [2]Pharmacy, ALTHAIA. Xarxa assistencial universitària de Manresa, Manresa, Spain, [3]Internal Medicine, ALTHAIA. Xarxa assistencial universitària de Manresa, Manresa, Spain

Background and Aims : The main purpose of the study is to evaluate the effectivity, safety and adherence in patients who undergoing treatment with PSCK9 inhibitors (iPCKS9), evolocumab and alirocumab, in our Lipid Unit of ALTHAIA. Xarxa assistencial universitarà de Manresa (Barcelona).

Methods: Prospective observational follow-up study since may 2016 until june 2021. Patients were on standard of care and didn't achieve cLDL goals, furthermore they met the local criteria (CAMHDA) to start treatment with iPCSK9. We took blood samples to assess lipid profile at 1,3,6 months and then every 6 months. We evaluated cLDL targets according to ESC/EAS 2019 Guidelines for the management of dyslipidaemias.

Results: N= 43. Women 17/43 (39,53%). 19/43 (44%) presented Heterozygous Familiar Hypercolesterolemia (FH). They were on secondary prevention 31/43 (72,09%), 10/31 (32%) of them with FH. 19/43 (44%) presented total intolerance to statins. Efectivity Patients presented a reduction of cLDL from baseline of 54,75% to 69,85%. Most of them (>63%) achieved cLDL goals time-maintained. We only observed 4 cases who presented a one-off increase. We observed 4 cases of MACE: 2/4 at the begining of iPCKS9 therapy, 1/4 in a patient who was active smoker and had poor drug adherence, and 1/4 in uncontrolled diabetis with cLDL <55mg/dl. Safety Evolocumab: 1/43 diarrhea, 1/43 flu syndrome Alirocumab: 1/43 myalgia, 1/43 severe skin reaction Adherence Patients presented an adherence >95% and felt comfortable with their administration regimen.

Conclusions: Most of patients who undergoing treatment with PCSK9 inhibitors achieve cLDL goals, present low rates of adverse effects and have a good adherence.

ID:876

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

VASCULAR ENDOTHELIAL FUNCTION AS AN EARLY SIGN OF VASCULAR AGEING IN PATIENTS WITH METABOLIC SYNDROME

POSTER VIEWING SESSION

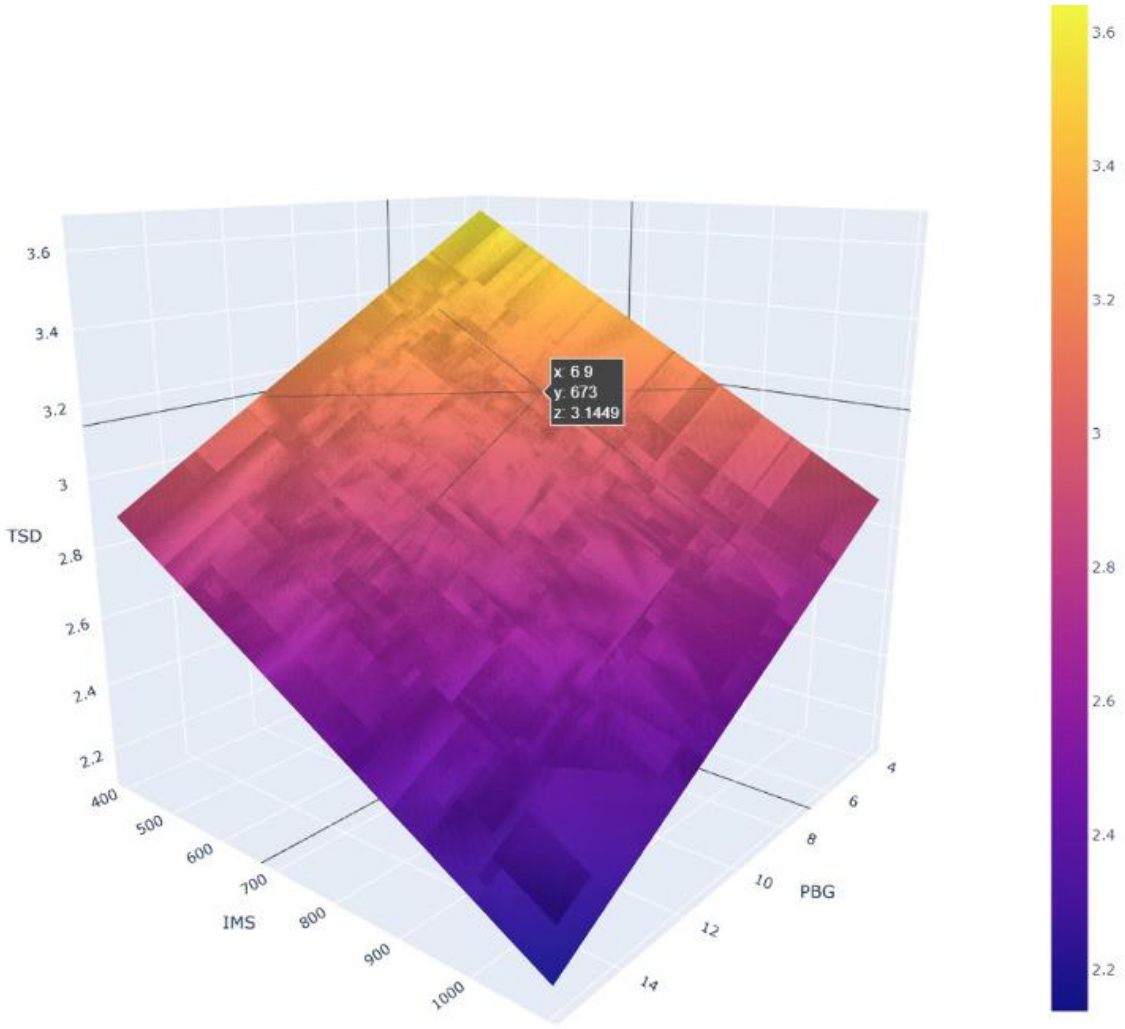
Kristina Pugaciauskaite[1], Jolita Badariene[1], Ligita Ryliskyte[1], Agne Laucyte-Cibulskiene[2,3], Jurgita Songailienė[4]
[1]Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Cardiology And Angiology; Nephrology, Vilnius University Hospital Santaros Klinikos; Lund University, Skane University Hospital, Vilnius, Lithuania, [3]Nephrology, Lund University, Skane University Hospital, Malmö, Sweden, [4]Department Of Human And Medical Genetics, Institute Of Biomedical Sciences, Vilnius university, Faculty of Medicine, Institute of Biomedical Sciences, Vilnius, Lithuania

Background and Aims : Objective is to evaluate signs of early vascular ageing, namely arterial stiffness, intima-media thickness and endothelial dysfunction, among people with metabolic syndrome by comparing the results of pulse wave velocity (PWV), intima-media thickness (IMT) and flow-mediated dilation FMD) techniques, respectively. Also, we aim to examine the correlation between these methods as well as relationship with cardiovascular risk factors.

Methods: The data of 4927 patients who were admitted to the Centre of Cardiology and Angiology at Vilnius University Hospital Santaros Klinikos was analysed. The patient cohort consisted of 2114 males and 2813 females aged 40-55 and 50-65, respectively. We evaluated the results of PWV, IMT and FMD techniques and their relationship with 6 cardiovascular risk factors.

Results: Endothelial dysfunction is more common among men than women ($p<0,001$). Abnormal values of FMD, PWV and IMT are associated with significantly higher frequency of atherosclerotic plaques in common carotid artery ($p=0,001$, $p=0,01$, $p<0,001$, respectively). There is a positive statistically significant correlation between total number of cardiovascular risk factors and both the extent of arterial stiffness ($p<0,001$) and intima-media thickness ($p<0,001$). We also found that intima-media thickness is correlated with arterial stiffness ($p=0,001$), while values obtained by both PWV ($p=0,001$) and IMT ($p=0,002$) methods are negatively linked with results of

FMD.



Correlation between FMD, IMT and PWV values.

TSD – flow mediated dilation (%), PWV – pulse wave velocity (m/s), IMS – intima-media thickness (μm).

Conclusions: Endothelial function is less impaired in women than in men. However, the latter were found to be associated with less stiffened arteries, lower prevalence of atherosclerotic plaques and thinner intima-media layers. There is a significant correlation between measures of endothelial dysfunction, arterial stiffness and intima-media thickness.

ID:1071

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

EXPRESSION PATTERN OF CHOLESTEROL METABOLISM GENES IN ADIPOSE TISSUE OF MORBIDLY OBESE PATIENTS WITH TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Kseniya V. Dracheva[1,2], Irina A. Pobozheva[1,2], Kristina A. Anisimova[3], Stanislav G. Balandov[3], Zarina M. Hamid[3], Alexandra A. Panteleeva[1,2], Dmitriy I. Vasilevsky[3], Sofya N. Pchelina[1,2], Valentina V. Miroshnikova[1,2]
[1]Laboratory Of Medical Genetics, Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation, [2]Laboratory Of Human Molecular Genetics, Petersburg Nuclear Physics Institute National Research Centre "Kurchatov Institute", Gatchina, Russian Federation, [3]Surgery Department, Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation

Background and Aims : Obesity is often complicated by concomitant pathologies such as metabolic syndrome (MS) and type 2 diabetes mellitus (DM2). Adipose tissue (AT) dysfunction in obesity is caused by accumulation of lipids as well as defective reverse cholesterol transport. ABCA1 and ABCG1 transporters and transcriptional factors PPARγ and LXRα/β are key players in cholesterol homeostasis in AT. Aim of the study was to investigate the *ABCA1, ABCG1, PPARG*, *LXRβ (NR1H2), LXRa (NR1H3)* gene expression in AT of patients with type 2 diabetes mellitus.

Methods: Subcutaneous and visceral AT (SAT and VAT) samples were obtained during bariatric surgery (N=33, age 43.3±11.2, BMI>35): morbidly obese without MS (N=8), with MS (N=6) and DM2 (N=19). Samples from the control group without obesity (N=11, age 41.7±7.3) were obtained during other intervention. mRNA levels of the studied genes were estimated by real-time PCR.

Results: SAT *PPARG* mRNA level was reduced in morbidly obese patients with DM2 (p=0,001), negatively correlated with BMI (r=-0,399, p=0,009), plasma glucose (r=-0,382, p=0,022) and triglyceride levels (r=-0,599, p=0,001). SAT *ABCG1* mRNA level in patients with DM2 was increased compared with patients with MS (p=0,009). SAT *ABCG1* mRNA level was positively correlated with *LXRα* mRNA level (r=0,386, p=0,009). SAT *LXRα* mRNA level in turn was positively correlated with plasma insulin concentration (r=0,510, p=0,013) and HOMA-IR (r=0,610, p=0,002). In multiple linear regression model DM2 diagnosis and *LXRα* mRNA level were independent predictors of SAT *ABCG1* expression (p<0,05).

Conclusions: DM2 is characterized by altered *PPARG* and *ABCG1* expression pattern in AT. Supported by Russian foundation for basic research [20-015-00502].

ID:1118

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

CUMULATIVE DYSGLYCEMIA, HYPERINSULINEMIA AND INSULIN RESISTANCE WITH ARTERIAL STIFFNESS PROGRESSION IN HEALTHY ADOLESCENTS: THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN (ALSPAC)

POSTER VIEWING SESSION

Andrew O. Agbaje
Institute Of Public Health And Clinical Nutrition, School Of Medicine, Faculty Of Health Sciences, University of Eastern Finland, Kuopio, Finland

Background and Aims : Altered metabolic indices have been associated with arterial stiffness progression in adults. However, longitudinal evidence among adolescents is limited. We investigated the longitudinal associations of cumulative fasting plasma glucose, insulin, and homeostatic model assessment of insulin resistance (HOMA-IR) with arterial stiffness progression among adolescents.

Methods: We studied 1779 British 15-year-olds (50% females) followed up for 9 years. Carotid-femoral pulse wave velocity (cfPWV) was repeatedly measured by Vicorder ultrasound device at ages 17 and 24 years. Fasting insulin and glucose were serially measured in line with standard protocols at ages 15, 17, and 24 years. HOMA-IR was computed for all time points. Metabolic indices were age and sex-specifically dichotimized as ≥75%, indicating high category and <75% indicating moderate or reference category. We conducted linear mixed-effect model analyses and adjusted for statistically significant determinants of cfPWV progression viz: sex, age, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, high sensitivity C-reactive protein, fat mass and lean mass measured with dual-energy Xray absorptiometry, heart rate, and sedentary time, light physical activity and moderate to vigorous physical activity measured with ActiGraphTM accelerometer.

Results: Cumulative high exposures to insulin: effect estimate -0.019mU/L; [95% CI -0.019 to -0.002; p = 0.033] and HOMA-IR: -0.021; [-0.039 to -0.004; p = 0.019] from 15 – 24 years of age were negatively associated with the 7-year cfPWV progression. However, cumulative high glucose exposure was unassociated with cfPWV progression 0.008mmol/L; [-0.008 to 0.025; p = 0.302].

Conclusions: Cumulative high insulin and HOMA-IR exposures from mid-adolescence through young adulthood appear protective of worsening arterial stiffness progression.

ID:1117

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

DISTRIBUTION OF OVERWEIGHT AMONG MEN AND WOMEN WITH CLINICAL DIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLAEMIA (FH) IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Egle Skiauteryte[3], Žaneta Petrulionienė[1,2,3], Dovile Gabartaite[2,3], Emilija Meskene[2,3], Juste Staigyte[2,3], Rimantė Čerkauskienė[2,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[3], Vilma Dzenkeviciute[2,3,5], Jolita Badariene[1,2,3], Sandra Kutkiene[3], Egidija Rinkuniene[1,2,3], Rusne Jakaite[3], Gabriele Jaskeviciute[2]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Clinic Of Internal Diseases, Family Medicine And Oncology, Vilnius University, Faculty of Medicine, Vilnius, Lithuania

Background and Aims : to determine the prevalence of overweight among men and women with clinically diagnosed FH.

Methods: Prospective observational cohort study enrolled patients with clinically diagnosed FH treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. According to Dutch Lipid Clinic Network (DLCN) diagnostic criteria for Familial Hypercholesterolemia, definite FH was diagnosed when a total point score was >8, probable FH – DLCN score 6-8, possible FH - 3-5 points, unlikely FH – DLCN score <3. Overweight was defined as body mass index (BMI) 25-29,9. Data of 220 study patients (mean age 45,3±12,6 years) were included in the analysis. The prevalence of overweight was compared in different groups according to clinical FH diagnosis. Statistical analysis was performed using R (v. 4.0.4) program package.

Results: Of 220 examined patients 54,5% (n=120) were women and 45,5% (n=100) were men. 25,5% (n=56) of patients had definite FH, 29,5% (n=65) - probable FH, 30,9% (n=68) possible and 14,1% (n=31) had unlikely FH. 44,5% (n=98) of the study population were overweight (55% of men and 37% of women, p=0,008). The prevalence of overweight in female group was: 20% (n=6) with definite FH, 43% (n=17) with probable FH, 51% (n=19) with possible FH and 17% (n=2) with unlikely FH. The prevalence of overweight in male group was: 48% (n=12) with definite FH, 63% (n=15) with probable FH, 47% (n=14) with possible FH and 68% (n=13) with unlikely FH.

Conclusions: almost half of the patients with clinical FH diagnosis were overweight with greater proportion of men compared to women.

ID:1111

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

PULSE WAVE VELOCITY CORRELATES IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA (FH).

POSTER VIEWING SESSION

Małgorzata Waluś-Miarka, Barbara Idzior-Waluś, Ewa Kawalec, Aleksandra Woźniak, Maria Kapusta
Metabolic Diseases, Jagiellonian University, Kraków, Poland

Background and Aims : Pulse wave velocity (PWV) is a measure of arterial stiffness and prognostic factor of cardiovascular events. The aim was to assess PWV correlates in patients with FH from Poland.

Methods: Material included 154 FH patients diagnosed with DLCN criteria(63 men,41%). In all patients standardized questionnaire, anthropometric measurements and blood test were performed. Presence of carotid arteries plaques was assessed by ultrasound, arterial stiffness by measurements of PWV between the carotid and femoral artery using Complior device.

Results: The mean(SD) values of PWV was 10.1(1,85)m/sec. In patients with presence of carotid plaques (61 persons) PWV was higher than in patients without: 10.5(1.86) vs 9.7(1.75)m/sec, p=0.0059. PWV was higher in patients with arterial hypertension and in patients with CAD than in patients without ($p<0.001$). There were no differences in PWV in patients according to presence of molecular confirmation of FH. In the whole group PWV correlated positively with age ($r=0.66, p<0.001$) and negatively with serum concentration of total cholesterol, LDL-C and apo B (correlation coefficients: $r=-0.23$, $p=0.007$, $r=-0.31$, $p<0.001$, $r=-0.22$, $p=0.011$ respectively). Significant positive association between PWV and BMI, triglyceride and apo A1 serum concentrations were found: correlation coefficients: $r=0.26$, $p=0,003$; $r=0.27$, $p=0.002$; $r=0.18$, $p=0.037$ respectively. Interestingly, we observed also correlation between PWV and apolipoprotein C: $r=0.27, p=0.023$. After adjustment for age these associations were not significant. In the whole group significant associations between systolic and diastolic blood pressure and PWV were observed and are still significant after adjustment for age.

Conclusions: The results indicate the important role of controlling blood pressure in FH patients to prevent arterial stiffening.

ID:1107

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

DISTRIBUTION OF NORMAL BODY MASS INDEX (BMI) ACCORDING TO CLINICAL FAMILIAL HYPERCHOLESTEROLAEMIA (FH) DIAGNOSIS IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Egle Skiauteryte[3], Žaneta Petrulionienė[1,2,3], Dovile Gabartaite[2,3], Emilija Meskene[2,3], Juste Staigyte[2,3], Rimantė Čerkauskienė[2,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[3], Vilma Dzenkeviciute[2,3,5], Jolita Badariene[1,2,3], Sandra Kutkiene[3], Egidija Rinkuniene[1,2,3], Rusne Jakaite[3], Goda Jackute[2]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Clinic Of Internal Diseases, Family Medicine And Oncology, Vilnius University, Faculty of Medicine, Vilnius, Lithuania

Background and Aims : to determine the prevalence of normal BMI among people with clinically diagnosed FH in Lithuania.

Methods: Prospective observational cohort study enrolled patients with clinically diagnosed FH treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. According to Dutch Lipid Clinic Network (DLCN) diagnostic criteria for FH, definite FH was diagnosed when a total point score was > 8, probable FH–6-8, possible FH - 3-5 and unlikely <3 points. Normal body mass index was defined as BMI 18,5-24,9 for both genders. Data of 220 study patients (mean age 45,3±12,6 years) were included in the analysis. The prevalence of normal BMI was compared in different groups according to FH diagnosis. Statistical analysis was performed using R (v. 4.0.4) program package.

Results: Prospective observational cohort study enrolled patients with clinically diagnosed FH treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. According to Dutch Lipid Clinic Network (DLCN) diagnostic criteria for Familial Hypercholesterolemia, definite FH was diagnosed when a total point score was greater than 8, probable FH – total point score was 6-8, possible FH - 3-5 points and unlikely FH was diagnosed when points were <3. Normal BMI was defined as 18,5-24,9 for both genders. Data of 220 study patients (mean age45,3±12,6 years) were included in the analysis. The prevalence of normal BMI was compared in different groups according to FH diagnosis. Statistical analysis was performed using R(v. 4.0.4) program package.

Conclusions: in our study, normal BMI was found in only one-third of the patients with clinicalFH diagnosis.

ID:1102

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

NUTRIGENETIC APPROACH OF ATHEROSCLEROSIS – CLINICAL CASE STUDY

POSTER VIEWING SESSION

Andreea Zamfirescu[1], Mihaela Roman[1], Ana Capisizu[1], Daniela C. Stoian[2]
[1]Geriatrics, University "Carol Davila" Bucharest Romania, Bucharest, Romania, [2]Genetics, International Academy of Nutrition Educators, Cambridge, United Kingdom

Background and Aims : Nutrigenetic studies the relationship between genes and nutrients, metabolism, individual predispositions, recommending appropriate nutrition and supplements in accordance with the unique human genetic structure. Nutrigenetic test is a modern and efficient evaluation which shows its usefulness in chronic pathologies by adding predictive value.

Methods: Clinical case study: 67y.o., male, multiple cardio-vascular risk-factors: diabetes(type-2); mixed-dyslipidemia, smoker(50PY), obesity(type-II), hypertension (grade-3-very-high-added-risk); disorganized lifestyle, high fat, sugar and alcohol consumption.

Results: Systemic atherosclerosis: chronic coronary syndrome(CCS), heart failure(HF), peripheral arterial disease(PAD): aorto-iliac occlusive disease(type III), carotid atherosclerosis, stroke(2000). Total cardiovascular risk estimation: HeartScore: 10% (very-high-risk). Medication for cardio-cerebro-vascular disease was according to guidelines. Nutrigenetic test at the age of 65 (2019) (Advanced Nutrigenomics LLC-SUA): genetic risk-variations for type-2-diabetes (table1), dyslipidemia (tabels2-3), and hypertension. The patient applied a part of the recommendations from the nutrigenetic test, supplementing: Omega-3 (1g/day) (table4), zinc (15mg/day), vitamin-C (1g/day), vitamin-D (4000UI/day); reduced intake of Omega-6, sugar, but continued smoking. Lower-limb duplex ultrasound scanning and arteriography (due to symptoms: IC=100meters) led to revascularization (2021): femuro-femoral bypass with prosthesis (PTFE-no.7), endarterectomy: common, superficial and deep right femoral-arteries, with good results.

Table 1. Nutrigenetic test result. Advanced Nutrigenomics LLC SUA, www.advancednutrigenomics.com, https://www.genetx.eu

TYPE 2 DIABETES

Test 83 (haplotype IRS1)		
Locus	Gene	Genotype
rs7578326	IRS1	A/G
rs2943641	IRS1	T/C
Haplotype AC:		Present

Resolution
The presence of this haplotype increases the risk of insulin resistance, then type 2 diabetes, compared to the general population.

Table 2. Nutrigenetic test result. Advanced Nutrigenomics LLC SUA, www.advancednutrigenomics.com, https://www.genetx.eu

CHOLESTEROL

Test 82 (haplotype PON1)		
Locus	Gene	Genotype
rs662	PON1	G/G
rs854560	PON1	A/T
Haplotype GA:		Present

Resolution
The presence of this haplotype is associated with higher levels of LDL cholesterol compared to the average values of general population.

Recommendation:
Continuous monitoring of cholesterol levels is necessary. It is recommended to consult with a specialist (nutritionist or nutritionist doctor) to address an appropriate lifestyle that minimizes the risk of increasing LDL cholesterol. If your LDL cholesterol is above normal, your doctor may use this information to personalize and streamline anti-hypercholesterolemic treatments and for proper nutritional management.

Table 3. Nutrigenetic test result. Advanced Nutrigenomics LLC SUA, www.advancednutrigenomics.com, https://www.genetx.eu

POSTPRANDIAL HYPERLIPEMIA

Test 86 (haplotype APOA5)		
Locus	Gene	Genotype
rs662799	APOA5	G/G
rs3135506	APOA5	G/G
Haplotype APOA5*1:		Absent

Resolution
The absence of this haplotype is associated with an increased risk of postprandial hyperlipemia, which may promote the appearance of some cardiovascular diseases.

Recommendation:
Significant reduction in the intake of foods rich in animal fats, depending on the specialist advice.

Table 4. Nutrigenetic test result. Advanced Nutrigenomics LLC SUA, www.advancednutrigenomics.com, https://www.genetx.eu

OMEGA3 - OMEGA 6 INTAKE

Recommendation:
The table below shows recommended nutritional values (including dietary supplements) of omega-6 and omega-3 unsaturated fatty acids, as well as the maximum ratio between omega-6 and omega-3. These values are specific only to you.

OMEGA-6 FATTY ACIDS (N6)		OMEGA-3 FATTY ACIDS (N3)		RATIO N6/N3
Linoleic acid (LA)	<4g/day	Alpha-linolenic acid (ALA)	> 1,1 g/day	< 4
		Eicosapentaenoic acid (EPA)	> 0,4 g/day	
		Docosahexaenoic acid (DHA)	> 0,88 g/day	

Foods rich in **omega-3** unsaturated fatty acids include **fish (especially mackerel, salmon, cod, herring, sardines, anchovies), shellfish, flax seeds/oil, nuts, hazelnuts and almonds (various varieties), chia seeds.**

Foods rich in **omega-6** unsaturated fatty acids include **corn oil, sunflower oil, avocado oil, soybean oil.**

Conclusions: The patient had genetic risk for diabetes, dyslipidemia and hypertension, which cumulated with unhealthy lifestyle, led to severe systemic atherosclerosis: CCS, HF, PAD needing revascularization, stroke. Applying all nutrigenetic test recommendations would ameliorate patient's prognosis. Younger patients with chronic pathologies risk (such as diabetes and dyslipidemia) determined through nutrigenetic test, could apply personalized early life style changes, which would improve outcomes (prevent or delay atherosclerotic pathology onset) by better lifestyle habits with lifelong impact.

ID:1099

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

PREVALENCE OF PREMATURE CORONARY ARTERY DISEASE (CAD) ACCORDING TO GENETIC FAMILIAL HYPERCHOLESTEROLAEMIA (FH) DIAGNOSIS IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Žaneta Petrulionienė[1,2,3], Egle Skiauteryte[3], Dovile Gabartaite[2,3], Emilija Meskene[2,3], Juste Staigyte[2,3], Rimantė Čerkauskienė[2,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[3], Jolita Badariene[1,2,3], Vilma Dzenkeviciute[1,2,3], Sandra Kutkiene[3], Egidija Rinkuniene[1,2,3], Rasa Strupaite-Sileikiene[2,5,6], Rusne Jakaite[3], Miglė Vilniškytė[2]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Centre Of Eye Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [6]Center Of Eye Diseases, Clinic Of Ear, Nose, Throat, And Eye Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, vilnius, Lithuania

Background and Aims : FH is known to be a predisposing cause of premature CAD. We aimed to determine the distribution of premature CAD according to genetic diagnosis of FH in Lithuania.

Methods: Prospective observational cohort study enrolled patients with clinically diagnosed FH according to Dutch Lipid Clinic Network (DLCN) criteria treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. Premature CAD was defined as occuring in men younger than 55 years and women younger than 60 years. Data of 60 study patients were included in the analysis. Obstructive Atherosclerotic CAD was defined as the presence of stenosis ≥50% in at least one coronary vessel in Coronary Computed Tomography Angiography (CCTA) or coronary angiography, as well as performed percutaneous coronary intervention (PCI) or coronary arteries bypass grafting (CABG). Genetic testing was performed using genomic DNA, which was enzymatically fragmented, and regions of interest were enriched using DNA capture probes. The final indexed libraries were sequenced on an Illumina platform. The prevalence of CAD according to genetic diagnosis of FH was analysed. Statistical analysis was performed using R (v. 4.0.4) program package.

Results: Of 60 examined patients 28,3% (n=17) had the genetic diagnosis of FH and 71,7% (n=43) had no FH mutation. Premature CAD was found in 47% (n=8) patients with genetic diagnosis of FH and in 19% (n=8) with no mutations determined (p=0,049).

Conclusions: Premature CAD was more prevalent among patients with genetically confirmed FH.

ID:1098

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

COLLABORATION OF CLINIC AND BIOBANK AS AN EFFECTIVE MODEL FOR DYSLIPIDEMIA RESEARCH

POSTER VIEWING SESSION

Oksana V. Kopylova[1], Alexandra Ershova[2], Alexey Meshkov[3], Maria Pokrovskaya[4], Anastasia Blokhina[2], Alena Limonova[2], Victoria A. Metelskaya[5], Oxana Drapkina[6,7]
[1]The Laboratory Of Clinomics, National Medical Research Center for Preventive Medicine, Moscow, Russian Federation, [2]The Laboratory Of Clinomics, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [3]The Laboratory Of Molecular Genetics, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [4]Bank Of Biological Material, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [5]Biochemistry, National Medical Center for Preventive Medicine, Moscow, Russian Federation, [6]Fundamental And Applied Aspects Of Obesity, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [7]Director, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation

Background and Aims : In the National Medical Research Center for Therapy and Preventive Medicine (NMRC TPM) the collaboration between clinic and biobank for collection of biospecimens was organized. **Aim**: To analyze results of new scheme of collection of biospecimens from patients with dyslipidemias in frame of the project “Interesting and rare clinical cases”.

Methods: Special criteria were developed for patient selection: total cholesterol >8 mmol/l, triglycerides (TG) >5.6 mmol/l, LDL-C >4.9 mmol/l or <1.5 mmol/l without lipid-lowering therapy, HDL-C <0.7/0.8 mmol/l in men/women, HDL-C ≥2.5/3.0 mmol/l in men/women, Lp(a) >30 g/l, patient has cutaneous or tendom xanthomas. The medical inpatient and outpatient records from 2016 June were analyzed. Eligible patients signed informed consent and donated blood samples which were prepared and stored in the biobank.

Results: In total 8112 biospecimens (plasma, serum, whole blood) from 507 patients with dyslipidemias have been collected to the moment. The maximum lipid levels were: LDL-C 14.74, HDL-C 3.1, TG 70.9 mmol/l, Lp(a) 355 mg/dl; the minimum: LDL-C 0.38, HDL-C 0,18 mmol/l. There are 47 patients with TG >10 mmol/l, 98 patients with low HDL-C, 319 patients with LDL-C >4.9 mmol/l, among them 233 patients with familial hypercholesterolemia. Detailed clinical information is collected for each biospecimen, structured and saved according to current international standards and rules. Such approach gives opportunities for research of monogenic and polygenic dyslipidemias, new biomarkers of atherosclerosis etc.

Conclusions: Collaboration of different structures: clinic and biobank may be an effective for research in the field of dyslipidemias and atherosclerosis.

ID:1090

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

THERAPEUTIC APHERESIS IN FAMILIAL COMBINED HYPERLIPIDEMIA AND PREGNANCY – A CASE REPORT AND REVIEW OF LITERATURE

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Goda Jackute[2], Gabriele Jaskeviciute[2], Žaneta Petrulionienė[1,2,3], Egle Skiauteryte[3], Dovile Gabartaite[2,3], Emilija Meskene[2,3], Jurate Barysiene[1,2,3]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Background and Aims : During pregnancy serum triglycerides and total cholesterol increase as physiological response to ensure fetal growth and placental function. However, elevated lipid levels in patients with a history of familial hyperlipidemia can result in pancreatitis, preterm birth, diabetes mellitus, preeclampsia and even death, both mother and child. Even though statins teratogenic effect is debatable, they should be avoided – treatment includes weight managing by low sodium diet, exercise, omega -3 acids. Authors chose to present a clinical case of 32-year-old pregnant patient with a history of familial combined hyperlipidemia, treated by therapeutic apheresis.

Methods: A 32-year-old woman diagnosed with familial combined hyperlipidemia and history of lipidemia induced pancreatitis was sent to cardiologist because of lipid correction due to planned pregnancy. Patient underwent biochemical tests, sonography of the heart and abdomen, echocardiogram, consultations of obstetrician, dietician.

Results: Biochemistry tests detected triglycerides (TG) 15,68 mmol/l, total cholesterol (TC) 5,88 mmol/l, LDL - C 0,44 mmol. Diet, regular physical activity, and Fenofibrate 200 mg. 1/d, Omega – 3 fatty acids 4,0/d was prescribed. After conception statins become contraindicated, hyperlipidemia persisted. It was adjusted with 18 therapeutic apheresis courses by a decision of multidisciplinary team. The newborn was born by vaginal delivery, patient was referred to cardiologist for further treatment.

Conclusions: The literature review revealed that even though therapeutic apheresis is expensive, requires specific terms, have potential risks, and is considered experimental, it’s effect to lower TG levels by 65 -85 % is highly appreciated in cases where other therapy possibilities are exhausted.

ID:1088

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

EVIDENCE OF PROATHEROGENIC INFLAMMATION IN VASCULAR ENDOTHELIUM OF CAVIAE PORCELLOUS INFECTED WITH HELICOBACTER PYLORI AND EXPOSED TO HIGH FAT DIET.

POSTER VIEWING SESSION

Agnieszka Krupa[1], Agata Tomaszewska[2], Weronika Gonciarz[3], Magdalena Chmiela[3], Tomasz Rechciński[4]
[1]Department Of Immunology And Infectious Biology,, University of Lodz, Lodz, Poland, [2]The Bio-med-chem Doctoral School, University of Lodz and Lodz Institutes of the Polish Academy of Sciences, Lodz, Poland, [3]Department Of Immunology And Infectious Biology,, Department of Immunology and Infectious Biology, University of Lodz, Lodz, Poland, [4]Clinic And Department Of Cardiology, Medical University of Lodz, Lodz, Poland

Background and Aims : Atherosclerosis is a lipid-driven inflammatory disease of vascular endothelium. Various infectious agents, including *Helicobacter pylori* (*HP)*, have been linked to atherosclerotic vascular disease, therefore the inflammatory aspect of Coronary Heart Disease is fundamental. The research done by our team indicated that bacterial components of *HP* and high fat substances acted synergistically in the initiating an early proatherogenic changes in the vascular endothelium. We were also the first group to show that *HP* antigens promoted macrophage transformation into foam cells. We aimed on investigating proatherogenic inflammation initiated in the vascular endothelium during infection with *HP* in the presence of high fat substances.

Methods: We used tissue samples from animals to analyze the expression of intercellular adhesion molecules 1 (ICAM-1) on aortic endothelial cells and looked for the evidence of oxidative stress. Moreover, we sought for the indication of non-alcoholic fatty liver disease, which is the most common chronic liver syndrome associated with subclinical and clinical cardiovascular disorder.

Results: Our results suggest that vascular endothelium of animals infected with *HP* and fed high fat diet showed dysregulation of expression of ICAM-1, and the evidence of oxidative stress - 4 Hydroxynonenal (4HNE). Finally, preliminary analysis of the liver indicated the presence of lipid droplets in the tissue sections of animals *HP* infected and exposed on a high fat diet.

Conclusions: We showed the evidence of proatherogenic inflammation of vascular endothelium of *HP* infected animals exposed to high fat diet. Also, we observed metabolic dysfunction in these animals, which is considered an early cardiovascular manifestation.

ID:1083

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-09 Aortic valve stenosis*

CARDIAC VALVES CALCIFICATION AND HDL-C IN PATIENTS WITH AORTIC VALVE SCLEROSIS

POSTER VIEWING SESSION

Symeon Evangelos Mavroudeas[1], Despina Kyriakopoulou[2], Dimitris Tzalas[1], Mirsini Stasinopoulou[1], Maria Drakopoulou[1], Panagiotis Toskas[1], Nikos Anousakis[1], Sotirios Tsalamandris[1], Spiridon Maragoudakis[3], Spiridon Tsiamis[4], Konstantinos Tsioufis[1], Konstantinos Toutouzas[1]
[1]Cardiology Department, Hippokratio University Hospital Athens Greece, Athens, Greece, [2]Cardiology Department, Hippokratio Hospital, Athens, Greece, [3]Cardiology Department, PAGNI Hospital, Athens, Greece, [4]Cardiology Department, Elpis General Hospital, Athens, Greece

Background and Aims : Growing evidence has demonstrated the influence of many atherosclerotic risk factors on cardiac valve calcification (CVC), which is correlated with higher cardiovascular and all-cause mortality risk. The aim of this study was to investigate the effect of high-density lipoprotein cholesterol (HDL-C) on both mitral and aortic valve calcification (AVC) in individuals with AVC.

Methods: Sixty-four patients with AVC, prior the intervention, were prospectively enrolled and underwent blood sampling for biochemical analysis and multi-slice computed tomography (MSCT) without contrast. Primary end points were the quantification of (1) mitral annulus calcification (MAC) and AVC, calculated by the median MAC and AVC scores (both were defined by Agatston units (AU) according to MSCT findings) and (2) the HDL-C level (defined by a direct enzymatic method). The study took place between 3 tertiary hospitals in Greece from October 2019 to November 2020.

Results: The median age of all participants was 75.3 years (IR=7.4). The median HDL-C, MAC and AVC score was 46.9 mg/dl (IR 12.4) and 737.4 AU (IR=1218.5), respectively. According to the bivariate analysis results, a statistically significant correlation was found between HDL-C levels and the MAC and AVC score, with increased levels of HDL-C being related to decreased levels of CVC (r=-0.318, p=0.014).

Conclusions: A significant inverse correlation between the HLD-C and CVC was confirmed in individuals with AVC. The above findings raise great interest for further research on pathophysiological mechanisms of valvular calcification and suggest that HDL-C may be an important treatment target to attenuate the development and progress of CVC.

ID:1080

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

A CASE REPORT OF A YOUNG MAN WITH THREE-VESSEL CORONARY ARTERY DISEASE (3VD) ASSOCIATED WITH FAMILIAL HYPERCHOLESTEROLEMIA (FH)

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Gabriele Jaskeviciute[2], Goda Jackute[2], Dovile Gabartaite[2,3], Egle Skiauteryte[3], Žaneta Petrulionienė[1,2,3], Emilija Meskene[2,3], Rasa Strupaite-Sileikiene[2,4,5], Rimantė Čerkauskienė[2,6], Viktoras Sutkus[6], Jurate Barysiene[1,2,3]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Centre Of Eye Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Center Of Eye Diseases, Clinic Of Ear, Nose, Throat, And Eye Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, vilnius, Lithuania, [6]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Background and Aims : FH is thought to be the most common inherited condition affecting the cardiovascular system and causing serious complications. The aim of this case report is to present a clinical case of a young man with 3VD caused by FH.

Methods: A 33-year-old man presented to the emergency department with the complaint of squeezing chest pain which lasted for 6 hours. The patient underwent biochemical tests, an ECG, a coronary angiography, a chest X-ray, a sonography of the heart and an examination of cardiologist.

Results: In anamnesis the patient revealed that he had a stable angina pectoris for 2 months before this event. Also, he had a positive family history for FH. First time hypercholesterolemia was detected 5 months before this event and Rosuvastatin was prescribed. Blood tests showed elevated troponin (65 ng/l), total cholesterol (5,87 mmol/l), LDL (3,91 mmol/l) levels, an ECG revealed myocardial ischemia. A coronary angiography was performed and the diagnosis of 3VD was made. A coronary arteries bypass grafting surgery was urgently performed and symptoms of angina pectoris relieved. For further hypercholesterolemia treatment Rosuvastatin and Ezetimibe were prescribed. After a few months a diagnosis of FH was confirmed.

Conclusions: The literature review revealed that coronary artery disease typically occurs between the ages of 40 and 45 years in men with FH. This case is unique because of an early onset of FH complications. It indicates that it is very important to early diagnose FH in order to prevent premature cardiovascular events.

ID:1077

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

THE ASSOCIATION BETWEEN IRISIN AND PULSE WAVE VELOCITY IN OBESE PATIENTS WITH ISCHEMIC HEART DISEASE

POSTER VIEWING SESSION

Borys Shelest[1], Yuliia Kovalova[2]
[1]Department Of Internal And Occupational Diseases, Kharkiv National Medical University, Kharkiv, Ukraine, [2]Department Of Internal Medicine No. 2, Clinical Immunology And Allergology Named After Academician L.t. Malaya, Kharkiv National Medical University, Kharkiv, Ukraine

Background and Aims : The pulse wave velocity (PWV) considered as a valuable marker of the vascular wall stiffness. Ischemic heart disease (IHD) leads to decreased level of irisin, herewith its association with pulse wave velocity in obese patients with IHD is not fully investigated. The aim of the study was to elucidate the association between irisin concentrations and PWV in obese patients with IHD.

Methods: 69 patients were enrolled into the study, 35 females, mean age 55.93 ± 7.11 years. The first group included 33 obese patients with IHD. 36 patients with only IHD without obesity – in the second group. The irisin levels were measured by ELISA. The carotid-femoral PWV was assessed by applanation tonometry. Obesity was indicated in accordance with WHO criteria.

Results: The serum irisin concentrations and PWV levels were 122.67 [104.38 – 137.01] ng / mL, 11.29 [7.55–13.59] m/s in the first group, while in the second group there were 131.72 [125.17–141.95] pg / mL, 10.34 [6.98–12.91] m/s respectively. The multivariate regression analysis pointed that dropped irisin level was significantly related with PWV escalation in both groups. It was found more pronounced association of irisin with PWV in the first group: OR 0.87, 95% CI 0.051–0.93, p = 0.023; while in the second group – OR: 0.93, 95% CI: 0.057–0.98, p = 0.041.

Conclusions: The irisin is significantly associated with PWV in obese and non-obese patients with IHD. It was found that the coexistent obesity leads to augmentation of irisin and PWV interrelation.

ID:1075

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

ASSESSMENT OF ADIPOKINES LEVELS AND LIPID PROFILE IN OVERWEIGHT AND OBESE PATIENTS DEPENDING ON THE PRESENCE OF CORONARY HEART DISEASE

POSTER VIEWING SESSION

Yulia Prus[1], Natalia Kurochkina[1], Igor V. Sergienko[1], Anna Popova[1], Diana Nozadze[1], T Scarf[2], Valerii Masenko[2], Aleksey Ansheles[3], Maria Tkacheva[4]
[1]Laboratory Of Atherosclerosis Phenotypes, National Medical Research Center of Cardiology of the Ministry of Health of Russian Federation, Moscow, Russian Federation, [2]Department Of Neurohumoral And Immunological Research, Russian Cardiology Research Center Ministry of Health of the Russian Federation, Moscow, Russian Federation, Moscow, Russian Federation, [3]Department Of Radionuclide Diagnostics And Positron Emission Tomography, National Medical Research Center of Cardiology, Moscow, Russian Federation, [4]Endocrinology Department, Academic Clinic of Neurology and Dentistry on the basis of N.N. Burdenko Neurosurgery Research Institute "Cecil +", Москва, Russian Federation

Background and Aims : To assess the secretory activity of adipose tissue in overweight and obese patients depending on the presence of coronary heart disease (IHD).

Methods: The study included 66 patients with a BMI of more than 25 kg/m^2, who were divided into two groups depending on the presence of CHD. The group of patients with CHD included 31 participants, the group of patients without CHD - 35 participants. All patients were measured levels of adipokines and lipids.

Results: Patients with CHD differed in a number of indicators, including age ($p < 0.001$), gender ($p = 0.002$), and smoking ($p < 0.001$). Myocardial infarction had been diagnosed in 45.2% of patients in the group with CHD. The group of patients without CHD tended to be overweight ($p = 0.08$), with an increased waist circumference ($p = 0.08$) and an increased BMI ($p = 0.02$). In patients without CHD, total cholesterol and LDL-cholesterol levels were significantly higher ($p < 0.001$ and $p = 0.001$, respectively, Figure 1), due to the fact that in the group with CHD, patients more often were taking statins ($p < 0.001$, figure 2). When assessing levels of adipokines in patients with CHD, there was an increase in the resistin level (7.9±3.5 ng/ml versus 5.5±2.5 ng/ml, $p < 0.001$) and a decrease in the leptin level (18.6±15.9 ng/ml versus 41.3±41.0 ng/ml, $p = 0.001$). Adiponectin levels in the studied subgroups did not differ statistically significantly (Figure
3).

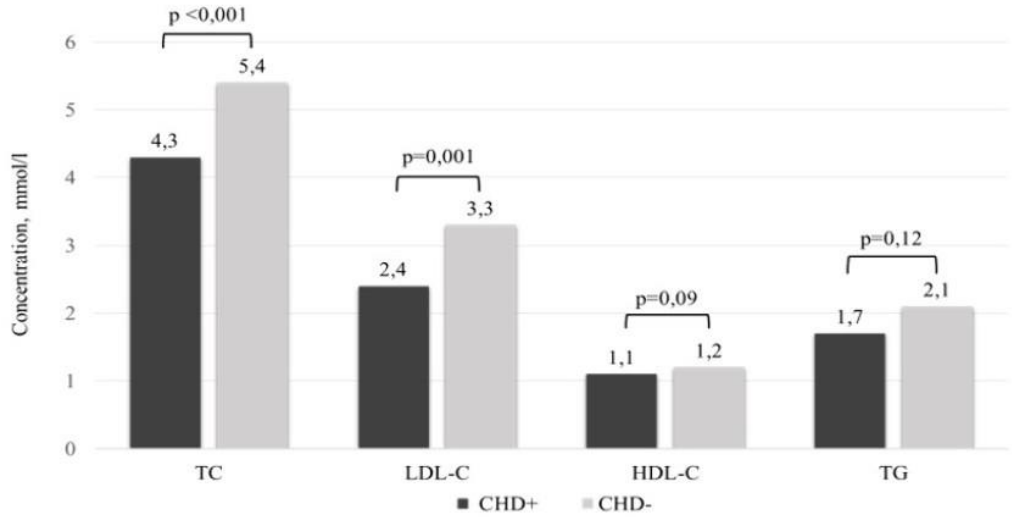


Figure 1. Comparison of lipid profile indices in overweight and obese patients depending on the presence of coronary heart disease.

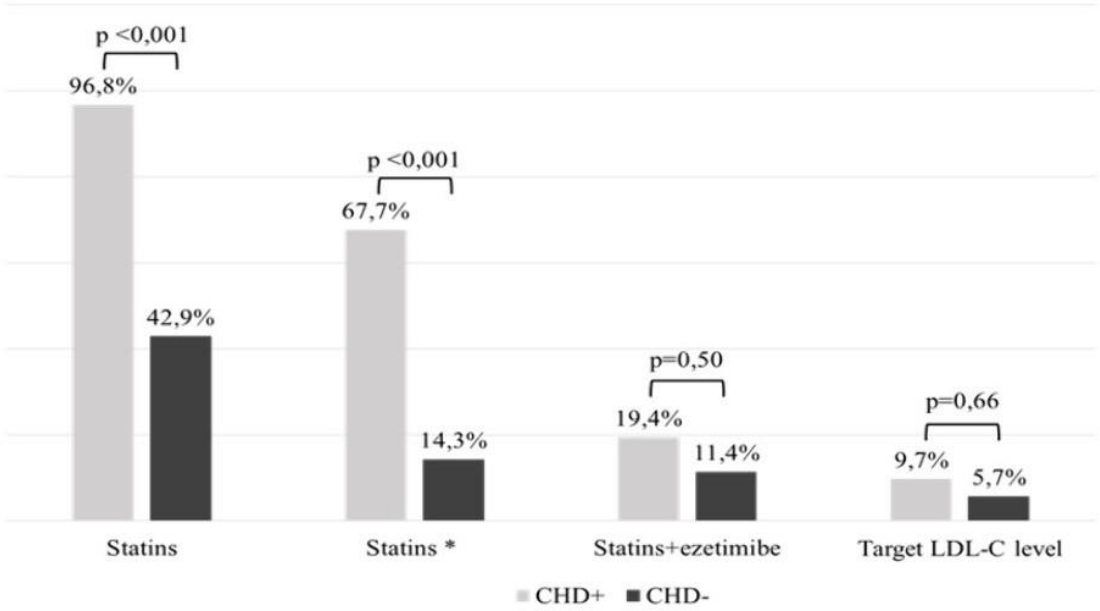


Figure 2. Frequency of lipid-lowering therapy and the achievement of target LDL-cholesterol levels in overweight and obese patients depending on the presence of coronary heart disease.

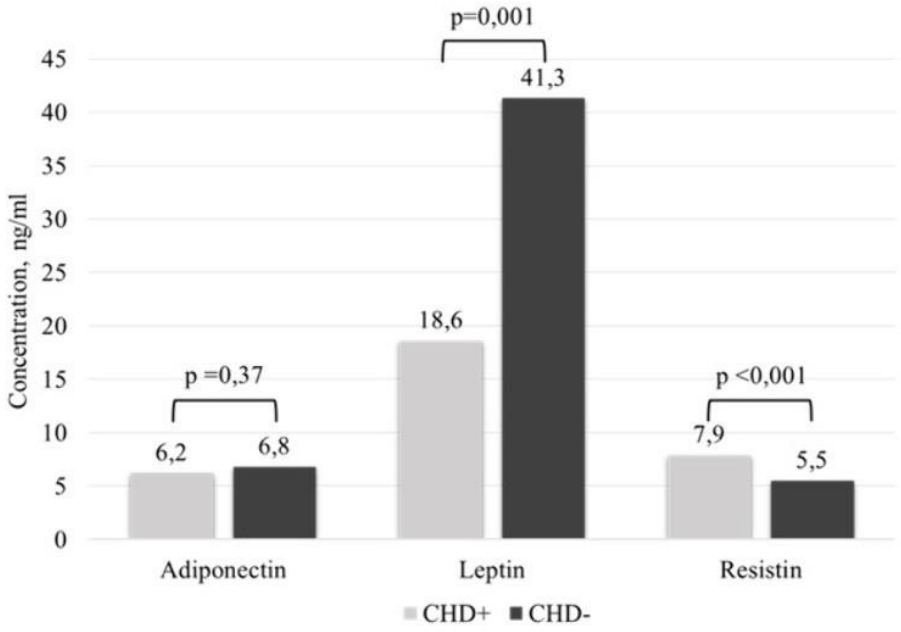


Figure 3. Comparison of adipokines levels in overweight and obese patients depending on the presence of coronary heart disease.

Conclusions: Resistin levels are elevated in patients with CHD. Lipid-lowering therapy reduces leptin levels.

ID:1072

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

IGM AUTOANTIBODIES AGAINST ATHEROGENIC LIPOPROTEINS AND EARLY MANIFESTATION OF CORONARY HEART DISEASE

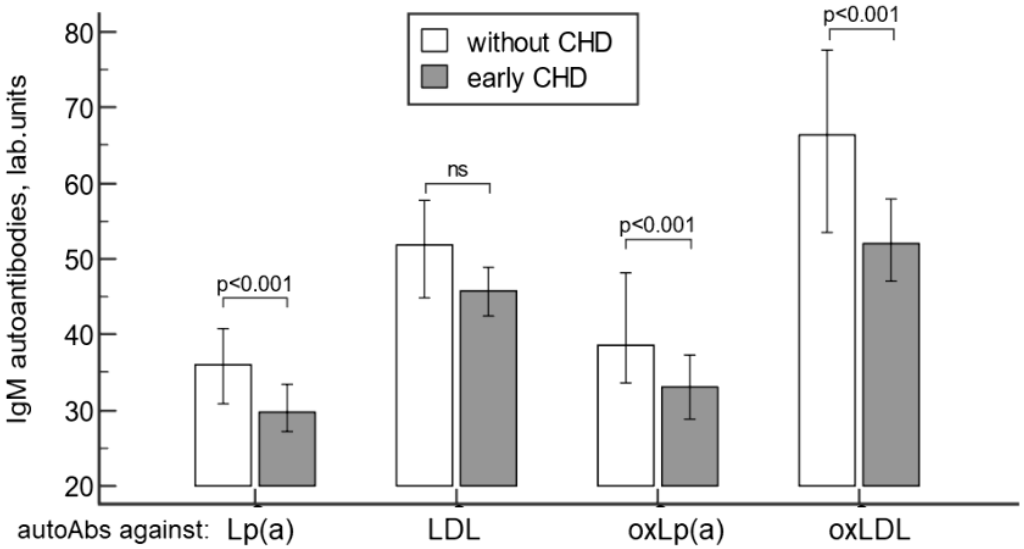
POSTER VIEWING SESSION

Elena A. Klesareva[1], Alexandra V. Tyurina[2], Olga I. Afanasieva[1], Marat V. Ezhov[2], Sergey N. Pokrovsky[1]
[1]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Moscow, Russian Federation, [2]Laboratory Of Lipid Disorders, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation

Background and Aims : To evaluate the association of autoantibodies (autoAbs) against atherogenic lipoproteins with early manifestation of coronary heart disease (CHD).

Methods: The study enrolled 300 patients aged 60±10 years. The CHD group included 200 patients with CHD debut before 55 years in men and before 60 years in women. The control group included 100 patients without CHD and stenotic atherosclerosis in any vascular beds. CHD risk factors, concentration of lipids, lipoprotein(a), immunoglobulins (Ig) A, G, M, and autoAbs against apoB100-containing atherogenic lipoproteins were determined in all patients.

Results: CHD patients were younger than control subjects (59 vs 64 years, p<0.001). All the classical risk factors were more frequent in the CHD group (p<0.001 for all). The concentration of IgM autoAbs did not differ between the groups, but the IgA and IgG autoAbs levels were significantly higher in CHD patients than in controls – 2.8 [2.3;3.0] vs 2.2 [0.9;2.8] g/L and 15.2 [13.5; 16.8] vs 13.9 [12.2;16.3] g/L, respectively, p<0.05 for both. The titers of IgM autoAbs, but not IgG autoAbs differed between the groups (figure).



Conclusions: A reduced titer of IgM autoAbs against atherogenic lipoproteins is associated with early manifestation of coronary heart disease.

ID:1070

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

THE “RATIO OF MONOCYTES TO TRIGLYCERIDES” IN OLDER PATIENTS WITH CHRONIC KIDNEY DISEASE AND CARDIOVASCULAR COMORBIDITY

POSTER VIEWING SESSION

Elena Efremova, Alexander Shutov
Department Of Therapy And Occupational Diseases, Ulyanovsk State University, Ulyanovsk, Russian Federation

Background and Aims : The "ratio of monocytes to triglycerides" (M/Tryg ratio) might predict the prognosis of patients with cardiovascular disease.The aim of this study was to investigate progonostic value of M/Tryg ratio in older patients with chronic kidney disease (CKD) and cardiovascular comorbidity.

Methods: 362 older patients with stable cardiovascular diseases (141 males, mean age 69,7±7,2 years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). Nutritional and metabolic status was assessed. Follow-up period was 1 year, primary endpoint - all-cause mortality.

Results: CKD with GFR less than 60 ml/min/1.73 m^2 was observed in 227 (62.7%) older patients with cardiovascular comorbidity. Abdominal obesity was observed in 186 (81.9%) patients, more often in women ($\chi 2 = 9.09$, $p = 0.003$), metabolic syndrome - in half of patients with CKD.Patients with CKD had higher triglyceride levels compared with patients without CKD: 1.2 (0.87; 1.71) and 1.01 (0.5; 1.78) mmol / l, resp., $p = 0.02$. M/Tryg ratio did not differ in older patients depending on CKD: 0.30 (0.18;0.53) and 0.33 (0.20%;0.64) resp., $p = 0.4$). M/Tryg ratio did not differ depending on stage of CKD ($p = 0.1$) and gender ($p = 0.22$) in patients with CKD. M/Tryg ratio more than 0.33 was associated with the annual mortality in patients with CKD (OR 10, 54; 95% CI 3.01-26.94; $p < 0.0001$); (sensitivity - 88%, specificity - 60.5% (AUC = 0.75); $p < 0.0001$).

Conclusions: The M/Tryg ratio in older patients with cardiovascular comorbidity does not depend on CKD and has a predictive value in assessing annual mortality.

ID:1015

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE STATE OF ENDOTHELIAL FUNCTION IN YOUNG PATIENTS WITH CORONARY ARTERY DISEASE, WITH A HISTORY OF HYPERTENSION AND WITHOUT

POSTER VIEWING SESSION

Valentin Oleynikov, Angelina Khromova, Nadezhda Burko, Kristina Polezhaeva, Alexey Kulyutsin
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : to study the parameters of endothelial function (EF) in patients with CAD younger than 50 years old, with long-term arterial hypertension or without a history of hypertension.

Methods: the study included 129 patients with CAD (mean age 43(40;48)) years. The patients were divided into 2 groups. Group 1 included 60 people without hypertension. Group 2 consisted of 69 patients with hypertension. The control (C) group consisted of 29 healthy individuals (mean age 42.4+2.8 years). EF was assessed by flow-mediated vasodilation (FMD) on the MyLab90 device (Esaote, Italy), with the registration of the following parameters: FMD, reactivity index (IR).

Results: In group C the IR was 2.2(95%CI 1.5;2.8). A negative reaction was detected in 1 (3.4%) patient. In group 1 IR - 1.7(95%CI 1.2;2.2) (p1-c=0.009); a negative reaction was registered in 13.3% (n=8) patients (p1-c=0.02), paradoxical - in 16.7% (n=10) (p1-c=0.001). In group 2, the IR was 1.5(95%CI 1.4;1.7) (p1-2=0.09); (p2-c=0.01). A negative reaction was detected in 7 (10.1%) patients (p1-2>0.05) (p2-c=0.03), paradoxical in 7(10.1%) patients (p1-2=0.1) (p2-c=0.004). In group C, the FMD index was 17.6(95% CI13.9;21.2)%; pathological values of FMD were registered in 6 (20.7%) patients. In group 1, FMD - 8.4(95%CI 5.8;10.8)% (p1-c=0.01); pathological values were found in 36 (60%) patients (p1-c=0.02). In group 2, FMD was 10.7(95%CI 8.7;12.6)%, (p2-c=0.02); (p1-2=0.99); in 32 (46.4%) patients, FMD was pathological (p1-2=0.001) (p2-c=0.01).

Conclusions: the parameters of endothelial function were significantly different in patients with coronary artery disease compared with healthy individuals. Pathological reactions of IR and FMD were recorded more often in patients.

ID:1035

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

TAMOXIFEN-INDUCED HYPERTRIGLYCERIDEMIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Miglė Vilniškytė[2], Milda Kovaite[3], Dovile Gabartaite[2,3], Egle Skiauteryte[3], Emilija Meskene[2,3], Žaneta Petrulionienė[1,2,3]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Background and Aims : The objective of the study was to determine the cause of hypertriglyceridemia in a patient undergoing Tamoxifen adjuvant chemotherapy following radical treatment of breast cancer with no previously diagnosed dyslipidemias.

Methods: The patient, a 45-year-old woman, developed severe hypertriglyceridemia and hypercholesterolemia during adjuvant Tamoxifen chemotherapy. The patient underwent biochemical tests, sonography of the heart, brachiocephalic vessels, veloergometry, and examination of cardiologist, endocrinologist, ophthalmologist.

Results: Severe hypertriglyceridemia (serum triglycerides 25,42 mmol/L, norm < 2,3 mmol/L) and hypercholesterolemia (serum cholesterol 19,23 mmol/L, norm < 5,2 mmol/L) were detected after the patient was put on Tamoxifen without enduring significant changes in dietary or lifestyle factors, hereditary dyslipidemias were not found either. Ultrasound examination revealed primary atherosclerotic changes in the right common carotid artery near bifurcation progressing to the right internal carotid artery. The patient had subclinical chronic autoimmune thyroiditis before starting Tamoxifen, but throughout adjuvant treatment, the disease progressed and required treatment with L-thyroxine. Increased physical activity, hypocaloric diet, and atorvastatin were used to adjust abnormally high lipid levels, whilst continuing Tamoxifen. Although a decrease in lipid levels was observed (serum triglycerides dropped to 6,52 mmol/L, serum cholesterol – 4,89 mmol/L), hypertriglyceridemia persisted. Ultimately, we decided to cease Tamoxifen, and immediately after withdrawal, lipid profile began to balance out.

Conclusions: Albeit Tamoxifen is a reliable option for adjuvant chemotherapy in rare cases Tamoxifen-induced hypertriglyceridemia may become apparent. Consequently, it is necessary to monitor the lipid profile of such patients and evaluate the potential risks and benefits of

treatment.

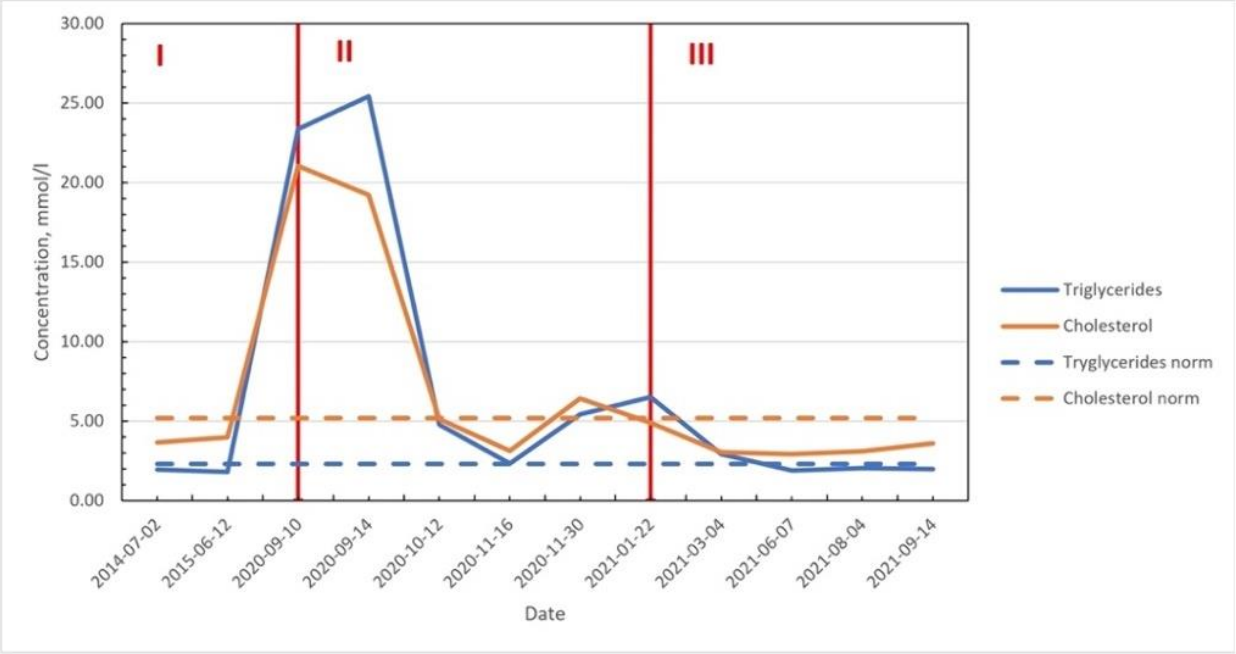


Figure 1. The changes in patient's concentration of triglycerides and cholesterol during observation period. Period I represents patient's lipid profile whilst being put on Tamoxifen. Period II – after identifying elevated lipid levels and introducing Atorvastatin, whilst continuing Tamoxifen. Period III – after ceasing Tamoxifen, whilst continuing Atorvastatin.

ID:1017

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

CARDIOVASCULAR OUTCOMES IN PATIENTS WITH HYPERLIPOPROTEINEMIA(A) DEPENDING ON ADHERENCE AND ADEQUACY OF STATIN THERAPY.

POSTER VIEWING SESSION

Alexandra V. Tyurina[1], Olga I. Afanasieva[2], Elena A. Klesareva[2], Marat V. Ezhov[1], Sergey N. Pokrovsky[2]
[1]Laboratory Of Lipid Disorders, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation, [2]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Moscow, Russian Federation

Background and Aims : Elevated Lp(a) is a recognized risk factor for ASCVD, but its contribution to the risk of MACE in patients with established CVD on statin therapy is not clear.

Methods: The study enrolled 200 patients aged 59 [53, 65] (median [25%;75%]) years with CHD manifestation before 55 years who were divided into two groups: with level of Lp(a)≥30 mg/dl and <30 mg/dl. Major adverse cardiovascular events (MACE) were defined as hospitalization for unstable angina, myocardial infarction, ischemic stroke, myocardial or carotid revascularization per person-year.

Results: The number of MACE per 1 person-year in the group with Lp(a) level<30 mg/dl was 0.33 and 0.52 in patients adherent and non-adherent to statin therapy, respectively, the minimum value of 0.21 was observed in patients with LDL-C below 1.4 mmol/L. In the group with Lp(a) level ≥30 mg/dl, the number of MACE in patients with the target level of LDL-C was 0.29. Statins intake in this group did not influence on the number of MACE: 0.34 vs 0.22 among patients who were adherent and non-adherent to statin.

Conclusions: Even in patients with a normal lipid profile there is a high residual risk of MACE associated with an increased level of Lp(a). It is necessary to develop new prognostic scales to identify patients at high risk of MACE and to restratify individuals depending on the concentration of Lp(a).

ID:1023

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

NUTRITIONAL FEATURES OF WOMEN WITH ARTERIAL HYPERTENSION AND ABDOMINAL OBESITY FROM THE STANDPOINT OF THE RISK OF CARDIOVASCULAR DISEASES ASSOCIATED WITH ATHEROSCLEROSIS

POSTER VIEWING SESSION

Marina Y. Penkova, Sergey N. Koval, Larysa A. Rieznik, Tatyana G. Starchenko
Department Of Arterial Hypertension And Prevention Of Its Complications, GI “L. T. Malaya Therapy National Institute of the NAMS of Ukraine”, Kharkiv, Ukraine

Background and Aims : The aim to study the content of fats (F) and dietary fiber (DF) in the daily diet (DD) of women (residents of Ukraine), patients with arterial hypertension (AH) with abdominal obesity (AO).

Methods: . 75 women with AH, aged 40 - 59 years were examined. The main group - 40 women with AO I-II degree. Comparison group - 35 women with normal body weight (BMW).

Results: . The contribution of F to the total energy value of DD was significantly higher in women with AO (34%) compared to women with BMW (22%), $p < 0.05$. The contribution of saturated fatty acids (SFA) to the total energy value of DD was 18% in women with AO and 10% in women with BMW ($p < 0.05$), and transsaturated fatty acids (TSFA) - 2% and 1.5%, respectively ($p > 0.05$). DF consumption was 28.8 [6.3; 38.4] g / day in the main group, and 39.2 [15.9; 52.5] g / day in the comparison group, $p < 0,05$.

Conclusions: . In women with AH and AO, the intake of F, including SFA and TSFA, exceeded the recommendations for a healthy diet, and the intake of DF was insufficient. In women with AH and BMW, excessive consumption of TSFA was observed, while the consumption of SFA did not exceed the norm, the amount of DF in the diet corresponded to the norms of healthy eating

ID:1024

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

COMPARATIVE EFFECT OF DELAPRIL-MANIDIPINE TREATMENT VERSUS TELMISARTAN-AMLODIPINE TREATMENT IN FASTING GLUCOSE, FASTING INSULIN, OGTT AND HBA1C LEVELS, IN PREDIABETIC HYPERTENSIVE PATIENTS

POSTER VIEWING SESSION

Angelos Liontos[1], Dimitrios Biros[1], Alexandros Papathanasiou[1], Christos Papagiannopoulos[1], Eleftherios Klouras[1], Lazaros Athanasiou[1], Stavros Tsourlos[1], Sempastien Filippas-Ntekouan[1], Valentini Samanidou[1], Nikolaos-Gavriil Kolios[1], Cornelia Veliani[1], Christiana Pappa[1], Athina Zarachi[2], Eirini Christaki[1], Evangelos Liberopoulos[3], Moses Elisaf[4], Haralampos Milionis[1], George Liamis[4]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece, [4]2nd Department Of Internal Medicine, University Hospital Of Ioannina, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece

Background and Aims : Introduction: The effect of various antihypertensive drugs on the glucose homeostasis has been discussed extensively. We present comparative data of the effect of delapril/manidipine versus telmisartan/amlodipine combination treatments, in fasting glucose, fasting insulin, OGTT and HbA1c levels, before and after the 3-month treatment, in hypertensive prediabetic patients.

Methods: METHODS: Data were collected from 104 patients from the outpatient clinic for lipid metabolism, hypertension and diabetes, during the period 2014-2018. 53 persons were randomized in the delapril/manidipine group 30/10 mg per day while 51 persons had been randomized in the group of telmisartan/amlodipine 80/5mg per day. All patients successfully completed the study. Baseline characteristics are presented in Table

1A.

Table 1A. *Patients' characteristics at the start of the study*

Characteristics/Combination of drugs	DEL/MANI	TEL/AMLO
N (Men-Women)	53(30-23)	51(35-16)
Age (Years)	58.08±11.73$$$	58.04±13. 6$$$
Smokers (%)	12(22.6%)	31(60.8%)
Alcohol Consumers (%)	7(13.2%)	16(31.4%)
Body Weight (Kg)	83.67± 13.21	84.72± 12.87
Height (m)	1.68[1.62-1.77]	1.72[1.6-1.77]
BMI (Kg/m^2)	28.73 [27.73-30.3]	29.32 [27.37-31.65]
SBP (mmHg)	156 [151-161]	163 [158-168]
DBP (mmHg)	100[88-101]	100[95-106]

Results: RESULTS: The resulting alternations in glucose, insulin, OGTT and HbA1c levels, before and after the 3-month treatment are presented

on **Table 1B**.

Table1B. Results of glycemic profiling tests before and after the three-month treatment

Parameter	Start of treatment	After 3 Months of Treatment	% Change	p-value
Glu (mg/dl)				
DEL/MANI	100[97-107]	98.45± 13.22	-1.55 % (-1.55)	0.004
TEL/AMLO	100[98-106]	98.22± 13.24	-1.78 % (-1.78)	0.005
INS (µIU/mL)				
DEL/MANI	8.6[6.3-11.4]	9[5.8-11.8]	4.65 % (0.4)	0.602^^
TEL/AMLO	13[9.5-14.9]	10[6.2-13.5]	-23.08 % (-3)	0.005**
HbAlc (%)				
DEL/MANI	5.6± 0.55	5.64± 0.57	0.71 % (0.04)	0.195
TEL/AMLO	5.67± 0.44	5.71± 0.46	0.71 % (0.04)	0.497
OGTT (mg/dl)				
DEL/MANI	136.22± 35.26	127.19± 37.89	-6.63 % (-9.03)	0.022^
TEL/AMLO	122.82± 26.88	124.7± 31.7	1.53 % (1.88)	0.206*

The data are presented as Average ± Standard Deviation, Median [25th-75th].

*p < 0.05 compared to DEL/MANI treatment, **p < 0.01 compared to DEL/MANI treatment,

***p < 0.001 compared to DEL/MANI treatment

^p < 0.05 compared to TEL/AMLO treatment, ^^p < 0.01 compared to TEL/AMLO treatment,

^^ <0.001 compared to TEL/AMLO treatment

Conclusions: CONCLUSIONS: comparison between the treatment groups showed a statistically significant difference in the change of INS levels (from the beginning of treatment and after 3 months) between the TEL/AMLO treatment group and the DEL/MANI treatment group (p-value<0.01), with increased levels in the DEL/MANI group compared to the TEL/AMLO group where a decrease was

observed. The change in OGTT levels showed a statistically significant difference (p-value<0.05), between the DEL/MANI group (decrease of 6.63%) compared to TEL/AMLO group (increase of 1.53%) after 3 months of treatment. No other significant differences were observed between treatment groups comparison, for the other parameters.

ID:1026

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

DETERMINING THE ROLE OF VON WILLEBRAND FACTOR IN THROMBOTIC POST TRANSPLANTATION COMPLICATIONS USING EX VIVO LUNG PERFUSION SYSTEM

POSTER VIEWING SESSION

Parnian Alavi[1], Sayed Himmat[2], Nader Aboelnazar[2], Max Buchko[2], Jayan Nagendran[2], Nadia Jahroudi[1]
[1]Department Of Medicine, University of Alberta, Edmonton, Canada, [2]Department Of Surgery, University of Alberta, Edmonton, Canada

Background and Aims : A major complication of lung transplantation is thrombosis, which may lead to allograft failure. Increased production of procoagulant molecules, such as von Willebrand factor (VWF), is a significant risk factor for thrombus formation. VWF is a pro-coagulant glycoprotein expressed only in endothelial cells and megakaryocytes, which mediates adhesion of platelets to the endothelium/sub-endothelium. External stimuli, including hypoxia can upregulate VWF. Since during organ-transplantation donor organs are under hypoxic conditions, we explored whether this may lead to alterations in VWF expression, and whether ex vivo lung perfusion (EVLP) as an innovative method for organ preservation prior transplantation can moderate the effect of VWF upregulation and its thrombogenic consequences.

Methods: Procured pig's lungs will be set in EVLP, and the tissue biopsies will be obtained at the beginning and the end of perfusion for RT-PCR, western blot and immunofluorescent analysis to investigate mRNA, protein, and vascular expression pattern of VWF. Similar analyses will be done on lungs that are preserved under the static cold condition (SCS).

Results: Analyses have demonstrated that VWF mRNA and protein levels are significantly reduced in lungs, which were perfused under ex vivo lung perfusion "EVLP" for 12 hours compared to control. Furthermore, IF analysis demonstrated that preservation of lungs under cold storage conditions prior to transplantation alters VWF expression pattern leading to increasing number of microvascular (indicated by CD31 staining) endothelial cells that express VWF.

Conclusions: Results will provide insights towards development of effective anti-thrombotic approaches that would be advantageous in organ transplant procedures.

ID:1030

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

FLOW-MEDIATED DILATION OF THE BRACHIAL ARTERY IN PATIENTS WITH OBESITY AFTER COVID-19

POSTER VIEWING SESSION

Olga Pogorelova[1], Izolda O. Kokaeva[2], Maria Tripoten[1], Yulia Zhernakova[2], Tatiana Balakhonova[1]
[1]Vascular Ultrasound Department, National Medical Research Center of Cardiology, MOSCOW, Russian Federation, [2]Department Of Hypertension, National medical research center of cardiology, MOSCOW, Russian Federation

Background and Aims : Endothelial dysfunction plays an important role in the pathogenesis of the novel coronavirus infection (COVID-19) and its complications. The aim of the study was to assess the contribution of obesity to the pathogenesis of endothelial dysfunction as one of the risk factors of a more severe disease.

Methods: We examined 19 patients with mild or moderate hypertension 1 month after their recovery from moderate COVID-19 (11m/8f, aged 45.4±9.0 years, without diabetes mellitus, non-smokers). 11 patients with hypertension had obesity (BMI≥30 kg/m^2) and 8 had normal body weight (BMI≤25 kg/m^2). We compared the endothelium-dependent flow-mediated dilatation (FMD) of the brachial artery in response to reactive hyperemia in the recovered group and in 20 age- and gender-matched healthy controls without cardiovascular risk factors.

Results: The FMD in 19 pts with hypertension was significantly lower than in healthy controls (5.3±3.4% vs 9.5±3.9%, $p<0.05$). FMD in pts with hypertension and obesity was significantly lower than in patients with hypertension and normal body weight (3.9±1.9% vs 7.3±3.7%, $p<0.05$) and in healthy controls ($p<0.05$). BMI, SBP, DBP, TC and TG levels were significantly higher in patients with hypertension and obesity than in participants with hypertension and normal body weight: 34.2±3.9 vs 22.7±2.8 kg/m2, 141.3±10 vs 123.5±17.3 mm Hg, 91.6±10.1 vs 79.4±12.8 mm Hg, 6.75±1.88 vs 5.12±0.82 mmol/l and TG 3.75±3.0 vs 1.18±0.24 mmol/l (all p-values <0.05).

Conclusions: In conclusion, moderate COVID-19 led to a disruption of the functional state of the endothelium in patients with hypertension, which was more pronounced in patients with obesity.

ID:1031

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

QUANTITATIVE CAROTID ATHEROSCLEROSIS ASSESSMENT FROM A CORONARY CT ANGIOGRAPHY (CTA) – OPTIMIZED CT PROTOCOL ACQUISITION – PROOF OF CONCEPT

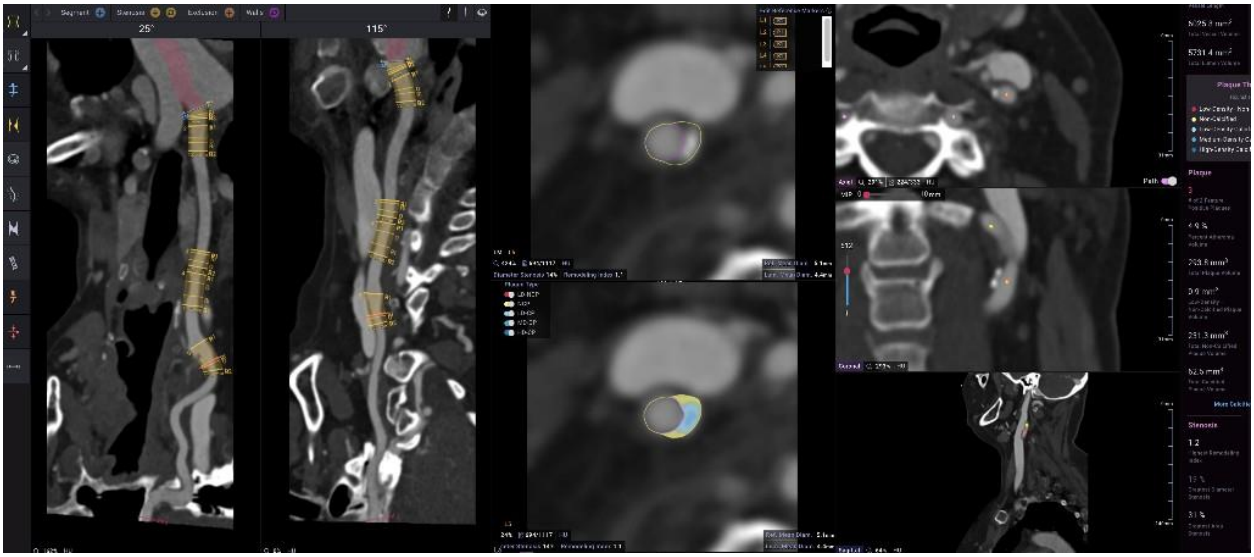
POSTER VIEWING SESSION

Hugo Marques[1,2], Carina Ruano[1], James Earls[3], James Min[4]
[1]Radiology, Hospital de Santa Marta - CHULC, Lisboa, Portugal, [2]Imaging, Católica Medical School, Lisboa, Portugal, [3]Radiology, George Washington University hospital, washington, United States of America, [4]Medical, cleerly inc, new york, United States of America

Background and Aims : Coronary and carotid atherosclerosis are the first and third cause of death. They share risk factors but disease involvement may be diverse. The aim was to assess the feasibility to evaluate the carotids in the same CT exam in people referred to coronary CTA

Methods: We imaged 26 patients (15 men) with mean age 57,7 Y referred for coronary CTA without changing the optimal coronary protocol. We followed the coronary CTA by a as soon as possible carotid CT acquisition (5 second interval determined by the CT machine, used to put the arms along the body), done caudo-cranially without further contrast administration. We evaluated carotid imaging quality by a 4 grade score [1-poor to 4-perfect] qualitative assessment by two >10Y experienced radiologists and by contrast and noise quantification. Quantitative carotids, and vertebral arteries plaque and stenosis evaluation was done in “Cleerly Labs-research”.

Results: Mean total contrast used was 95 ml. Mean radiation dose for the carotids acquisition was 193 DLP. One carotid acquisition had motion artifacts (movement of arms), all others were of at least good quality. Mean density and noise values were respectively: aorta (274HU; 25); left internal carotid (342HU; 25); right internal carotid (336HU;29); internal jugular vein (520HU;26). Mean total plaque was 189mm3; (147mm3 of non calcified plaque) Highest stenosis was 51% at the right internal carotid and 27% on the left.



Conclusions: Quantitative Carotid atherosclerosis CT assessment following coronary CTA acquisition is feasible without needing extra contrast, with all segments evaluable.

ID:1038

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

COMPARATIVE EFFECT OF DELAPRIL-MANIDIPINE TREATMENT VERSUS VALSARTAN-AMLODIPINE TREATMENT IN FASTING GLUCOSE, FASTING INSULIN, OGTT AND HBA1C LEVELS, IN PREDIABETIC HYPERTENSIVE PATIENTS

POSTER VIEWING SESSION

Angelos Liontos[1], Dimitrios Biros[1], Alexandros Papathanasiou[1], Christos Papagiannopoulos[1], Eleftherios Klouras[1], Stavros Tsourlos[1], Lazaros Athanasiou[1], Sempastien Filippas-Ntekouan[1], Nikolaos-Gavriil Kolios[1], Cornelia Veliani[1], Christiana Pappa[1], Athina Zarachi[2], Valentini Samanidou[1], Eirini Christaki[1], Maria Christaki[1], Ioannis Vagias[1], Evangelos Liberopoulos[3], Moses Elisaf[4], Haralampos Milionis[1], George Liamis[4]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece, [4]2nd Department Of Internal Medicine, University Hospital Of Ioannina, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece

Background and Aims : Introduction: The effect of various antihypertensive drugs on the glucose homeostasis has been discussed extensively. Dual combination treatment is adviced with current guidelines. We present comparative data of the effect of delapril/manidipine versus valsartan/amlodipine combination treatments, in fasting glucose, fasting insulin, OGTT and HbA1c levels, before and after the 3-month treatment, in hypertensive prediabetic patients.

Methods: METHODS: Data were collected from 107 patients from the outpatient clinic for lipid metabolism, hypertension and diabetes, during the period 2014-2018. 53 patients were randomized in the delapril/manidipine group 30/10 mg per day while 54 patients had been randomized in the group of valsartan/amlodipine 160/5mg per day. All patients successfully completed the study. Baseline

characteristics are presented in Table 1A.

Characteristics/Combination of drugs	DEL/MANI	VAL/AMLO
N (Men-Women)	53(30-23)	54(33-21)
Age (Years)	58.08±11.73	64.44±11.64
Smokers (%)	12(22.6%)	14(25.9%)
Alcohol Consumers (%)	7(13.2%)	8(14.8%)
Body Weight (Kg)	83.67± 13.21	80.83±11.80
Height (m)	1.68[1.62-1.77]	1.69[1.62-1.75]
BMI (Kg/m^2)	28.73 [27.73-30.3]	28.09[26.81-29.89]
SBP (mmHg)	156 [151-161]	162 [159.25-165]
DBP (mmHg)	100[88-101]	100[92-103.75]

Results: RESULTS: The resulting alternations in glucose, insulin, OGTT and HbA1c levels, before and after the 3-month treatment are presented

on **Table 1B**.

Table1B. Results of glycemic profiling tests before and after the three-month treatment

Parameter	Commencement	After 3 Months of Treatment	% change	p-value
Glu (mg/dl)				
DEL/MANI	100[97-107]	98.45± 13.22	-1.55 % (-1.55)	0.004
VAL/AMLO	104[96.25-110.75]	103.96± 10.51	-0.04 % (-0.04)	0.622
INS (µIU/mL)				
DEL/MANI	8.6[6.3-11.4]	9[5.8-11.8]	4.65 % (0.4)	0.602
VAL/AMLO	6.2[4.2-9.23]	7.2[4.77-10.47]	16.13 % (1)	0.136
HbAlc (%)				
DEL/MANI	5.6± 0.55	5.64± 0.57	0.71 % (0.04)	0.195
VAL/AMLO	5.79± 0.33	5.75± 0.32	-0.69 % (-0.04)	0.236
OGTT (mg/dl)				
DEL/MANI	136.22± 35.26	127.19± 37.89	-6.63 % (-9.03)	0.022
VAL/AMLO	139.95± 26.9	131.61± 26.05	-5.96 % (-8.34)	0.053

The data are presented as Average ± Standard Deviation, Median [25th-75th].

*p < 0.05 compared to DEL/MANI treatment, **p < 0.01 compared to DEL/MANI treatment,

***p < 0.001 compared to DEL/MANI treatment

$p < 0.05 compared to VAL/AMLO therapy, $$p < 0.01 compared to VAL/AMLO therapy, $$$p

< 0.001 compared to VAL/AMLO therapy

Conclusions: CONCLUSIONS: Form the studied population, no significant differences were observed between treatment groups' comparison, for all parameters after the 3-month treatment. In the DEL/MANI treatment group there was observed a statistically significant decrease in FPG (p-value=0.004<0.01) with a change of -1.55 mg/dl which corresponds to a percentage of reduction of -1.55%. In the same group a

statistically significant decrease in OGTT levels was also observed, (p-value<0.05), with a change of -9.03 mg/dl which corresponds to a reduction rate of -6.63%,that was, while the changes in the VAL/AMLO group were not.

ID:1069

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-09 Aortic valve stenosis*

CORRELATION BETWEEN AORTIC VALVE CALCIFICATION AND ROUTINE LABORATORY TEST RESULTS IN PATIENTS WITH AORTIC VALVE SCLEROSIS.

POSTER VIEWING SESSION

Symeon Evangelos Mavroudeas[1], Dimitris Tzalas[2], Despina Kyriakopoulou[1], Mirsini Stasinopoulou[3], Kanela Sotirakou[4], Irene Feskou[5], George Benetos[1], Panagiotis Toskas[1], Sotirios Tsalamandris[1], Spiridon Maragoudakis[6], Spiridon Tsiamis[7], Konstantinos Tsioufis[1], Konstantinos Toutouzas[1]
[1]Cardiology Department, Hippokratio University Hospital Athens Greece, Athens, Greece, [2]Cardiology Department, Hippokratio Hospital, Athens, Greece, [3]Radiology Department, Agios Savvas General Hospital, Athens, Greece, [4]Radiology Department, Elpis General Hospital, Athens, Greece, [5]Haematology Department, Agios Savvas General Hospital, Athens, Greece, [6]Cardiology Department, PAGNI Hospital, Athens, Greece, [7]Cardiology Department, Elpis General Hospital, Athens, Greece

Background and Aims : Aortic valve calcification (AVC) has been associated with increased risk for cardiovascular disease and vascular thrombosis and has also been proposed as a predictor of adverse outcomes in many interventional cardiology procedures,such as the transcutaneous aortic valve replacement (TAVR).The aim of this study was to investigate and correlate biochemical measurements in patients with aortic sclerosis

Methods: Sixty-four patients with aortic valve sclerosis found on bedside cardiac echocardiogram were enrolled and underwent non-contrast ECG-guided MSCT to quantify the aortic valve calcium score, defined by Agatston units (AU).Blood samples were drawn and basic biochemical measurements were made with standard methods. The study took place in Greece from October 2019 to November 2020 in three tertiary hospitals

Results: Median age of patients was 75.3 years (IR=7.4) and 71,9% were men. After analysis of the CT images, median aortic valve Agatston score was 673.5 (IR=872). According to the results of the bivariate analyses, a statistically significant relation was found between aortic valve calcification and HDL, C-reactive protein (CRP) and blood calcium (Ca) levels. Increased levels of CRP were related with increased aortic valve AU (p=0.028), while increased levels of HDL and serum calcium were found to be negatively related with aortic valve calcium, corresponding to lower AU (p=0.004 and p=0.014, respectively)

Conclusions: Inflammation,calcium metabolism and lipid disorders could possibly correlate with the course of AVC.Given that aortic valve calcification is being studied as a predictor of major CVD outcomes,more studies are needed to clarify the underlying pathophysiology mechanisms in order to efficiently diagnose,categorize and monitor these patients.

ID:1041

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

QUALITY OF LIFE IN OLDER PATIENTS WITH OBESITY AND CHRONIC KIDNEY DISEASE

POSTER VIEWING SESSION

Elena Efremova, Alexander Shutov, Alexey Semenov, Ksenia Yafarkina
Department Of Therapy And Occupational Diseases, Ulyanovsk State University, Ulyanovsk, Russian Federation

Background and Aims : Obesity is a risk factor for chronic kidney disease (CKD). The aim of this study was to investigate quality of life and psychological status in older patients with CKD and obesity.

Methods: 472 older patients with stable cardiovascular diseases (231 males, mean age 69,6±7,3years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). Nutritional status (presence and type of obesity, body composition) was assessed. Quality of life, psychological status and defense mechanisms were studied.

Results: CKD with GFR less than 60 ml/min/1.73 m^2 was diagnosed in 277 (58.7%) patients. Overweight was observed in 111 (40.1%) patients, obesity - in 118 (42.6%) patients with CKD. More than half had grade 1 obesity (70; 59.3%), every fourth (30; 25.4) - grade 2, 18 (15.3%) - grade 3 among obese patients with CKD. All older patients with CKD had an increase in adipose tissue. Obesity in patients with CKD was associated with immature psychological defense mechanisms "denial" (36 (18; 55) and 27 (9; 45)% scores, resp., p = 0.005) and "substitution "(10 (0; 20) and 0 (0; 10)% scores, resp., p = 0.01) compared with patients without obesity. Patients with obesity were characterized by "passive aggressiveness", difficulties of social adaptation. Older patients with CKD and obesity had lower indicators on the social functioning scale (quality of life questionnaire "SF-36") (37.5 (37.5; 50) and 50 (37, 5; 62.5) points, resp., p = 0.03) compared with patients without obesity.

Conclusions: Older patients with CKD are characterized by sarcopenic obesity, which leads to impaired social functioning.

ID:1043

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

DOUBLE TROUBLE: PATHOGENIC LDLR AND SCARB1 VARIANTS IN THE SAME FAMILY

POSTER VIEWING SESSION

Olga N. Ivanova[1], Tatiana Pawhun[2], Ekatherina Y. Zakharova[1]
[1]Hereditary Metabolic Diseases Laboratory, Research Centre for Medical Genetics, Moscow, Russian Federation, [2]Cardiology Department State Healthcare Institution, Ulyanovsk Regional Children's Clinical Hospital named after political and public figure Yu.F. Goryachev, Ulyanovsk, Russian Federation

Background and Aims : LDLR and SCARB1 are the key membrane receptors LDL and HDL. Mutations in the LDLR and SCARB1 genes are identified in 80% of patients with familial hypercholesterolemia and in <<< 1% of patients with hyperalphalipoproteinemia. Mutations in the both genes act co-dominantly, heterozygous carriers demonstrate intermediate levels of LDL-C or HDL-C between wild-type and homozygous individuals. Here we describe a family with extremely high levels of lipoproteins (above the 90th percentile for age and sex) with a rare variant in one or both genes.

Methods: NGS was performed by Ion S5 system. Variant validation was performed by PCR-direct sequencing.

Results: The proband was admitted to the cardiology department with recurrent fainting and elevated LDL-C levels. We identified two pathogenic variants in a heterozygous state – LDLR(NM_000527.5):c.986G>A (p.Cys329Tyr) (HGMD - CM981186) and SCARB1(NM_005505.5):c.727-2A>C (rs201068540, according to the ACMG criteria the variant is pathogenic). We then determined that sibling is also the carrier of both mutations, the mother has only the SCARB1 variant, the father has only the LDLR variant. Segregation of variants correlates with the lipid profile of patients. The mutation in the SCARB1 gene correlates with a high HDL-C phenotype, and the LDLR mutation with a high LDL-C phenotype.

Conclusions: Our findings suggest mutations in the SCARB1 gene are a rare but recurring cause of elevated HDL-C levels. The finding of the combined variants in LDLR/SCARB1 genes triggering hypercholesterolemia and hyperalphalipoproteinemia phenotypes is essential to elaborate the spectrum of variants causing dyslipidemia and to understand the genotype-phenotype correlation.

ID:1045

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

PSORIATIC NEPHROPATHY: A HISTOPATHOLOGICAL UPDATE

POSTER VIEWING SESSION

Liliya Volos
Pathological Anatomy, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Background and Aims : Psoriasis is one of the most common dermatoses and accounts for 12 to 15% of all skin diseases. Visceral pathology, manifested in patients with psoriasis, has been attracting increasing attention from many researchers for many years. One of the central places in the visceral lesions in psoriasis is the pathology of the kidneys - psoriatic nephropathy. Our aim was to examine histological changes of kidneys in patients with psoriasis vulgaris.

Methods: We have performed a clinical-morphological studied of outpatient card data, disease histories and autopsy reports of 18 cases with psoriasis vulgaris at the life. Structural changes in the kidneys in psoriasis vulgaris have been studied in all 18 cases. The histological specimens of kidneys were collected during necropsy and fixed in a solution of IHC Zinc Fixactive (PharMingen, USA), paraffin embedding, 5±1 μm thick-section cutting, and stained by Hematoxylin–Eosin, Congo Red, and IHC methods.

Results: Psoriatic nephropathy is represented by the following basic morphological forms: minimal changes of the kidneys, mesangioproliferative, membranous, membranoproliferative, diffuse fibroplastic glomerulonephritis, and amyloidosis. The most characteristic type of glomerulopathy in psoriasis is focal-segmental mesangioproliferative glomerulitis (IgA - nephropathy), which accounts for 61.1% of the structural pathological findings of autopsy material of psoriatic disease.

Conclusions: In the pathogenesis of psoriatic nephropathy, the basis mechanism is the deposition of immune complexes and a direct cell-mediated cytotoxic response, which manifests in the kidneys and skin with morphologically identical angiopathy at the level of the microcirculatory bed, an increase in the level of Ig, in particular IgA, activation of system complement.

ID:1051

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

HISTOLOGICAL FEATURES OF CEREBRAL ISCHEMIC STROKE IN TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Liliya Volos[1], Tetyana Mykhaylichenko[2]
[1]Pathological Anatomy, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine, [2]Department Of Internal Medicine N2, Donetsk National Medical University, Kramatorsk, Ukraine

Background and Aims : Diabetes mellitus (DM) leads to a significant increase in mortality and a deterioration in the quality of life of patients, due to the development of cardiovascular complications. Ischemic stroke in diabetic patients occurs 2-4 times more often than in the general population. Mortality in ischemic stroke is 50 - 60%, in hemorrhagic form 70 - 95%. The prognosis for stroke patients with diabetes is more pessimistic than for those without diabetes. **The aim** of this study was to identify the morphological features of cerebral stroke in diabetes mellitus.

Methods: Twenty-five cases of ischemic stroke on diabetes mellitus background were selected from the archive of Pathology Department. Medical records and histories of diseases were reviewed to retrieve information regarding patient and the cause of death. Information obtained from the autopsy protocol included macroscopic characteristics, status of intracranial arteries and general autopsy findings.

Results: In the cortical-medullary arteries of the zone of ischemic necrosis of the brain tissue segmental fibrinoid necrosis, parietal and occlusive thrombi, perivascular fibrosis and hyalinosis were present. In most of the cases were the presence of focal perivascular encephalolysis and lacunar infarcts, the fusion of small foci with the formation of large ischemic foci of colliquation necrosis. The shadow cells, pyknosis, compaction of the Nissl tigroid, lipofuscin in neurons, atrophy of the neuronal cytoskeleton, intraneuronal inclusions, single neuronal plaques were found outside the stroke zone.

Conclusions: The most significant morphological features in cerebral stroke are a combination of pathology of the microvasculature with a dominant damage to the intracerebral arteries.

ID:1063

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

PREVALENCE OF PREMATURE CORONARY ARTERY DISEASE (CAD) ACCORDING TO CLINICAL FAMILIAL HYPERCHOLESTEROLAEMIA (FH) DIAGNOSIS IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Žaneta Petrulionienė[1,2,3], Egle Skiauteryte[3], Dovile Gabartaite[2,3], Emilija Meskene[2,3], Juste Staigyte[2,3], Rimantė Čerkauskienė[2,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[3], Jolita Badariene[1,2,3], Vilma Dzenkeviciute[2,3,5], Sandra Kutkiene[3], Egidija Rinkuniene[1,2,3], Rusne Jakaite[3], Rasa Strupaite-Sileikiene[2,6,7], Gabriele Jaskeviciute[2]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Clinic Of Internal Diseases, Family Medicine And Oncology, Vilnius University, Faculty of Medicine, Vilnius, Lithuania, [6]Centre Of Eye Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [7]Center Of Eye Diseases, Clinic Of Ear, Nose, Throat, And Eye Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, vilnius, Lithuania

Background and Aims : We aimed to determine the prevalence of CAD according to clinical diagnosis of Familial Hypercholesterolemia(FH) in Lithuania.

Methods: Prospective observational cohort study enrolled patients with clinically diagnosed FH treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. According to Dutch Lipid Clinic Network (DLCN) diagnostic criteria for FH, definite FH was diagnosed when a total point score was>8, probable–6-8, possible-3-5,unlikely<3 points. Premature CAD was defined as occuring in men <55 years and women <60 years. Obstructive Atherosclerotic CAD was defined as the presence of stenosis ≥50% in at least one coronary vessel in Coronary Computed Tomography Angiography(CCTA) or coronary angiography, as well as performed percutaneous coronary intervention(PCI) or coronary arteries bypass grafting(CABG). Data of 119 study patients were included in the analysis. The prevalence of premature CAD was compared in different groups according to FH diagnosis. Statistical analysis was performed using R(v. 4.0.4) program package.

Results: Of 119 examined patients 52,1%(n=62) were women and47,9%(n=57) were men.In the study population, premature CAD was diagnosed for 26%(n=31) patients. 21,8%(n=26) of study patients had definite FH diagnosis, 37,8%(n=45) had probable FH, 28,6%(n=34) - possible FH and11,8% (n=14) had unlikely FH diagnosis. Premature CAD was diagnosed to 38,5%(n=10) patients with definite FH, 33,3%(n=15) with probable FH, 14,7%(n=5) with possible FH and 7,1%(n=1) among people with unlikely FH.

Conclusions: Our findings indicate that among individuals with premature CAD there is an opportunity to detect an index case for initiation of cascade FH screening, especially in definite and probable FH cases.

ID:1068

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

THE EFFECT OF IATROGENIC HYPOTHYROIDISM ON LIPOPROTEIN SUBFRACTIONS AND SERUM PARAOXONASE ACTIVITY IN PATIENTS WITH DIFFERENTIATED THYROID CANCER

POSTER VIEWING SESSION

Mónika Katkó[1], Annamária Gazdag[1], Mariann Harangi[1], Anita Szentpéteri[1], Erika Galgóczi[1], Annamária Erdei[1], Eszter Berta[1], Miklós Bodor[1], Harjit Pal Bhattoa[2], Endre V. Nagy[1]
[1]Department Of Internal Medicine, University of Debrecen, Faculty of Medicine, Debrecen, Hungary, [2]Department Of Laboratory Medicine, University of Debrecen, Faculty of Medicine, Debrecen, Hungary

Background and Aims : The development of atherogenic lipid profile has a major role in hypothyroidism induced accelerated atherosclerosis. In a group of patients with differentiated thyroid cancer (DTC) subclinical hyperthyroidism is maintained after thyroidectomy, interrupted annually with short-term overt hypothyroidism for diagnostic purposes. The effects of short-term overt hypothyroidism on lipid parameters, lipoprotein subfractions and paraoxonase-1 (PON1) activity were studied in these patients.

Methods: Twenty-one patients who underwent total thyroidectomy and ablative radioiodine therapy for DTC were enrolled in the study. Blood samples were collected during continuous TSH-suppressive levothyroxine (L-T4) therapy and after four weeks of L-T4 withdrawal. Thyroid hormones, lipid parameters and PON1 paraoxonase and arylesterase activity were measured, analysis of lipoprotein subfractions was performed by Lipoprint system.

Results: Compared to values measured during continuous L-T4 therapy, total cholesterol, HDL-C, LDL-C, ApoA1, ApoB levels were significantly elevated during iatrogenic hypothyroidism. Differences in the subfraction pattern of lipoproteins were also observed: in hypothyroidism, the mean LDL size decreased (26.9±0.4 nm vs 27.1±0.4 nm, $p<0.01$) and the proportion of small and medium-sized HDL subfractions decreased (29.5±9.9% vs 33.8±8.6%, $p<0.001$, and 43.8±4.6% vs 46.1±5.1%, $p=0.005$, respectively), while the proportion of large HDL subfractions increased (26.8±9.8% vs 20.0±6.9%, $p<0.0001$). The PON1 paraoxonase and arylesterase activities were increased during L-T4 withdrawal (113±67 U/L vs 106±67 U/L, $p=0.005$; and 159±44 U/L vs 134±21 U/L, $p<0.01$; respectively).

Conclusions: In short-term overt hypothyroidism both atherogenic and anti-atherogenic changes were found: the shift toward lower density LDL subfractions is atherogenic, while the increased proportion of larger HDL subfractions and increased paraoxonase activity are anti-atherogenic.

ID:878

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

PRESENCE OF SUBCLINICAL ATHEROSCLEROSIS BEFORE 45 YEARS. ANALYSIS FROM A COHORT STUDY IN ARGENTINA

POSTER VIEWING SESSION

Gustavo A. Giunta[1], María Florencia Aguiló[2], Laura Brandani[1], Daniel Antokoletz[1], Daniel Pirola[1], Pablo Cutine[1], Ariel Kraselnik[1], Nahuel Messina[1], Lorena Helman[1]
[1]Unidad Metabólica, Fundación Favaloro, Ciudad Autónoma de Buenos Aires, Argentina, [2]Nutrición, Fundación Favaloro, Ciudad Autónoma de Buenos Aires, Argentina

Background and Aims : Subclinical atherosclerosis (SA) has important implications in recent cardiovascular prevention guidelines. Young people with SA may be at increased long-life risk for cardiovascular disease. The aim of the present study is to evaluate the frequency and clinical characteristics of young people with SA.

Methods: In a cross-sectional design, male and female adults 45 years old or younger were included. Medical records were used as source for general data collection. Presence of SA was evidenced by the finding of carotid plaques on vascular ultrasound.

Results: A total of 1788 patients (pat) were included (Female 49.3%, with average age 30.1+/-8.6 years). SA was detected in 3.1%. This percentage was associated with age (<30y = 0.6%, 30 to < 40y = 1.8% and > 40y = 11.7%). Patients with SA had higher frequency of arterial hypertension (3% vs. 9%, p< 0.01), with similar prevalence of smoking (23.2% vs. 29.1%, p=ns), familiar antecedents of premature coronary disease (7.1% vs. 12.7%, p=ns) and metabolic syndrome (10% vs. 20%, p=ns). Higher total cholesterol (182.5±35.8mg/dL vs. 212.9±38.4mg/dL, p<0.0001) and triglycerides (105.3±65.3mg/dL vs. 150±92mg/dL, p<0.0001) was observed in SA group. In addition, HDL was lower for SA pat (54.7±13.6mg/dL vs. 49.2±11mg/dL, p<0.0001). Also, statin use was higher in these patients (.7% vs. 3.6%, p<0.05).

Conclusions: Even in low frequency, SA is present in young patients. Male sex, age and risk factors are associated with SA in this subpopulation.

ID:875

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-12 Adipose tissue biology and pathology*

BIOACTIVE LIPIDS AND LIPOPROTEIN LIPASE IN EPICARDIAL ADIPOSE TISSUE FROM PATIENTS WITH CORONARY ARTERY DISEASE: UNFOLDING A MISSING LINK

POSTER VIEWING SESSION

Gabriela Berg[1], Magali Barchuk[1], Patricia Ancel[2], Ljubica Svilar[2], Veronica Miksztowicz[3], Daniel Yñon[4], Juan Patricio Nogueira[5], Miguel Rubio[4], Laura E. Schreier[1], Anne Dutour[2], Jean Charles Martin[2], Bénédicte Gaborit[2]
[1]Clinical Biochemistry, Lipids and Atherosclerosis Laboratory, Faculty of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, Argentina, [2]Inrae, Aix-Marseille University, INSERM, INRAE, C2VN, France, Marseille, France, [3]Instituto De Investigaciones Biomédicas (biomed) Conicet, Lab. de Patología Cardiovascular Experimental e Hipertensión Arterial., Buenos Aires, Argentina, [4]División De Cirugía Cardiovascula, Hospital de Clínicas “José de San Martín”, Argentin, Buenos Aires, Argentina, [5]Conicet, Universidad Nacional de Formosa , Argentina, Formosa, Argentina

Background and Aims : Epicardial adipose tissue (EAT) contributes to atherosclerotic cardiovascular disease (ASCVD). EAT presents a specific lipidomic signature, with increased proinflammatory lipids, such as ceramides (Cer). Besides the activity of lipoprotein lipase (LPL) in EAT, supplying fatty acids to the tissue, would contribute to its expansion. Our aim was to evaluate links among LPL activity and bioactive lipids in EAT from coronary disease (CAD) patients.

Methods: We studied patients undergoing coronary by-pass graft (CAD, n=25) and patients without CAD (noCAD, n=14). EAT and subcutaneous AT (SAT) were obtained, tissue LPL activity and its regulators expression (ANGPTL4, GPIHBP1 and PPARγ) were assessed. Tissue lipidomes were evaluated by UHPLC-MS, in positive and negative ionization modes. For statistics, the MetaboAnalyst software was used

Results: LPL activity was higher in EAT from CAD ($p<0.001$), and in EAT than SAT in both groups ($p<0.001$). ANGPTL4 levels were lower, GPIHBP1 and PPARγ levels were higher in EAT from CAD ($p<0.001$). In both groups EAT exhibited more Cer ($p=0.01$), directly associated to LPL activity, being the strongest association with Cer18:1/24:1 ($p<0.001$). EAT Cer18:1/16:0 to Cer18:1/24:0 and Cer18:1/24:1 to 18:1/24:0 indexes were higher in CAD ($p=0.03$; $p<0.001$, respectively), the latter directly associated with LPL activity ($r=0.63$, $p<0.001$) GPIHBP1 levels ($r=0.68$, $p<0.001$), and inversely to EAT ANGPTL4 expression ($r=-0.49$, $p=0.03$).

Conclusions: The association between LPL activity, total Cer and the atherogenic Cer indexes highlights the importance of the enzyme and these bioactive lipids contributing to the deleterious phenotype of EAT in ASCVD.

ID:1120

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

GUT MICROBIOTA METABOLITES AND PROINFLAMMATORY CYTOKINES LEVELS ROLE IN PATIENTS WITH ATHEROSCLEROSIS AND ATRIAL FIBRILLATION

POSTER VIEWING SESSION

Iryna Melnychuk, Victoriia Kramarova, Viktor Lizogub
Internal Medicine # 4, O.O.Bogomolets National Medical University, Kiev, Ukraine

Background and Aims : To determine connections of gut microbiota metabolites and proinflamatory cytokines levels in patients with atherosclerosis and atrial fibrillation

Methods: 258 patients were investigated. They were divided into 3 groups: control group – 50 patients without atherosclerosis (AS); comparable group – 72 patients with AS but without arrhythmias and mean group – 136 patients with AS and atrial fibrillation (AF). Carotid ultrasound and Holter ECG monitoring were used for diagnosis verification. Plasma Trimetylamine N-oxide (TMAO) and trimetylamine (TMA) levels were determined by gas chromatography with mass electron detection.

Results: Compared with controls, IL-6 (392±29 pg/ml) and CRP (5.35±0.96 mg/l) were significantly elevated in comparable and mean groups (525±41 pg/ml 6.84±0.78 mg/l respectively). There was no difference in CRP between those with comparable and mail groups. Nevertheless, IL-6 levels were significantly higher in mean group (p=0.02). Compared with controls, TMA was significantly elevated in comparable (23,94±1,56 mmol/l) and mean (25,85±1,18 mmol/l) groups. TMAO (4,22±0,30 mmol/l) was significantly elevated in mean group comparable with controls and comparable group. Significant direct strong correlation were determined between IL-6 and TMAO levels (r=0,634; p<0,01).

Conclusions: Gut microbiota metabolites (TMAO, TMA) and proinflamatory cytokines were increased in patients with AS. That shows us connections between inflammatory proses and changes of intestinal microbiota in patients with AS. In case of AS and AF combination proinflamatory cytokines are increased even more than for patients without rhythm abnormalities. TMAO and IL-6 strong direct correlation and their growth in AS and AF patients.

ID:705

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

COMPARATIVE EFFECT OF VALSARTAN-AMLODIPINE TREATMENT VERSUS TELMISARTAN-AMLODIPINE TREATMENT IN FASTING GLUCOSE, FASTING INSULIN, OGTT AND HBA1C LEVELS, IN PREDIABETIC HYPERTENSIVE PATIENTS

POSTER VIEWING SESSION

Angelos Liontos[1], Dimitrios Biros[1], Alexandros Papathanasiou[1], Christos Papagiannopoulos[1], Eleftherios Klouras[1], Stavros Tsourlos[1], Lazaros Athanasiou[1], Sempastien Filippas-Ntekouan[1], Athina Zarachi[2], Nikolaos-Gavriil Kolios[1], Christiana Pappa[2], Valentini Samanidou[1], Eirini Christaki[1], Evangelos Liberopoulos[3], Moses Elisaf[4], Haralampos Milionis[1], George Liamis[4]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece, [4]2nd Department Of Internal Medicine, University Hospital Of Ioannina, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece

Background and Aims : Introduction: According to the latest ESC guidelines for hypertension treatment, it is recommended to use combination therapy of 2 antihypertensive agents as a starting point for most patients. The effect of these drugs on the glucose homeostasis has been discussed extensively. We present comparative data of the effect of valsartan/amlodipine versus telmisartan/amlodipine combination treatments, in fasting glucose, fasting insulin, OGTT and HbA1c levels, before and after the 3-month treatment, in hypertensive prediabetic patients.

Methods: METHODS: Data were collected from 105 patients who visited our outpatient clinic for lipid metabolism, hypertension and diabetes, during the period 2014-2018. 54 persons were randomized in the valsartan/amlodipine group 160/5 mg per day while 51 persons had been randomized in the group of telmisartan/amlodipine 80/5mg per day. All patients successfully completed the

study.

Table 1A. *Patients' characteristics at the start of the study*

Characteristics/Combination treatment	TEL/AMLO	VAL/AMLO
N (Men-Women)	51(35-16)	54(33-21)
Age (Years)	58.04±13. 6	64.44±11.64
Smokers (%)	31(60.8%)	14(25.9%)
Alcohol Consumers (%)	16(31.4%)	8(14.8%)
Body Weight (Kg)	84.72± 12.87	80.83±11.80
Height (m)	1.72[1.6-1.77]	1.69[1.62-1.75]
BMI (Kg/m^2)	29.32 [27.37-31.65]	28.09[26.81-29.89]
SBP (mmHg)	163 [158-168]	162 [159.25-165]
DBP (mmHg)	100[95-106]	100[92-103.75]

Results: RESULTS: The results of the alternations in glucose, insulin, OGTT and HbA1c levels, before and after the 3-month treatment are presented

Table 1B. Results of glycemic tests before and after the 3-month treatment

Parameter	Start of treatment	After 3 Months of Treatment	% Change	p-value
Glu (mg/dl)				
TEL/AMLO	100[98-106]	98.22± 13.24	-1.78 % (-1.78)	0.005
VAL/AMLO	104[96.25-110.75]	103.96± 10.51	-0.04 % (-0.04)	0.622
INS (µIU/mL)				
TEL/AMLO	13[9.5-14.9]	10[6.2-13.5]	-23.08 % (-3)	0.005$$$
VAL/AMLO	6.2[4.2-9.23]	7.2[4.77-10.47]	16.13 % (1)	0.136^^^
HbAlc (%)				
TEL/AMLO	5.67± 0.44	5.71± 0.46	0.71 % (0.04)	0.497
VAL/AMLO	5.79± 0.33	5.75± 0.32	-0.69 % (-0.04)	0.236
OGTT (mg/dl)				
TEL/AMLO	122.82± 26.88	124.7± 31.7	1.53 % (1.88)	0.206
VAL/AMLO	139.95± 26.9	131.61± 26.05	-5.96 % (-8.34)	0.053

The data are presented as Average ± Standard Deviation, Median [25th-75th].
^p < 0.05 compared to TEL/AMLO therapy, ^^p < 0.01 compared to TEL/AMLO therapy, ^^ < 0.001 compared to TEL/AMLO therapy
$p < 0.05 compared to VAL/AMLO therapy, $$p < 0.01 compared to VAL/AMLO therapy, $$$p < 0.001 compared to VAL/AMLO therapy

on **Table 1B**.

Conclusions: CONCLUSIONS: regarding the change in insulin levels for the TEL/AMLO group there was a decrease of 23.08% (p=0.005) after the 3-month treatment while in the VAL/AMLO group there was

an increase but not statistically significant (+16.13%, p=0.136). Comparison between the treatment groups showed a statistically significant difference in the change of INS levels (from the beginning of treatment and after 3 months) between the TEL/AMLO treatment group and the VAL/AMLO treatment group (p-value<0.001). No other significant differences were observed between treatment groups for the other parameters.

ID:739

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

A MULTIPLE CASE STUDY OF THE EFFECT OF PHYSICAL ACTIVITY BEFORE AND AFTER COVID 19 ON PULSE WAVE VELOCITY IN BLIND PEOPLE LIVING INDEPENDENTLY

POSTER VIEWING SESSION

Akira Kimura, Itsuki Takada
Graduate School Of Health Sciences Sciences, GUNMA PAZ UNIVERSITY, Takasaki, Japan

Background and Aims : COVID19 has been prevalent since 2020. The effect of health education on pulse wave velocity(PWV) in blind people who have been living independently for more than 5 years using a case study. To determine the effect of physical activity on PWV before and after COVID19 in blind people.

Methods: The subjects were Five people who were not infected with COVID19 after 5 years of health education in a population of blind people living in a suburban area of Japan. The study design was a case study, a 3-year cohort at two consecutive time points. Anthropometric measurements, PWV measurements (PR203-2), and interviews about lifestyle in November 2021. Descriptive statistics, Characteristic behaviors are described.

Results: The mean(SD) age was 68(11) years (SD). Height ,163(5.1) cm, weight, 64.6(8.1) kg, BMI 24(2), body fat, 33.7(3.8)%, muscle mass percentage 23.3(3.8)%. change from November 2018 was +4 years, +0(1.6)cm, +0.4(2.3)kg, +0.4(3.3), +0.4(3.3)%, and +0.6(1.6)%, respectively. Left BaPWV was 1486 (102) cm/sec, right was 1476 (91) cm/sec, left ABI was 1.11 (0.11), right ABI was 1.12 (0.15), and the changes from November 2018 were -28.6 (148) cm/sec, 16 (198) cm/sec, -0.05 (0. 07) and -0.06 (0.1), respectively. As a characteristic behavior, all but one of the patients who lost the opportunity to walk outdoors due to the COVID19 epidemic reported doing 20 minutes of low-intensity squatting exercise daily.

Conclusions: 80% reported doing light indoor exercise even though they lost the opportunity to walk outdoors due to the COVID19 epidemic, and maintained good pulse wave velocity over spontaneous exacerbations.

ID:738

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

LEFT VENTRICULAR MASS INDEX AND RISK OF COGNITIVE DECLINE IN A GENERAL ELDERLY POPULATION: TANUSHIMARU COHORT STUDY

POSTER VIEWING SESSION

Nagisa Morikawa, Mika Enomoto, Ako Fukami, Maki Yamamoto, Hiromi Sato, Hisashi Adachi, Yoshihiro Fukumoto
Division Of Cardiovascular Medicine, Department Of Internal Medicine, Kurume Univiersity School of Medicine, Kurume, Fukuoka, Japan

Background and Aims : Elevated cardiovascular disease risk factor burden is a recognized contributor to poorer cognitive function. Recent cohort study suggested that higher N-terminal pro-B-type natriuretic peptide levels predicted incident dementia. However, there is little study of the longitudinal association between left ventricular (LV) structure and future cognitive decline. Therfore, we hypothesied that LV structure is associated with cognitive decline.

Methods: We recruited 1943 participants (mean age: 65.8±11.3 years, male 39.9%) as a population-based sample of Tanushimaru, Japan in 2009 and followed 837 adults in 2018 after excluding those with heart disease history. The subjects received 2-dimensional echocardiography to quantify LV mass index (LVMI) in 2009. The 30-point Mini-Mental State Examination (MMSE) was used to assess cognitive function in 2009 and in 2018. We classified MMSE scores ≦23, 24–27, ≥28 as dementia, mild cognitive impairment (MCI) and normal cognition (NC). Multivariable logistic regression analyses were performed to examine the association between LVMI and cognitive decline.

Results: Mean MMSE scores in 2009 and in 2018 among 837 participants were 28.1±2.0 and 28.4±2.3, respectively. Cognitive status progressed from NC to MCI/dementia in 19.3% (96/498) or from NC/MCI to dementia in 2.9% (24/826). Conversion from NC to MCI/dementia was not associated with LVMI, while larger LVMI was significantly associated with the progression from NC/MCI to dementia (p=0.002). Age, sex-adjusted odds ratio for progression to dementia was 1.50 (95% confidence interval, 1.16-1.97) as LVMI increased. The association was independent of body mass index, systolic blood pressure, and microalbuminuria.

Conclusions: Larger LVMI can be a risk factor for dementia.

ID:733

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

CIRCULATING MICRO-146A AND PRO-INFLAMMATORY CYTOKINES IN PATIENTS WITH CORONARY ARTERY DISEASE WITH TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Serhii Serik, Vladyslav Riabukha, Viktoria Malko
Department Of Ischemic Heart Disease And Metabolic Disorders, Government Institution "L.T. Malaya Therapy National Institute of The National Academy of Medical Sciences of Ukraine", Kharkiv, Ukraine

Background and Aims : Circulating microRNAs were suggested as modulators of coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM). The aim of the study was to investigate the association of circulating microRNA-146a with interleukin-6 (IL-6) and interleukin-18 (IL-18) levels in patients with CAD with T2DM.

Methods: The study included 52 patients with CAD with T2DM, 20 CAD patients without diabetes and 15 healthy individuals as control. microRNA-146a-5p was determined in plasma by real time PCR. Results expressed in relative units. IL-6 and IL–18 levels were measured by ELISA.

Results: MicroRNA-146a levels in CAD patients with T2DM (19,52 [12,51; 36,93]) and without diabetes (39,64 [18,29; 103,84]) were higher than in the controls (5,41 [3,48; 7,63]), p=0,0001, p=0,000003). But in CAD patients with T2DM microRNA-146a level was decreased compared to patients without diabetes (p=0,0133). IL-6 and IL-18 levels in patients with T2DM were increased compared with controls (p=0,0015, p=0,0315) and did not differ significantly in comparison to non-diabetic patients. Only in CAD patients with T2DM microRNA-146a was negatively correlated with IL-6 (R=-0,42, p=0,035) and IL-18 (R=-0,41, p=0,040). In diabetic patients lower microRNA-146a level (the 1st tertile) was associated with the increase of IL-6 and IL-18 levels in comparison with the 3rd tertile (p=0,0207, p=0,0148) and with non-diabetic patients (p=0,0194, p=0,0337).

Conclusions: Circulating microRNA-146a level in CAD patients with T2DM was increased compared to controls but decreased in comparison with CAD patients without diabetes. The lowest microRNA-146a levels in CAD patients with T2DM was associated with the significant elevation of IL-6 and IL-18 levels.

ID:732

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

PREGNANCY IN HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA – A CASE SERIES

POSTER VIEWING SESSION

Kateřina Veletová[1], Milan Bláha[2], Vladimír Blaha[1], Miriam Lánská[2], Pavel Žák[2]
[1]The 3rd Department Of Internal Medicine - Metabolic Care And Gerontology, University Hospital Hradec Králové, Hradec Králové, Czech Republic, [2]The 4th Department Of Internal Medicine - Hematology, University Hospital Hradec Králové, Hradec Králové, Czech Republic

Background and Aims : Familial hypercholesterolemia (FH) is an autosomal codominant lipid metabolism disorder mostly caused by defects of a low-density lipoprotein (LDL) receptor gene. This condition results in lifelong elevation of plasmatic LDL-cholesterol (LDL-C) levels, followed by premature atherosclerosis and an increase in cardiovascular risk. Management of women suffering from the homozygous form of FH (HoFH) poses difficult demands on physicians, regarding specific phases of their patients´ lives. Periods of pregnancy and lactation represent an additional risk due to association of physiological changes in pregnancy, pre-existing dyslipidemia and limited therapeutic possibilities and experiences. Methods of extracorporeal LDL-apheresis represent a suitable therapeutic approach.

Methods: We present our experience in case reports of 6 HoFH women and their 13 pregnancies (9 successful, 3 abortions and 1 interruption).

Results: One of the 6 patients experienced a lethal complication of her pregnancy, which was associated with her HoFH disease. Of the 9 successful pregnancies, 9 children with standard birth weight and psychomotor development were born. Two of these successful pregnancies were treated by a lipid-lowering method – LDL-apheresis. We provide graphs describing the development of the pregnancy lipidogram before and after LDL-aphereses.

Conclusions: Pregnancy in HoFH women represents substantial risk, however, patients without signs of decompensated cardiovascular disease can have a good prognosis. Such pregnancies can proceed until in-term spontaneous delivery without any major complication. LDL-apheresis plays an important role in the management of pregnancy in HoFH.

ID:729

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-06 Gender and cardiovascular risk*

SEX-DEPENDENT DIFFERENCES ON THE IMPACT OF MINOCYCLINE ADMINISTRATION IN THE DEVELOPMENT OF CORONARY ARTERY DISEASE IN A MURINE MODEL OF ACCELERATED ATHEROSCLEROSIS

POSTER VIEWING SESSION

Laura M. Parra[1], Leticia A. Gonzalez Jara[2,3], Marcelo E. Andia[2,3], Sergio Uribe[2,3]
[1]School Of Medicine, Pontificia Universidad Católica, Santiago, Chile, [2]Millennium Nucleus Cardio Mr, Biomedical Imaging Center, Radiology, School Of Medicine, Pontificia Universidad Catolica, Santiago, Chile, [3]Radiology, Pontificia Universidad Catolica de Chile, Santiago, Chile

Background and Aims : Cardiovascular risk considerably increases in women after menopause, even surpassing that of men, suggesting an effect of age and sex. We seek to compare sex-dependent differences of minocycline administration on survival, inflammation, oxidative stress and monocyte population in young male and female mice, using a diet-induced model of atherosclerosis.

Methods: Male and female SRB1 KO/apoE-hypomorphic mice, aged 2-3 months, were randomly assigned to 2 groups: Control (AT-Control) and minocycline (AT-MIN). Minocycline was administered in the drinking water at a dose of 0.05 mg/mL. Atherosclerosis was induced by feeding an atherogenic diet (15% fat, 1.25% cholesterol, 0.5% cholate). Survival was evaluated by the Kaplan-Meier method, and the log-rank test was used to compare survival curves. Differences in weight post intervention were compared by Mann–Whitney U test.

Results: Female SRB1 KO/apoE-hypomorphic mice have better survival than male mice when fed an atherogenic diet (33.4 vs 30.4 days, respectively). Minocycline administration significantly improved survival in male (Minocycline n=8, 30.4 days vs. Control n=4, 19 days, $P<0.001$) and female (Minocycline n=8, 33.4 days vs Control n=8, 26.5 days, $P<0.022$) (Figure 1). There were no significant differences in weight after intervention (Median weight difference, male: 1.5 grs, P=0.68, female: 1.2 grs, P=0.65, Figure

2).

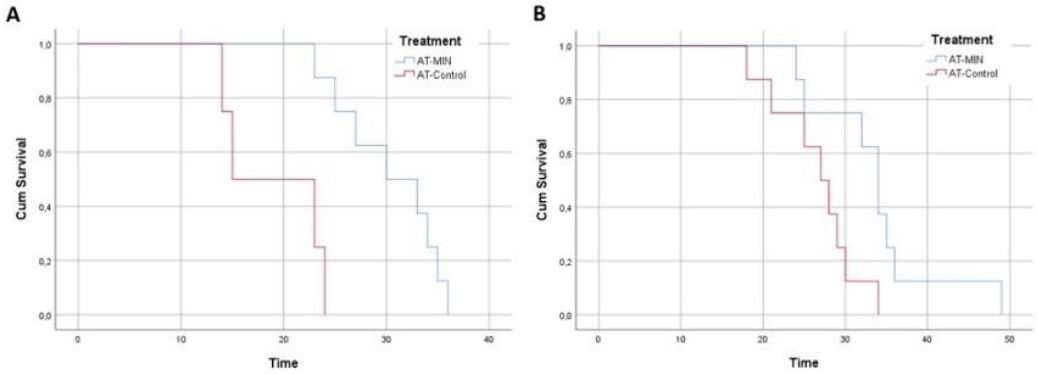


Figure 1. Effect of minocycline on survival of male and female SRB1 KO/apoE hypomorphic mice fed atherogenic diet. Kaplan–Meier survival curves of (A) Male AT-Control (n=4), AT-MIN (n=8) and (B) Female AT-Control (n=8), AT-MIN (n=7). **P<0.001 *P<0.022 respectively.

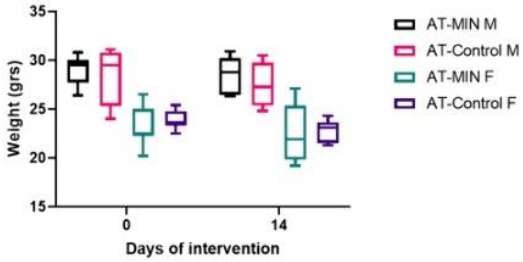


Figure 2. Effect of minocycline on weight in SRB1 KO/apoE hypomorphic mice fed atherogenic diet. Male: AT-Control M (n=4), AT-MIN M (n=8), Female: AT-Control F (n=8) and AT-MIN F (n=7). P<0.68

Conclusions: Minocycline improved survival in both male and female SRB1 KO/apoE-hypomorphic mice fed an atherogenic diet, with a higher baseline survival in females. This study is under development and the next step is to compare the inflammatory profile, oxidative stress and monocyte population, and finally to compare with old mice. Acknowledgement: FONDECYT 1180525

ID:725

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

THE SYNERGISTIC ROLE OF IRRATIONAL BELIEFS AND HEALTH ANXIETY REGARDING FAMILY HISTORY OF DIABETES ON TYPE 2 DIABETES; THE ATTICA EPIDEMIOLOGICAL STUDY.

POSTER VIEWING SESSION

Christina Vassou[1], Thomas Tsiampalis[1], Ekavi N. Georgousopoulou[2], Christina Chrysohoou[3], Mary Yannakoulia[1], Christos Pitsavos[3], Mark Cropley[4], Demosthenes B. Panagiotakos[1]
[1]Department Of Nutrition And Dietetics, Harokopio University, Athens, Greece, Kallithea, Greece, [2]School Of Medicine Sydney, University of Notre Dame, Sydney, Australia, Sydney, Australia, [3]First Cardiology Clinic, School Of Medicine, University of Athens, Greece, Athens, Greece, [4]School Of Psychology, University of Surrey, Guildford, UK, Guildford, United Kingdom

Background and Aims : To investigate the path between family history of diabetes and diabetes incidence, in relation to irrational beliefs and healthy anxiety.

Methods: During the ATTICA prospective cohort study (2002-2012) that was carried out in Greece, 845 participants (18-89 years) without evidence of diabetes at baseline underwent psychological evaluation through the Irrational Beliefs Inventory (IBI, range 0-88) and the Whitley Index scale (WI, range 0-14). Incidence of diabetes was based on the criteria of the American Diabetes Association.

Results: Mean IBI score was 53±10/88 in men and 51±11/88 in women (p=0.68). Mean WI score 3.7±3/14 in men and 3.6±3/14 in women. The 10-year incidence of type 2 diabetes was 13.4% in men and 12.4% in women (p=0.57). Interaction analysis revealed that when focused on those with high levels of irrational beliefs, family history of diabetes was associated with 3.7-times (Hazard Ratio 3.70; 95%CI 1.83, 7.48) higher odds of T2DM among those with low health anxiety, when focused on those with high levels of irrational beliefs, family history of diabetes was associated with 2.8-times (HR 2.81; 95%CI 1.74, 4.54) higher odds of T2DM in the entire sample, while when focused on those with high levels of irrational beliefs, family history of diabetes was associated with 2.4-times (HR 2.38; 95%CI 1.33, 4.27) higher odds among those with high health anxiety levels.

Conclusions: This work strongly suggests, for the first time in the literature, the synergistic role of irrational beliefs and health anxiety in the relationship between family history of diabetes and the development of T2DM.

ID:721

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

NEBIVOLOL PREVENTS RESTENOSIS BY INHIBITING INFLAMMATION, PROLIFERATION AND PLATELET AGGREGATION IN HIGH GLUCOSE-INDUCED HUMAN SAPHENOUS VEIN GRAFTS

POSTER VIEWING SESSION

Caglar Bintepe[1], Buket Reel[2], Cagatay Engin[3], Nevin Ersoy[4], Hüsnü A. Bagriyanik[4,5]
[1]Pharmacology, Ege University Institute of Health Sciences, Izmir, Turkey, [2]Clinical Pharmacy, Ege University Faculty of Pharmacy, Izmir, Turkey, [3]Cardiovascular Surgery, Ege University School of Medicine, Izmir, Turkey, [4]Histology And Embryology, Dokuz Eylul University School of Medicine, Izmir, Turkey, [5]Histology And Embryology, Izmir Biomedicine and Genome Center, Izmir, Turkey

Background and Aims : Netrins, slits, semaphorins and ephrins were recently described as guidance molecules involved in the pathogenesis of atherosclerosis. Ephrin-A2 causes atherosclerosis by stimulating proliferation, migration and extracellular matrix deposition. Conversely, Semaphorin-3A (Sema-3A) inhibits proliferation and migration. On the other hand, matrix metalloproteinase-2 (MMP-2) is activated by MMP-14, but this activity is controlled by tissue inhibitor of metalloproteinase-2 (TIMP-2). In our previous study, we demonstrated that nebivolol inhibited atherosclerotic netrin-1 and inflammatory MMP-2,-9 expressions, while upregulating protective Slit-2 expression in high glucose-induced human saphenous vein (HSV) grafts. In the present study, we aimed to investigate antiplatelet (CD41/CD61), antiproliferative α-smooth muscle actin (α-SMA), anti-inflammatory (MMP-14/TIMP-2) and anti-atherosclerotic (Ephrin-A2/Sema-3A) effects of nebivolol in high glucose-induced HSV grafts.

Methods: HSV graft segments (n=7) from patients undergoing coronary artery bypass grafting (CABG) surgery were divided into five rings and incubated in DMEM containing 30 mM glucose and/or 10 µM nebivolol or 0.1 % DMSO for 24hrs after gently removal of the endothelium. Control rings were incubated in DMEM only. Protein expressions were determined by immunostaining/immunoscoring in paraffin embeded HSV transverse sections.

Results: In contrast to high glucose, nebivolol reduced the expressions of Ephrin-A2, α-SMA, CD41/CD61 and MMP-14, but increased the expressions of Sema-3A and TIMP-2 in HSV grafts.

Conclusions: Nebivolol may contribute to the maintenance of long-term graft patency by preventing inflammation, proliferation and platelet aggregation in diabetic patients undergoing CABG surgery. **The authors* would like *to* thank *to the* Scientific Research Projects Coordination *Unit,* Ege University*, Turkey (B.Reel, TDK-2020-21833) for* financial *support.*

ID:720

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

EFFECTS OF MINOCYCLINE IN PREVENTING THE DEVELOPMENT OF CORONARY ARTERY DISEASE IN A MURINE MODEL OF ACCELERATED ATHEROSCLEROSIS

POSTER VIEWING SESSION

Laura M. Parra[1], Leticia A. Gonzalez Jara[2,3], Marcelo E. Andia[2,3], Sergio Uribe[2,3]
[1]School Of Medicine, Pontificia Universidad Católica, Santiago, Chile, [2]Radiology, Pontificia Universidad Catolica de Chile, Santiago, Chile, [3]Millennium Nucleus Cardio Mr, Biomedical Imaging Center, Radiology, School Of Medicine, Pontificia Universidad Catolica, Santiago, Chile

Background and Aims : Experimental and clinical evidence supports the critical role of inflammation in atherosclerosis, independent of the cholesterol level. The purpose of this study is to evaluate the effect of short-term treatment with minocycline, a tetracycline antibiotic, that has been shown to possess anti-inflammatory properties, on survival, inflammation, oxidative stress and monocyte population in a diet-induced myocardial infarction mouse model.

Methods: SRB1 KO/apoE hypomorphic mice, aged 2-3 months, were randomly assigned to 2 groups: Control (AT-Control) and minocycline (AT-MIN). Minocycline was administered in the drinking water at a dose of 0.05 mg/mL. Atherosclerosis was induced by feeding a high fat, high cholesterol diet (15% fat, 1.25% cholesterol, 0.5% cholate). Survival analysis was evaluated by the Kaplan-Meier method, and the log-rank test to compare survival curves. Additionally, differences in weight post intervention were compared by Mann–Whitney U test.

Results: Minocycline administration significantly improved mean survival in SRB1 KO/apoE hypomorphic mice fed an atherogenic diet (Minocycline n=8, 30.4 days vs. Control n=4, 19 days, P<0.001, Figure 1). There was no significant difference in weight between both groups post diet intervention (Median weight difference= 1.5 grs, P=0.68, Figure 2).

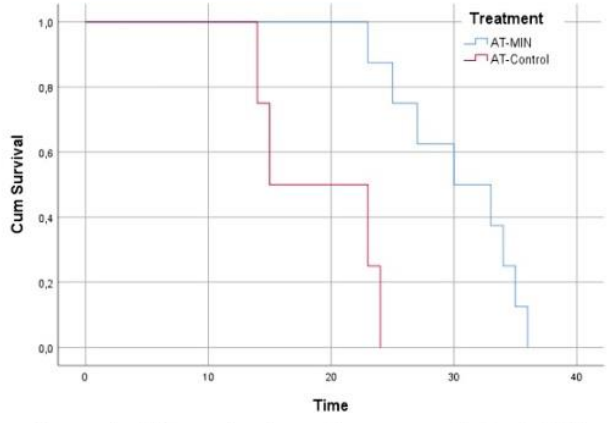


Figure 1. Effect of minocycline on survival of SRB1 KO/apoE hypomorphic mice fed atherogenic diet. Kaplan–Meier survival curves of AT-Control (n=4) and AT-MIN mice (n=8). *P<0.001

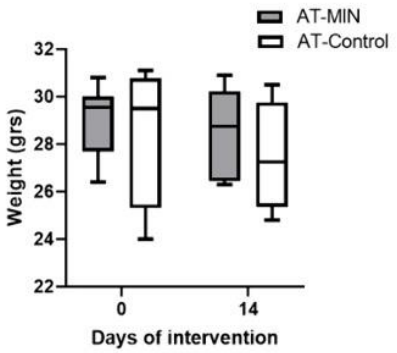


Figure 2. Effect of minocycline on weight in SRB1 KO/apoE hypomorphic mice fed atherogenic diet. AT-Control (n=4) and AT-MIN mice (n=8). P=0.68

Conclusions: Short-term treatment with minocycline successfully improved survival in SRB1 KO/apoE-hypomorphic mice fed an atherogenic diet, without significantly affecting body weight. This study is under development and the next step is to evaluate systemic and local inflammation and oxidative stress biomarkers and monocyte sub-populations. We expect the results to be comparable to statin management, as has been previously proposed. Acknowledgement: FONDECYT 1180525

ID:716

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE ROLE OF RIPC IN PREVENTING ORGAN DAMAGE, INFLAMMATION AND OXIDATIVE STRESS DURING LOWER LIMB DSA: A RANDOMISED CONTROLLED TRIAL

POSTER VIEWING SESSION

Karl Kuusik[1,2,3], Teele Kasepalu[1], Mihkel Zilmer[2], Jaan Eha[1,3], Mare Vähi[4], Liisi Anette Torop[5], Jüri Lieberg[6], Jaak Kals[2,6,7]
[1]Heart Clinic, Tartu University Hospital, Tartu, Estonia, [2]Centre Of Excellence For Genomics And Translational Medicine, Institute Of Biomedicine And Translational Medicine, Department Of Biochemistry, University of Tartu, Tartu, Estonia, [3]Institute Of Clinical Medicine, Department Of Cardiology, University of Tartu, Tartu, Estonia, [4]Institute Of Mathematics And Statistics, University of Tartu, Tartu, Estonia, [5]Pathology Service, Tartu University Hospital, Tartu, Estonia, [6]Surgery Clinic, Department Of Vascular Surgery, Tartu University Hospital, Tartu, Estonia, [7]Department Of Surgery, Institute Of Clinical Medicine, University of Tartu, Tartu, Estonia

Background and Aims : Diagnostic digital subtraction angiography (DSA) and DSA with percutaneous transluminal angioplasty (DSA-PTA) are common procedures for diagnosing and treating symptomatic lower extremity arterial disease (LEAD). However, organ damage following DSA and DSA-PTA is often under-recognised and hence undiagnosed. The aim of the current study was to assess the effect of remote ischemic preconditioning (RIPC) intervention on the organ damage markers profile, oxidative stress and inflammation biomarkers in LEAD patients undergoing DSA and DSA-PTA procedure.

Methods: The RIPC intervention was performed by inflating a standard blood pressure cuff on the patient´s upper arm to 200 mmHg for 5 minutes four times with 5-minute perfusion between each cycle. The sham intervention was performed similarly, but the cuff was inflated to 20 mmHg.

Results: A total of 111 (RIPC 54, sham 57) patients with symptomatic LEAD scheduled for endovascular procedure were randomized, and 102 patients (RIPC 47, sham 55) completed the study protocol. RIPC significantly limited the increase of adiponectine levels after DSA and DSA-PTA, compared to sham intervention (p=0.020), but CK-MB levels were markedly lower in the sham group (p=0.047) after procedure. There was no significant difference between the RIPC and the sham group in mean changes in hs-Troponin-T (p=0.25), NT-proBNP (p=0.24), creatinine (p=0.76), eGFR (p=0.61), urea (p=0.95), beta-2-microglobuline (p=0.34) or cystatine C (p=0.24) levels.

Conclusions: In this controlled clinical study RIPC failed to improve the profile of renal and cardiac biomarkers in patients with LEAD periprocedurally. RIPC significantly limits the rise in adiponectin levels and may influence the decrease of CK-MB levels.

ID:714

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

ROUTINE USE OF FRIBROSIS-4 INDEX IN LIPID CLINIC

POSTER VIEWING SESSION

Tina Mazaheri[1], Ruvini N. Ranasinghe[2], Amy Jennings[2], Wiaam Alhasani[2], Nandini Rao[3], Georgios K. Dimitriadis[4], Royce P. Vincent[3]
[1]Clinical Biochemistry Department, King's College Hospital NHS Foundation Trust, London, United Kingdom, [2]Clinical Biochemistry, King's College Hospital NHS Foundation Trust, London, United Kingdom, [3]Clinical Biochemistry, King's College Hospital, London, United Kingdom, [4]Endocrinology, Kings College Hospital, London, United Kingdom

Background and Aims : Non-alcoholic fatty liver disease (NAFLD), the hepatic manifestation of metabolic syndrome, is a common cause of chronic liver disease and abnormal liver function test (LFT) in UK, yet it remains underdiagnosed. The number of patients presenting to lipid clinic with metabolic syndrome is increasing. Non-invasive biomarkers such as Fribrosis-4 (FIB-4) index is a helpful screening tool to exclude advanced fibrosis in high-risk patients. Therefore, we assessed the clinical utility of FIB-4 in a secondary care lipid clinic.

Methods: In this retrospective study, 208 patients presenting to the lipid clinic in 2021 were reviewed. Those with history of excess alcohol intake, pre-existing liver disease or incomplete laboratory data were excluded. FIB-4 was calculated using aspartate aminotransferase (AST), alanine aminotransferase (ALT) and platelet counts. 62% of patients were excluded due to lack of paired AST and ALT. A FIB-4 score <1.45 was used to rule out advanced fibrosis, with FIB-4 >3.25 indicating high risk for advanced fibrosis.

Results: 49 patients (22M) were included aged 52(38-62) [median (IQR)] years.35% had BMI ≥30 Kg/m^2, 45% had pre/type 2 diabetes and 43% had metabolic syndrome.FIB-4 was >1.45 in 24% of patients with metabolic syndrome vs. 4% without metabolic syndrome. There was no difference in FIB-4 between genders/BMI.

Conclusions: Nearly a quarter of patients presenting to the lipid clinic with metabolic syndrome had a FIB-4 score prompting further assessment for liver fibrosis. We recommend wider use of FIB-4 in lipid clinics and LFT panels to include both AST and ALT to facilitate this.

ID:710

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

PROGRESSIVE EARLY CORONARY ATHEROSCLEROSIS IN THE PATIENT WITH CHRONIC PERIODONTITIS

POSTER VIEWING SESSION

Elena V. Baranova[1], Irina V. Alekseeva[2], Mariya V. Muzalevskaya[3], Valeria D. Shurygina[4], Irina E. Mikhailova[4], Alexey V. Tregubov[3,4], Soreiia A. Urazgildeeva[3,4,5]
[1]Cardiology, Limited Liability Company MEDICOM, Gatchina, Leningrad region, Russian Federation, [2]Diagnostic Center, Center for cardiac medicine Chernaya Rechka, Saint Petersburg, Russian Federation, [3]Center Of Atherosclerosis And Lipid Disorders, Northwest District Scientific and Clinical Center named after L.G. Sokolov, Saint Petersburg, Russian Federation, [4]Scientific, Clinical, And Educational Center Cardiology, St.Petersburg State University, Saint Petersburg, Russian Federation, [5]Center Of Clinical Lipidology, Center for cardiac medicine Chernaya Rechka, Saint Petersburg, Russian Federation

Background and Aims : Interrelationship between periodontal infection and cardiovascular morbidity has become increasingly appreciated in recent years. Chronic inflammatory and microbial burden caused by the dental plaque may predispose to the enhanced atherosclerotic process. Periodontal pathogens could induce the production of antiphospholipid antibodies, e.g., to oxidized low-density lipoproteins (AT-oxLDL), and stimulate the autoimmune disorders leading to early atherosclerosis. In order to illustrate above mentioned position, we report a case of 37-year-old smoking man with a history of acute myocardial infarction (AMI) and chronic periodontitis (CP).

Methods: The patient has a history of AMI at the age of 36 resulted in the development of left ventricular aneurysm and severe heart failure (ejection fraction by Echocardiography - 13%). Restenosis has been developed at the site of BMS implantation in the anterior interventricular artery a year later. A cardioverter-defibrillator has been implanted due to the paroxysmal ventricular tachycardia. The patient has no family history of cardiovascular diseases or diabetes.

Results: The patient's LDL cholesterol level is 1.85 mmol/l (resulted in taking atorvastatin 80 mg). AT-oxLDL was measured by enzyme immunoassay. Its level - 48.22 U/l - is more than twice above upper limit of the norm. Bacterial DNA of the following periodontal pathogens is identified in subgingival samples: Peptostreptococcus micros – $1,4x10^6$, Porphiromonas gingivalis – $3,89x10^7$, Prevotella intermedia – $2,86x10^4$, Treponema denticola – $1,77x10^5$. The patient has no signs of any inflammatory diseases except CP.

Conclusions: The progressive early coronary atherosclerosis in the smoking patient without severe hypercholesterolemia and diabetes can be partly linked to immune inflammatory response to periodontal pathogens.

ID:709

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-07 Nutrition, nutraceuticals*

THE EFFECTS OF ONE-DAY FASTING IN YOUNG AND MIDDLE-AGE PATIENTS WITH OVERWEIGHT AND OBESITY

POSTER VIEWING SESSION

Lolita Matiashova, Anna Isayeva
Department Of Comprehensive Risk Reduction For Chronic Non-communicable Diseases, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine

Background and Aims : Background There is insufficient data on the effect of intermittent fasting on blood lipids and inflammation. **Aim**. To study the effect of one-day intermittent fasting on blood lipids, inflammation markers, and well-being in middle-age patients with overweight and obesity.

Methods: A cohort study of 105 (40 male) overweight and obese individuals (BMI=30±5kg/m2) who never practiced intermittent fasting (IF) before were included. Fasting glucose (FG), total cholesterol (TC), lipoprotein low density (LDL), triglyceride (TG), lipoprotein high density (HDL), creatinine, urea (U), high sensitive C-reactive protein (hCRP) and interleukin 1 beta (IL-1B) were measured before and after fasting. After the day of fasting, all participants in the study rated their difficulty of practicing fasting from 1 to 10. Statistical analyses were conducted by IBM SPSS Statistics 19

Results: The basic level of hCRP was 10.6±8.7 mg/L and IL-1B 2.7±0.7 pg/mL. After fasting the hCRP level decreased in all patients to 4.7±3.2 mg/L (p=0.04) and IL-1B to 2.6 ±0.7 pg/mL (p>0.05). The patients were divided into 2 groups by age: 1-st group age median 26 (25:40) and 2-nd group 57 (50:60) years old. Younger patients (1-st) rate fasting practice from 5 to 10 and older patients from 1 to 5 points. The data presented in table 1 showed that blood lipids improved in the 2-nd group. The urea level decreased in both groups, while creatinine level did not change.

Table 1. The mean and standard deviation of laboratory analysis before and after fasting (F) in two groups (*p<0.05: **p<0.001).

Group	TC	TC F	HDL	HDL F	TG	TG F	LDL	LDL F	FG	FG F	U	U F
1	4.9±0.9	5.1±0.9*	1.3±0.3	1.4±0.4	1.3±1.0	1.3±0.9	2.9±0.8	3.1±0.9*	4.7±0.5	4.6±0.6	5.9±1.8	3.9±6.2*
2	4.8±1.1	4.4±1.3*	1.5±1.2	1.2±0.3*	1.7±0.7	1.3±0.4*	3.2±1.5	2.5±1.2*	5.4±61	5.4±0.7	7.9±2.3	10.5±12.

Conclusions: The effect of one-day intermittent fasting differs in young and middle-aged patients. Middle-age patients tolerate intermittent fasting favorably and have more positive changes in blood lipids.

ID:708

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

LIPID PROFILES AND THE PREVALENCE OF DYSLIPIDEMIA IN PREGNANCY

POSTER VIEWING SESSION

Tetyana Ternushchak[1], Marianna Tovt-Korshynska[2]
[1]Internal Medicine, Uzhhorod National University, Uzhhorod, Ukraine, [2]Internal Medicine, Uzhhorod National University, Ужгород, Ukraine

Background and Aims : Physiological changes in the lipid metabolism (elevated low-density lipoprotein cholesterol (LDL-C), triglycerides (TG) and lipoprotein(a) Lp(a)) occur during pregnancy. However, dyslipiemia is associated with gestational diabetes, hypertension, preeclampsia and preterm birth. High level of total cholesterol due to greater concentrations of LDL-C and reduced level of high-density lipoprotein cholesterol (HDL-C) promote atherosclerosis. Moreover, severe hypertriglyceridemia (SHTG) is a potent risk factor for development of acute pancreatitis. The aim of this study was to evaluate serum lipid profiles and the prevalence of dyslipidemia among middle aged pregnant females without established cardiovascular diseases.

Methods: We retrospectively analyzed the medical records of 147 middle-aged women during pregnancy and 24-months after delivery. Fasting blood samples were assayed for total cholesterol, LDL-C, TG, HDL-C, apolipoprotein A1 (Apo A1) and Apo B concentrations during the first, second, third trimesters and 24-months after delivery. The atherogenic index of plasma (AIP) was calculated as log (TG/HDL-C). Free T4, T3 and TSH were measured for detecting subclinical hypothyroidism.

Results: The prevalence of dyslipidemia was observed in 37%. Moreover, 29% of them had subclinical hypothyroidism. Current knowledge on the relationship between lipids and both thyroid hormones and THS is insufficient. The prevalence of dyslipidemia was significantly higher in pregnant females aged 42 years and older (TC, OR=2.5; HDL-C less than 1, OR=1.8; LDL-C greater than 3,9, OR=1.7). The TG, LDL-C, Apo A1 and Apo B levels raised significantly between 19 to 37 weeks and maintained high during next 16 months.

Conclusions: Dyslipidemia is associated with advanced age of pregnant female and subclinical hypothyroidism.

ID:707

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

SIGNIFICANCE OF LDL-C IN APPEARANCE OF MYOCARDIAL INFARCTION IN COVID-19 PATIENTS IN BOSNIAN POPULATION – ONE CENTER EXPERIENCE

POSTER VIEWING SESSION

Lamija (Pojskic) Ferhatbegovic[1], Belma Pojskic[1], Denis Mrsic[2]
[1]Department For Internal Diseases, Cantonal Hospital Zenica, Zenica, Bosnia and Herzegovina, [2]Clinic For Internal Diseases, University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina

Background and Aims : To asses risk factors for myocardial infarction(MI) in COVID-19 patients.

Methods: We compared 2 groups of patients with MI.In Group1 were patients infected with SARS-CoV-2 and in Group2 were patients without SARS-CoV-2.Data were collected from medical records from Cantonal Hospital Zenica.Following parameters were age,sex,hypertension,total cholesterol(TC),high density lipoprotein(HDL-C),low density lipoprotein(LDL-C),triglycerides(TG),diabetes,smoking.Statistical analysis was performed with SPSS 19.0.

Results: There were 43 pts in Group1 (28 males,65% and 15 females,35%) and 50 patients in Group2 (29 males,58% and 21 females 42%).Pts in Group1 were older than in Group2 without significant difference (most patients in Group1 were between 70-79y/o,in Group2 most patients were between 50-59 y/o).In both groups hypertension was similarly represented(Group1 70%,Group2 76%)as well as diabetes(Group1 37%;Group2 28%).Mean level of TC in Group1 was 4.7 mmol/L,in Group2 was 5.1mmol/L and there was no significant difference.There was no significant difference between Group1 and Group2 in mean level of HDL-C(in both groups1.2 mmol/L) and TG (Group 1 1,9 mmol/l;Group2 2.1 mmol/L).LDL-C was significantly higher in Group1 than in Group2(3.0mmol/L vs 1.2mmol/L respectively;$p<0.005$).There were significantly more smokers in Group2(54%)compared to Group1(16%).

Conclusions: LDL-C is established risk factor for atherosclerosis and MI, but in this research LDL-C has been shown as prominent risk factor for MI in patients infected with SARS-COV-2. Possible explanation could be that cholesterol can indirectly increase the liability of patients to SARS-CoV-2 and can help in virus cell membrane penetration. Regular monitoring of LDL-C levels and its adequate treatment would likely affect the weaker impact of COVID-19 on the occurrence of MI.

ID:703

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

LIPOPROTEIN (A) LEVEL DEPENDING ON CLINICAL FEATURES AND LEVEL OF PLASMA SPHINGOLIPIDS IN PATIENTS WITH EARLY ATHEROSCLEROSIS

POSTER VIEWING SESSION

Anastasia Rogozhina[1], Alice Alessenko[2], Larisa Minushkina[3], Uliana Gutner[2], Maria Shupik[2], Iliya Kurochkin[2], Olga Maloshitskaya[4], Sergey Sokolov[4], Albert Lebedev[4], Ludmila Ivanova[1], Victoria Braznik[1], Dmitry Zateyshchikov[1]
[1]Cardiology, City Clinical Hospital 51, Moscow, Russian Federation, [2]Biochemical Physics, Institute of Biochemical Physics of the Russian Academy of Sciences, Moscow, Russian Federation, [3]Cardiology, Central State Medical Academy of Department of Presidential Affairs, Moscow, Russian Federation, [4]Chemistry Department, Lomonosov Moscow state University, Moscow, Russian Federation

Background and Aims : Premature atherosclerosis is a complex multifactorial condition. The study aimed to distinguish more subgroups of the disease by measuring lipoprotein (a) (Lp(a)) and sphingolipid (SP) profile in addition to usual clinical factors.

Methods: We measured Lp(a) and SP levels in 85 (51±6.4 yrs) premature coronary artery disease (CAD) and in 10 severe dyslipidemia patients (pts) using immunoturbidimetric and the chromatography-mass spectrometry methods for Lp(a) and SP, respectively.

Results: 27 (28,4%) pts had Lp (a)> 30 mg/dL. They were more likely to have family history of cardiovascular disease (70.4% vs 41.2%, p = 0.04) and peripheral atherosclerosis (29.6% versus 10.3%, p = 0.029). The level of sphingosine-1-phosphate (S1P) was higher in pts with Lp (a) <30 mg/dL (19.195 ± 3.818 vs 17.135 ± 6.003; p=0.037). 10 from 18 diabetes mellitus pts had Lp(a)<5.16 mg/dl (p=0.025).

Conclusions: We speculate that the burden of high lp(a) level can be the reason for early CAD manifestation in 1 of 3 pts without DM and abnormal SP levels. Funding: RFBR grant 19-04-00870A

ID:744

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

INITIAL SERUM FERRITIN LEVEL AS A PREDICTOR OF IN-HOSPITAL MORTALITY IN PATIENTS PRESENTED BY ST-ELEVATION MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Mahmoud Abdelnabi[1,2], Abdallah Almaghraby[3], Juthipong Benjanuwattra[1], Yehia Saleh[4], Ahmed Mokhtar Abd El Azeem[3]
[1]Internal Medicine Department, Texas Tech University Health Science Center, Lubbock, United States of America, [2]Cardiology And Angiology Unit, Clinical And Experimental Internal Medicine Department, Medical Research Institute Alexandria University, Alexandria, Egypt, [3]Cardiology Department, Faculty of Medicine Alexandria University, Alexandria, Egypt, [4]Cardiology Department, Houston Methodist DeBakey Heart & Vascular Center, Houston, United States of America

Background and Aims : In addition to iron homeostasis, an iron-storage protein, ferritin, plays a role in various pathological conditions including inflammatory and malignant diseases. Several studies showed that elevated serum ferritin level was associated with a higher risk of coronary artery disease. Recently, it has been shown that high serum ferritin levels in men independently correlated with an increased risk of cardiovascular mortality. The study aimed to investigate the possible correlation between the initial serum ferritin level and the in-hospital mortality in patients presented by ST-elevation myocardial infarction (STEMI).

Methods: A total number of 890 patients presented by acute STEMI from the period from 1/5/2020 to 1/5/2021 and underwent successful primary percutaneous coronary intervention (PPCI) according to the standard techniques. Initial serum ferritin level was measured in all patients at the time of admission. Patients with a history of anemia or on iron supplemental therapy were excluded from the study.

Results: 41 patients had in-hospital mortality while 849 patients survived. There was no significant difference between both groups regarding baseline clinical characteristics. By comparing initial serum ferritin levels in the 2 groups, it was higher in deceased patients (p-value=

0.0004*).

Baseline Clinical Characteristics			
	Survived (*n*=849)	**Deceased (*n*=41)**	***P*-value**
Age (years)	59.3 ± 13	60.5 ± 12.2	0.56
Male Sex	636 (74.9)	29 (70.7)	0.55
Anterior STEMI	670 (78.9)	30 (73.2)	0.38
Inferior STEMI	153 (18)	11 (26.8)	0.16
Lateral STEMI	17 (2)	0 (0)	0.36
Posterior STEMI	9 (1.1)	0 (0)	0.5
Diabetes Mellitus	466 (54.9)	22 (53.7)	0.88
Hypertension	634 (74.7)	30 (73.2)	0.83
Smoking	556 (65.5)	25 (61)	0.55
Ejection fraction (%)	45 ± 12	44 ± 15	0.61
Pain to balloon (minutes)	120.1 ± 65	115.3 ± 62	0.64
Hemoglobin (g/dl)	12.8 ± 1.1	12.8 ± 1.5	1
Serum creatinine (mg/dl)	0.7 ± 1.1	0.85 ± 0.8	0.39
Platelet count (10^3 /ml^{-3})	250 ± 114	231 ± 93	0.29
Serum Ferritin (ng/ml)	457 ± 361	255 ± 286	0.0004*
Data are number (%) or mean ± S.D., STEMI: ST-elevation myocardial infarction			

Conclusions: There was a positive correlation between initial serum ferritin level and in-hospital mortality in acute STEMI patients**.** Further studies are required to determine the prognostic impact of ferritin levels in patients with stable coronary artery disease and acute coronary syndromes.

ID:673

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

STIMULATION OF ENDOTHELIAL PROGENITOR CELLS: A NEW PUTATIVE THERAPEUTIC EFFECT OF HMG CO-A REDUCTASE INHIBITOR IN ANKYLOSING SPONDYLITIS: STAT-AS STUDY

POSTER VIEWING SESSION

Devaansh Syngle[1,2], Nidhi Garg[2]
[1]Intern, Government Multi Speciality Hospital -16, Chandigarh, India, [2]Volunteer, Healing Touch Foundation, Chandigarh, India

Background and Aims : CVD is the leading cause of premature death in AS. EPCs that protect against atherosclerotic vascular damage are depleted in AS contributing to enhanced CV-risk. Therapeutic potential of augmenting EPCs to treat the heightened CV-risk of AS has not yet been explored. This study investigates the effect of rosuvastatin on EPC population, vascular endothelial dysfunction and inflammation (surrogates of atherosclerosis) in AS.

Methods: Randomized and placebo-controlled study, 36 AS patients randomized (1:1) to receive either rosuvastatin (10mg/day, n=18) or placebo (n=18) for 6-months as an adjunct to existing stable sDMARDs. Primary efficacy endpoint included: EPCs (CD34+/CD133+) quantified by Flow-Cytometry. Secondary outcome variables included: nitrite, lipids, ICAM-1 and VCAM-1, ASDAS, BASDAI, BASFI and pro-inflammatory cytokines (TNF-α, IL-6 and IL-1).

Results: At baseline, inflammatory measures, pro-inflammatory cytokines, adhesion molecules and nitrite were elevated and EPCs impaired among both groups. After treatment with rosuvastatin, EPCs increased significantly from 0.023±0.0013% to 0.033±0.0014%, p=0.001 as compared to placebo (fig. 1). At 6-months, ASDAS, BASDAI, BASFI, ESR, CRP, TNF-α and IL-6 improved significantly in rosuvastatin group. Concentration of serum nitrite and ICAM-1 was significantly lower in rosuvastatin treated group. Rosuvastatin exerted a positive effect on lipid spectrum. Significant negative correlation observed

between EPCs and BASDAI, CRP, TNF-α and nitrite after treatment with rosuvastatin (fig.

Fig. 1 Effect of Rosuvastatin and Placebo on Endothelial Progenitor Cells (EPCs) in Ankylosing Spondylitis

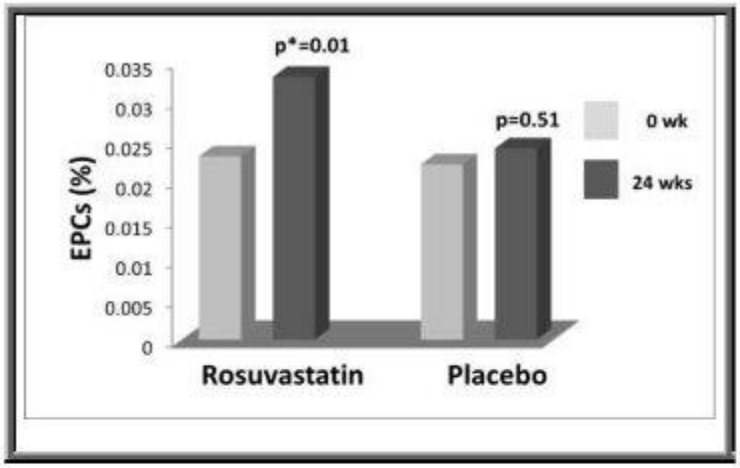


Fig. 2 Correlation between EPCs and markers of inflammation and endothelial dysfunction after 24-weeks of treatment with rosuvastatin in AS.

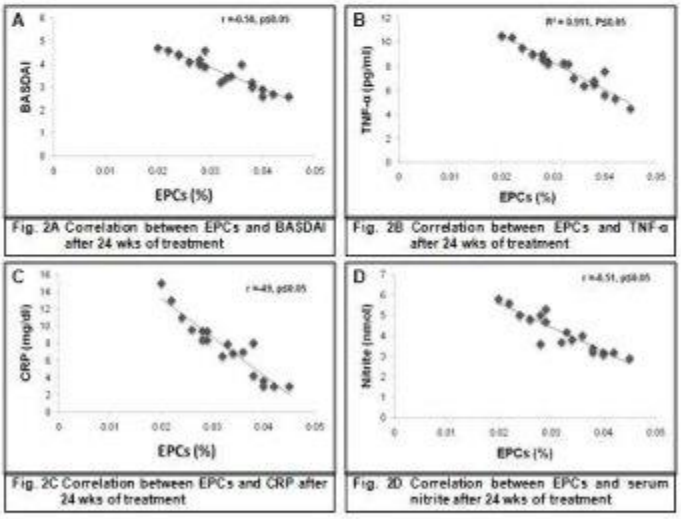


Fig. 2A Correlation between EPCs and BASDAI after 24 wks of treatment

Fig. 2B Correlation between EPCs and TNF-α after 24 wks of treatment

Fig. 2C Correlation between EPCs and CRP after 24 wks of treatment

Fig. 2D Correlation between EPCs and serum nitrite after 24 wks of treatment

BASDAI - Bath Ankylosing Spondylitis Disease Activity Index; TNF-α – tumor necrosis factor-α; CRP - C-reactive protein. p≤ 0.05 statistically significant*

2).

Conclusions: First study to demonstrate that rosuvastatin augments EPC population in AS mediated by lowering pro-inflammatory cytokines, which down regulates adhesion molecules, ESR, CRP and NO

production. The augmentation of EPCs by rosuvastatin may provide novel strategy to prevent cardiovascular events in AS.

ID:633

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

SDLDL PARTICLES ARE ASSOCIATED WITH RESIDUAL INFLAMMATORY RISK IN PATIENTS WITH SEVERE ATEROSCLEROSIS AND OPTIMAL LEVELS OF LDL

POSTER VIEWING SESSION

Leticia A. Gonzalez Jara[1], Maria Fernanda Menares[2], Juan Francisco Bulnes[3], Attilio Rigotti R[4], Marcelo E. Andia[1], Gonzalo Martinez R[3]
[1]Millennium Nucleus Cardio Mr, Biomedical Imaging Center, Radiology, School Of Medicine, Pontificia Universidad Catolica, Santiago, Chile, [2]School Of Medicine, Pontificia Universidad Catolica, Santiago, Chile, [3]Division Of Cardiovascular Diseases, Pontificia Universidad Catolica, Santiago, Chile, [4]Nutrition, Diabetes And Metabolism, School Of Medicine, Pontificia Universidad Catolica, Santiago, Chile

Background and Aims : Background: Elevated hsCRP (>2 mg/dL) is associated with increased cardiovascular risk, even in patients with controlled traditional risk factors. High levels of circulating triglycerides are linked to increased cardiovascular risk, inflammation and to circulating levels of sdLDL, a variant of LDL, considered an emerging risk factor for cardiovascular disease. **Objective:** To evaluate the relationship between sdLDL cholesterol (sdLDL-C) and residual inflammatory risk in a cohort of patients with atherosclerosis under proper medical treatment (average LDL 70 mg/dL, all receiving statins).

Methods: Methods: 47 subjects were analyzed from a prospective cohort of patients with moderate carotid artery disease (NASCET 30-70%). Basal total cholesterol, HDL and triglycerides were evaluated. Levels of lipoprotein-associated cholesterol were calculated using the Sampson formula. Statistical analysis included Mann-Whitney Test, ANOVA, and logistic regression.

Results:

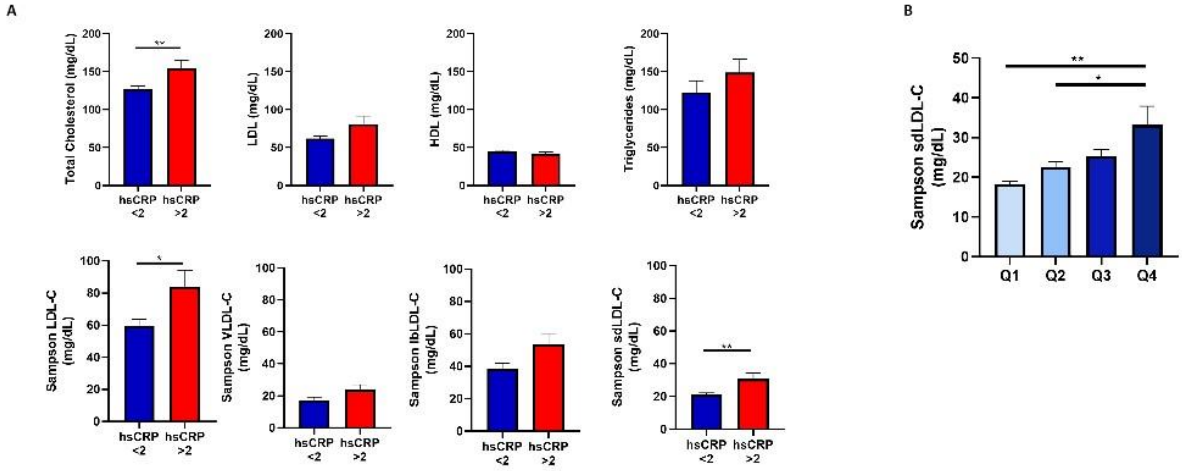


Figure 1: A. Lipid analysis based on circulating levels of hsCRP in a cohort of patients with atherosclerosis and optimal medical treatment. **B.** Cholesterol levels associated with sdLDL according to triglyceride quartiles. Q1(< 85.3), Q2 (85.3-120.5), Q3 (120.6-155.5), Q4 (>155.5). Results are shown as mean ± SEM. *p<0.05. **p<0.01

Results: 38% of the patients presented hsCRP >2 mg/L. This residual inflammatory risk was associated with elevated total cholesterol (p=0.0068), Sampson LDL-C (p=0.02) and Sampson sdLDL-C (p=0.0059), figure 1A. Only sdLDL-C levels were independently associated with elevated hsCRP (p=0.002). When subjects were separated according to triglycerides quartiles (p25%, 85.25; median 120.5; p75% 155.5

mg/dL), the upper quartile showed significantly higher levels of sdLDL when compared to lower quartiles, figure 1B.

Conclusions: Conclusion: sdLDL-C is independently associated with elevated hsCRP in a cohort of patients with moderate carotid artery disease, which might partially explain the residual inflammatory risk. sdLDL levels cannot be managed with statins, unlike LDL, and their management is mostly associated to circulating triglycerides, opening new possibilities for optimizing the treatment of high-risk patients.

ID:642

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

THE RELATIONSHIP BETWEEN NONALCOHOLIC FATTY LIVER DISEASE WITH VISCERAL FAT DEPOTS OF OTHER LOCALIZATION, METABOLIC PARAMETERS AND MARKERS OF RENAL DYSFUNCTION IN PATIENTS WITH OBESITY.

POSTER VIEWING SESSION

Polina E. Erbes, Sofia G. Shulkina, Elena N. Smirnova, Angelica A. Antipova, Natalya A. Koryagina
Therapy, Perm State Medical University named after E. A. Wagner (PSMU) of the Ministry of Healthcare of the Russian Federation., Perm, Russian Federation

Background and Aims : To assess the relationship between non-alcoholic fatty liver disease (NAFLD) with visceral fat, metabolic parameters, markers of renal dysfunction in patients with obesity.

Methods: The study included 105 people aged 44.8±6.4 years. The group №1-patients with NAFLD, BMI 36.1±3.2kg/m². The group №2- without NAFLD with BMI 35.5±3.9kg/m². The TNF, β2 microglobulin, ACRU, IL 6, MCP-1, leptin, resistin and cystatin C was determined by ELISA. GFR was calculated by CKD-EPI formula and cystatin C. The examination of visceral adipose tissue: VAT- measurement at the level of the navel from the inner surface of the rectus abdominis to the posterior wall of the aorta and L4; the thickness of the posterior perirenal fatty tissue and perirenal fatty tissue on both sides.

Results: Fat stores in groups are shown in Table 1. Metabolic parameters and renal markers are presented in Table 2. In the group with NAFLD stage F1 is established in 20% of patients, indicators F-4,2[3,7;5,3]кPa., In the group 2- indicators F-1,7[0,7;3,3] кPa. In group 1 the relationship between F1 and cystatin C (r=0.46), resistin (r=0.7), TG (r=0.39); VAT with ALT (r=0.40); AST (r=0.52); HDL (r=-0.67); TG (r=0.38); MCP-1 (r=0.28). Perirenal fat depot associations with LDL (r=0.40), glucose (r=0.49), ACRU (r=0.43), cystatin C (r=0.28). In a 2 group- associations between the perirenal adipose tissue with TG (r=0.35), cystatin C (r=0.29), MCP-1

(r=0.36).

Table 1. Visceral fat depots in groups (M ± σ)

index	Group 1	Group 2	P
Epicardial fat depot; mm	3.5 ± 1.1	2.5 ± 0.8	P = 0.03
Pericardial fat depot; mm	4.0 ± 1.3	3.0 ± 1.0	P = 0.04
VAT; mm	81.1 ± 17.3	50.6 ± 13.7	P <0.0001
Posterior perenal fat depot on the right; mm	11.1 ± 3.6	7.3 ± 2.2	P <0.01
Posterior perenal fat depot on the left; mm	11.3 ± 5.6	7.7 ± 2.8	P <0.01
Perirenal adipose tissue volume on the right; cm²	15.3 ± 4.4	10.4 ± 3.0	P <0.01
Perirenal adipose tissue volume on the left; cm²	16.6 ± 5.2	10.9 ± 3.1	P <0.01

Note: VAT - measurement at the level of the navel from the inner surface of the rectus abdominis to the posterior wall of the aorta and L4; P is an indicator of reliability.

Table 2. Indicators of hormonal activity of adipose tissue and renal markers in groups (M ± σ)

index	Group 1	Group 2	p
Leptin, ng ml	32.2 ± 15.3	30.5 ± 10.4	P =0.05
Resistin, ng/ml	4.0 ± 1.2	2.3 ± 0.9	P = 0.01
HOMA index	4.6 ± 1.2	1.7 ± 0.4	P <0.001
GFR CKD-EPI ml/min/1.73m²	90.4 ± 11.5	87.2 ± 12.7	P> 0.05
GFR – Hoek ml/min/1.73 m²	87.1 ± 9.8	98 ± 11.0	P = 0.03
Cystatin C in blood, ng/ml	910 ± 120	833 ± 100	p = 0.04
Cystatin C in urine, ng/ml	91.8 ± 67	51.6 ± 34	P <0.01
TNF, pg/ml	0.3 ± 0.01	0.2 ± 0.05	P = 0.05
MCP-1, pg/ml	138.2 ± 55.4	114.1 ± 50.0	P <0.01
IL6, pg/ml	2.3 ± 1.5	0.7 ± 0.5	P = 0.03
albumin/creatinine ratio urine, mg/g	0.9 ± 0.5	0.4 ± 0.2	P = 0.04
β2 microglobulin, μg/ml	1.17 ± 0.6	0.86 ± 0.6	P = 0.04

Note: TNF - tumor necrosis factor, IL 6 - interleukin 6, MCP-1 - monocytic hematoxic factor-1, GFR - glomerular filtration rate, p - reliability of results.

Conclusions: In patients with NAFLD, the parameters of the lipid profile and renal dysfunction deteriorate, which can contribute to the development of atherosclerosis.

ID:645

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

PREVALENCE AND FACTORS ASSOCIATED WITH ASPIRIN PRESCRIBING FOR THE PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE AMONG PATIENTS WITH TYPE 2 DIABETES

POSTER VIEWING SESSION

Surarong Chinwong, Narawith Somrith, Narinthorn Plodkhan, Sinwisuth Sutheechai, Dujrudee Chinwong
Department Of Pharmaceutical Care, Faculty of Pharmacy, Chiang Mai University, Muang Chiang Mai, Thailand

Background and Aims : Cardiovascular disease is a major complication among diabetes mellitus type 2 (DMT2) patients, and guidelines recommend aspirin to prevent cardiovascular complications in DMT2 patients. However, it remains unclear and controversial as aspirin can increase the risk of bleeding. This cross-sectional study aimed to determine the prevalence of aspirin use for primary prevention of cardiovascular disease and investigate the factors associated with aspirin use among patients with DMT2.

Methods: Data were retrospectively collected from medical records in patients diagnosed with DMT2 but no diagnosis of cardiovascular disease treated at a tertiary teaching hospital in northern Thailand from January 1, 2017, to December 31, 2019.

Results: Of 286 patients, 57% were female, mean age of 57.2±11.2 years, 60% being diabetes less than five years, mean HbA1C of 7.1±1.6%, mean plasma glucose of 134.5±38.1, mean 10-year CV risk score of 13.9±9.1%. The CV risk score ≥10% was 57%. The prevalence of aspirin use was 16.78%, 95% confidence interval (CI):12.87-21.59%. Three factors were significantly associated with the use of aspirin for primary prevention of cardiovascular disease among patients with DMT2. Patients with more than five years of diabetes were less likely to receive aspirin (adjusted odds ratio (aOR)=0.23, 95%CI:0.09-0.56, p=0.002); patients with fasting plasma glucose higher than 130 mg/dl were more likely to receive aspirin (aOR=2.18, 95%CI:1.06-4.50, p=0.034); patients with hypertension were more likely to be prescribed aspirin (aOR=2.72, 95%CI:1.07-6.95, p=0.036).

Conclusions: In conclusion, three factors associated with prescribing aspirin for primary prevention were the shorter duration of diabetes, the higher in plasma glucose, and being hypertension.

ID:653

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

VITAMIN D DEFICIENCY AS A RISK FACTOR FOR ARTERIAL HYPERTENSION AND CHRONIC KIDNEY DISEASE IN OBESE PATIENTS.

POSTER VIEWING SESSION

Elena Byvaltseva[1], Sofia G. Shulkina[2], Elena N. Smirnova[2], Vladimir Jelobov[2], Nadezhda Kolomeets[2]
[1]Polyclinc Therapy, Perm State Medical University named after E. A. Wagner (PSMU) of the Ministry of Healthcare of the Russian Feaderation., Perm, Russian Federation, [2]Therapy, Perm State Medical University named after E. A. Wagner (PSMU) of the Ministry of Healthcare of the Russian Federation., Perm, Russian Federation

Background and Aims : To establish a relationship between serum vitamin D levels and risk factors for cardiovascular disease in obese patients of working age.

Methods: The study included 100 people aged 44.8±6.4 years, BMI 33.1±3.2kg/m² without disorders of carbohydrate metabolism, atherosclerosis, arterial hypertension, kidney damage.The level of vitamin D, leptin, resistin, HOMA index, GFRwere investigated. The examination of visceral adipose tissue: the epi- and pericardial fat depots; VAT1 - measurement at the level of the navel from the inner surface of the rectus abdominis to the posterior wall of the aorta and L4; the thickness of the posterior perirenal VAT on the right and left and the area of perirenal fat on both sides.

Results: Fat stores in groups are shown in Table 1.The vitamin D level- 28.4±11.6 ng/ml. Vitamin D deficiency (level<20 ng/ml) - 24% of patients, vitamin D deficiency (level 20-29 ng/ml) - in 46%, optimal values - in 30%. The SBP-125±18.2 mm.Hg, DBP-80.5±9.2 mm.Hg, leptin-19.6[13.3;27.5],HOMA index-2.18[1.1;3.2], cystatin C- 890[810; 940] ng/ml.Correlations of vitamin D with SBP (r=−0.42), DBP (r=−0.30), TG (r=−0.30), HDL (r=0.33), GFR (r=−0.36), cystatin C (r=−0.30)б with epicardial fat (r=−0.40) and perenal fat (r=−0.40). Leptin correlated with pericardial fat (r=0.29), VAT-(r =0.39), perenal (r= 0.32)

and perineal fat depots (r =0.37). Cystatin C had associations with epicardial fat (r=0.32), VAT (r=0.32).

Table 1. Visceral fat depots in groups (M ± σ)

index	Group
Epicardial fat depot; mm	3.5 ± 1.1
Pericardial fat depot; mm	3,5 ± 1.3
VAT; mm	76,2.1 ± 17.3
Posterior perenal fat depot on the right; mm	9.1 ± 3.6
Posterior perenal fat depot on the left; mm	8.3 ± 5.6
Perirenal adipose tissue volume on the right; cm²	12.3 ± 4.4
Perirenal adipose tissue volume on the left; cm²	13.6 ± 5.2

Note: VAT - measurement at the level of the navel from the inner surface of the rectus abdominis to the posterior wall of the aorta and L4; P is an indicator of reliability.

Conclusions: In obese patients, a low level of vitamin D is associated with an increase in markers of metabolic distress, increase BP and a decrease in renal function.

ID:657

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

HETEROPLASMY OF ATHEROSCLEROSIS-ASSOCIATED MITOCHONDRIAL DNA MUTATIONS AND ITS EFFECTS ON RESPIRATION AND VIABILITY OF CYBRIDS.

POSTER VIEWING SESSION

Evgeny Bezsonov[1,2], Elena Zhigmitova (Erdyneeva)[1], Evgeny Borisov[1], Damir Lyukmanov[3], Nelya R. Yakhina[4], Natalia O. Zheleznyak[5], Anastasia S. Vlasova[6], Vasily V. Sinyov[1], Alexander N. Orekhov[1]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P.Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Department Of Biology And General Genetics, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation, [3]«mirea — Russian Technological University», The Federal State Budget Educational Institution of Higher Education, Moscow, Russian Federation, [4]Faculty Of Medical Biology, Pirogov Russian National Research Medical University, Moscow, Russian Federation, [5]Faculty Of Bioingeneering And Bioinformatics, Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [6]Faculty Of Pediatrics, Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

Background and Aims : Atherosclerosis is a disease that is one of the leading causes of death in Russia (as well as in other developed countries). The pathogenesis of atherosclerosis is associated with a thickening of the inner surface of large arteries, leading to a decrease in blood flow and impaired circulation. It should be noted that the final mechanism of atherogenesis at the molecular and cellular levels has yet to be clarified. Mitochondrial mutations can be the first link in a series of pathological changes, including the activation of the immune response, which ultimately lead to the development of atherosclerosis. Recently, an association of certain mitochondrial DNA (mtDNA) mutations with atherosclerosis was found and cybrid lines carrying these mutations were created in our laboratory.

Methods: PCR based detection of heteroplasmy of mtDNA mutations, detection of cellular viability, detection of oxygen consumption. 10 cell lines of cybrids carrying combinations of 10 atherosclerosis-associated mtDNA mutations and THP-1 control line.

Results: The data on cell viability and respiration were determined for 10 cybrids and parental cell lines. Cell lines (cybrids) were ranked on the basis of data on their growth rates and respiration. The percentage of heteroplasmy was determined for each of the 10 selected mitochondrial DNA mutations in each cell line.

Conclusions: The data obtained allowed us to make a conclusion about the effect of mitochondrial mutations associated with asymptomatic atherosclerosis on the rate of cell division and respiration. **The research was supported by Russian Science Foundation, grant # 22-25-00457.**

ID:664

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

REAL-WORLD DATA ON THE COMPARISON OF LDL-C LOWERING EFFECTS BETWEEN ALIROCUMAB AND EVOLOCUMAB

POSTER VIEWING SESSION

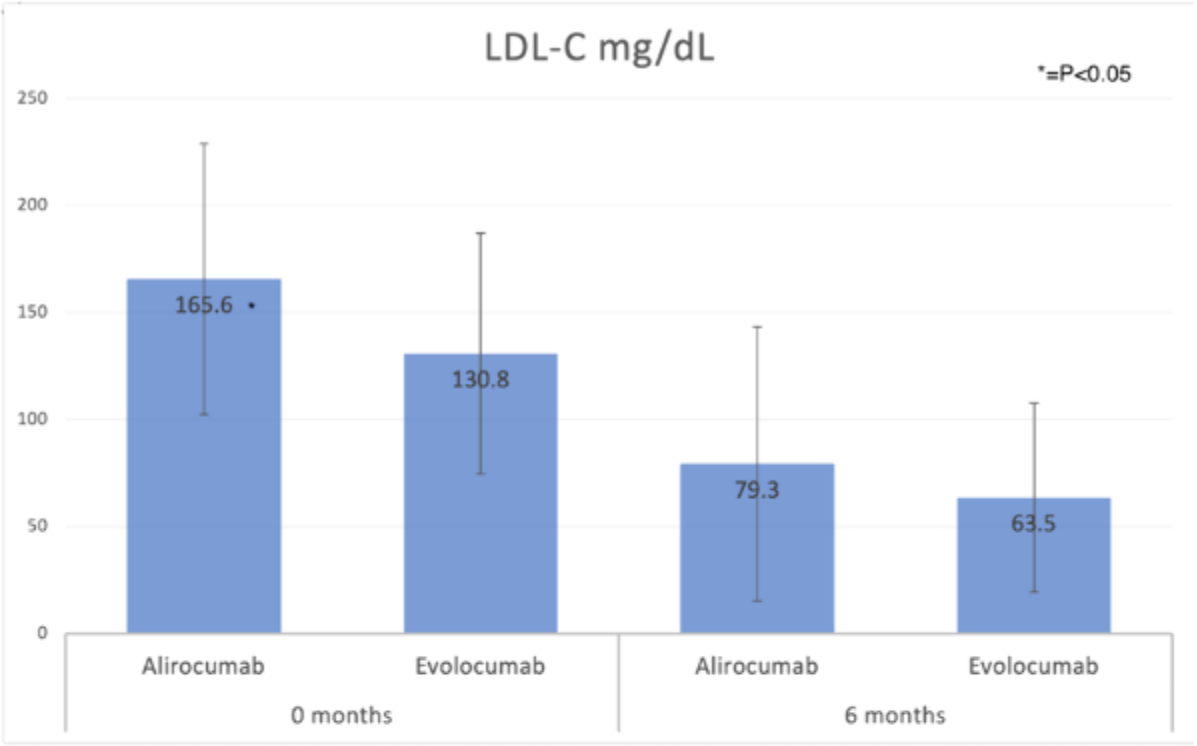
Dai-Yi Lin[1], Chia-Ling Tsai[1], Jen-Yu Chuang[2], Chih-Hung Liang[2], Yi-Han Chen[3], Ya-Hui Chang[4], Hung-I Yeh[1], Chao-Feng Lin[5,6]
[1]Department Of Cardiology, MacKay Memorial Hospital, Taipei, Taiwan, [2]Department Of Medical Education, MacKay Memorial Hospital, Taipei, Taiwan, [3]School Of Public Health, College Of Public Health, Taipei Medical University, Taipei, Taiwan, [4]Department Of Pharmacy, MacKay Memorial Hospital, Taipei, Taiwan, [5]Cardiology Department, MacKay Memorial Hospital, Taipei, Taiwan, [6]Department Of Medicine, MacKay Medical College, New Taipei City, Taiwan

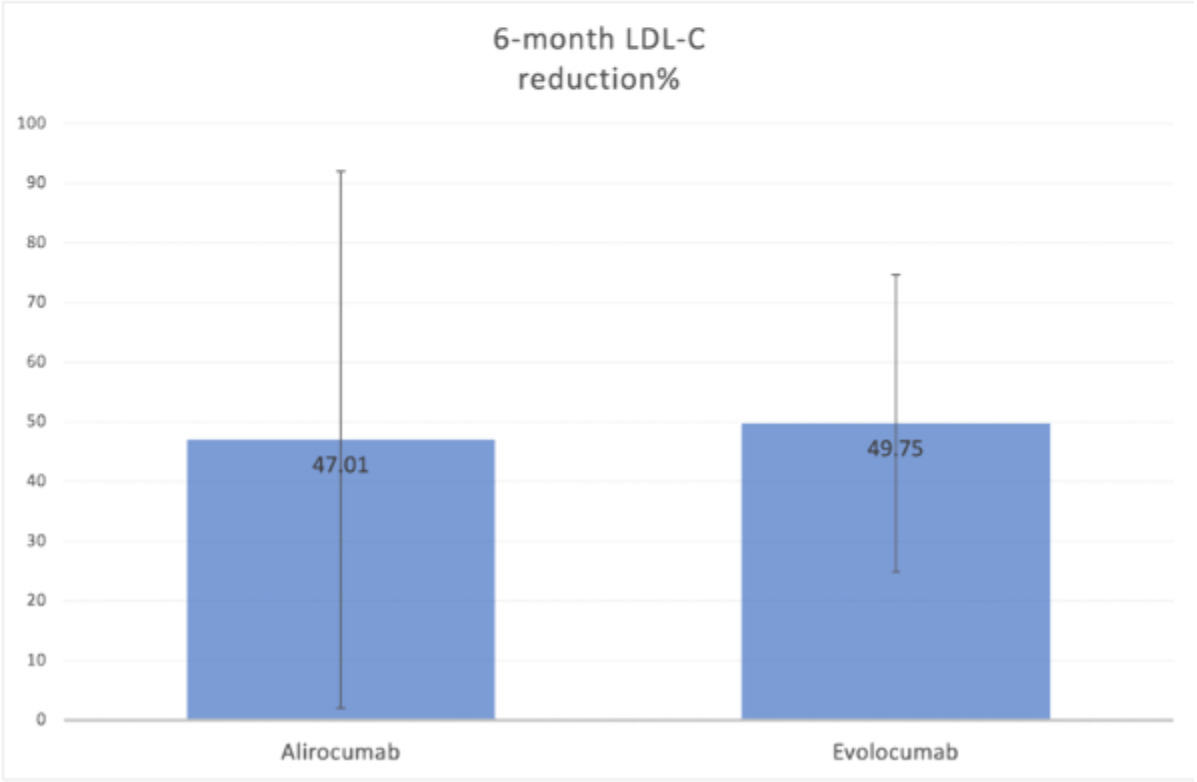
Background and Aims : Despite proprotein convertase subtilisin/Kexin type 9 (PCSK9) inhibitors, alirocumab and evolocumab, have been approved to further reduce serum low-density lipoprotein cholesterol (LDL-C) levels and significantly reduce the risk of atherosclerotic cardiovascular disease in high-risk patients, there are still few studies to compare the LDL-C lowering effects between alirocumab and evolocumab in clinical practice. The present study was aimed to report a real-world data on the comparison of LDL-C lowering effects between the abovementioned 2 PCSK9 inhibitors.

Methods: Between Feb 2018 and Sep 2022, 44 patients, including 22 patients receiving alirocumab and 22 patients receiving evolocumab, were enrolled. Each patient received observation and a 6-month follow-up. The patients' baseline characteristics, prescribed lipid-lowering medications, and serum LDL-C levels were recorded and compared between alirocumab users and evolocumab users.

Results: The baseline demographic data were similar between alirocumab users and evolocumab users, except patients receiving alirocumab had received more frequent ezetimibe treatment at baseline. Compared with patients receiving evolocumab, patients receiving alirocumab had higher baseline serum LDL-C (165.6±63.2 vs. 130.8±56.3 mg/dL, p = 0.046) levels. At 6-month follow-up, the serum LDL-C levels of patients receiving alirocumab were similar to those of patients receiving evolocumab (79.3±64.0 vs. 63.5±44.0 mg/dL, p = 0.481). Additionally, the percentages of LDL-C reduction were also similar between alirocumab users and evolocumab users (52.1%±45.0% vs. 51.5±24.85%). These results were

consistent irrespective of the background intensity of statin use.





Conclusions: Our study showed that the LDL-C lowering effects of alirocumab were similar to those of evolocumab.

ID:680

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

DECREASE SERUM ANTI-OXLDL ANTIBODY IS AN INDEPENDENT MARKER OF PERIPHERAL ARTERIAL DISEASE IN PERITONEAL DIALYSIS PATIENTS

POSTER VIEWING SESSION

Chih-Hsien Wang, Chiu-Huang Kuo, Bang-Gee Hsu
Division Of Nephrology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan

Background and Aims : Autoantibodies to oxidized low-density lipoprotein (oxLDL) has an inverse associated with carotid artery atherosclerosis and predict development of future cardiovascular disease. Peripheral arterial disease (PAD), defined by low ankle-brachial index (ABI), is associated with increased mortality in patients with chronic renal failure. The present study aimed to determine the relationship between serum anti-oxLDL antibody level and PAD in peritoneal dialysis (PD) patients.

Methods: The present cross-sectional, single-center study included 90 PD patients. Serum IgG anti-oxLDL antibody levels were measured using a commercial enzyme immunoassay. ABI values were measured using an automated oscillometric device. Patients with ABIs of <0.9 were categorized into the low ABI group.

Results: In the study, 23 of the 90 patients (25.6%) had low ABIs. The rates of diabetes mellitus ($P = 0.010$) as well as the older age ($P = 0.006$), serum levels of triglyceride ($P = 0.008$), fasting glucose ($P < 0.001$), and C-reactive protein ($P < 0.001$) were higher, while serum levels of anti-oxLDL antibody ($P = 0.008$) were lower in the low ABI group compared with the normal ABI group. The multivariable logistic regression analysis revealed that serum levels of anti-oxLDL antibody (odds ratio [OR]: 0.978, 95% confidence interval [CI]: 0.958–1.000, $P = 0.046$) and C-reactive protein (each 0.1 mg/dL increase, OR: 1.662, 95% CI: 1.151–2.398, $P = 0.007$) were independently associated with PAD in PD patients.

Conclusions: Serum anti-oxLDL antibody level is negatively associated and C-reactive protein is positively associated with PAD in PD patients.

ID:701

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

ADRENAL ABNORMALITIES AND STROKE

POSTER VIEWING SESSION

Hamza Chaudhry[1,2], Tehniyat Baig[1,2], Hooman Kamel[1]
[1]Neurology, Weill Cornell Medicine, New york, United States of America, [2]Neurology, Weill Cornell Medicine- Qatar, Doha, Qatar

Background and Aims : Adrenal lesions are increasingly recognized as a potential cause of hyperaldosteronism and hypercortisolism, with adverse metabolic effects potentially increasing the risk of cardiovascular events. We examined the association of adrenal abnormalities with ischemic stroke and intracerebral hemorrhage (ICH).

Methods: We performed a cross-sectional study using data from the Cornell Acute Stroke Academic Registry (CAESAR), which includes patients with ischemic stroke and ICH at our medical center since 2018. As controls, we included randomly selected patients hospitalized with traumatic brain injury (TBI). We included patients who had undergone an abdominal CT with and without contrast. Imaging reports were reviewed for any mentions of adrenal abnormalities by reviewers blinded to the study hypothesis. We calculated prevalence rates of adrenal abnormalities by group and used logistic regression models, adjusted for demographics and vascular risk factors, to evaluate the association of adrenal abnormalities with ischemic stroke and ICH, in reference to those control patients with TBI.

Results: Among 75 IS patients, 75 ICH patients, and 75 TBI controls, adrenal abnormalities were found in 12% of the TBI patients, 13% of the ICH patients, and 15% of the IS patients (P = 0.89). In multiple logistic regression models, adrenal abnormalities were not associated with ischemic stroke (OR, 1.1; 95% CI, 0.4-3.0) or ICH (OR, 1.1; 95% CI, 0.4-2.9).

Conclusions: We found that patients with ischemic stroke or ICH did not have a higher prevalence of adrenal abnormalities than control patients. Future studies may be warranted to further investigate the role of occult hypercortisolism and hyperaldosteronism in stroke risk.

ID:682

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

LIPOPROTEIN(A) ASSOCIATED WITH ARTERIAL STIFFNESS BY CARDIO-ANKLE VASCULAR INDEX IN PERITONEAL DIALYSIS PATIENTS

POSTER VIEWING SESSION

Chih-Hsien Wang, Chiu-Huang Kuo, Bang-Gee Hsu
Division Of Nephrology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan

Background and Aims : Arterial stiffness predicting future cardiovascular disease. Elevated lipoprotein(a) [Lp(a)] was independently associated with the risk of cardiovascular events in chronic kidney disease. Cardio-ankle vascular index (CAVI) is a marker of arteriosclerotic disease and is associated with cardiovascular events. The aim of this study is to examine the relationship between serum Lp(a) levels and arterial stiffness measuring by CAVI in peritoneal dialysis (PD) patients.

Methods: Eighty-six adult PD patients who received regular PD for more than 3 months were enrolled in this study. CAVI values was derived using the waveform device (VaSera VS-1000). Left or right CAVI values that were > 0.9 were included in the high CAVI group. Serum Lp(a) levels were measured using a commercial enzyme-linked immunosorbent assay kit.

Results: Among 86 PD recipients, 35 patients (40.7%) were in the high CAVI group. Compared with PD patients in the normal CAVI group, PD patients in the high CAVI group had higher serum total cholesterol ($P = 0.003$), triglyceride ($P = 0.044$), C-reactive protein ($P < 0.001$), and Lp(a) levels ($P < 0.001$), while lower serum albumin ($P = 0.026$) levels. Multivariate logistic regression analysis, serum Lp(a) level (Odds ratio [OR]: 1.022, 95% confidence interval [CI]: 1.011–1.034, $P < 0.001$), total cholesterol (OR: 1.030, 95% CI: 1.000–1.061, $P = 0.047$), and C-reactive protein (each 0.1 mg/dL increase, OR: 1.200, 95% CI: 1.001–1.438, $P = 0.049$) were the independent predictors of arterial stiffness in PD patients.

Conclusions: Serum Lp(a) level was proved to be involved in the pathogenetic process of arterial stiffness in PD patients.

ID:684

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

INTERACTION BETWEEN HOMOCYSTEINE, ANTIOXIDANTS AND LIPIDS IN PATIENTS WITH CAROTID ATHEROSCLEROSIS

POSTER VIEWING SESSION

Manana Akhvlediani[1], Dudana Gachechiladze[2], Marika Emukhvari[1], Tamar Kvantaliani[3], Nino Zabakhidze[4]
[1]Clinical Laboratory, Todua Clinic, Tbilisi, Georgia, [2]Ultrasound, Todua Clinic, Tbilisi, Georgia, [3]Kardiology, Clinic on Lars, Tbilisi, Georgia, [4]Clinical Lboratory, Todua Clinic, Tbilisi, Georgia

Background and Aims : The purpose of this study were find relationship between homocysteine, total antioxidant status(TAS), superoxide dismutase(SOD), glutation peroxidase(GPX) and lipids in patients with carotid atherosclerosis.

Methods: 89 patients with ACA (age 59.4±1.7 years) were divided into 2 groups. Group I comprised 51 patients, with hemodynamically insignificant stenosis of CA (<50%) and IMT 0.95±0.04mm. Group II 38 patients with hemodynamically significant stenosis (>50%), IMT was 1.1±0.1mm. Control group 49 healthy patients.

Results: In group I Correlation was positive(from r=0.500 to r=0.628). Homocysteine increased up to 17.0±0.3 mkmol/l. TAS up to 2.20±0.03mmol/l, SOD 280.2±0.3E/L. Tchol, LDL were 6.24±0.14 and 4.8±0.15 mmol/l. The relation between these parameters and CA stenosis were positive(from r = 0.473, to r = 0.533). HDL 1.11±0.04 mmol/l and GPX 3423.2±1.1E/L. The correlation between HDL, GPX , CA stenosis and IMT was negative (r= - 0.433,r = - 0.401, r = - 0.452). In Group II, The homocystein was 24.0±0.3 mkmol/l, TAS level 2.4 ±0.03mmol/l SOD 293.1±0.4E/L, Tchol 6.97±0.04 and LDL 5.63±0.05 mmol/l. Correlation between these parameters and CA stenosis was positive(r= 0.505, r = 0.621). HDL was 0.84±0.02mmol/l, GPX 3493.1±0.7E/L. Correlation between HDL, CA stenosis and IMT was negative(r = -0.531, r = -0.491).

Conclusions: Taking into consideration the result obtained, we think it is possible to use positive correlation between lipids, D dimer, homocystein, TAS and SOD, also negative correlation between HDL,GPX and the degree of CA stenosis, as the markers of development of carotid atherosclerosis in patients with carotid atherosclerosis

ID:688

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

ASSOCIATION OF SIRT6 SNP RS107251 WITH HYPOECHOIC CAROTID PLAQUE: AN EXPLORATORY STUDY

POSTER VIEWING SESSION

Ana Kolakovic[1], Tamara Djuric[1], Igor Koncar[2], Ivan Zivotic[1], Ana Djordjevic[1], Maja Zivkovic[1]
[1]Department Of Health And Environment, Laboratory For Radiobiology And Molecular Genetics, University Of Belgrade, Belgrade, Serbia, Vinca Institute of Nuclear Sciences -National institute of the Republic of Serbia, University of Belgrade, Belgrade, Serbia, Belgrade, Serbia, [2]Clinic For The Vascular And Endovascular Surgery, Clinical Centre of Serbia, Medical Faculty, University of Belgrade, Belgrade, Serbia, Belgrade, Serbia

Background and Aims : As a member of sirtuin family of class III histone deacetylase enzymes, SIRT6 has been involved in all key pathways that are (dis)regulated during atherogenesis. Its multiple effects mostly exert by deacetylating histone 3 at the promoter region of its target genes including those regulating DNA damage, telomere maintenance, aging, inflammation, cell proliferation, apoptosis, glucose, and lipid metabolism. Recent study has shown that overexpression of SIRT6 in mice model of unstable carotid plaque, promotes angiogenesis and intraplaque hemorrhage. SIRT6 SNP rs107251 has been previously associated with increased risk for carotid plaque presence, the number of plaques, and the total plaque area measured by ultrasound. The study aimed to examine whether rs107251 SNP is associated with different, ultrasonographically defined plaque phenotypes in patients with advanced carotid atherosclerosis.

Methods: Our study group comprised 298 patients with advanced atherosclerosis (202 hyperechoic and 96 hypoechoic (dominantly echolucent plaques). Genotyping for rs107251 C/T was performed by real-time PCR using Taqman ® technology.

Results: We have found a significant and independent association of rs107251 C/T variant with presence of hypoechoic plaque, according to the T allele as a dominant model with an adjusted (OR=1.91, 95 % CI 1.03-3.55, p=0.04) to gender, BMI, total cholesterol, hypertension, and smoking status.

Conclusions: Our findings indicate that SIRT6 rs107251 might impact the development of hypoechoic human carotid plaque phenotype in patients with advanced carotid atherosclerosis.

ID:691

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

BODY COMPOSITION, LIPIDS AND ADIPOKINE PROFILE IN YOUNG OVERWEIGHT AND OBESE INDIVIDUALS

POSTER VIEWING SESSION

Vasilii S. Chulkov[1], Elena S. Gavrilova[2], Vladislav Chulkov[1], Ekaterina D. Pankova[2], Elena E. Minina[3], Elizaveta A. Lenets[1], Polina E. Tkachenko[2], Sergei A. Martynov[1]
[1]Faculty Therapy Department, South Ural State Medical Universiry, Chelyabinsk, Russian Federation, [2]Policlinic Therapy And Clinical Pharmacology, South Ural State Medical Universiry, Chelyabinsk, Russian Federation, [3]Faculty Of Pediatrics Named After N.s. Tyurina, South Ural State Medical Universiry, Chelyabinsk, Russian Federation

Background and Aims : Aim. To compare body composition, lipids and adipokine levels in young individuals with normal weight, overweight and obesity.

Methods: . Study design: a cross-sectional study. The study included 254 patients. Patients were divided into two groups: gr. 1 - individuals with normal body weight (n = 175), aged 31.8 ± 7.1 years; gr. 2 - individuals with overweight/obesity (n = 79), aged 36 ± 7.0 years. Anthropometric data, body composition parameters, blood levels of lipids and adipokines were compared among two groups. MedCalc statistical software package (2021). $p<0.05$ were taken as statistically significant.

Results: . Individuals overweight/obese had higher levels of systolic BP, visceral fat percentage and total fat percentage compared to normal-weight subjects. We found that subjects in the overweight/obese group had the highest levels of triglycerides and LDL-C ($p < 0.05$). Adiponectin and resistin levels in the overweight/obese subject group were significantly lower ($p < 0.05$). Plasma levels of leptin and PAI-1 were not different among the two groups.

Conclusions: . In overweight/obese young individuals, adipokine imbalance along with traditional risk factors could be a good predictor of cardiovascular and metabolic risk assessment.

ID:692

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

PERCEIVED STRESS, LOW PHYSICAL ACTIVITY, AND PREVALENCE OF OBESITY IN POLICE OFFICERS

POSTER VIEWING SESSION

Miroslaw Janczura[1], Rafal Rosa[2], Jerzy Dropinski[3], Katarzyna Kotula-Horowitz[4], Andrzej Stanisz[5], Teresa Domagała[6]
[1]Clinical Department Of Thoracic And Oncological Surgery, Pulmonary Rehabilitation Unit, Faculty of Health Sciences, Jagiellonian University School of Medicine,, Krakow, Poland, [2]Department Of Anesthesiology And Intensive Care, Health Care Centre of the Ministry of the Interior and Administration, Krakow, Poland, [3]Immunology And Hypercoagulability Outpatient Department, Jagiellonian University, Kraków, Poland, [4]Department Of Internal Medicine, Health Care Centre of the Ministry of the Interior and Administration, Krakow, Poland, [5]Department Of Bioinformatics And Telemedicine, Jagiellonian University School of Medicine, Krakow, Poland, [6]Medical Biochemistry, Jagiellonian University School of Medicine, Kraków, Poland

Background and Aims : Police work is exposed to more stressors than other occupations. Associations between perceived stress and metabolic syndrome (MetS) and physical activity in police officers were investigated.

Methods: Cross-sectional data from a cohort of non-diabetic subjects (n=233; 19F; aged 27 - 58 years) were analysed. MetS was consistent with IDF criteria, perceived stress with Cohen's 10-item Perceived Stress Scale. The International Physical Activity Questionnaire-Long Form (IPAQ-LF) was used to evaluate a subject's estimated metabolic equivalent of Task (MET), based on 5 select domains of physical activity. Non-parametric (Mann–Whitney U, Kruskal–Wallis) tests, and univariate linear analyses were applied.

Results: Obesity was established in 100 (42.92%), hypertension in 111 (47.44), whereas MetS in 104 (44.63%) study subjects. The median [interquartile range] level of perceived stress was also significantly higher in the MetS subjects, as compared to the non- MetS ones (18.00 [15.00–22.00], and 16.00 [12.00–20.00], p=0.02). Perceived stress was positively associated with waist circumference (B=0.326, p=0.03), blood pressure (B=0.622 and B=0.369, p=0.01) for systolic and diastolic, respectively. Negative associations were established between waist circumference and leisure-time (B=−0.074, p=0.04), total walking (B=−0.032, p=0.02), and total (B=−0.013, p=0.03) physical activity. Similar associations between those domains of physical activity and plasma triglycerides level were also observed (p=0.04, p=0.03 and p=0.02). No associations were established between the select domains of physical activity and other variables, e.g. systolic (diastolic) blood pressure, glucose, HDL cholesterol.

Conclusions: Perceived stress, and low physical activity promoted obesity in police officer.

ID:696

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

ASSOCIATION OF NEUROPHYSIOLOGICAL PARAMETERS AND NEUROLOGICAL DEFICIENCY IN ATHEROSCLEROTIC CAROTID DISEASE

POSTER VIEWING SESSION

Nikita Solianik, Igor Suchkov, Alexander Pshennikov, Roman Zorin, Roman Kalinin, Andrey Egorov
Vascular Surgery, ryazan state medical university, Ryazan, Russian Federation

Background and Aims : Carotid atherosclerosis is the main reason about 20–30 % of strokes. One-fifth of ischemic strokes affect the vertebrobasilar area. The aim of the study was to assess the relationship of neurological deficit and changes of neurophysiological parameters of the brain in carotid atherosclerosis.

Methods: This retrospective, single-center study enrolled patients with carotid atherosclerosis. Thirty-five patients divided into groups based on severity of cognitive performance and the degree of stenosis. The patients had spectral analysis and analysis of the coherence function of the electroencephalogram, cognitive evoked potentials P300, and heart rate variability. For determination of association between signs and severity of the disease carried out using neural networks.

Results: The patients divided on 2 groups by use cluster analysis based on parameters of neurological status and degree of stenosis in the selected patients. For assessment of significance of indicators, it ranked in descending order of their importance. In the group of indicators with high prognostic significance, the characteristics of the cognitive evoked potential has a prevalence in 40%, the second place was taken by the indicators of the cross-correlation function of the EEG (30%), then the spectral characteristics of the EEG (20%) and HRV (10%).

Conclusions: Search of predisposing factors for development of neurological disorders is important for patient's treatment and changing quality of life, social adaptation. This allows us to single out the most significant neurophysiological parameters of neurological functions insufficiency, which primarily include the indicators of the P300 cognitive evoked potential.

ID:741

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-05 Extracellular matrix and calcification*

REGULATION OF MDM2 E3 LIGASE-DEPENDENT VASCULAR CALCIFICATION BY MSX1/2

POSTER VIEWING SESSION

Duk-Hwa Kwon[1], Nakwon Choe[1], Sera Shin[1], Juhee Ryu[2], Yongwoon Lee[1], Anna Jeong[1], Yun-Gyeong Lee[1], Eun-Mi Kim[1], Young-Kook Kim[3], Hyun Kook[1]
[1]Pharmacology, Chonnam National University Medical School, Hwasun, Korea, Republic of, [2]College Of Pharmacy, Kyungpook National University, Daegu, Korea, Republic of, [3]Biochemistry, Chonnam National University Medical School, Hwasun, Korea, Republic of

Background and Aims : Calcium deposition to the vascular smooth muscle matrix, or vascular calcification, makes vessels rigid and increases morbidity and mortality in patients with cardiovascular and renal diseases. Previously, we reported that histone deacetylase (HDAC) 1 prevents vascular calcification, whereas its E3 ligase, mouse double minute 2 homolog (MDM2), induces vascular calcification by repression of HDAC1. The regulatory mechanism for this action of MDM2 remained unclear. In the present study, we investigated whether MDM2-induced vascular calcification is dependent on the ubiquitination activity of MDM2 and determined the upstream regulator of MDM2.

Methods: We generated vascular smooth muscle cell (VSMC)-specific conditional MDM2 knockout mouse and three different transgenic mouse lines, TgMDM2 WT, TgMDM2 Y489A and TgMDM2 ΔR to observe effects vascular calcification.

Results: Using cellular models and transgenic mice, we confirmed that E3 ligase activity is required for the vascular calcification. By promoter mapping analysis, we found that both Msx1 and Msx2 bound to the MDM2 promoter region, which resulted in the transcriptional activation of MDM2. Both Msx1 and Msx2 were increased in mouse models of vascular calcification and in calcified human coronary artery. Msx1 and Msx2 potentiated vascular calcification in cellular or mouse models in an MDM2-dependent manner.

Conclusions: Our results establish a novel role for MSX1/MSX2 in the transcriptional activation of MDM2 and a resultant increase in MDM2 E3 ligase activity during vascular calcification.

ID:745

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

POINT OF CARE TESTING FOR HYPERLIPIDEMIA :LIMITATIONS AND BENEFITS

POSTER VIEWING SESSION

Tania Martinez[1], Bernardo M.M. Almeida[1,2], Anita Saldanha[1], Carolina Q. Cardoso[1], Marileia Scartezini[1], Lucca Malucelli[1], Caio C. Klosovski[1], Ana Paula P. Margeotto[1], Andre L. Gasparoto[1], Abel Pereira[1], Tereza Bellincanta[1]
[1]Nephrology, Hospital Beneficiencia Portuguesa de Sao Paulo, Sao Paulo, Brazil, [2]Nephrology, BP - Hospital Beneficiência de São Paulo, Sao Paulo, Brazil

Background and Aims : Point od Care testing has become a form of technique universally used not only for epidemiological research but as follow up control for patients under treatment. It has limitations aswell as to presenting results only between two values,a lower and an upper value limits.Even so,focusing in its official purposes ,it is a most important way of mapping epidemiologically a country or a prefixed region,in which Brazil can be a good example for profiting from a large scale screening.

Methods: In this study 8547 individuals ,ages from 20 to 93 years old ,went spontaneously to the collection points for lipid profiles results from the five regions in Brazil.The particular technique was performed using a colorimetric test strip by the Hilab equipment that connects to the internet of things technology that recognizes resultsby each the unique QR code that is sent via cloud to the central resarch center.Linear ranges(mg-ml):Cholesterol and Triglycerides from 120 to 400 and HDLc 20 to 100.Statistical tests applied:chi square,Student t and ANOVA.Results

Results: Focusing in limitations ,the numbers of participants below(B) and upper(U) the range limits were, in order of numbers and percentiles:Total Cholesterol-B: 1703 and 19,94;U-35 and 0.41%.Triglycerides-B:1692 and 19,81%;U-862 and 10,09%.HDLc-B 111 and 1,3%;U-135 and 1,58%. Benefits:awareness for Familiar Hypercholesterolemia and Familiar Chylomicronemia Syndrome,the limitations can turn out to be a benefit for prevention of cardiovascular diseases and pancreatitis.

Conclusions: Point of care tests for lipid profile can be not only a screening for dyslipidemias but an important signalizer too of genetic hyperlipidemias such as Familial Hypercholesterolemia and Familial Chylomicronemia Syndrome .

ID:873

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MANAGEMENT OF LIPID-LOWERING TREATMENT IN PATIENTS WITH ISCHEMIC STROKE IN CATALONIA AND BALEARIC ISLANDS, SPAIN. MALIC STUDY PHASE 2. PRELIMINARY RESULTS.

POSTER VIEWING SESSION

Angels Pedragosa[1], Carolina Guerrero[1], Rosa Borrallo[1], Marta Mauri[1], Amelia Boix[2], Xabi Urra[3], Laura Redondo[4], Ana Rodriguez-Campello[5], David Canovas[6]
[1]Internal Medicine, Consorci Sanitari de Terrassa, Terrassa, Spain, [2]Neurology, Hospital Universitari Son Espases, Palma, Spain, [3]Neurology, Hospital Clínic Barcelona, Barcelona, Spain, [4]Internal Medicine, Hospital Universitari de Vic, Vic, Spain, [5]Neurology, Hospital del Mar, Barcelona, Spain, [6]Neurology, Consorci Corporació Sanitaria Parc Taulí, Sabadell, Spain

Background and Aims : Patients with non-cardioembolic ischemic stroke or TIA have a very high-risk with LDL-C target goal to<55mg/dL and achieving a 50% reduction from baseline.
Our main objective is to know the lipid-lowering treatment received in this group of patients.

Methods: Observational, epidemiological, cross-sectional, multicenter study of in-hospital care performed with the collection of 30 consecutive cases per center of patients with non-cardioembolic ischemic stroke or TIA.

Results: Since July 2021, 250 patients have been included from 14 sites. The mean age was 71(36-93) years, 63% men.
History of vascular risk factors and previous vascular disease: 55,5% smokers, 77% hypertensive, 39% diabetics, 60% dyslipidemia, 10% obesity, 11% ischemic heart disease, 16% ischemic stroke or TIA, 0,8% hemorrhagic stroke, 10% peripheral arterial disease and 12% chronic kidney disease.
Previous lipid-lowering treatment: 44% statins, 4% ezetimibe, 3,6% fibrates.
At admission, 85% had LDL-C determined [mean 104 (35-230)mg/dL]. 93% LDL-C > 55mg/dL, 70% LDL-C >100mg/dL.
89% high-potency statin (atorvastatin or rosuvastatin at medium-high doses), 11% associated ezetimibe, 4% fibrates and in a single case alirocumab were started.

Conclusions: The majority of patients with non-cardioembolic ischemic stroke and TIA are outside of LDL-C therapeutic targets at the time of the acute event. After, few patients had combined lipid-lowering treatment despite the fact that 70% had LDL-C levels> 100mg / dL.
It's necessary to shift the paradigm for very high-risk patients from 'an intensive statin therapy first' approach to an 'intensive lipid-lowering therapy' approach.

ID:807

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

TELOMERE LENGTH IN ATHEROSCLEROTIC LESIONS OF HUMAN AORTIC INTIMA

POSTER VIEWING SESSION

Igor A. Sobenin[1], Zukhra B. Khasanova[1], Taisiya V. Tolstik[2], Ulyana S. Zotova[2], Alexander M. Markin[2], Natalya A. Doroshchuk[3]
[1]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [2]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [3]Laboratory Of Pathomorphology Of Cardiovascular Diseases, National Medical Research Center of Cardiology, Moscow, Russian Federation

Background and Aims : The early studies of atherosclerotic plaques have demonstrated that the cells in advanced atherosclerotic lesions display changes of senescence, and telomere shortening is generally believed to be the molecular mechanism that triggers the onset of cellular senescence. This study was undertaken to test the hypothesis on the association of telomere length and the type of atherosclerotic lesion of human aorta.

Methods: Nine autopsy samples of human thoracic aorta were divided into zones differing by the type of atherosclerotic lesion (unaffected areas - UA, initial lesions, fatty streaks, lipofibrous and fibrous plaques). Up to 25 zones were obtained from each autopsy sample, and DNA was isolated from intimal layer. Telomere length was measured by qPCR with SYBR Green I.

Results: Initial lesions did not differ from unaffected areas by telomere length (P=0.89 vs UA), but the 1.30-fold increase of telomere length was observed in fatty streaks (P=0.040), the 1.22-fold increase in lipofibrous plaques (P=0.13), and the further 1.67-fold increase in fibrous plaques (P=0.033). There was a significant relationship between the telomere length and the progression of atherosclerotic lesions (regression analysis: adjusted R-square 0.750, P<0.001; ANOVA: F= 99.87, P<0.001).

Conclusions: Positive association telomere length with atherosclerosis progression can be explained at least by migration of smooth muscle and pericyte-like cells and macrophages into the zone of emerging atherosclerotic lesions, by the resulting changes in the cellular composition of the intima, and also by inhibition of the functional activity of cells in advanced atherosclerotic lesions. This study was supported by Russian Ministry of Health, Project 121031300062-9

ID:862

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

THE ASSOCIATION OF PANCREATIC STEATOSIS WITH TYPE 2 DIABETES AND HYPERTENSION

POSTER VIEWING SESSION

Yurgita R. Varaeva[1], Antonina V. Starodubova[1,2], Svetlana D. Kosyura[2], Tamara D. Kiknadze[1], Elena N. Livantsova[1], Natalia V. Polenova[1], Svetlana A. Derbeneva[1], Georgiy E. Leonov[1]
[1]Department Of Cardiovascular Pathology And Diet Therapy, Federal Research Centre for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation, [2]Internal Diseases Department, Pirogov Russian National Research Medical University, Moscow, Russian Federation

Background and Aims : According to published international data, Pancreatic Steatosis (PS) is associated with visceral fat accumulation, Obesity, and Type 2 Diabetes. This research project's aim was to compare the rates of Type 2 Diabetes and Hypertension in PS and non-PS groups in Russian population.

Methods: 64 obese (mean BMI 41.35±0.92 kg/m^2) participants (26 males and 38 females) with mean age 48.12±1.17 years old were recruited: 31 in PS-group and 33 in non-PS-group. In addition, participants' medical histories were collected. The ultrasound scan and computer tomography were used for the PS diagnostics via the assessment of pancreas density compared to liver and spleen tissue density. The 40 HU pancreas tissue CT-density was used as cut-offs for the PS diagnosis. Grant information: Research work carried out within the state assignment of the Ministry of Education and Science of the Russian Federation (N 0410-2022-0005 and N 0410-2020-0013).

Results: The groups were comparable according to their age, body weight, BMI, fat mass, and gender distribution. The prevalence of type 2 diabetes was significantly higher in the PS-group (66.7% compared to 35.5%, p-value 0.040), the same as Hypertension rates (93,9% compared to 51.6%, p-value 0.004). Also, Hypertension negatively correlated with the pancreas tissue CT-density (R^2 -0.272, p-value 0.003).

Conclusions: In the Russian population, Type 2 Diabetes and Hypertension rates are significantly higher among obese patients with Pancreatic Steatosis. In addition, Hypertension rates negatively correlate with pancreas CT-density.

ID:861

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-06 Gender and cardiovascular risk*

SEX DIFFERENCES IN SUBCLINICAL ATHEROSCLEROSIS

POSTER VIEWING SESSION

Ying Jie Chee, Rinkoo Dalan
Endocrinology, Tan Tock Seng Hospital, Singapore, Singapore

Background and Aims : There is emerging evidence demonstrating the sex dichotomy in atherosclerotic cardiovascular diseases (ASCVD) among individuals with diabetes mellitus (DM). However, the mechanisms are unclear. We aimed to evaluate the impact of sex on the associations and possible mechanisms modulating ASCVD risk factors and subclinical atherosclerosis in DM.

Methods: We recruited 398 individuals from a diabetes centre in Singapore. Carotid ultrasonography, applanation tonometry, endothelial function test, cholesterol efflux studies, oxidative stress index (osi) and high-sensitivity C-reactive protein (hsCRP) were assessed. Subclinical atherosclerosis (SA) was defined as maximal carotid intima-media thickness (CIMT) > 0.8mm or presence of plaques or both. Multiple logistic regression was used to evaluate associations between ASCVD risk factors and SA.

Results: There were 196 men and 202 women (mean age 54.2 and 54.5 years respectively). CIMT and SA were higher in men despite having lower osi, hsCRP and higher cholesterol efflux capacity as compared to women (table 1). Using multiple logistic regression, age, systolic blood pressure (SBP), hsCRP and non-high-density lipoprotein cholesterol were associated with SA in men. In women, age, SBP and osi were associated with SA, after adjusting for body mass index, waist circumference, HbA1c, cholesterol efflux capacity and statin

use.

Table 1: Comparison between males and females

	Total (N = 398)	Male (N=196)	Female (N=202)	p-value
Age (years)	54.4 (10.4)	54.2 (10.2)	54.5 (10.7)	0.82
BMI	26.9 (24.1-30.2)	26.4 (24.0-29.5)	27.4 (24.5-30.5)	0.14
SBP (mmHg)	132 (122-141)	131.5 (122.3-140)	132 (122-142.5)	0.57
DBP (mmHg)	75 (70-80.5)	77 (71.5-82.5)	73.5 (68.5-78.5)	0.61
Total cholesterol (mmol/L)	4.2 (3.7-4.9)	4 (3.5-4.7)	4.4 (3.9-5.0)	0.38
LDL cholesterol (mmol/L)	2.4 (2.0-2.9)	2.3 (1.9-2.8)	2.4 (2.1-3.0)	0.013
HDL cholesterol (mmol/L)	1.1 (1.0-1.2)	1.0 (0.9-1.2)	1.1 (1.0-1.4)	0.000
Non-HDL cholesterol (mmol/L)	3.0 (2.6–3.7)	3.0 (2.5–3.7)	3.2 (2.6–3.8)	0.053
Triglyceride (mmol/L)	1.3 (1.0-2.0)	1.3 (1.0-2.0)	1.4 (1.0-2.0)	0.73
HbA1c (%)	8.4 (7.2-9.7)	8.6 (7.2-9.6)	8.3 (7.0-9.7)	0.55
Oxidative stress index	1.00 (0.85-1.15)	0.94 (0.80-1.07)	1.06 (0.91-1.23)	< 0.000
hsCRP (mmol/L)	1.8 (0.8-4.0)	1.2 (0.5-3)	2.4 (1.1-4.7)	< 0.000
Statin use	287 (76.7)	135 (73.8)	152 (80)	0.13
CIMT (mm)	0.617 (0.55-0.70)	0.650 (0.55-0.70)	0.617 (0.55-0.70)	0.004
Presence of subclinical atherosclerosis	191 (50.9)	106 (57.3)	85 (44.7)	0.015
Reactive hyperaemia index	0.65 (0.46-0.83)	0.65 (0.46-0.81)	0.66 (0.45-0.86)	0.64
Cholesterol efflux capacity	8.50 (4.83-12.01)	9.80 (5.48-12.69)	7.78 (4.34-11.04)	0.018

Values are mean (SD) or median (IQR) or N (%). Chi-square (for categorical variables) and independent sample Student's/Mann-Whitney test (for continuous variables)

Conclusions: There appears to be distinct mechanisms mediating SA between men and women with DM. In men, atherosclerosis may be driven to a larger extent by inflammation, whereas oxidative stress may be more pivotal in women. An individualized, sex-based approach that targets different aspects of atherosclerosis may be required to optimize ASCVD risk.

ID:859

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ARTERIAL STIFFNESS INDICATORS AS MARKERS OF CARDIOVASCULAR PATHOLOGY IN PEOPLE OF DIFFERENT AGE GROUPS

POSTER VIEWING SESSION

Valentin Oleynikov, Angelina Khromova, Kristina Polezhaeva, Ksenia Pavlenko, Luidmila Salyamova, Nadezhda Burko
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : to identify parameters of arterial stiffness that can predict the development of cardiovascular diseases in individuals with a relatively low risk in different age cohorts.

Methods: the study included 55 healthy individuals (mean age 49.9±8.9 years) and 101 patients with CAD without a history of cardiovascular pathology (mean age 51±9.2 years). All persons included in the study were divided by age: 30-40 years old and 40-50 years old. The state of the common carotid arteries (CCA) was assessed using RF technology with an ultrasound scanner MyLab 90 "Esaote", Italy, with the registration of the following parameters: intima-media thickness (IMT), local pulse wave velocity (PWV), transverse distensibility coefficient (DC) and stiffness index β.

Results: In the group of 30-40 years old, in healthy individuals IMT was 409.9(95%CI 381.2;491.3) μm, PWV - 5.1(95%CI 4.6;6.9) m/s, DC - 0.04(95%CI 0.03;0.05) 1/kPa, β index - 4.9(95%CI 4.1;6.8), in patients with CAD: IMT - 599.1(95%CI 498.3;634.2) μm (p=0.005), PWV - 6.4 (95% CI 5.7;7.8) m/s (p=0.027), DC - 0.03(95%CI 0.01;0.04) 1/kPa (p=0.009), β index - 7.8(95%CI 6.1;8.9) (p=0.006). In a cohort of 40-50 years in healthy, BMI was 483.4(95%CI 441.6;587.7) μm, PWV - 5.6(95%CI 4.7;7.1) m/s, DC - 0.03 (95%CI 0.02;0.04) 1/kPa, β index - 5.8(95% CI 4.7;6.9), in patients: TCIM - 642.3(95%CI 591.3;691.7) μm (p=0.011), PWV - 7.0(95%CI 5.7;8.2) m/s (p=0.019), DC - 0.02(95%CI 0.01;0.03) 1/kPa (p=0.037), β index - 8.0(95%CI 7.1;11.8) (p=0.012).

Conclusions: In patients with coronary artery disease, significant changes in CCA were revealed in comparison with healthy individuals in all age cohorts.

ID:853

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

INDICATORS OF REGIONAL ARTERIAL STIFFNESS IN YOUNG PATIENTS WITH DIFFERENT TYPES OF CORONARY HEART DISEASE

POSTER VIEWING SESSION

Angelina Khromova, Luidmila Salyamova, Irina Matrosova, Kristina Polezhaeva, Nadezhda Burko, Valentin Oleynikov
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : to study the indices of regional arterial stiffness and biological age in CAD patients under 50 years of age with and without history of cardiovascular diseases (CVD).

Methods: the study included 129 patients with confirmed CAD (mean age 43(CI95% 40;48)). The patients were divided into 2 groups: the first included 60 people without previous history of cardiovascular pathology, group 2 consisted of 69 patients with a history of CVD. The control (C) group consisted of 29 healthy individuals (mean age 42.4+2.8 years). Regional arterial stiffness was assessed by volume sphygmography ("Fukuda Denshi", Japan) according to the following indicators: B-PWV - PWV in muscular arteries, R/L-PWV - PWV in elastic arteries, L-/CAVI-1 - cardio-ankle vascular index, biological age.

Results: In healthy individuals: B-PWV - 6.5(95% CI 6.1;6.9), R/L-PWV - 10.2(95% CI 9.5;10.9) m/s. In group 1: B-PWV - 7.2(95%CI 6.8;7.7) m/s, R/L-PWV was 12.2(95% CI 11.8;12.6) m/s. In group 2: B-PWV - 7.0(95%CI 7.0;7.9) m/s (p1-c,2-c,$p<0.05$), R/L-PWV - 12.1(95%CI 11.9;12.7) m/s (p1-c,2-c,$p<0.05$). The L-/CAVI-1 in group C was 6.4(95% CI 6.1;6.7), in group 1 - 7.4(95%CI 7.1;7.7), in group 2 - 10.6(8.9;12.4) (p1-c,2-c,1-2<0.05). The biological age in healthy people was 40.9(95%CI 39.0;42.6) years, in group 2 - 45.6(95%CI 43.2;47.9) years (p2-c<0.05) and in group 1 - 44.3(95%CI 41.4;47.3) years (p1-c,2-c<0.05).

Conclusions: Differences in the parameters of regional arterial stiffness were recorded in healthy individuals under 50 years old compared to patients with CAD, while more pronounced changes were found in patients without a history of CVD, with differences is average and biological ages.

ID:851

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

IN PATIENTS WITH CARDIOVASCULAR DISEASE AND HEART FAILURE DENTAL STATE (TOOTH LOSS) MAY EXACERBATE INFLAMMATORY SYNDROME

POSTER VIEWING SESSION

Ioan I. Gutiu[1,2], Anton I. Gutiu[3], Flavian S. Radulescu[4]
[1]Medical Emergencies, Centrul Medical G&G SRL, Bucuresti, Romania, [2]Family Medicine, Centrul Medical G&G SRL, Bucuresti, Romania, [3]Family Medicine, Privat Medical Office, Bucuresti, Romania, [4]Biopharmacy, University of Medicine and Pharmacy "Carol Davila", Bucuresti, Romania

Background and Aims : Background: We hypothesized that dental state overall appreciated by simple counting of dental loss may have a role in cardiac failure pathogenesis by chronic inflammation generated by gum chronic infection (periodontosis, periodontitis).

Methods: Methods: We studied 1786 subjects with cardiovascular disease (CVD) investigated by clinical examination, laboratory investigations, echocardiography and dental state appreciated mainly by teeth loss number (TLN). The mean age of the group was 59.6 years; 527 (29,5%) were male, 482 had heart failure with clinical simptoms.. Functional classification of heart failure (NYHA) was applied: 227 (47%)-class II, 207 (43%)-class III, 48 (10%)-class IV. For inflammatory syndrome appreciation, we used serum fibrinogen (F), C reactive protein (CRP) and TLN determination.

Results: Results: We found that inflammatory syndrome expressed by F, CRP and TLN is present in cardiac failure of patients with CVD: F is increased in cardiac failure versus no cardiac failure patients (423,8+/-131,6 vs 398,6+/-122,2-P<0.0002); TLN is increased in cardiac failure patients versus normal functional patients (15,1+/-10,5 vs 13,7+/-8,6-P<0,0071), CRP (6,6+/-4,4 vs 5,7+/-4,1-P<0,006). The multivariate analysis noted that, after confounding adjusting, only age, TLN and F are the factors remained in the equation. A posthoc analysis noted a progressively increased relationship between F, TLN and cardiac failure functional class.

Conclusions: Conclusion: Inflammatory syndrome is present in cardiac failure from CVD by increased TLN, serum F, and CRP level. TLN intervention is explained by a inflammatory state generated by gum inflammation and germs discharged in circulation. Preventive measures are considered.

ID:850

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

DETECTION OF COMORBIDITIES IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA IN THE UKRAINIAN FAMILIAL HYPERCHOLESTEROLEMIA REGISTRY

POSTER VIEWING SESSION

Nataliia Chulaievska, Olena Mitchenko, Vadym Romanov, Kateryna Timokhova
Endocrine Cardiology And Dyslipidemia, State Institution National Scientific Center «The M.D. Strazhesko Institute of Cardiology National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine

Background and Aims : Early diagnosis and treatment of familial hypercholesterolemia (FH) is necessary to reduce severe complications of the rapidly progressing atherosclerotic process.

Methods: 284 patients with FH (12 children, 272 adults: 243 (89.3%) with Heterozygous FH (HeFH), 29 (10.6%) with Homozygous FH (HoFH)) were included to the Ukrainian FH Registry. Clinical characteristics of patients, lipid/carbohydrate profile, TSH, ApoB, Lp (a), coronary angiography, genetic testing were analyzed.

Results: Among 243 HeFH patients there were 166 (68.3%) women, 77 (31.7%) men. The HoFH group included 29 patients: 19 (65.5%) women, 10 (34.5%) men, which indicates a significant FH predominance in women in the Ukrainian FH Registry. Clinical characteristics of HoFH (45.6±2.5years) were more severe than in HeFH (44.7±0.8years). A higher percentage of HoFH patients had ASCVD (79.3% vs. 47.7%), myocardial infarction (13.8% vs. 6.2%), peripheral atherosclerosis (100% vs. 52.7%), higher LDL-C (13.1±0.7mmol/l vs. 6.6±0.1mmol/l). In contrast to HoFH patients of comparable age, HeFH patients had higher incidence of diabetes mellitus (DM) -16.0 vs. 10.3% and obesity -33.7% vs. 26.9% (only in HoFH women). Hypertension was registered in 65% of cases and in both groups prevailed in women. The 4 most severe HoFH patients (females of reproductive age) with LDL-C>20mmol/l, ApoB-1.7±0.2g/l, Lp(a)-119.5±31.4nmol/l and 100% positive genetics showed the most severe atherosclerotic process, coronary revascularization, atherosclerotic heart valve defects, the highest DLCN scores and the least incidence of comorbidities.

Conclusions: DM and obesity are significantly more common among HeFH. FH patients should receive specific treatment of concomitant conditions in addition to combined high-intensity lipid-lowering therapy to reduce cardiovascular risk.

ID:847

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

OBESITY AND PROGNOSIS IN OLDER PATIENTS WITH CARDIOVASCULAR COMORBIDITY AND CHRONIC KIDNEY DISEASE

POSTER VIEWING SESSION

Elena Efremova, Alexander Shutov
Department Of Therapy And Occupational Diseases, Ulyanovsk State University, Ulyanovsk, Russian Federation

Background and Aims : Chronic kidney disease (CKD) worsens the prognosis of patients with cardiovascular comorbidity.The aim of this study was to investigate relationships between obesity and prognosis in older patients with CKD and cardiovascular diseases.

Methods: 472 older patients with stable cardiovascular diseases (231 males, mean age 69,6±7,3years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). Nutritional status was assessed: presence and type of obesity, body composition. Follow-up period was 1 year, primary endpoint - all-cause mortality.

Results: CKD with GFR less than 60 ml/min/1.73 m^2 was observed in 277 (58.7%) patients. Overweight was observed in 111 (40.1%) patients, obesity - in 118 (42.6%) patients with CKD. More than half had grade 1 (70; 59.3%), every fourth (30; 25.4) - grade 2, 18 (15.3%) - grade 3 among obese patients with CKD. Patients with CKD had higher percentage of fat mass (42.6 (35.3; 48.2) and 38.4 (32.9; 44.8)%, resp., p = 0.0002) and lower lean body mass index 18.6 (17.0;20.6) and 19.7 (17.8;21.8) kg / m^2, resp., p =0.004) compared to patients without CKD.The presence of obesity in patients with CKD was associated with a significant risk of death (OR 2.69; 95% CI 1.32-5.51; p = 0.005). Lean body mass index less than 20.6 kg / m^2 was associated with higher annual mortality in older patients with CKD (OR 3.94; 95% CI 1.90–8.18; p = 0.0003); (sensitivity - 52.6%, specificity - 81.7% (AUC = 0.67); p = 0.0015).

Conclusions: Older patients with CKD are characterized by sarcopenic obesity, which worsens the prognosis of annual mortality.

ID:842

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

NOVEL PATHOGENIC VARIANTS OF THE LDLR GENE IDENTIFIED IN PUTATIVE FH SUBJECTS

POSTER VIEWING SESSION

Tommaso Fasano[1], Efrem Bonelli[1], Emanuele Alberto Negri[2], Chiara Trenti[2], Roberta Gnoni[1], Sebastiano Calandra[3], Stefano Bertolini[4]
[1]Diagnostic Imaging And Laboratory Medicine, AUSL - IRCCS REGGIO EMILIA, REGGIO EMILIA, Italy, [2]Internal Medicine, AUSL - IRCCS REGGIO EMILIA, REGGIO EMILIA, Italy, [3]Biomedical Science, University od Modena and Reggio Emilia, Modena, Italy, [4]Department Of Internal Medicine, University of Genova, Genova, Italy

Background and Aims : Familial hypercholesterolemia (FH) is a common inherited disorder of low-density lipoprotein (LDL) catabolism causing elevated LDL-cholesterol (LDL-C) and premature atherosclerotic cardiovascular disease. FH is typically caused by deleterious variants of LDLR, APOB or PCSK9 genes and its prevalence is of about 1:300 in the general population. Aim of this study was the genetic characterization of suspected FH patients.

Methods: From 2014 to 2019 we collected 186 subjects with suspected FH (122 index cases and 64 relatives, aged ³18 years) who were clinically examined at the Lipid Clinic and tested by Next Generation Sequencing for genes associated with FH (LDLR, APOB, PCSK9, APOE, LDLRAP1, ABCG5, ABCG8, LIPA, CYP27A1, MYLIP).

Results: Overall, 107 subjects (54 index patients/53 relatives) resulted to be heterozygous carriers of pathogenic variants of LDLR (103, 96.3%), APOB (3, 2.8%), or PCSK9 (1, 0.9%) genes. Five (likely)pathogenic variants of LDLR were not reported previously. Three of these caused frameshift with the occurrence of a premature termination codon (Gln33Profs*17, Cys243Trpfs*12, Val365Argfs*20). The other two were missense variants (Pro608His, Ala684Asp), involving highly conserved amino acids, which were found to be deleterious by “in silico” analysis (REVEL score 0.962 and 0.817, respectively).

Conclusions: Clinical and genetic identification of FH patients represents a challenging task in clinical practice. In the present study we report 5 novel LDLR variants. Three of them can be regarded as deleterious due to the formation of a truncated protein. Clinical phenotypes and “in silico” analysis suggested that novel missense mutations can also be considered pathogenic.

ID:840

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

TYPE 2 DIABETES, HFPEF, AND ENDOTHELIAL DYSFUNCTION: AN OBSERVATIONAL STUDY

POSTER VIEWING SESSION

Antonio Cutruzzolà[1], Pietro P. Cozza[1], Salvatore De Rosa[2], Stefan Moraru[1], Martina Parise[3], Agostino Gnasso[1], Concetta Irace[3]
[1]Clinical And Experimental Medicine, Magna Graecia University, Catanzaro, Italy, [2]Medical And Surgical Sciences Department, Magna Graecia University, Catanzaro, Italy, [3]Health Sciences, Magna Graecia University, Catanzaro, Italy

Background and Aims : The risk of heart failure (HF) in diabetic patients is two-fold higher. The HFpEF (preserved ejection fraction) is the most common form, and is associated with endothelial dysfunction (ED). Recently the HFA-PEFF score has been proposed for the diagnosis of HFpEF. We evaluated the association between ED and HFA-PEFF score in subjects with type 2 diabetes (T2D).

Methods: We enrolled 24 patients with T2D and 24 controls matched for age, sex, and BMI. Exclusion criteria were previous cardiovascular events, significant valvular diseases, and chronic severe illness. Participants underwent echocardiography to evaluate the morphological and functional criteria of the HFA-PEFF. The ED was assessed with the flow-mediated dilation (FMD) technique.

Results: Patients with T2D had mean age of 58±6 years, disease duration of 10±7 y, HbA1c 7.0±0.9%, six had microvascular complications. Cardiovascular risk factor were comparable, except for a higher prevalence of hypertension in T2D, 58 vs. 33%, though not significant (p=0.08). FMD was significantly lower in T2D vs. controls (mean±SD: 4.7±3.5 vs 8.7±4.3%, p=0.001). Conversely, the HFA-PEFF score was significantly higher (median (IQR): 3(1) vs. 1(2.5), p=0.001). We observed lower values of FMD for higher HFA-PEFF scores, even when adjusted for hypertension: HFA-PEFF 0-1, FMD 7.4±1.5%; HFA-PEFF 2-4, FMD 3.7±0.7% (p=0.04). FMD also significantly correlated in T2D with E/e' (r=0.57, p=0.004).

Conclusions: Patients with T2D have higher scores of HFpEF, which are associated with worse endothelial function status. The assessment of endothelial function might be useful to disclose early alterations in cardiac function, and to better understand the evolution towards HFpEF in T2D.

ID:839

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

MONOCYTES WITH LOW MITOCHONDRIAL MEMBRANE POTENTIAL ARE ASSOCIATED WITH ATHEROSCLEROSIS AND SHOW SIGNS OF CELLULAR SENESCENCE

POSTER VIEWING SESSION

Nikita Nikiforov[1,2,3,4], Y Chegodaev[1], A Zhuravlev[1], Zukhra B. Khasanova[5], Y Yegorov[6], Alexander N. Orekhov[1]
[1]Laboratory Of Cellular And Molecular Pathology Of The Cardiovascular System, Institute of Human Morphology, Moscow, Russian Federation, [2]Laboratory Of Angiopathology, Institute Of General Pathology And Pathophysiology, Moscow, Russian Federation, [3]Institute Of Experimental Cardiology, National Medical Research Center of Cardiology, Moscow, Russian Federation, [4]Russian Academy Of Sciences, Institute of Gene Biology, Moscow, Russian Federation, [5]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [6]Russian Academy Of Sciences, Engelhardt Institute of Molecular Biology, Moscow, Russian Federation

Background and Aims : Recently, we have identified two subpopulations of monocytes differ in mitochondrial membrane potential (MMP) in human blood. Moreover, the content of monocytes with low potential (MMP-low) was higher in the blood of patients with atherosclerotic plaques. In this research, we studied this subset of monocytes in more detail.

Methods: The study included 25 healthy and 20 patients with atherosclerosis characterized by carotid intima-media thickness (cIMT). Monocytes were isolated from blood using CD14+ magnetic separation. Vital staining with the potential-dependent dye Mitotracker Orange was used to determine MMP. The proportions of MMP-low and -high monocytes, classical and non-classical monocytes were assessed using FACS and confocal microscopy. Cell sorting was used for subsequent detailed study of the cellular functions.

Results: Interestingly, the percentage of MMP-low monocytes directly correlated with patients' cIMT. Compared to MMP-high monocytes, MMP-low monocytes had a decreased pro-inflammatory secretory activity. MMP-low monocytes had a decreased oxygen consumption and had a reduced viability in cell culture. Evaluation of the percentage of CD16 + and CD16- cells showed that MMP-low monocytes include 35-50% of non-classical monocytes, while MMP-high monocytes include 10-20% of non-classical monocytes. Evaluation of 10 associated with atherosclerosis mitochondrial DNA mutations showed no difference between MMP-low and -high monocytes.

Conclusions: Atherosclerosis is associated with an increased level of blood monocytes with both immunological and mitochondrial dysfunction. These cells are probably senescent. The accumulation of such dysfunctional cells may contribute to chronification of inflammation in the vascular wall. Supported by RSF (Grant No. 22-15-00273).

ID:831

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

THE STUDY OF THE INFLUENCE OF ANTIOXIDANTS ON VIABILITY AND RESPIRATION OF CELLS WITH ATHEROSCLEROSIS-ASSOCIATED MITOCHONDRIAL MUTATIONS.

POSTER VIEWING SESSION

Evgeny Bezsonov[1,2,3], Elena Zhigmitova (Erdyneeva)[1], Evgeny Borisov[1], Damir Lyukmanov[4], Nelya R. Yakhina[5], Vasily V. Sinyov[1], Alexander N. Orekhov[1]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P.Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Department Of Biology And General Genetics, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation, [3]Laboratory Of Angiopathology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation, [4]«mirea — Russian Technological University», The Federal State Budget Educational Institution of Higher Education, Moscow, Russian Federation, [5]Faculty Of Medical Biology, Pirogov Russian National Research Medical University, Moscow, Russian Federation

Background and Aims : The pathogenesis of atherosclerosis, the leading disease in mortality in the world, is associated with a thickening of the inner surface of large arteries, leading to a decrease in blood flow and impaired circulation. Mitochondrial mutations can be the first link in a series of pathological changes that involve the activation of the immune response and lead to the development of atherosclerosis. Our laboratory created a set of cybrids carrying atherosclerosis-associated mitochondrial mutations. It has been shown by different groups that addition of certain antioxidants and vitamins to cybrids carrying mitochondrial mutations associated with other than atherosclerosis diseases promoted the survival of cells, normalized the level of ROS generation, increased the content of mtDNA, restored mitochondrial functions including aerobic respiration and ATP synthesis. Thus, the study of the effect of antioxidants and agents-modulators of mitochondrial metabolism on cell cybrids with specified mitochondrial mutations (particularly atherosclerosis-associated) is promising in terms of practical application.

Methods: The detection of the viability of cells and oxygen consumption in the presence of antioxidants.

Results: Using 13 cybrid lines carrying atherosclerosis-associated mitochondrial mutations, as well as THP-1 parental cell line, the effects of different antioxidants (chosen on the basis of the analysis of related publications) on the rate of cell growth and consumption of oxygen were studied.

Conclusions: The results obtained will expand the understanding of new therapeutic possibilities for the treatment of atherosclerosis and other diseases associated with mitochondrial mutations. **The research was supported by the Russian Science Foundation, grant number 22-25-00480.**

ID:821

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

POSTPRANDIAL APOLIPOPROTEIN(A) METABOLISM IN FAMILIAL HYPERCHOLESTEROLAEMIA: THERAPEUTIC EFFECT OF OMEGA-3 FATTY ACID SUPPLEMENTATION

POSTER VIEWING SESSION

Qidi Ying[1], Mikaël Croyal[2,3,4], Dick C. Chan[1], Valentin Blanchard[5], Jing Pang[1], Michel Krempf[6], Gerald F. Watts[1,7]
[1]University Of Western Australia, School of Medicine, Faculty of Health and Medical Sciences, Perth, Australia, [2]Chu Nantes, Inserm, Cnrs, Sfr Santé, Inserm Ums 016, Cnrs Ums 3556, F-44000, Université de Nantes, Nantes, France, [3]F-44000, CRNH-Ouest Mass Spectrometry Core Facility, Nantes, France, [4]Chu Nantes, Cnrs, Inserm, L'institut Du Thorax, F-44000, Université de Nantes, Nantes, France, [5]Departments Of Medicine, Centre For Heart Lung Innovation, Providence Healthcare Research Institute, St. Paul's Hospital, University of British Columbia, Vancouver, Canada, [6]Groupe Elsan, Clinique Bretéché, Nantes, France, [7]Department Of Cardiology And Internal Medicine, Royal Perth Hospital, Lipid Disorders Clinic, Perth, Australia

Background and Aims : Lipoprotein(a) [Lp(a)] is a low-density lipoprotein (LDL)-like particle containing apolipoprotein(a) [apo(a)] that increases risk of atherosclerotic cardiovascular disease (ASCVD) in familial hypercholesterolaemia (FH). Postprandial redistribution of apo(a) protein from Lp(a) to triglyceride-rich lipoproteins (TRL) may also increase the atherogenecity of TRL particles. Omega-3 fatty acid (ω-3FA) supplementation improves postprandial TRL metabolism in FH subjects. However, its effect on postprandial apo(a) metabolism has not yet to be investigated.

Methods: We carried out an 8-week open-label, randomized, cross-over trial to test the effect of oral supplementation with 4 g/day ω-3FA supplementation on postprandial apo(a) responses in FH patients following ingestion of an oral fat load. Postprandial plasma total and TRL-apo(a) concentrations were measured by liquid chromatography-tandem mass spectrometry, and the corresponding area under-the-curve (AUC) (0-10hr) determined using the trapezium rule.

Results: Compared with no ω-3FA treatment period, ω-3FA supplementation significantly lowered concentrations of postprandial TRL-apo(a) at 0.5hr (-17.9%), 1hr (-18.7%), 2hr (-32.6%) and 3hr (-19.2%) ($P<0.05$ for all). Postprandial TRL-apo(a) AUC was significantly reduced with ω-3FA supplementation by 14.8% ($P<0.05$). By contrast, ω-3FA had no significant effect on total AUC of plasma total apo(a). The decrease in postprandial TRL-apo(a) AUC was significantly associated with the changes in the AUC of triglycerides ($r=0.600$; $P<0.01$) and apoB-48 ($r=0.616$; $P<0.01$).

Conclusions: Supplementation with ω-3FA reduces postprandial Lp(a) response to a fat meal in FH patients on statin and/or ezetimibe treatment; this may have implications for decreasing residual risk of ASCVD in FH.

ID:816

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

RISK FACTORS OF DEEP VEIN THROMBOSIS IN COVID-19 PATIENTS.

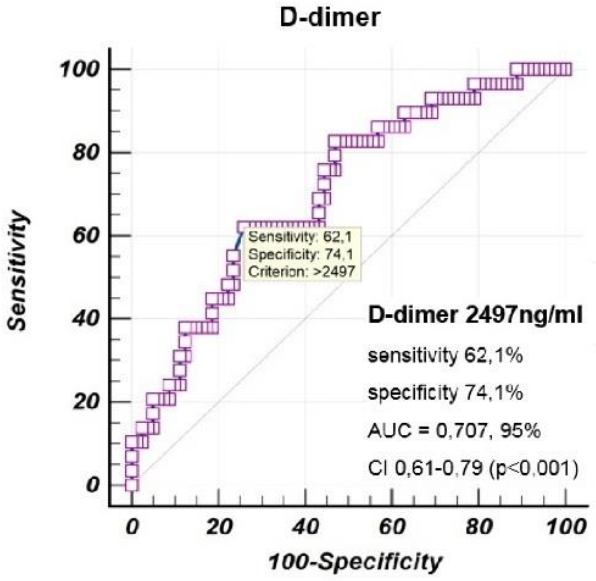
POSTER VIEWING SESSION

Maria Tripoten, Olga Pogorelova, Tatiana Balakhonova
Department Of Ultrasonography Diagnostic Methods, Federal State Budgetary Institution NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY Ministry of Health of the Russian Federation, moscow, Russian Federation

Background and Aims : COVID 19 infection characterized by activation of the hemostasis system and critical increase D-dimer, which increased risk of deep vein thrombosis (DVT) and pulmonary embolism.

Methods: The patients were observed in our COVID hospital from April 15 - June 15, 2020. The study included patients with risk factors for DVT: increase D-dimer more than 2500 ng/ml (or increase more than 5-6 times), the presence of clinical symptoms of DVT, bed rest more than 5 days, stay in the intensive care unit (ICU)) for more than 3 days. These patients were observed for asymptomatic DVT with compression doppler ultrasound (CUS).

Results:



The study comprised 114 patients (51% male). CUS was positive for DVT in 31 patients (27%), of whom 17 (54,8%) was proximal DVT, 12 patients (38,7%) had distal DVT. Median days of hospitalization was 19±8,13. 12 patients died (10,5%). Patients with DVT were significant more frequently to be in the ICU (8(26%) vs 7(8,4%), p=0,03), on bed rest (14(45%) vs 18(21,7%), p=0,02). Patients with DVT had significant higher CRP (mg/L) 145,9 [62,7;161,3] vs 90,6 [41,7;150,9] p=0,06, D-dimer (ng/mL) 2596 [1416;4395] vs 1000 [469;2500] p<0,001, fibrinogen (g/L) was lower 3,25[2,44;3,62] vs 4,27[3,32;5,53] p=0,02. D-dimer levels 2497 ng/ml were associated with asymptomatic DVT (sensitivity 62,1%, specificity

74,1%). D-dimer showed an acceptable discriminative capacity (area under the ROC curve 0,707, 95% CI 0,61–0,79 (p<0,001)).

Conclusions: In patients with COVID-19 pneumonia and risk factors for DVT, the frequency of asymptomatic DVT was 27%. D-dimer levels 2497 ng/ml were associated with asymptomatic DVT with sensitivity 62,1%, specificity 74,1%.

ID:809

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

HEALTHY LIFESTYLE CHANGES CAN IMPROVE CARDIOVASCULAR MARKERS WITHIN 10 WEEKS

POSTER VIEWING SESSION

Christian Koeder[1], Andreas Hahn[2], Heike Englert[1]
[1]Department Of Nutrition, University of Applied Sciences Münster, Muenster, Germany, [2]Institute Of Food Science And Human Nutrition, Leibniz University Hannover, Hannover, Germany

Background and Aims : Cardiovascular disease (CVD) is the leading cause of death worldwide. Healthy lifestyle changes, especially dietary changes, are an underutilized tool to improve CVD markers. In addition, more effective strategies are needed to overcome translational barriers to healthy lifestyle changes and to empower citizens to successfully put these changes into practice. The objective of the study was to fill this gap.

Methods: We conducted exploratory subgroup analyses (ANCOVA) of a non-randomized, community-based, controlled trial with a strong focus on a largely plant-based diet (Healthy Lifestyle Community Programme, cohort 2), including participants with high baseline values of 16 different CVD markers. Participants were mostly middle-aged, recruited from the general population in rural northwest Germany.

Results: Compared to control, after 10 weeks, significant reductions were observed for cholesterol (total-C, measured and calculated LDL-C, non-HDL-C, remnant-C), HbA1c, body mass index, waist circumference, and resting heart rate (RHR) ($p < 0.03$), with no significant between-group differences in HDL-C, triglycerides, glucose, insulin, blood pressure (systolic and diastolic), or pulse pressure. In the intervention group, measured LDL-C, calculated LDL-C, non-HDL-C, and RHR decreased by -20 (95% CI -27, -13) mg/dl, -27 (-35, -19) mg/dl, -29 (-40, -18) mg/dl, and -13 (-18, -8) bpm, respectively ($p < 0.02$).

Conclusions: The intervention programme successfully facilitated lifestyle changes which lead to relevant improvements in CVD markers.

ID:801

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

TOWARDS AN SI-TRACEABLE REFERENCE MEASUREMENT SYSTEM FOR SERUM APOLIPOPROTEINS (A), A-I, B, C-I, C-II, C-III AND E

POSTER VIEWING SESSION

Renee Ruhaak[1], Fred Romijn[1], Ilijana Begcevic-Brkovic[2], Zsusanna Kuklenyik[3], Julia Dittrich[4], Uta Ceglarek[5], Andrew Hoofnagle[6], Harald Althaus[7], Eduardo Angles-Cano[8], Stefan Coassin[9], Vincent Delatour[10], Liesbet Deprez[11], Ioannis Dikaios[11], Gerhard Kostner[12], Florian Kronenberg[9], Alycia N. Lyle[3], Urban Prinzing[13], Hubert W. Vesper[3], Christa Cobbaert[1]
[1]Clinical Chemistry And Laboratory Medicine, LUMC, Leiden, Netherlands, [2]Institute Of Laboratory Medicine, Clinical Chemistry And Molecular Diagnostics, University Hospital Leipzig, Leiden, Germany, [3]Division Of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, United States of America, [4]Institute Of Laboratory Medicine, Clinical Chemistry And Molecular Diagnostics, LUMC, Leiden, Netherlands, [5]Institute Of Laboratory Medicine, Clinical Chemistry And Molecular Diagnostics, LUMC, Leipzig, Netherlands, [6]Department Of Laboratory Medicine And Pathology, University of Washington, Seattle, United States of America, [7]-, Siemens Healthcare Diagnostics products GmbH, Marburg, Germany, [8]French Institute Of Health And Medical Research (inserm), Université Paris Descartes, Paris, France, [9]Institute Of Genetic Epidemiology, Medical University of Innsbruck, Innsbruck, Austria, [10]-, Laboratoire National de Métrologie et d'Essais, Paris, France, [11]-, European Commission, Joint Research Centre (JRC), Geel, Belgium, [12]Gottfried Schatz Research Center (for Cell Signaling, Metabolism And Aging) Division Of Molecular Biology And Biochemistry, Medical University of Graz, Graz, Austria, [13]-, Roche Diagnostics GmbH, Penzberg, Germany

Background and Aims : Reference measurement systems (RMS) are essential to ensure accurate test results for IVD-manufacturers, clinicians and laboratory professionals . Apolipoproteins (apos) are increasingly recognized as relevant functional biomarkers for cardiovascular risk assessment, and new insights and therapies increase clinical measurement frequency. As former WHO-IFCC RMS for apos A-I, B and Lp(a) are no longer available, there is an unmet need for a higher order, globally available, RMS for conventional and emerging apolipoproteins.

Methods: A mass spectrometry-based candidate reference measurement procedure (cRMP) was developed using bottom-up proteomics. Proteins in serum were denatured, reduced and alkylated prior to digestion. Thirty-one peptides representing seven apolipoproteins were quantified relative to stable isotope labelled synthetic peptides. Calibration is currently done with value-assigned, serum-based commutable calibrators. The method is provisionally validated according to CLSI guidelines.

Results: Interpeptide correlation within individual proteins showed Pearson's Rs > 0.975, except for apoC-I (R = 0.953) and one comparison for C-III (R = 0.970). The quantitation of apo(a) is independent of its size polymorphism by design and was linear between 3.4 and 450 nmol/L, the LoQ for apo(a) was 3.4 nmol/L. Total imprecision for apo(a) was 8.5, 10.2, 10.1, 10.4 and 9.7%, at concentrations of 8.4, 15.6, 49.3, 252 and 364 nmol/L. Average total imprecision for other apos ranged between 3.7 and 7.4%.

Conclusions: A next generation, 7-plex, proteomics-based cRMP was developed that allows molecular measurement of targeted apos. As serum apolipoproteins are measured directly through their proteotypic peptides, molar and accurate quantitation of apo(a) and the other apolipoproteins is enabled with this cRMP.

ID:750

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EFFECT OF SAFFRON ETHANOLIC EXTRACT ON BODY WEIGHT, LIPID PROFILE AND ATHEROSCLEROTIC LESIONS IN EARLY AND ESTABLISHED ATHEROSCLEROTIC NEW ZEALAND WHITE RABBITS

POSTER VIEWING SESSION

Iman Nabilah Abd Rahim, Noor Alicezah Mohd Kasim, Effat Omar, Suhaila Abdul Muid, Hapizah Nawawi
Faculty Of Medicine, Institute of Pathology, Laboratory and Forensic Medicine (I-PPerForM), Sungai Buloh, Malaysia

Background and Aims : Dyslipidaemia and obesity play a major role in the development of atherosclerosis. Saffron, an ancient traditional herb has been used before to treat cardiovascular disease but scientific reports on its effect is scarce. This study aims to investigate the effect of saffron ethanolic extract (SEE) on the weight, lipid profile and atherosclerotic lesions in New Zealand white (NZW) rabbits.

Methods: Forty-five male NZW rabbits were divided into 2 groups; control; G0(n=15) and treatment groups; G1(n=30). G0 were used for tissue control. G1 were fed high-cholesterol diet for 4 and 8 weeks to induce early; G1a(n=15) and established atherosclerosis; G1b(n=15) respectively. G1 then were treated with various solutions for 8 weeks (i)distilled water (ii)50mg/kg/day SEE and (iii)100 mg/kg/day SEE. Lipid profile and body weight were measured at baseline, before and after administration of each solution. The rabbits then were euthanized. The aorta was excised from the ascending aorta down to the bifurcation of the iliac arteries and stained with Sudan IV. The percentage of atherosclerotic lesions was analysed using ImageJ.

Results: 50 and 100mg/kg/day SEE decreased the percentage mean body weight of G1a and G1b compared to baseline ($p>0.05$). Both doses of SEE significantly ameliorated LDL and TC levels (>100%) of atherosclerotic NZW rabbits ($p<0.05$). However, 100mg/kg/day SEE proportionally reduced more LDL and TC levels compared to 50mg/kg/day SEE ($p>0.05$). SEE in both doses decreased the percentage of atherosclerotic lesion in G1a and G1b compared to baseline ($p>0.05$).

Conclusions: SEE exerted anti-obesity, hypolipidemic and anti-atherogenic effects. Therefore, saffron could become a promising cardioprotective agent.

ID:769

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EVALUATION OF FRACTIONAL FLOW RESERVE IMPACTS ENDOVASCULAR MANAGEMENT OF PATIENTS WITH STABLE CORONARY ARTERY DISEASE IN THE CLINICAL PRACTICE

POSTER VIEWING SESSION

Mykola Stan[1], Andrii Khokhlov[1], Oleg Zharinov[2], Kyrylo Mikhaliev[3], Oksana Stan[1], Oleg Zelenchuk[4], Borys Todurov[5]
[1]Interventional, Endovascular And Angiography Department, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine, [2]Department Of Functional Diagnostics, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine, [3]Internal Medicine, SIS "RPC PCM" SAD, Kyiv, Ukraine, [4]Department Of Cardiosurgery, X-ray And Extracorporeal Technologies, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine, [5]Ceo, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine

Background and Aims : To evaluate the impact of fractional flow reserve (FFR) assessment upon stenting interventions in patients with stable coronary artery disease (SCAD) in clinical practice.

Methods: A cohort study included 120 patients with SCAD (stable angina), in whom selective coronary angiography revealed stenoses of large subepicardial coronary arteries ≥50% and <80%. FFR was measured in patients of the main group (n = 70), and in the case of FFR less than 0,8 stenting of stenosed vessels was performed. In the control group (n = 50), decisions on revascularization or continuation of optimal drug therapy were made only on the basis of clinical and angiographic data.

Results: The studied groups were comparable by age, gender, body mass index and left ventricular ejection fraction. Single-vessel lesions were found in 42 (60%) patients in the main and 16 (32%) in the control group (p=0,029), multivessel – in 28 (40%) and 34 (68%), respectively (p=0,003). Revascularization interventions were performed in 33 (47%) patients in the main group and 43 (86%) in the control group (p<0,001).

Conclusions: The majority of patients with additional FFR assessment had a single-vessel disease. Evaluation of FFR affects the treatment of patients with intermediate stenotic lesions of the coronary arteries and has been associated with significant reduction of the number of implanted stents.

ID:751

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-10 Modified lipoproteins*

VIRAL SIALIDASES AND ATHEROSCLEROSIS.

POSTER VIEWING SESSION

Evgeny Bezsonov[1,2,3], Dmitry A. Kashirskikh[1], Tatiana V. Kirichenko[1,2], Veronika A. Myasoedova[4], Alexandra Melnichenko[1], Varvara Orekhova[1], Alexander N. Orekhov[1]
[1]Laboratory Of Angiopathology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation, [2]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P.Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [3]Department Of Biology And General Genetics, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation, [4]Unit For Study Of Aortic, Valvular And Coronary Pathologies, Centro Cardiologico Monzino IRCCS, Milan, Italy

Background and Aims : Sialidases play an important role in atherosclerosis development due to modification of low-density lipoproteins (LDL). Removal of sialic acid residues from native LDL leads to the formation of atherogenic desialylated LDL. But the exact details of the formation of these modified LDL are still to be clarified. The aim of this study was to explore the contribution of viral sialidases to the total sialidase activity in blood plasma.

Methods: The total sialidase activity was measured using commercially available kits. The work was carried out in accordance with the principles of good clinical practice on volunteers showing increased sialidase activity of blood plasma in preliminary screening.

Results: There were no significant changes in the sialidase activity of plasma when it was measured immediately after oral administration of oseltamivir phosphate, a selective inhibitor of neuraminidases of influenza A and B viruses, after 4 hours and after 6 hours (8 volunteers). The study of neuraminidase activity during a 6-week clinical study using oseltamivir phosphate was carried out. In 6 volunteers, no significant changes of the sialidase activity of plasma were found when it was measured immediately after taking the drug, on days 7, 14 and 42.

Conclusions: The data obtained indicate the possible absence of the determining role of viral neuraminidases in the appearance of modified (desialylated) LDL. Apparently, desialylated LDL appear due to an increased activity of endogenous sialidases. **Research was supported by the Russian Science Foundation (grant#18-15-00254).**

ID:752

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-02 Smooth muscle cell biology*

INTEGRATION OF CAD-ASSOCIATED GWAS LOCI AND DECONVOLUTION FROM HUMAN CAROTID PLAQUES TO STUDY SMOOTH MUSCLE CELL FUNCTION IN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Sampath Narayanan[1], Sofija Vuckovic[2], Robert Wirka[3], Mariette Lengquist[1], Thomas Quertermous[4], Ulf Hedin[1], Ljubica P. Matic[1]
[1]Molecular Medicine And Surgery, Karolinska Institutet, Stockholm, Sweden, [2]Molecular Medicine And Surgery, Karolinska Institutet, Stockholm, Netherlands, [3]Division Of Cardiology, UNC School of Medicine, Chapel Hill, United States of America, [4]Division Of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, United States of America

Background and Aims : A central role of smooth muscle cells (SMCs) in atherosclerosis has recently evolved implying genetic and causal links in the disease. Here, we hypothesized that coronary artery disease (CAD)-related gene polymorphisms influence SMC function in atherosclerosis and investigated the role of genes harboring such variants in SMCs *in vitro*.

Methods: An integrative bioinformatic approach was applied to deconvolve cellular fractions from microarray data of carotid plaques in the Biobank of Karolinska Endarterectomies (BiKE) using single-cell sequencing data from coronary plaques (n=5). Genetic variants in genes with high correlations to mesenchymal cell fractions were identified, followed by functional analyses of these genes in SMCs *in vitro* using migration and proliferation assays.

Results: We identified 5 mesenchymal cell-specific variants associated with CAD-related GWAS risk loci, BiKE patient symptomatology and gene expression eQTLs from BiKE plaques and GTex normal arteries. These variants were harbored in genetic loci of *ARNTL*, *LDLR*, *MIA3*, *PAK1* and *ARHGAP15*. Microarray analysis revealed increased expression of *ARHGAP15* and *PAK1* and decreased levels of *LDLR* in carotid plaques compared with normal arteries (n=127 vs. 10 respectively, student's t-test). Immunohistochemistry demonstrated increased expression of corresponding proteins in fibrous cap of plaques compared to normal arteries (n=5). To investigate their function in SMCs, the genes were silenced, followed by migration and proliferation assays. Preliminary results indicated that silencing of *MIA3* and *PAK1* inhibited SMC migration, while it was accelerated by *ARHGAP15* knockdown.

Conclusions: The results of this project may reveal novel SMC-specific therapeutic targets and genetic links to the disease, to be explored for improved treatment of atherosclerosis.

ID:756

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ABDOMINAL OBESITY AS A RISK FACTOR OF THE DEVELOPMENT OF CARDIOVASCULAR AND METABOLIC DISORDERS IN PATIENTS WITH ARTERIAL HYPERTENSION

POSTER VIEWING SESSION

Tatiana Petelina[1], Natalia Musikhina[2], Ksenia Avdeeva[1], Maria Lyapina[3], Elena Dorodneva[3], Liana Valeeva[1], Elena Samoilova[1], Ekaterina Mikova[1], Luidmila Gapon[1]
[1]Arterial Hypertension Department, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tyumen, Russian Federation, [2]Urgent Cardiology Department, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tyumen, Russian Federation, [3]Internal Medicine Department, Federal State Budgetary Educational Institution of Higher Education "Tyumen State Medical University" of the Ministry of Healthcare of the Russian Federation, Tyumen, Russian Federation

Background and Aims : To study the role of abdominal obesity (AO) in the development of cardiovascular and metabolic disorders (MD) in patients with arterial hypertension (AH).

Methods: 154 patients (57.1±7.0) were randomized into 3 groups. Gr.1 included 43 healthy patients, Gr.2 - 58 subjects with AH without MD and Gr.3 - 53 subjects with AH and AO. Body mass index (BMI), parameters of sphygmography, 24-hour blood pressure monitoring; biochemical parameters; inflammatory markers; sex hormones; MDRD were estimated.

Results: In Gr.2 and 3 there were registered significant increase in PWV, CAVI and decrease in ankle-brachial index; increase in mean 24-hour and daytime SBP, in day and night time SBP and DBP variability. In biochemical parameters increase in total cholesterol, LDL, triglycerides level and in inflammatory markers - homocysteine, hs-CRP, decrease in HDL-chol. was detected compared to group 1 patients. Besides in groups there were registered correlation between lipid and inflammatory markers with parameters of sphygmography (positive associations of PWV and CAVI with LDL, homocysteine, IL6, endothelin-1 and negative with sex hormones). In patients with AH and AO, elevated levels of leptin, uric acid, IL1b and MDRD were also detected. The positive interrelations of BMI with hs-CRP, leptin; leptin with IL6, daytime SBP and DBP with the level of hs-CRP, glucose and uric acid, daytime SBP variability; BMI with daytime SBP and variability, PWV ($p<0.05$ for all) were revealed.

Conclusions: A multilateral approach to the study of the development of cardiovascular and metabolic disorders in patients with AH indicates that AO is a pathogenetic link in their relationship.

ID:758

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-08 Platelets, thrombosis and atherosclerosis*

FEATURES OF THE PRODUCTION OF PLASMINOGEN ACTIVATOR INHIBITOR-1 BY LOCAL FAT DEPOTS OF VARIOUS LOCALIZATION IN CARDIOVASCULAR DISEASES

POSTER VIEWING SESSION

Olga V. Gruzdeva[1], Ekaterina Belik[1], Yulia Dyleva[1], Maxim Y. Sinitsky[2], Anton V. Sotnikov[3], Olga L. Barbarash[4]
[1]Department Of Experimental Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [2]Laboratory Of Molecular, Translational, And Clinical Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [3]Cardiac Surgery Department, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, Kemerovo, Russian Federation, [4]Clinical Cardiology, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Background and Aims : It is assumed that the increase the circulating level of PAI-1 due to the excessive production of PAI-1 by AT induce atherosclerosis. Aim:To determine the expression and secretion of PAI-1 by subcutaneous, epicardial, perivascular adipocytes, its relationship with the systemic PAI-1 in CAD and heart defects

Methods: Examined 84 patients with CAD, 50 with heart defects. During CABG or heart valve replacement adipocytes of subcutaneous (SAT), epicardial (EAT) and perivascular adipose tissue (PVAT) were isolated. Expression of PAI-1 was determined by qPCR using TaqManTM in a ViiA 7 Real-Time PCR (Applied Biosystems, USA). The concentration of PAI-1 in AT supernatants and plasma was measured ELISA (Invitrogen, California)

Results: The maximum levels mRNA PAI-1 were observed in EAT relative to the SAT and PVAT. In heart defects the lowest level of mRNA PAI-1 was found in PVAT. The expression of PAI-1 in SAT did not differ. The secretion of PAI-1 in the SAT, EAT, PVAT in CAD was higher than in heart defects. EAT adipocytes in CAD were characterized the maximum level of PAI-1 relative to SAT and PVAT. The secretion of PAI-1 in SAT in heart defects was higher than in the EAT and PVAT. The systemic level of PAI-1 in CAD exceeded that in heart defects.Direct correlations were found between PAI-1 expression and PAI-1 secretion in EAT and PVAT, plasma PAI-1 and secretion in EAT regardless of nosology. Plasma PAI-1 correlated with PVAT secretion only in CAD

Conclusions: PAI-1 can be used to develop methods for correcting pathological activation of AT in CAD

ID:759

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

CAROTID INTIMA-MEDIA THICKNESS IS ASSOCIATED WITH PREVALENCE OF ATRIAL FIBRILLATION

POSTER VIEWING SESSION

Maki Yamamoto[1], Mika Enomoto[1], Ako Fukami[1], Nagisa Morikawa[1], Hiromi Sato[1], Hisashi Adachi[2], Yoshihiro Fukumoto[1]
[1]Division Of Cardiovascular Medicine, Department Of Internal Medicine, Kurume Univiersity School of Medicine, Kurume, Fukuoka, Japan, [2]Cardiology, Keikokai, Hara Hospital, Fukuoka, Japan

Background and Aims : Objective: Carotid intima-media thickness (IMT) is one of the useful marker for atherosclerosis and increased IMT predicts for cardio-vascular disease (CVD). Prevalence of atrial fibrillation (AF) is increasing with age, and the elderly have complications such as CVD and AF. We investigated whether IMT was related with prevalence of AF.

Methods: We performed a health check-up in Tanushimaru in 2018. A total of 1368 subjects were measured IMT by using ultrasonography, and were examined electrocardiography and echocardiography.

Results: Mean IMT was 0.72±0.21 mm, 18 subjects (1.3%) had AF. The characteristics of age ($p<0.001$), systolic blood pressure ($p<0.001$), LDL-cholesterol ($p=0.0026$), E/A ratio ($p<0.001$), Left ventricular end-diastolic diameter ($p=0.0199$), Left Atrial Dimension ($p<0.001$) and prevalence of AF ($p<0.001$) were significantly associated with the IMT quartiles. After adjustment for age and sex, the significances of factors were remained.

Conclusions: Conclusion: This study demonstrated that increased IMT was associated with prevalence of AF. A prospective study is needed to examine whether increasing IMT predicts for incidence of AF.

ID:761

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

ADIPOCYTOKINE PROFILE OF LOCAL FAT DEPOTS OF THE HEART AND CALCIFICATION OF CORONARY ARTERIES IN PATIENTS WITH CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Olga V. Gruzdeva[1], Yulia Dyleva[1], Ekaterina Belik[1], Aleksandr Kokov[2], Maxim Y. Sinitsky[1], Kiril Kozyrin[3], Olga L. Barbarash[4]
[1]Department Of Experimental Medicine, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [2]Department Of Radiation Diagnostics, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian, Kemerovo, Russian Federation, [3]Department Of Cardiac Surgery, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian, Kemerovo, Russian Federation, [4]Director, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian, Kemerovo, Russian Federation

Background and Aims : Aim: to study the relationship between the adipocytokine profile of epicardial AT (EAT) and perivascular AT (PVAT) with the severity of coronary artery calcification (CC) in patients with coronary artery disease (CAD).

Methods: The study included 125 patients with CAD, whose mean age was 59.12 (53.35; 66.41) years. Coronary artery (CA) calcification degree was assessed by multislice spiral computed tomography (MSCT) method (Siemens AG Medical Solution, Germany). During coronary artery bypass grafting, biopsies of subcutaneous adipose tissue (SAT), EAT and PVAT were obtained in all patients. Adipocytes were isolated under sterile conditions. The expression of *ADIPOQ*, *LEP, IL6* was determined using PCR with detection of products in real time and the level of adipocytokine secretion in the culture medium using test systems "R&D Systems" (Canada) by enzyme-linked immunosorbent assay.

Results: The highest level of expression of the *ADIPOQ* in all types of fat stores was observed in patients with moderate/medium CC compared to those with massive CC; the maximum expression of *ADIPOQ* was observed in the culture of PVAT adipocytes. Expression of the *LEP* and *IL6* in massive CC was higher, with the maximum values in the culture of EAT adipocytes relative to SAT and PVAT adipocytes. Decreases in the levels of *ADIPOQ* and its secretion, increases in the levels of *LEP* and *IL6* and their secretion in adipocytes of the EAT and PVAT were associated with the development of CC in patients with CAD.

Conclusions: High expression and secretion of leptin and IL6 and low adiponectin are associated with massive coronary calcification.

ID:771

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

HYPERLIPOPROTEINEMIA(A) AND LYMPHOCYTE MONOCYTE RATIO ARE ASSOCIATED WITH CARDIOVASCULAR OUTCOMES IN PATIENTS WITH EARLY MANIFESTED CORONARY HEART DISEASE.

POSTER VIEWING SESSION

Olga I. Afanasieva[1], Alexandra V. Tyurina[2], Elena A. Klesareva[1], Oksana A. Razova[1], Marat V. Ezhov[2], Sergey N. Pokrovsky[1]
[1]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Moscow, Russian Federation, [2]Laboratory Of Lipid Disorders, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation

Background and Aims : Повышенная концентрация липопротеинов (а) [Lp (a)] является генетическим фактором риска ASCVD и может быть триггером системного воспаления. Самым простым маркером системного воспаления является количество лейкоцитов. Мы стремились оценить связь Lp (a) и соотношения моноцитов лимфоцитов (LMR) с сердечно-сосудистыми событиями у пациентов с ранними проявлениями ИБС.

Methods: В исследование были включены 200 пациентов в возрасте 59 [53; 65] лет (медиана [25%; 75%]) лет с проявлениями ИБС до 55 лет, 83% составляли мужчины. Все пациенты получали гиполипидемическую терапию. Среднее время от проявления ИБС до включения в исследование составило 11 [5; 17] лет. Такие серьезные сердечно-сосудистые события (MACE), как инфаркт миокарда, ишемический инсульт, аортокоронарное шунтирование и госпитализация по поводу нестабильной стенокардии, рассматривались как первичные конечные точки. Определяли концентрацию Lp (a), липидов, количество лейкоцитов и их соотношение.

Results: Patients were divided into two groups depending on the presence (n=121) or absence (n=79) of MACE during the follow-up. The groups didn't differ in age, gender, most clinical and laboratory parameters. Lp(a) concentration and LMR were higher in patients with vs without MACE: 44.2 [13.0;98.6] vs 24.9 [8.0;78.5] mg/dL, 3.9 [2.7; 5.0] vs 4.8 [3.2;5.8], respectively, $p<0.05$ for both. Multivariate adjustment confirmed the independent association of Lp(a) and monocyte count with MACE. Patients with Lp(a)$\geq$30 mg/dL and LMR below 4.6 had the highest risk of MACE than those with Lp(a)<30 mg/dL and LMR≥4.6 (OR=2.9 (1.3-6.7), p=0.01.

Conclusions: Elevated lipoprotein(a) level and lymphocyte monocyte ratio are associated with increased risk of cardiovascular events in patients with early manifestation of CHD.

ID:799

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

ACHIEVEMENT OF THE TARGET LEVEL OF LDL CHOLESTEROL AND PLEIOTROPIC EFFECTS OF HIGH-DOSE ATORVASTATIN THERAPY IN PATIENTS WITH PRIMARY MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Luidmila Salyamova, Olga Kvasova, Karina Korenkova, Kristina Polezhaeva, Valentin Oleynikov
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : To study the hypolipidemic and pleiotropic effects of atorvastatin depending on the achievement of the LDL-C target level in patients with STEMI.

Methods: The study included 125 patients with STEMI (mean age 51.2±8.8 years) in the first 24-96 hours from STEMI. Total cholesterol, HDL-C, triglycerides, LDL-C, non-HDL-C, brain natriuretic peptide (BNP), creatinine with GFR calculation by CKD-EPI formula have been determined on the 7th-9th day, 24, 48 weeks after. The patients were divided into three groups. Group 1 included 41 patients who achieved LDL-C <1.5 mmol/l and/or a decrease by 50% both after 24 and 48 weeks of follow-up. Group 2 consisted of 35 people who reached the target LDL level at only one of two visits. Group 3 included 49 people with LDL below target values**.**

Results: The number of patients with abnormal BNP in group 1 decreased from 17 (41.5%) to 7 (17%) (p=0.015) and in group 2 from 17 (48.6%) to 8 (23%) (p=0.026) by the 48th week; in the 3rd group initially - in 18 (37%), after 48 weeks - in 12 (24.5%; p=0.18). The GFR in the 1st group was initially 83.6(CI% 76.7;90.6) ml/min, after 48 weeks - 86.3(CI% 81.0;91.6)ml/min (p=0.524); in group 2 - 87.8(CI% 81.3;94.4) and 86.9(CI% 80.9;93.0)ml/min (p=0.726), in group 3 - 84.5(CI% 79.3;89.6) and 77.7(CI% 73.9.9;81.4)ml/min (p=0.011).

Conclusions: In patients with primary STEMI, only the achievement of target LDL values throughout the 48-week follow-up was accompanied by the most pronounced pleiotropic effect of atorvastatin, which was manifested by an improvement in the laboratory parameters.

ID:773

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-06 Gender and cardiovascular risk*

FEMALE PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA HAVE HIGHER CHOLESTEROL BURDEN AT 19 AND 30 YEARS OF AGE: DATA FROM 12-YEARS FOLLOW-UP

POSTER VIEWING SESSION

Anja K. Johansen[1,2], Martin P. Bogsrud[3], Kjetil Retterstøl[2,4], Gisle Langslet[4], Kirsten B. Holven[1,2]
[1]National Advisory Unit On Familial Hypercholesterolemia, Oslo University Hospital, Oslo, Norway, [2]Department Of Nutrition, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway, [3]Unit For Cardiac And Cardiovascular Genetics,, Oslo University Hospital, Oslo, Norway, [4]Lipid Clinic, Oslo University Hospital, Oslo, Norway

Background and Aims : It is the cumulative exposure to low-density lipoprotein cholesterol (LDL-C) that defines the risk of cardiovascular disease (CVD). Patients with familial hypercholesterolemia (FH) have increased risk of premature CVD, and the highest excess risk is observed in young FH women. The aim of our study was to calculate lifelong LDL-C burden in FH individuals and investigate possible sex differences.

Methods: LDL-C burden was calculated based on untreated LDL-C and repeated LDL-C measurements during follow-up. Data were obtained from medical records of 438 young FH individuals <18 years at first visit to the Lipid Clinic, Oslo University hospital. Results presented as means (SD).

Results: Patients were 11.0 (3.9) years at first visit to the Lipid Clinic and had been followed up for 12.0 (7.0) years. Girls with FH had accumulated a significant higher LDL-C burden compared to boys at 19 years of age (112 [27] vs. 101 [25] mmol-years, P<0.001) and at 30 years of age (175 [36] vs. 157 [34] mmol-years, P=0.02).

Conclusions: Young women with FH had a higher accumulated cholesterol burden compared to young men, potentially explaining the excess CVD risk in this group. This underscores the importance of early treatment initiation among girls with FH and furthermore the need for careful follow-up to ensure that statin-free periods (e.g. in relation to pregnancy and breastfeeding) are limited.

ID:778

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

STUDY OF THE EFFECT OF IL7 ON CHANGES IN THE CONTENT OF CHOLESTEROL IN CELLS AND THE INFLAMMATORY MEDIATORS GENES EXPRESSION.

POSTER VIEWING SESSION

Alexander M. Markin[1,2], Anastasia I. Bogatyreva[1], Taisiya V. Tolstik[1], Ulyana S. Zotova[1], Yulia V. Markina[1,3], Anton Y. Postnov[1], Alexander N. Orekhov[1,3,4]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Department Of Histology, Cytology And Embryology, Peoples' Friendship University of Russia (RUDN University), Moscow, Russian Federation, [3]Laboratory Of Angiopathology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation, [4]Institute For Atherosclerosis Research, Institute for Atherosclerosis research, Moscow, Russian Federation

Background and Aims : Our goal is to analyze the relationship of pro-inflammatory activation and changes in cholesterol content in primary monocytes obtained from healthy donors. An assessment of cholesterol accumulation was carried out by adding modified LDL to cells isolated from plasma patients with atherosclerosis. We believe that various interleukins are able to influence the degree of accumulation of lipids in macrophages.

Methods: Experiments were carried out on human monocytes obtained from healthy donors. To monocytes, which were previously differentiated into macrophages, were added or interleukins and modified LDLs, or interleukins without LDL. Negative control contained a clean environment, there were only LDL in positive control. The accumulation of lipids was estimated by measuring cholesterol in cells. Gene expression was measured using qPCR.

Results: In our work, we used Il7. This Il caused a decrease in cholesterol content in cells while simultaneously incubated with LDL. Analysis of expression of IL1B and TNFa genes, basic inflammation mediators, showed that an increase in their expression does not occur.

Conclusions: When adding Il7 to the cell medium, where LDL was also added, in cells there is a significant decrease of cholesterol content compared with positive control. Thus, the IL7 may be in some kind of anti atherosclerotic effect. This work was supported by the Russian Science Foundation («Research Institute of Human Morphology» Grant # 22-25-00190).

ID:779

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

BURDEN OF ASCVD IN ENGLAND

POSTER VIEWING SESSION

Divyagiri Seshagiri[1], Adeline Durand[2], Christopher L. Morgan[3], Raquel Lahoz[1]
[1]Rwe, Novartis Pharma AG, Basel, Switzerland, [2]Health Economics & Outcomes Research, Novartis Pharmaceuticals UK Ltd, London, United Kingdom, [3]Epidemiology, Pharmatelligence, Cardiff, United Kingdom

Background and Aims : This study describes the epidemiology, healthcare resource utilization (HRU) and its associated costs in patients with atherosclerotic cardiovascular disease (ASCVD) in England.

Methods: This retrospective non-interventional cohort study included adult patients with ASCVD from the Clinical Practice Research Datalink (CPRD) Aurum database (January 2011 – December 2019). ASCVD was defined as patients who had at least one encounter of ASCVD and have hypercholesterolemia (defined by formal diagnosis using SNOMED or ICD-9/10 diagnosis, being prescribed cholesterol-lowering treatments or with a test result of LDL-C ≥1.8 mmol/L 3 months prior or post-index date). Index date was first ASCVD encounter during Jan 2015 – Dec 2019.

Results: ASCVD incidence and prevalence evaluated in 2019 showed similar trends. Both were found to be higher in males compared to females and within these two groups, 65+ years age group had predominantly higher incidence rate than younger age group. From 2015 to 2018, 155,651 patients with incident ASCVD and potential 12 months follow-up (42% females) with mean age of 71.4 years and LDL-C 2.7 mmol/L were identified. Less than 2% of patients had LDL-C ≥2.6 mmol/L and were treated with high-intensity statins at baseline. During the 376,622 years follow-up, 63% of patients had all-cause and 16% ASCVD-related inpatient admissions, 40% cardiology outpatient appointments, and 96% were seen in primary care. ASCVD-related inpatient admissions had a total cost of £105

million.

Table: Epidemiology in 2019, and healthcare resource use and costs for incident ASCVD patients in 2015-2018

	Incidence rate (per 1,000 PY)		Prevalence rate (per 1,000 PY)	
Age groups	**Males**	**Females**	**Males**	**Females**
18-24 years	0.02	0.02	0.04	0.03
25-34 years	0.12	0.11	0.37	0.22
35-44 years	0.94	0.4	3.38	1.53
45-54 years	4.45	2	20.82	9.72
55-64 years	11.2	5.26	67.02	30.19
65-74 years	21.7	11.96	145.07	72.17
75+ years	38.56	26.12	253.04	159.82
18-64 years	3.81	1.9	17.88	8.03
65+ years	28.37	18.37	193.52	116.55
Overall	8.71	6.09	53.35	33.24
Healthcare resource utilization (N patients=155,638)	**N (patients)**	**%**		
Inpatient admissions, n (%)	97,222	62.5%		
ASCVD inpatient admissions, n (%)	24,485	15.7%		
Outpatient patients, n (%)	138,784	89.2%		
Cardiology outpatients, n (%)	61,975	39.8%		
Primary care patients, n (%)	149,835	96.3%		
Costs (N patients=155,638)	**N (contacts)**	**Total costs (376,622 PY)**	**Cost per person year**	
Inpatient admissions	360,831	£636,381,713	£1,689.7	
ASCVD inpatient admissions	33,125	£105,322,388	£279.7	
Outpatient appointments	2,240,453	£248,456,591	£659.7	
Cardiology outpatient appointments	263,519	£29,850,115	£79.3	
Primary care appointments	5,416,118	£130,026,123	£345.2	

Conclusions: Incidence and prevalence of ASCVD was substantially higher in males and in 65+ age group and resource utilization and cost burden were higher in inpatient care setting.

ID:792

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 Cholesterol efflux and reverse cholesterol transport*

DIMERIZATION OF CHOLESTEROL PERMITS ITS BINDING TO LIPID-FREE APOA-I

POSTER VIEWING SESSION

Veronika B. Baserova, Alexander D. Dergunov
Structural Fundamentals Of Lipoprotein Metabolism, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation

Background and Aims : To model the interaction of lipid-free apoA-I with cholesterol molecules that exist in various self-associated forms in extracellular space. Cholesterol dimerization is exploited to reconcile the existing experimental data on cholesterol binding to apoA-I with extremely low critical micelle concentration of cholesterol.

Methods: The interaction of differently self-associated lipid-free apoA-I with cholesterol monomer and tail-to-tail (TT) or face-to-face (FF) cholesterol dimer was modelled with Schrödinger package. Two crystal structures of 1-43 N-truncated apolipoprotein Δ(1-43)A-I tetramer (PDB ID: 1AV1, structure B), 185-243 C-truncated apolipoprotein Δ(185-243)A-I dimer (PDB ID: 3R2P, structure M) were exploited.

Results: Cholesterol monomers bind to multiple binding sites in apoA-I monomer, dimer and tetramer with low, moderate and high energy, still insufficient to overcome the thermodynamic restriction by cholesterol micellization (-52.8 kJ/mol). However, apoA-I monomer and dimer existing in structure B, that contain nonoverlapping and non-interacting pairs of binding sites with high affinity for TT and FF cholesterol dimers, can bind in common 14 cholesterol molecules that correspond to existing values. ApoA-I monomer and dimer in structure M can bind in common 6 cholesterol molecules. The values of respective total energy of cholesterol binding for both B and M structures exceed the free energy of cholesterol micellization.

Conclusions: Cholesterol dimers may simultaneously interact with extracellular monomer and dimer of lipid-free apoA-I, that accumulate at acid pH in atheroma. The thermodynamically allowed apolipoprotein-cholesterol interaction outside the macrophage may represent a new mechanism of cholesterol transport by apoA-I from atheroma, in addition to ABCA1-mediated cholesterol efflux.

ID:793

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

LEU351ARG IN APOB, A NEW MISSENSE VARIANT CAUSING FAMILIAL HYPOBETALIPOPROTEINEMIA

POSTER VIEWING SESSION

Xavier Vanhoye[1], Alexandre Janin[1,2], Amandine Caillaud[3], Antoine Rimbert[3], Fabienne Venet[4,5], Morgane Gosset[4,5], Wienecke Dijk[3], Oriane Marmontel[1,6], Séverine Nony[1], Charlotte Chatelain[1], Pierre Lindenbaum[3], Bertrand Cariou[3,7], Philippe Moulin[6,8], Mathilde Di Filippo[1,6]
[1]Service De Biochimie Et De Biologie Moléculaire, Laboratoire De Biologie Médicale Multisites, Hospices Civils de Lyon, BRON, France, [2]Cnrs Umr5310, Inserm U1217, Institut Neuromyogène, Université Claude Bernard Lyon 1, Université de Lyon, LYON, France, [3]Inserm U1087 - Cnrs 6291 - Nantes University, Institut du thorax, Nantes, France, [4]Laboratoire D'immunologie, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, France, [5]Centre International De Recherche En Infectiologie (ciri), Inserm U1111, Cnrs, Umr5308, Ecole Normale supérieure de Lyon, Université Claude Bernard-Lyon 1, Lyon, France, [6]Inserm U1060, Université Lyon 1, Inrae U1397, Laboratoire CarMen, Oullins, France, [7]L'institut Du Thorax, NANTES UNIVERSITY - CHU NANTES, Nantes, France, [8]Service D'endocrinologie, De Diabétologie Et Des Maladies Métaboliques, Hôpital Louis Pradel, Bron cedex, France

Background and Aims : Familial hypobetalipoproteinemia (FHBL) is mostly caused by premature termination codons in the *APOB* gene, a condition associated with fatty liver and steatohepatitis. Here, we identified a rare missense variant in *APOB*, p.Leu351Arg, in a family presenting with a FHBL phenotype. Despite its co-segregation with FHBL in the proband and her two children, this variant was classified as variant of uncertain significance (VUS) according to the The American College of Medical Genetics and Genomics (ACMG) guidelines. To test if the FHBL phenotype resulted from p.Leu351Arg, we edited hepatic cells and tested the impact of this variant on the full length apoB-100 hepatic synthesis and secretion.

Methods: We generated *APOB* knock-out (KO) and *APOB*-p.Leu351Arg knock-in HuH7 cells using CRISPR-Cas9 technology. ApoB synthesis and secretion were explored by digital droplet PCR and ELISA quantification.

Results: *APOB* expression was decreased by 70% in heterozygous *APOB*-KO cells and almost abolished in homozygous-KO cells, with a consistent decrease in apoB production and secretion. *APOB*-p.Leu351Arg homozygous cells presented with a 40% decreased *APOB* expression and undetectable apoB levels in cellular extracts and supernatant.

Conclusions: As the p.Leu351Arg impairs apoB secretion, we classified this new variant as likely pathogenic, proposed a hepatic follow-up and a cascade screening of relatives in this family. To date, this is the first assessment the pathogenicity of VUS in FHBL, using genome editing of human liver cells. This proof-of-principle experiment will allow a global exploration of others VUS found in dyslipidemic patients and to propose a personalized follow-up of these patients.

ID:797

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

FEATURES OF INDICATORS OF CENTRAL PRESSURE AND STIFFNESS IN PATIENTS WITH PRIMARY MYOCARDIAL INFARCTION IN COMBINATION WITH COVID-19

POSTER VIEWING SESSION

Valentin Oleynikov, Luidmila Salyamova, Marina Lukyanova, Karina Korenkova, Alexey Kulyutsin
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : To conduct a comparative analysis of indicators of central (aortic) pressure and stiffness in patients with primary acute myocardial infarction (MI) with and without COVID-19.

Methods: The study included 45 patients with myocardial infarction (with and without ST-segment elevation), mean age - 57.7±9.6 years. The patients were divided into groups: Group 1 (n=22) - MI developed within two weeks after a confirmed COVID-19 or during hospitalization for MI a positive PCR test for COVID-19 was detected; Group 2 (n=23) - patients with MI without SARS-Cov-2. Applanation tonometry using a Sphygmocor device (AtCor Medical, Australia) was performed. The aortic systolic (SBPao), pulse (PPao) pressure, carotid-femoral pulse wave velocity (cfPVV) were analyzed. The survey was carried out 4-6 weeks after myocardial infarction to exclude the effect of drug therapy for COVID-19.

Results: In group 1 mean age was 62.9(CI% 59.4;66.4), in group 2 - 52.7(CI% 49.3;56.2) years (p=0.0003). Arterial hypertension was diagnosed in 20 patients of group 1 (91%) and in 18 patients in group 2 (78.3%) (p=0.53). According to applanation tonometry, the SBPao level in group 1 was 124.6(CI% 119.2; 130.0) mmHg, in group 2 - 111.6(CI% 106.4;116.9) mmHg (p=0.001); PPao - 41.1 CI% 37.5;44.6) and 30.9(CI% 27.4;34.4) mmHg, respectively (p=0.0003). The prevalence of pathological cfPWV (>10 m/s) in the 1st group - 68.2% (n=15) versus 21.7% (n=5) in the 2nd group (p=0.003).

Conclusions: Patients with MI and COVID-19 were diagnosed with a predominance of central pressure indicators and a high frequency of pathological PWV in the aorta according to the applanation tonometry data.

ID:1119

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

LABORATORY FINDINGS AND CLINICAL OUTCOMES OF 681 COVID-19 PATIENTS WITH DYSLIPIDEMIA REQUIRING HOSPITALIZATION

POSTER VIEWING SESSION

Angelos Liontos[1], Dimitrios Biros[1], Orestis Milionis[1], Stavros Tsourlos[1], Lazaros Athanasiou[1], Alexandros Papathanasiou[1], Nikolaos-Gavriil Kolios[1], Christiana Pappa[1], Cornelia Veliani[1], Valentini Samanidou[1], George Siopis[1], Eleni Pargana[1], Maria Nasiou[1], Nikol-Natalia Armata[1], Stavros-Periklis Anagnostopoulos[1], Aikaterini Poulopoulou[1], Sempastien Filippas-Ntekouan[1], Maria Christaki[1], Iro Rapti[1], Aikaterini Panteli[1], Maria Kosmidou[1], Ilias Tsiakas[1], Ioannis Vagias[1], Evangelos Liberopoulos[2], Eirini Christaki[1], Haralampos Milionis[1]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece

Background and Aims : COVID-19 pandemic has been one of the most emerging issues of the scientific community for the past two years. Patients with dyslipidemia are at risk for acute cardiovascular events during hospitalization, due to stress and atherosclerosis. The aim of this study is to describe the main clinical findings and outcomes of these patients, while hospitalized for COVID-19.

Methods: Data of 681 hospitalized patients were collected from the University Hospital of Ioannina. The diagnosis of dyslipidemia was documented if present in the patients' past medical history. The data were analyzed using independents samples t-test and chi-square test, on IBM SPSS Statistics 26.

Results: The diagnosis of dyslipidemia was present in 230 patients, 126 of which were male. The patients' mean age was 69.7 years and BMI 29.8 kg/m^2. The most frequently used statins were atorvastatin (n=117), rosuvastatin (n=35) and simvastatin (n=35). The presence of dyslipidemia was associated with a higher incidence of anorexia and lower incidence of dry cough, as presenting symptoms of COVID-19 (OR=1.89, p=0.02 and OR=0.70, p=0.03). 37 of these patients eventually passed away during hospitalization, while dyslipidemia was associated with a higher probability of death (OR=1.56, p=0.05). A higher value of CRP/HDL ratio was documented in the group of deceased patients with dyslipidemia compared to the rest of the patients (3.79 vs 2.02, p=0.007). lipid values at baseline are presented at table

1.

Table1

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age	230	18.00	95.00	69.7870	12.26928
BMI	81	17.58	55.56	29.8522	5.74572
TCHOL_FIRST	148	56.00	283.00	144.5608	42.22232
TRG_FIRST	152	33.00	524.00	129.5526	72.05772
HDL_FIRST	146	12.00	149.00	37.1301	14.86271
LDL_FIRST	136	15.00	272.00	83.6691	35.43718
Valid N (listwise)	48				

Conclusions: While our data is not enough to extract a definitive answer it is possible that dyslipidemia can negatively affect the prognosis of patients with COVID-19.

ID:1123

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

PREVALENCE OF OBESITY AMONG MEN AND WOMEN WITH CLINICAL DIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLAEMIA (FH) IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Žaneta Petrulionienė[1,2,3], Egle Skiauteryte[3], Dovile Gabartaite[2,3], Emilija Meskene[2,3], Juste Staigyte[2,3], Rimantė Čerkauskienė[2,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[3], Vilma Dzenkeviciute[2,3,5], Sandra Kutkiene[3], Jolita Badariene[1,2,3], Egidija Rinkuniene[1,2,3], Rusne Jakaite[3], Goda Jackute[2]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Clinic Of Internal Diseases, Family Medicine And Oncology, Vilnius University, Faculty of Medicine, Vilnius, Lithuania

Background and Aims : we aimed to determine the distribution of obesity among different genders with clinically diagnosed FH.

Methods: Prospective observational cohort study enrolled patients with clinically diagnosed FH treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. According to Dutch Lipid Clinic Network (DLCN) diagnostic criteria for Familial Hypercholesterolemia definite FH was diagnosed when a total point score was >8, probable FH – DLCN score 6-8, possible FH - 3-5 points, unlikely FH – DLCN score <3. Obesity was defined as body mass index (BMI) ≥30. Data of 220 study patients (mean age 45,3±12,6 years) were included in the analysis. The prevalence of overweight was compared in different gender groups according to FH diagnosis. Statistical analysis was performed using R (v. 4.0.4) program package.

Results: Of 220 examined patients 54,5% (n=120) were women and 45,5% (n=100) were men. 25,5% (n=56) of study patients had definite FH diagnosis, 29,5% (n=65) - probable FH, 30,9% (n=68) had possible and 14,1% (n=31) had unlikely FH diagnosis. 15% (n=33) of the whole population were obese (12% of men and 18% of women, p=0,270). The prevalence of obesity in female group was: 20% (n=6) with definite FH, 20% (n=8) with probable FH, 11% (n=4) with possible FH and 25% (n=3) with unlikely FH. The prevalence of obesity in male group was: 8% (n=2) with definite FH, 13% (n=3) with probable FH, 17% (n=5) with possible FH and 11% (n=2) with unlikely FH.

Conclusions: 5% of the patients with clinical FH diagnosis were obese, without statistically significant difference between genders.

ID:619

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

THE FREQUENCIES OF INFGAMMA-PRODUCING T-HELPERS 17 AND LP(A) CONCENTRATION IN BLOOD IN PATIENTS WITH ATHEROSCLEROSIS.

POSTER VIEWING SESSION

Anastasiia Y. Filatova[1], Alexandra V. Tyurina[2], Olga I. Afanasieva[3], Nataliya Y. Ruleva[1], Elena A. Klesareva[3], Marat V. Ezhov[2], Tatiana I. Arefieva[1]
[1]Laboratory Of Cell Immunology, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation, [2]Laboratory Of Lipid Disorders, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation, [3]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Moscow, Russian Federation

Background and Aims : Chronic inflammation accompanied by the innate and adaptive immune response as well as lipid disorders are key players in atherogenesis. We analyzed the content of minor T-cell populations with pro- and ant-inflammatory activity, the concentration of lipoprotein(a) [Lp(a)] and markers of neutrophil activation in patients with atherosclerosis.

Methods: 76 male patients were categorized into two groups: 1 – patients (63 (57;65) years, n=20) without CHD and stenotic atherosclerosis in coronary, carotid and low limb arteries, 2 – patients (58 (54;64) years, n=56) with early manifestation of CHD. Lp(a) and myeloperoxidase (MPO)-DNA complexes were assessed by ELISA. T-lymphocyte subpopulations were analyzed with direct immunofluorescence and flow cytometry after activation of mononuclear leukocytes in vitro.

Results: Patients of both groups were comparable in age, BMI, arterial hypertension, lipids. The concentration of Lp(a) was higher in group 2 compared to group 1 (49.3 (10.4;102.1) mg/dL versus 12.0 (4.3;32.1) mg/dL, $p<0.05$). The content of INFγ-producing T-helpers (Th) 17 (Th17/1) was higher in group 2 compared to group 1 (19.4 (15.6;24.5) versus 13.4 (11.7;22.0), % of Th17, $p=0.05$). The same tendency was found for absolute values of Th17/1. There were no differences in the content of CD4+ T-cells, regulatory T-cells, Th17, Th1 and MPO-DNA complexes between groups. The positive correlation was observed between the content of Th17, Th17/1 and the concentration of MPO-DNA complexes ($r=0.23$ and $r=0.27$, respectively, $p<0.05$).

Conclusions: We hypothesize that the increased content of Th17/1 may contribute to the progression of atherosclerosis via neutrophil activation. Further investigations are needed to confirm the phenomena identified.

ID:1359

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

INTERMEDIATE STAGE ATHEROSCLEROSIS REGRESSION USING PHOTOFRIN II - MEDIATED ULTRASOUND SONODYNAMIC THERAPY AND GOLD NANOPARTICLES- MEDIATED X- RAYS-BASED AUGER ELECTRON THERAPY

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : In atherosclerosis, local inflammation and associated macrophage activity can lead to foam cell- rich lesion formation, making inflammation an important target in cardiovascular diseases.In this study, we developed an experimental sonodynamic therapy system, and investigated its effectiveness on intermediate stage atherosclerosis regression accompanied by lipid based encapsulated gold nanoparticles- mediated X- rays- based Auger electron therapy, wherein diagnostic B- mode ultrasound is combined with ultrasound therapy system, with a goal of increased safety.

Methods: In this study, common carotid arteries of hamsters submitted to intermediate stage atherosclerosis using intravascular balloon injury and high- cholesterol diet injury. Then common carotid arteries of the treatment group (n= 10) at the injured region, underwent pulsed low level focused ultrasound (F= 1.1 MHz, P= 20 W, PD= 120 ms) - mediated sonodynamic therapy accompanied by intravenous lipid- based encapsulated photofrin II administration and lipid based encapsulated gold nanoparticles- mediated X- rays (25 Gy)- based Auger electron therapy.

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for wall mean thickness, percentage of luminal cross-sectional area of stenosis, lipid- laden cells and lipid droplets density at the stenotic region in the treatment group compared with the other groups ($P<0.05$)

Conclusions: Enhanced apoptotic and anti- proliferative effect of photofrin II, induced by enhanced inertial cavitation effect of pulsed focused ultrasound, due to collapsed lipid capsules accompanied by enhanced apoptotic effect of Auger electron therapy, can cause to regress of the intermediate stage atherosclerosis and significantly dilate the luminal cross-sectional area of stenosis.

ID:1448

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

A NEW CLINICAL DECISION SUPPORT SYSTEM BASED ON PERSONALIZED EVIDENCE-BASED MEDICINE IN LIPID LOWERING THERAPIES

POSTER VIEWING SESSION

Kseniya Benimetskaya, Igor Mikheenko, Andrey Ponomarenko, Yuri Krivosheev, Dmitry Ponomarev, Denis Losik
Research Team, LLC MedicBook, Novosibirsk, Russian Federation

Background and Aims : Widespread obstacle to take entire advantages of LDL-C-lowering-drug therapy (LLT) is suboptimal lipid management. Clinical decision support systems (CDSS) are promising tools to augment clinicians in their decision-making processes and improve healthcare delivery. Aim was to develop emerging CDSS to resolve the issue of insufficient LLT effectiveness.

Methods: MedicBK CDSS was developed as software that is able to detect patient parameters and specific disease characteristics from electronic health records (EHRs) and suggest therapeutic strategies on the basis of the latest clinical guidelines and high-quality randomized clinical trials data related to certain cases.

Results: MedicBK CDSS detects from EHRs patient parameters. Some indicators are calculated at this stage, such as eGFR and SCORE. MedicBK CDSS defines the patient risk category using a set of obtained parameters. Then the system determines corresponding treatment goals for LDL-C and non-HDL-C or ApoB in some particular cases. MedicBK CDSS defines indications for lifestyle intervention and drug intervention. The system suggests an optimal drug therapy according to clinical guidelines taking into consideration exhaustive patient characteristics and previously conducted therapy. MedicBK CDSS performs indirect efficacy and safety comparison between treatment strategies through network meta-analysis by R-statistic program. Additionally the system evaluates adherence of ongoing therapy to clinical guidelines.

Conclusions: MedicBK CDSS is a promising novel tool for improving healthcare delivery by exhaustive analysis of patient parameters, promoting adherence to clinical guidelines and precise usage of clinical trials data. MedicBK CDSS apparently is capable to make a significant contribution to proper lipid management.

ID:1393

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

EARLY ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN HIGH-RISK WOMEN WITH POLYCYSTIC OVARY SYNDROME

POSTER VIEWING SESSION

Donna F. Vine[1], Paolo Raggi[2], Harald Becher[2], Mahua Ghosh[3], Xiaoying Wu[1]
[1]Metabolic And Cardiovascular Disease Laboratory, U of Alberta, Edmonton, Canada, [2]Medicine-cardiology, University of Alberta, Edmonton, Canada, [3]Division Of Endocrinology And Metabolism, U of Alberta, Edmonton, Canada

Background and Aims : Background: Polycystic Ovary Syndrome (PCOS) is associated with increased cardiometabolic risk factors and cardiovascular disease (CVD). Currently, there is a need to assess early CVD in high-risk women with and without PCOS to effectively prevent morbidity from CVD. **Objective:** The aim of this study was to provide evidence-based research to aid assessment guidelines for early detection of dyslipidaemia, cardiac dysfunction and subclinical atherosclerosis in women with and without PCOS.

Methods: Design, Setting, participants: A case-control study in high-cardiometabolic risk women aged 25-45 years with and without PCOS, matched for age and body mass index.
Main outcome measures: ACVD was measured using carotid intima-media thickness (cIMT), carotid plaque and cardiac function using ultrasound and 2D/3D echocardiography.

Results: Results: Preliminary data (n= 35 PCOS, and n=10 control) shows those with PCOS have a 5 fold higher presence of carotid plaque and early left ventricular global longitudinal strain (LVGLS, 21.1±0.18%) compared to controls (22.4±0.48). Although, there was no difference in mean cIMT, a higher maximum cIMT was observed in PCOS. PCOS tended to have higher plasma triglycerides, LDL-C, total ApoB, non-HDL and remnant cholesterol compared to controls.

Conclusions: Conclusion: Our preliminary data shows early impairment in global LV function and ACVD in PCOS compared to controls, and this is associated with atherogenic dyslipidemia. These results suggest early screening and a risk-stratification model may be warranted in this high-risk population of young women.

ID:1391

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EARLY STAGE ATHEROSCLEROSIS REGRESSION, USING B- MODE ULTRASOUND- GUIDED CHLOR- ALUMINIUM SULFONATED PHTHALOCYANINE - MEDIATED CATHETER- BASED LOW LEVEL RED LASER PHOTODYNAMIC THERAPY

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : Excessive lipid accumulation by macrophages plays a crucial role in atherosclerosis. Foam cells are generated by uncontrolled uptake of modified LDL, especially oxidized LDL (oxLDL). Photodynamic therapy is a treatment that uses photosensitizing agents, along with light to kill cancerous and hyperplasia cells.The aim of this study was to evaluate the effect of chlor- aluminium sulfonated phthalocyanine (CASPc)- mediated photodynamic therapy on early stage atherosclerotic regression, wherein diagnostic B- mode ultrasound is combined with laser system, with a goal of increased safety.

Methods: Golden Syrian Hamsters underwent primary balloon dilatation injury at the right common carotid artery followed by a 1.5% cholesterol-rich diet injury for three weeks. Histopathology results showed development of macrophages- derived foam cells in intimal layer and early stage atherosclerosis formation in all of the hamsters' arteries. Then common carotid arteries of the treatment group (n= 10) at the injured segment, treated using B- mode ultrasound- guided CASPc - mediated catheter- based low level red laser (λ= 670 nm, E/A= 15 J/cm^2) photodynamic therapy. Foam cells density were evaluated in the treatment group compared with the control group using B-mode ultrasonography and histopathology.

Results: Ultrasonography and histopathology results showed a significant reduction in the mean value for foam cells density within the atherosclerotic lesion in the treatment group compared with the control group ($p < 0.05$).

Conclusions: Apoptotic effect of CASPc, induced by low level red laser, can cause to early stage atherosclerosis regression and significantly reduce the foam cells- mediated inflammation.

ID:1390

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ULTRASOUND- GUIDED POLYHYDROXY FULLERENE – LOADED MICROBUBBLES- MEDIATED PULSED LOW LEVEL FOCUSED ULTRASOUND SONODYNAMIC THERAPY OF NEOINTIMAL HYPERPLASIA ACCOMPANIED BY CATHETER- BASED RADIUM-226 BRACHYTHERAPY

POSTER VIEWING SESSION

Hossein Mehrad[1,2], Hossein Ahmadi Noubari[3]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [3]Electrical And Computer Engineering Faculty, University of British Columbia, Vancouver, Canada

Background and Aims : Neointimal hyperplasia is usually defined in an artery as thickening of the intimal layer after an injury such as angioplasty, stenting or surgical repair. In this study, we investigated effect of sonodynamic therapy combined with brachytherapy on neointimal hyperplasia reduction.

Methods: Briefly, rats underwent perivascular severe cold injury using liquid nitrogen at the abdominal aorta (approximately 0.5 cm superior to the iliac bifurcation). After eight weeks, the histopathology results showed progressive inflammation and smooth muscle cells proliferation in intimal layer, resulting in vessel wall thickening. Then treatment group underwent catheter- based gamma ray brachytherapy (^{226}Ra, 25 Gy) in combination with pulsed low level focused ultrasound (P= 15 W, PD= 250 ms)- mediated sonodynamic therapy accompanied by sonosensitizer polyhydroxy fullerene- loaded PESDA (Perfluorocarbon- Exposed Sonicated Dextrose Albumin) microbubbles (100ml/kg, 2-5 $\times 10^5$ bubbles/ml) administration and simultaneously B- mode ultrasound imaging.

Results: from ultrasonography and histopathology, showed a significant reduction in the mean value for wall mean thickness and percentage of luminal cross-sectional area of stenosis at the neointimal hyperplasia region in the treatment group compared with the other groups ($P< 0.05$). Moreover, cell morphology with electron microscopy showed the apoptosis of smooth muscle cells in intimal layer after combination therapy.

Conclusions: Apoptotic effect of gamma ray brachytherapy in combination with enhanced anti-inflammatory effect of polyhydroxy fullerene, induced by enhanced sonodynamic therapy effect of ultrasound, due to collapsed microbubbles, can cause to reduce the hyperplastic smooth muscle cells in intimal layer and significantly dilate the luminal cross-sectional area of stenosis.

ID:1388

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

OUTCOME OF CARDIOVASCULAR DISEASE RISK DEFINED BY SOME INFLAMMATORY MARKERS IN YOUNG MONGOLIAN PEOPLE

POSTER VIEWING SESSION

Shuumarjav Uurtuya[1], Galbadrakh Munkhtuul[1], Dagdanbazar Nyamdorj[2]
[1]Department Of Pathophysiology, school of biomedicine, Ulaanbaatar, Mongolia, [2]Department Of Human Anatomy, school of biomedicine, Ulaanbaatar, Mongolia

Background and Aims : Cardiovascular diseases (CVD) treatment and diagnostic methods have been increasing so far. Researchers have been studying markers and risk scores for determine the CVD risks. Morbidity and mortality rate did not decreasing all the developed and developing country. The world medical biggest problem is we could not decrease the number of young adults with CVD and mortality rate is getting younger. C reactive protein (CRP) and serum amyloid A protein (SAA) are predictors cardiovascular disease. Elevated SAA increases the risk of atherosclerotic ischemia. . Therefore, aim of this study was to determine the risk of CVD in young adults aged 18-25 years with biomarkers.

Methods: Aim of this study was to determine the risk of CVD in young adults aged between 18-25 years with biomarkers. A total of 116 people were surveyed, including 45 men (38.79%) and 71 women (61.2%), with an average age of 21.96±1.85.

Results: CVD risk is <1%-2.8% by Framingham risk score. The prevalence of overweight was 5.2%, hypertension 7.8%, triglyceride 16.4%, LDL 3.5%, and glucose 38.8%. Framingham risk scores are weakly correlated with LDL and diastolic pressure, respectively.CRP is strongly correlated with SAA ($r = 0.87$, $p < 0.0001$).CRP varied depending on LDL and glucose levels ($p = 0.006$ and $p = 0.03$, respectively).

Conclusions: Therefore, in young people, CRP may be a potential marker for CVD risk.

ID:1377

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

FT-IR SPECTROSCOPIC STUDY OF ATHEROMATIC PLAQUE FORMATION AND THE RISK OF COVID-19 MORTALITY OF PATIENTS WITH CARDIOVASCULAR DISEASES. A MATHEMATICAL SIMULATION APPROACH

POSTER VIEWING SESSION

Ioannis Mamarelis[1], Jane Anastassopoulou[2], E Mylonas[3], Vasiliki Mamareli[4], K. Spiliopoulos[3], Theophilos Theophanides[5]
[1]Cardiology, GENERAL ARMY HOSPITAL OF ATHENS, ATHENS, Greece, [2]Cardiology, GENERAL ARMY HOSPITAL, ATHENS, Greece, [3]Cardiology, Δρ., ΓΕΡΑΚΑΣ ΑΤΤΙΚΗΣ, Greece, [4]Cardiology, GENERAL ARMY HOSPITAL, ΝΕΑ ΣΜΥΡΝΗ, Greece, [5]Cardiology, Δρ., ΝΕΑ ΣΜΥΡΝΗ, Greece

Background and Aims : Background/Aim: COVID-19 various, a pandemic disease since 2019, attacks the patients with cardiovascular disease. However, the mechanism of this sensitivity has not yet been clear. The aim is focused to describe the relationship between the clinical history and atherosclerosis development with the survival.

Methods: Materials and method. To carry out we used the nationwide date for three categories of patients: diabetic with coronary events, diabetic and hypertensive. Fourier-Transform-Infrared spectra were used for patients of 54-74 years. The simulation was performed with ODE-(SIR) using the Λ fractional derivative. The arteries were received from patients who underwent to endarterectomy during Coronary Artery Bypass Grafting (CABG).

Results: Results: FT-IR spectra showed that in diabetic cardiovascular patients the oxidative stress produces amyloid protein and AGEs (Advanced Glycation End product**s**). The AGEs contain increasing number of -OH and -NH groups, which could bind to spike glycoptrotein of COVID-19 as donor-acceptor by hydrogen bonds (Scheme). Moreover, from the patients' damaged ATP the PO_4^{3-} and bases are used from viral RNA for its replication.

Conclusions:

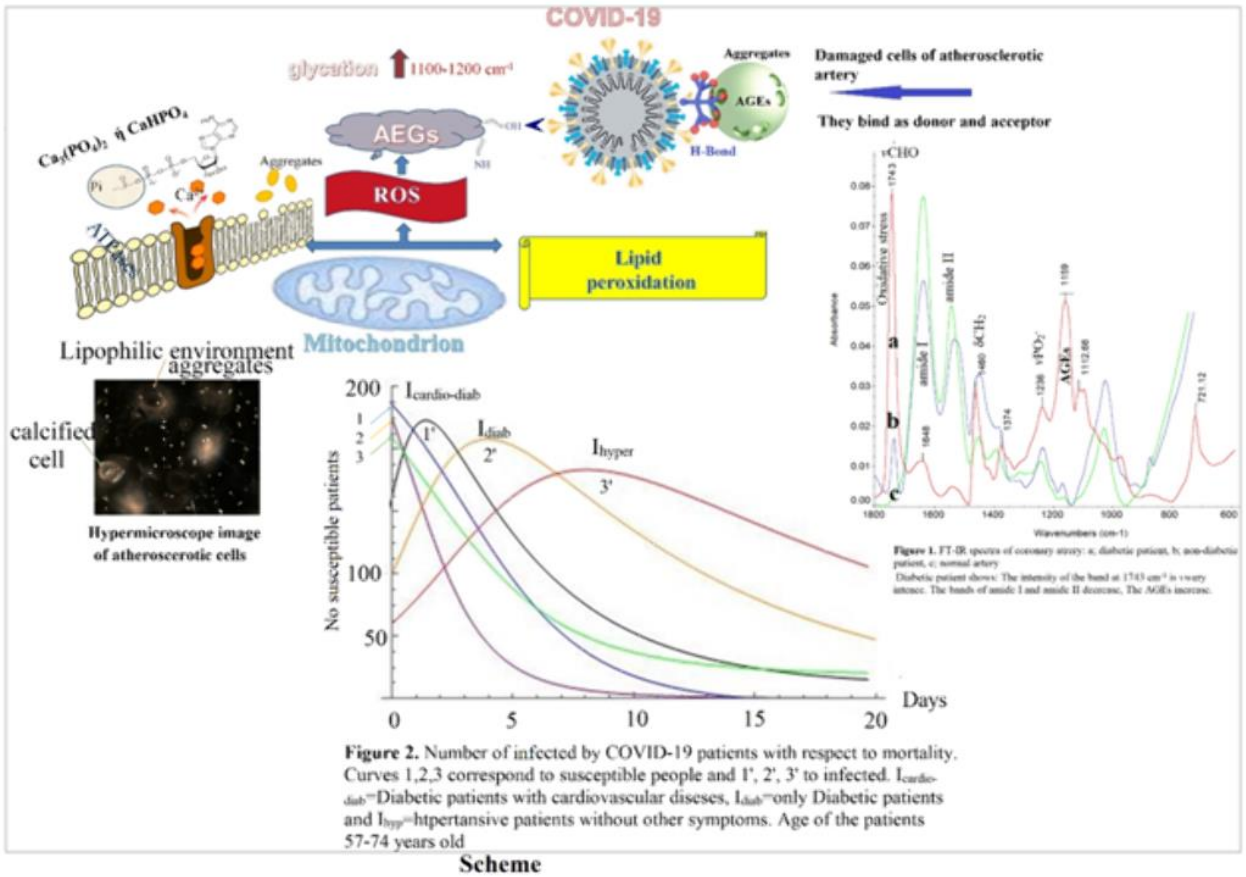


Figure 2. Number of infected by COVID-19 patients with respect to mortality. Curves 1,2,3 correspond to susceptible people and 1', 2', 3' to infected. $I_{cardio-diab}$=Diabetic patients with cardiovascular diseses, I_{diab}=only Diabetic patients and I_{hyp}=htpertansive patients without other symptoms. Age of the patients 57-74 years old

Scheme

Conclusions: Mathematical simulation of an association between the risk of COVID-19 infection in combination with FT-IR data showed amyloid proteins and AGEs of atheromatic plaques increased the risk of the influence in a higher order in diabetic patients with cardiovascular disease, diabetic and hypertensive. The onset time of the disease is significantly reduced from 8.5 days for hypertensive patients to 4.5 for diabetic and 2.5 for diabetic heart patients.

ID:1376

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

CARDIOPULMONARY EXERCISE TEST ALTERATIONS IN YOUNG SMOKERS WITH OBESITY

POSTER VIEWING SESSION

Elena N. Livantsova[1], Yurgita R. Varaeva[1], Peter A. Kelekhsaev[1,2], Tamara D. Kiknadze[1], Antonina V. Starodubova[1,2]
[1]Department Of Cardiovascular Pathology And Diet Therapy, Federal Research Centre for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation, [2]Department Of Intermediate Level Therapy, Pirogov Russian National Research Medical University, Moscow, Russian Federation

Background and Aims : Our study aims to investigate cardiopulmonary parameters in obese patients according to smoking status.

Methods: The study included 19 obese adults (mean age 35.2 years). All participants underwent a comprehensive examination, including anthropometry, bioimpedance measurement, biochemical analyses, lipid profile, spirometry, cardiopulmonary exercise testing.

Results: We included 42.1% non-smokers, 42.1% were current smokers, and 15.8% ex-smokers. The gender ratio was comparable between the three groups. The resting oxygen consumption rate for non-smokers was significantly lower compared to both smokers and ex-smokers (0.26 L/min, 0.50 L/min, and 0.56 L/min, respectively; p = 0.032). The resting O2 pulse for non-smokers was significantly lower compared to both smokers and ex-smokers (2.8 ml/bpm, 5.3 ml/bpm, and 4.8 ml/bpm, respectively; p = 0.032). Also, for non-smokers, the majority have a good heart rate recovery, which indicates an optimal level of adaptation of the cardiovascular system to stress. But among smokers in 14.3% of cases and ex-smokers in 100% of cases, there is a weak post-exercise heart rate recovery, which indicates a reduced adaptive capacity of the cardiovascular system.

Conclusions: Our data demonstrated that smokers are characterized by hypoxia at rest, non-optimal autonomic nervous system functioning, and a reduced adaptive capacity of the cardiovascular system. The results of cardiorespiratory exercise testing allow us to personalize the training mode. **Funding:** Research work was carried out at the expense of a subsidy for the implementation of the state task within FR No. 0410-2022-0005 and ASR No. 0410-2020-0003. **Disclosure of Interest:** None Declared

ID:1373

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 Cholesterol efflux and reverse cholesterol transport*

MOROCCAN POMEGRANATE (SEFRI VARIETY) POLYPHENOLS PREVENT HYPERLIPIDEMIA, OXIDATIVE STRESS AND ENHANCE CHOLESTEROL EFFLUX PROCESSES

POSTER VIEWING SESSION

Lamiae Benchagra[1], Mehdi Alami[1], Samira Boulbaroud[1], Abdelouahed Khalil[2], Mhamed Ramchoun[1], Hicham Berrougui[1]
[1]Department Of Biology, University of Sultan Moulay Slimane, Beni Mellal, Morocco, [2]Department Of Medicine, Faculty of Medicine and Biological Sciences, Sherbrook, Canada

Background and Aims : The present study aimed to investigate the effect of phenolic-rich extract from pomegranate peels (PEPP) and arils (PEPA) on lipid profile in high fat-high fructose diet (HFFD) induced hyperlipidemia in *Wistar* rats and to provide a molecular explanation for their effects.

Methods: Potent antioxidative and antiatherogenic effects of pomegranate phenolic-rich extracts against lipid peroxidation in whole plasma were assessed in *wistar* rats (n= 30) after pomegranate extracts consumption for 12 wk.

Results: Our results showed that pomegranate phenols rich-extract administration to HFFD-rats, significantly reduced the plasma levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), triglycerides (TG), atherogenic index (AI), and increased plasma high-density lipoprotein cholesterol (HDL-C) concentration when compared to the control group. Moreover, pomegranate polyphenols are shown to enhance significantly cholesterol efflux from J774 loaded [^{3}H]-cholesterol to apoA1 ($p< 0.0001$) and promote ABCA1, ABCG1, and SR-B1 protein expression on macrophages. In another hand, we investigated the effect of pomegranate phenols-rich extract on the oxidative stress process and our results showed a significant reduction of TBARS and ROS formation in the stressed J82 cell line.

Conclusions: These results reflect the protective effect of pomegranate extract against the atherosclerosis process confirming its potential beneficial effect as a health nutritional supplement rich in phenolic bioactive compounds.

ID:1371

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-04 Lipoprotein receptors*

MICRORNA 33A CONTROLS SREBP-2 AND LXR DEPENDENT REGULATION OF THE LDL RECEPTOR PATHWAY

POSTER VIEWING SESSION

Vimal Ramachandran[1,2], Melanie Modder[3], Li Zhang[4], Christopher Krumm[5], Wietse In Het Panhuis[3], Milena Schönke[3], Yi-Chien Lu[6], Timothy Hla[7], Ann-Hwee Lee[2], Patrick Rensen[3], Peter Tontonoz[4], Sander Kooijman[3], Hani Najafi-Shoushtari[1,2]
[1]Qatar, Weill Cornell Medicine, Doha, Qatar, [2]Cell And Developmental Biology, Weill Cornell Medicine, New York, United States of America, [3]Medicine, Leiden University Medical Centre, Leiden, Netherlands, [4]Pathology And Laboratory Medicine, UCLA, Los Angeles, United States of America, [5]Pathology And Laboratory Medicine, Weill Cornell Medicine, New York, United States of America, [6]Laboratory Medicine, Yale University, New Haven, United States of America, [7]Surgery Harvard Medical School, Boston's Children Hospital, Boston, United States of America

Background and Aims : Coordinated cellular mechanisms that regulate LDLR transcription and degradation remain largely obscure. We sought to assess the effect of miR-33a on the LDLR pathway given the concerted action of SREBP-2 and miR-33a in elevating cellular cholesterol levels.

Methods: The role of miR-33a in LDLR expression and (V)LDL-uptake was assessed in a series of gain and loss of function studies. Post-transcriptional inhibition through direct binding to target mRNAs was determined and validated by vector-based and Par-Clip assays. The effect on plasma cholesterol and triglyceride levels was evaluated in DIO, *Ldlr*$^{+/-}$ and E3L.CETP mice.

Results: MiR-33a-3p/5p modulated LDLR protein abundance and LDL uptake without a change in mRNA. Intrinsic binding sites predominantly positioned within the PCSK9 coding sequence and IDOL 3'-UTR, facilitated inhibition and interrupted sustained LDLR repression in hepatocytes. MiR-33a-3p, but not 5p, also directly inhibited ANGPTL3 expression. Liver-targeted miR-33a-3p mimic reduced hepatic and circulating PCSK9 levels and lowered LDL levels. In E3L.CETP mice, it also attenuated postprandial TG and non-HDL-C levels as a consequence of increased triglyceride-derived fatty acid uptake by white adipose tissue and subsequent hepatic uptake of lipoprotein remnants, accompanied by reduced plasma ANGPTL3.

Conclusions: Our findings reveal a compensatory control mechanism in the LDLR pathway and highlights miR-33a-3p mimics as alternative therapeutic inhibitors of LDL-cholesterol in hypercholesterolemia.

ID:1370

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

LIPID DISORDERS IN YOUNG OBESE PATIENTS DEPENDING ON SMOKING STATUS

POSTER VIEWING SESSION

Elena N. Livantsova[1], Yurgita R. Varaeva[1], Peter A. Kelekhsaev[1,2], Tamara D. Kiknadze[1], Georgiy E. Leonov[1], Antonina V. Starodubova[1,2]
[1]Department Of Cardiovascular Pathology And Diet Therapy, Federal Research Centre for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation, [2]Department Of Intermediate Level Therapy, Pirogov Russian National Research Medical University, Moscow, Russian Federation

Background and Aims : Our study aims to evaluate the association between lipid parameters and smoking status in obese patients.

Methods: 19 young obese adults (mean age 35.2 years) were examined. We collected the data of anthropometry, body composition analysis, biochemical markers, and lipid profile.

Results: We included 42.1% non-smokers, 42.1% current smokers, and 15.8% ex-smokers. The proportion of women was 68%. The average BMI was 34.0 kg/m2. Lipid parameters were comparable in three groups (median total cholesterol: 5.3 mmol/L, 5.2 mmol/L, and 5.6 mmol/L; median LDL cholesterol: 3.5 mmol/L, 3.6 mmol/L, and 3.9 mmol/L for non-smokers, current smokers, and ex-smokers, respectively). Hypercholesterolemia was found in 11 (58%) patients: 4 (50%) non-smokers and 5 (62.5%) current smokers. Hyper-LDL-C was detected in 10 (52.6%): 3 (37.5%) non-smokers and 5 (62.5%) current smokers.

Conclusions: The results of our study confirm the important contribution of smoking to dyslipidemias for young people. Further research is required to clarify the features of smoking-associated metabolic disorders. **Funding:** Research work was carried out at the expense of a subsidy for the implementation of the state task within FR No. 0410-2022-0005 and ASR No. 0410-2020-0003. **Disclosure of Interest:** None Declared

ID:1369

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

APPROACH OF THERAPEUTICS GOALS IN A GROUP OF PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA UNDER PCSK9 INHIBITORS TREATMENT.

POSTER VIEWING SESSION

Adriana C. Puente, Pedro I. Olivares, Rafael Trujillo
Cardiology, NATIONAL MEDICAL CENTER 20 DE NOVIEMBRE, ISSSTE, MEXICO CITY, Mexico

Background and Aims : Background. Patients with Familial hypercholesterolemia are a group of high cardiovascular risk, they require multiple lipid-lowering treatments and has difficulty reaching therapeutic goals. PCSK9i are currently a treatment option. Aim. To evaluate the achievement of therapeutic goals in a group of patients with familial hypercholesterolemia under PCSK9 inhibitors treatment.

Methods: . We retrospectively evaluated 22 patients with familial hypercholesterolemia under PCSK9i treatment. We evaluated sex, age, associated cardiovascular risk factors, previous cardiovascular disease, and concomitant pharmacological treatment. LDL-C levels were measured before and one year after treatment. Statistical analysis: SPSS system, continuous data as mean ± SD, percentages were rounded; Chi-square and Student's t-tests.

Results: . Mean age 51.4±16.6 years old, 11 (50%) men; 13 (59%) heterozygotes, 9 (41%) familial homozygotes. Cardiovascular risk factors: 11 patients arterial hypertension (50%),4 diabetes mellitus (18%), obesity and overweight 211 (50%). Previous cardiovascular disease: coronary artery disease 16 (72%), peripheral artery disease 1 (4.5%), cerebrovascular disease 3 (13.6%). All patients were under previous statins and ezetimibe treatment. Initial mean C-LDL levels: heterozygotes 187.30 mg/dl and 279.28 mg/dl. One year C-LDL levels: heterozygotes 109.33 mg/dl and 142.35 mg/dl. There was a C-LDL reduction of - 41% and – 49% in the heterozygotes and homozygotes respectively. Three patients (13.6%) reached therapeutic goals.

Conclusions: Conclusion. PCSK9 inhibitors treatment is an efficacy therapeutic option to treat dyslipidemia in high-risk patients. There was a significant reduction in C-LDL levels around 50%. The achievement of therapeutic goals was 13.6%, therefore this group of patients must be treated intensively as soon as possible.

ID:1366

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

PHYSICAL ACTIVITY AND CARDIAC ARRHYTHMIAS IN PATIENTS WITH INOCA ON THE MANAGEMENT WITH RANOLAZINE

POSTER VIEWING SESSION

Tetiana Pylova[1], Vira Tseluyko[2]
[1]Cardiology, Kharkiv Medical Academy of Post-graduate Education, Kharkiv, Ukraine, [2]Cardiology, V. N. Karazin Kharkiv National University, Kharkiv, Ukraine

Background and Aims : The **aim** of the study was to evaluate the effect of basic ranolazine therapy in INOCA patients on exercise stress test and Holter ECG monitoring.

Methods: 53 patients with INOCA were examined, including 17 men (32.7%) and 35 (67.3%) women, the average age was 57 (± 9.68) years. In addition to physical and laboratory examination, exersise stress test, Holter ECG monitoring were included in the examination of patients. Patients were divided into 2 groups: group I - patients who in addition to standard therapy received ranolazine at a dose of 1000 mg twice a day for 6 months, and group II patients with standard antianginal therapy. The examination was performed at 6-month follow-up.

Results: Before treatment in group I, the duration of the exercise test was 356.51± 180.24s, and after treatment 414.32± 142.10s (p = 0.03). In group II, the duration of the test before treatment was 361.4± 160.24s, and after 380.5± 152.2s (p= 0.15). The duration of the test differed significantly in group I after treatment of patients from group II after treatment of patients with a standard treatment (p= 0.04). In group I the frequency of ventricular arrhythmias: before treatment n=1142[30; 2012], after treatment n=729[23; 1420], in group II a significant difference between the number of extrasystoles before and after treatment not detected(n=1026[17; 1920], n=985[15; 1680], respectively) p= 0.18.

Conclusions: The addition of ranolazine to the basic therapy of patients with INOCA helps to increase exercise tolerance and contributes to a significant reduction in the number of ventricular arrhythmias.

ID:1361

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-05 Extracellular matrix and calcification*

DIFFERENTIAL EXPRESSION OF EXTRACELLULAR MATRIX-RELATED GENES IN TISSUE OF STABLE AND UNSTABLE ATHEROSCLEROTIC PLAQUES

POSTER VIEWING SESSION

Elena Shakhtshneider, Dinara Ivanoshchuk, Veniamin Fishman, Yuliya I. Ragino, Yana V. Polonskaya, Elena V. Kashtanova, Alexandr Chernyavsky, Ivan Murashov, Mikhail Voevoda
Laboratory Of Medical Genetics, Institute of Internal and Preventive Medicine - Branch of the ICG SB RAS, Novosibirsk, Russian Federation

Background and Aims : The goal of the current study was to examine the differential expression of extracellular matrix genes in tissue of stable and unstable atherosclerotic plaques.

Methods: The group of men with coronary atherosclerosis consisted of 181 patients, age 45-65 (57±1.3). Clinical diagnosis of coronary atherosclerosis was evaluated by percutaneous coronary angiography. All of patients were individuals free of ACS and had stable exertional angina classes II-IV. The tissue of atherosclerotic plaques was collected during surgery in the presence of intraoperative indications. Histological examination of plaques was performed. Transcriptome profile in the tissue of atherosclerosis plaques was carried out on an Illumina HiSeq1500 instrument (Illumina, USA). The enrichment and library preparation were performed using the TruSeq RNA Sample Preparation Kit (Illumina, USA).

Results: The expression level of EFEMP1 (EGF containing fibulin extracellular matrix protein 1), FMOD (Fibromodulin) and FBLN5 (fibulin 5) genes was higher in stable atherosclerotic plaque of fibrous type vs unstable atherosclerotic plaque of dystrophic-necrotic type (p <0,0001). Table 1. Expression of extracellular matrix-related genes in atherosclerotic plaques

Gene	SAP v1	SAP v2	UAP v1
EFEMP1	1920,3	1931,3	1085,3
FMOD	1650,3	1663,8	685,3
FBLN5	1006,3	1023,9	408,9

Note: NAB - unstable atherosclerotic plaques of dystrophic-necrotic type SAB - stable fibrous atherosclerotic plaques v1, v2 - technical repeat

Conclusions: Expression of extracellular matrix genes was different between stable and unstable atherosclerotic plaques. This study was conducted as part of the main topic in state assignment No. AAAA-A17-117112850280-2.

ID:1360

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

NOVEL PROGNOSTIC CUT-OF LEVEL FOR THE LDL CHOLESTEROL IN YOUNG STEMI PATIENTS

POSTER VIEWING SESSION

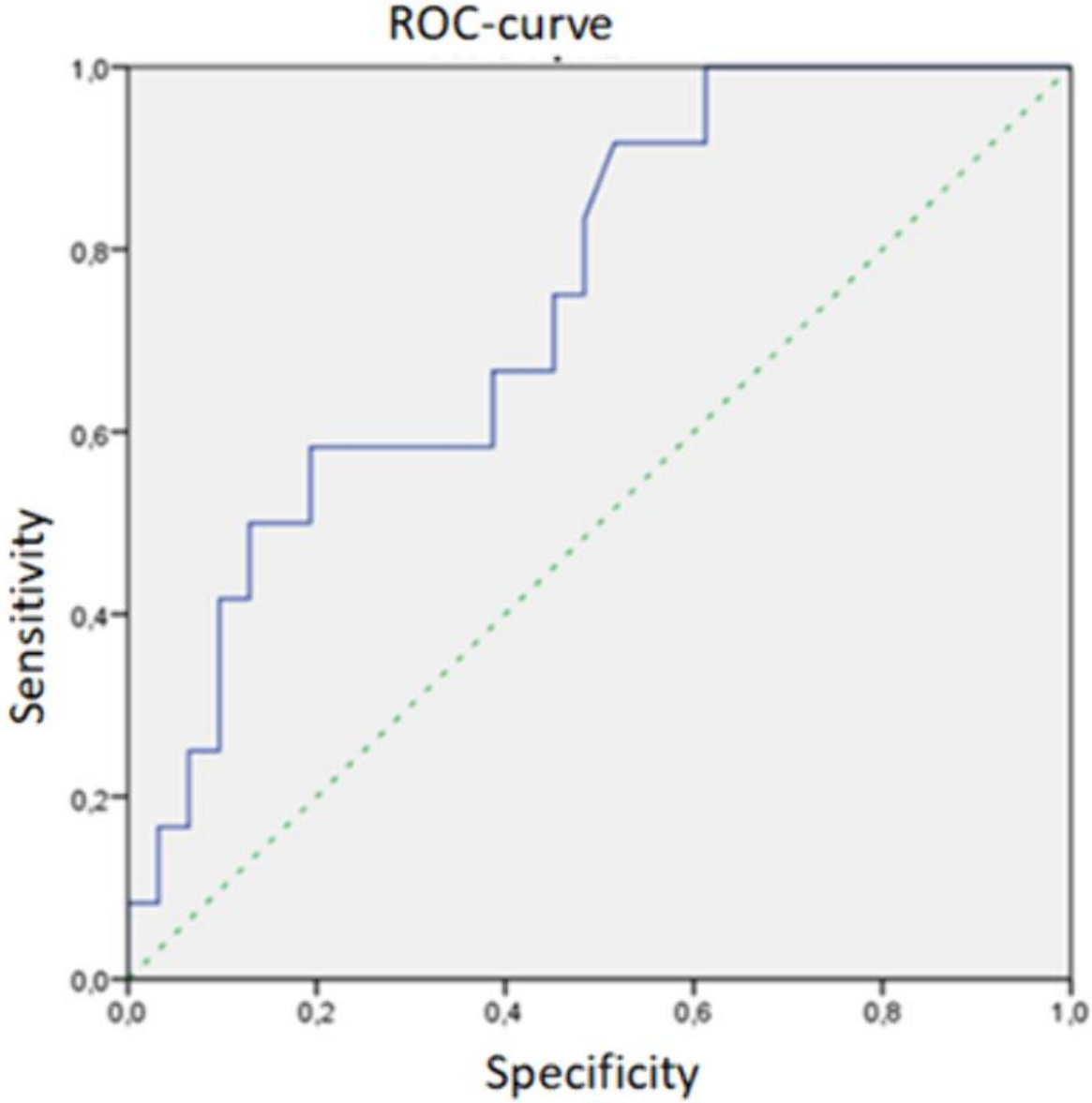
Dmytro Bilyi, Alexander Parkhomenko, Oleg Irkin, Yaroslav Lutai, Anton Stepura
Intensive Care Unit, NSC “Institure of cardiology n.a. M.D.Strazhesko” NMAS of Ukraine, Kyiv, Ukraine

Background and Aims : The aim was to identify and evaluate the effect of lipid metabolism on long-term prognosis in young STEMI patients.

Methods: 142 STEMI patients depending on the age divided into the 2 groups: 1st (n=55) <45 and 2nd (n=87)≥45 years. Depending on the baseline LDL higher or less than 4.0mmol/l, 4 subgroups were obtained: 1A(n=21) with LDL≥4.0, 1B(n=34)<4.0, 2A(n=42)≥4.0 and 2B(n=45)<4.0mmol/L. All patients were followed during 3 and 5 years and the development of endpoints (death from any cause and combined CV events- CV death, MI, stroke) assessed. ROC-analysis was performed with determination of specificity and sensitivity of predictor of development of complications.

Results: Young patients (group 1A) within 3 years of FU more frequently had a death from any cause (Log-rank test; p=0.017) and CV events (Log-rank test; p=0.021) compared with subgroup 1B. For 5 years of FU the development of CV events observed more often in patients <45years with LDL≥4.0mmol/L (group 1A) (Log-rank test; p=0.002 and p=0.021, respectively) compared with patients of 1B group. Patients ≥45years had no dependence of development of complications on the baseline LDL higher (group 2B) or less than 4.0mmol/L (group 2A). The LDL 4.125mmol/L proved to be prognostically significant for the development of CV events within long FU period of MI only in young patients (area under the ROC curve 0.746(95% CI 0.59–

0.90).



Conclusions: Baseline LDL level≥4.125mmol/l in young patients with STEMI, but not older than 45 years, has a negative impact on prognosis during the 5years of FU with increased number of CV events.

ID:1356

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

HYPERLIPOPROTEINEMIA(A) IS RELATED TO SEVERE CORONARY AND CAROTID ARTERY DISEASES IN FAMILIAL HYPERCHOLESTEROLEMIA PATIENTS.

POSTER VIEWING SESSION

Uliana V. Chubykina[1], Olga I. Afanasieva[2], Elena A. Klesareva[2], Narek A. Tmoyan[1], Marat V. Ezhov[3]
[1]Laboratory Of Lipid Disorders, National Medical Research Center of Cardiology, Moscow, Russian Federation, [2]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Moscow, Russian Federation, [3]Laboratory Of Lipid Disorders, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation

Background and Aims : Familial hypercholesterolemia (FH) and elevated lipoprotein(a) level are hereditary disorders of lipid metabolism associated with the premature development of atherosclerotic cardiovascular diseases. The aim of this study was to evaluate the effect of hyperlipoproteinemia(a) on coronary and carotid artery diseases.

Methods: The study included 206 FH patients according to the Dutch Lipid Clinic Network criteria (average age 43±11 years, males 45%) from the Russian FH Registry. Stenotic atherosclerosis was considered in case of presence of stenosis ≥50%. Multivessel coronary disease was classified if two or three vessels had stenosis ≥50%. The concentration of lipoprotein(a) was measured by enzyme-linked immunosorbent assay in serum. The lipoprotein(a) concentration ≥30 mg/dLwas considered as hyperlipoproteinemia(a).

Results: FH patients with hyperlipoproteinemia(a) were older, no significant differences in risk factors were found. The Table presents data on atherosclerotic lesions of coronary and carotid artery in FH patients depending on the presence of hyperlipoproteinemia(a). The Figure shows the data of ROC analysis with the optimal threshold value of lipoprotein(a) concentration for predicting multivessel coronary disease and stenotic atherosclerosis of carotid arteries. In FH patients with hyperlipoproteinemia(a) the odds ratios of multivessel coronary artery disease and stenotic atherosclerosis of carotid arteries were 3.11 (95% CI: 1.60 -6.06, p <0.001) and 2.26 (95% CI: 1.10-4.66, p <0.05),
respectively.

Table. Coronary and carotid artery diseases in FH patients depending on lipoprotein(a) level.

Parameter	Lp(a)<30 mg/dL	Lp(a)≥30 mg/dL	p
Coronary heart disease	36 (28%)	34 (44%)	**<0.05**
Stroke/transient ischemic attack	6 (5%)	5 (6%)	0.8
Percutaneous coronary intervention	27 (21%)	21 (27%)	0.3
Coronary artery bypass grafting	7 (5%)	15 (19%)	**<0.01**
Stenosing carotid atherosclerosis, %	4 (3%)	11 (14%)	**<0.01**
Multivessel coronary artery disease	20 (16%)	28 (36%)	**<0.001**

Note: Data are present as n (%). Lp(a) - lipoprotein(a).

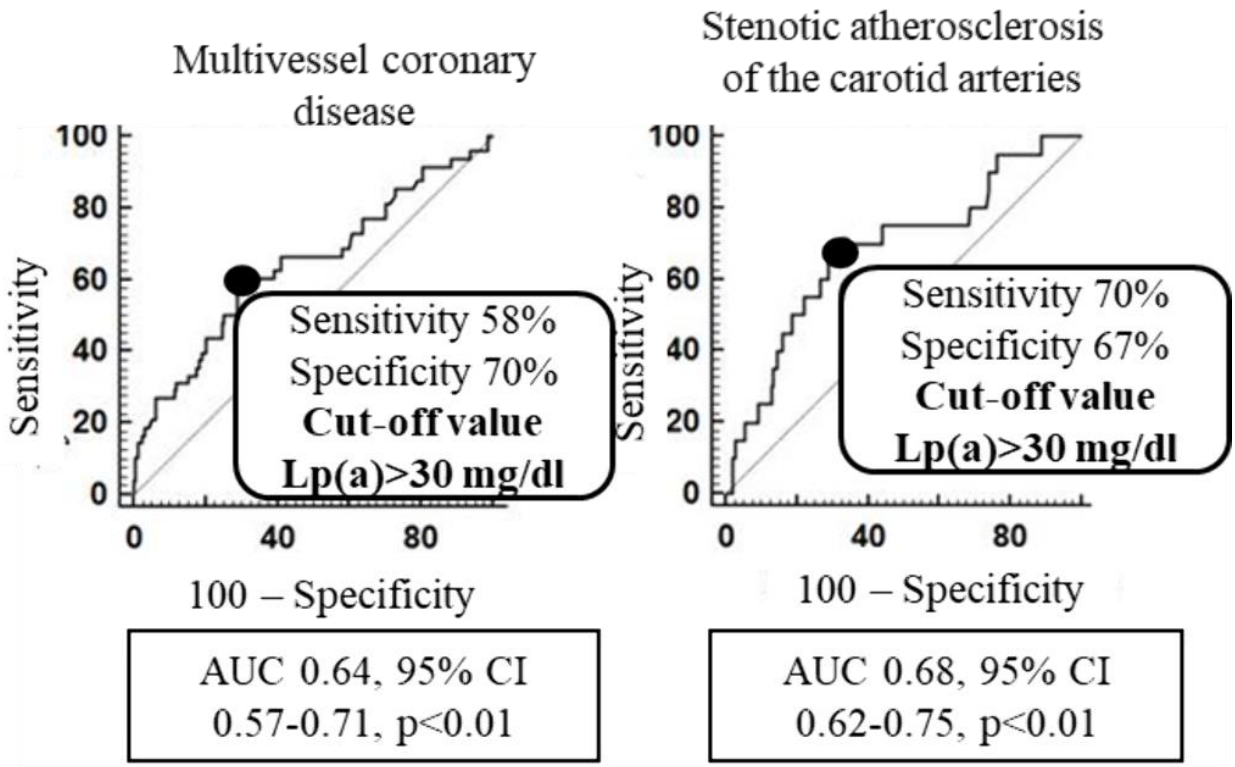


Figure. ROC analysis

Conclusions: Lipoprotein(a) concentration ≥30 mg/dL in FH patients is associated with more severe coronary and carotid artery diseases.

ID:1460

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

ADIPOKINE'S LEVEL IN PATIENTS WITH OVERWEIGHT AND OBESITY, DEPENDING ON THE PRESENCE OF TYPE 2 DIABETES MELLITUS

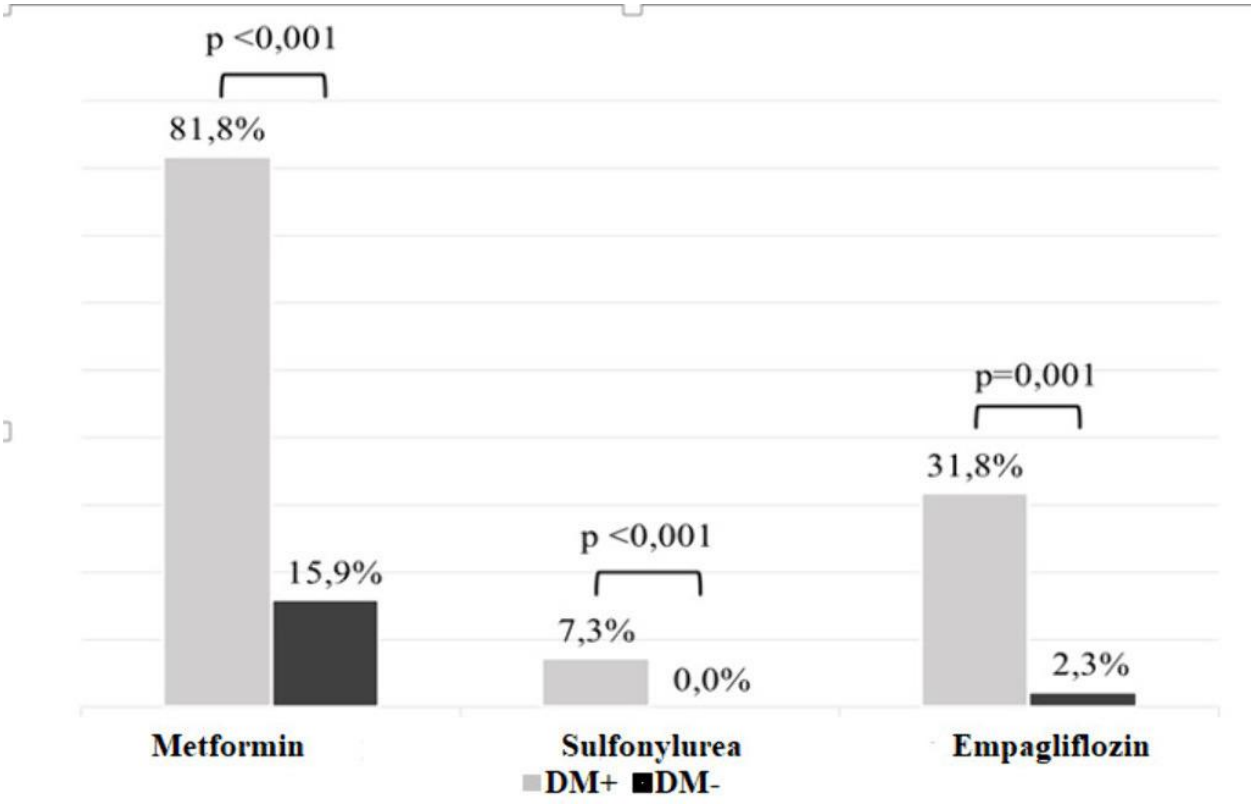
POSTER VIEWING SESSION

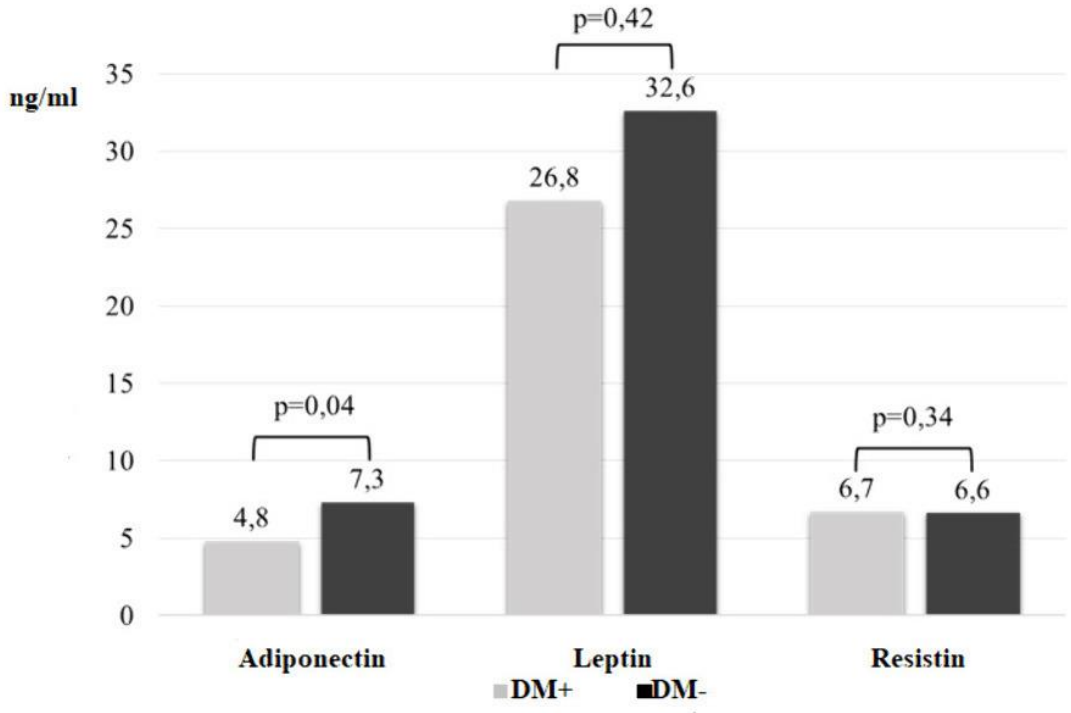
Natalia Kurochkina[1], Yulia Prus[1], Diana Nozadze[1], Anna Popova[1], Igor V. Sergienko[1], Aleksey Ansheles[2], Valerii Masenko[3], Tatiana Sharf[3], Mariia Tkacheva[4]
[1]Laboratory Of Atherosclerosis Phenotypes, National Medical Research Center of Cardiology of the Ministry of Health of Russian Federation, Moscow, Russian Federation, [2]Department Of Radionuclide Diagnostics And Positron Emission Tomography, National Medical Research Center of Cardiology, Moscow, Russian Federation, [3]Department Of Neurohumoral And Immunological Research, Russian Cardiology Research Center Ministry of Health of the Russian Federation, Moscow, Russian Federation, Moscow, Russian Federation, [4]Endocrinology Department, Academic Clinic of Neurology and Dentistry on the basis of N.N. Burdenko Neurosurgery Research Institute "Cecil+", Moscow, Russian Federation

Background and Aims : assessment of adipose tissue secretory activity and it's effect on the severity of atherosclerosis and on the lipid spectrum in patients with type 2 diabetes mellitus

Methods:

Parameters	Type 2 diabetes mellitus n=22	Non Type 2 diabetes mellitus – n=44	p
Age, years	57±11	55±13	0,67
Male	14 (63,6%)	26 (59,1%)	0,79
Weight, kg	101,7±18,5	95,4±17,4	0,33
Waist circumference, cm	107,8±11,4	105,8±14,6	0,53
BMI, kg/m2	33,6±5,4	32,6±5,5	0,52
Smoking	3 (13,6%)	13 (29,5%)	0,23
Arterial hypertension	19 (86,4%)	40 (90,9%)	0,68
CHD	11 (50,0%)	20 (45,5%)	0,80
Atherosclerosis of the carotid arteries	4 (18,2%)	12 (27,3%)	0,55
Laboratory indicators			
TC, mmol/l	4,4±1,00	5,2±1,6	**0,03**
LDL-C, mmol/l	2,5±1,0	3,1±1,3	0,07
HDL-C, mmol/l	1,1±0,2	1,2±0,3	0,06
TG, mmol/l	1,9±1,1	1,9±1,0	0,62
Target values LDL-C	3 (13,6%)	3 (6,8%)	0,39
Glucose, mmol/l	6,6±1,8	5,4±0,9	**0,005**
Glycated hemoglobin, %	7,2±1,4	5,9±1,2	**<0,001**
HOMA-IR	4,3±1,2	2,7±0,8	**<0,001**
Lipid-lowering therapy			
Statins	18 (81,8%)	27 (61,4%)	0,16
Statins and esetimib	5 (22,7%)	5 (11,4%)	0,28





The study included 66 patients with a body mass index (BMI) over 25 kg/m2 (observation group, mean age 56± 12 years). All patients were divided into two subgroups depending on the presence of type 2

diabetes (DM group, n=22 and non DN, n=44). The patient's risk factors were assessed and biochemical blood test was performed (including adipokine levels)

Results: DM type 2 and non DM groups did not differ in age and gender, in indicators such as weight, BMI, smoking and comorbidity. In patients without type 2 DM, the level of TC was significantly higher ($p=0.03$), and there was also a tendency to higher levels of LDL and HDL cholesterol ($p=0.07$ and $p=0.06$, respectively). The level of blood glucose, HbA1c and the HOMA-IR index were significantly higher in the group of patients with type 2 diabetes ($p <0.01$), despite antidiabetic therapy. In patients without type 2 diabetes, the serum adiponectin level was significantly higher compared to patients with type 2 diabetes (7.3±5.3 ng/ml versus 4.8±3.6 ng/ml, $p=0.04$). The levels of leptin and resistin did not differ statistically significantly between groups

Conclusions: In patients with DM type 2, the level of adiponectin was significantly reduced compared to non DM. There were no differences in the levels of leptin and resistin between the groups of patients with DM type 2 and non DM.

ID:1344

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

COMPARATIVE EFFECT OF DELAPRIL-MANIDIPINE TREATMENT VERSUS TELMISARTAN-AMLODIPINE TREATMENT IN HOMA-IR, HOMA-B, HOMA-S AND QUICKI INDEXES IN PREDIABETIC HYPERTENSIVE PATIENTS.

POSTER VIEWING SESSION

Angelos Liontos[1], Sempastien Filippas-Ntekouan[2], Dimitrios Biros[1], Nikolaos-Gavriil Kolios[1], Cornelia Veliani[1], Christos Papagiannopoulos[1], Valentini Samanidou[1], Alexandros Papathanasiou[1], Stavros Tsourlos[1], Lazaros Athanasiou[1], Christiana Pappa[1], Eleni Pargana[1], Maria Nasiou[1], Athina Zarachi[2], Ilias Tsiakas[1], Eirini Christaki[1], Moses Elisaf[3], Evangelos Liberopoulos[4], Haralampos Milionis[1], George Liamis[3]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]2nd Department Of Internal Medicine, University Hospital Of Ioannina, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [4]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece

Background and Aims : Introduction: Hypertensive patients often suffer from other metabolism related comorbidities characterized by insulin resistance (e.g., diabetes mellitus, metabolic syndrome). The pharmaceutical combination of telmisartan/amlodipine has been associated with beneficiary effects on glucose metabolism and insulin resistance**.** Dual combination treatment is advised with current guidelines. ARB and CCB combination are considered to have a beneficial affect on glucose homeostasis. We present comparative data of the effect of delapril/manidipine versus telmisartan/amlodipine combination treatments, in HOMA-IR, HOMA-B, HOMA-S and QUICKI indices before and after the 3-month treatment, in hypertensive prediabetic patients.

Methods: METHODS: Data were collected from 104 patients from the outpatient clinic for lipid metabolism, hypertension and diabetes, during the period 2014-2018. 53 persons were randomized in the delapril/manidipine group 30/10 mg per day while 51 persons had been randomized in the group of telmisartan/amlodipine 80/5mg per day. All patients successfully completed the study. Baseline characteristics are presented in Table

1A.

Table 1A. *Patients' characteristics at the start of the study*

Characteristics/Combination of drugs	DEL/MANI	TEL/AMLO
N (Men-Women)	53(30-23)	51(35-16)
Age (Years)	58.08±11.73$$$	58.04±13. 6$$$
Smokers (%)	12(22.6%)	31(60.8%)
Alcohol Consumers (%)	7(13.2%)	16(31.4%)
Body Weight (Kg)	83.67± 13.21	84.72± 12.87
BMI (Kg/m^2)	28.73 [27.73-30.3]	29.32 [27.37-31.65]
Glucose (mg/dl)	100[97-107]	100[98-106]
Insulin (*μIU/mL*)	8.6[6.3-11.4]	13[9.5-14.9]

Results: RESULTS: The resulting alternations in HOMA-IR, HOMA-B, HOMA-S, QUICKI, before and after the 3-month treatment are presented

on **Table 1B**.

Table1B. Results of insulin resistance indices before and after the three-month treatment

Parameter	Start of treatment	After 3 Months of Treatment	% Change	p-value
HOMA-IR				
DEL/MANI	2.14[1.52-2.89]	2.17[1.35-2.74]	1.4 % (0.03)	0.577^
TEL/AMLO	3.06[2.27-3.91]	2.37[1.44-3.61]	-22.55 % (-0.69)	0.005*
HOMA-B (%)				
DEL/MANI	81.63[52.62-103.52]	88.24[63.91-137]	7% (6.61)	0.006^
TEL/AMLO	118.33[85.23-144.86]	95.57[65.66-142.61]	-24% (22.76)	0.283*
HOMA-S				
DEL/MANI	0.01[0.01-0.02]	0.01[0.01-0.02]	0% (0)	0.389
TEL/AMLO	0.01[0.01-0.01]	0.01[0.01-0.02]	0% (0)	0.381
QUICKI				
DEL/MANI	0.34[0.33-0.36]	0.34(0.33-0.37)	0% (0)	0.177
TEL/AMLO	0.32(0.31-0.34)	0.34(0.32-0.36)	6% (0.02)	0.186

The data are presented as Average ± Standard Deviation, Median [25th-75th].

*p < 0.05 compared to DEL/MANI treatment, **p < 0.01 compared to DEL/MANI treatment,

***p < 0.001 compared to DEL/MANI treatment

^p < 0.05 compared to TEL/AMLO treatment, ^^p < 0.01 compared to TEL/AMLO treatment,

^^ <0.001 compared to TEL/AMLO treatment

Conclusions: CONCLUSIONS: comparison between the treatment groups showed a statistically significant difference in the change of HOMA-IR (from the beginning of treatment and after 3 months) between the TEL/AMLO treatment group and the DEL/MANI treatment group (p-value<0.05), with increased insulin sensitivity in the TEL/AMLO group. Furthermore, HOMA-B was significantly increased in

the DEL/MANI group compared with the TEL/AMLO group ($p<0.05$). No other significant changes were evident.

ID:1331

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

THE IMPACT OF SNP RS3798220 ON THE LPA GENE IN ATHEROSCLEROTIC DISEASE

POSTER VIEWING SESSION

Rafael S. Knack[1], Henrique Grinberg[1], Renata S. Knack[2], Ricardo Egidio S. Knack[1], Kamilla M.M. Sá[3], Taliê Z.B. Hanada[3]
[1]Clinical Staff, Hospital Israelita Albert Einstein, São Paulo, Brazil, [2]Molecular Biology And Genetics, FAEPE - Fundação de Apoio a Pesquisa e a Extensão de Serviços da Comunidade FAMERP, São José do Rio Preto, Brazil, [3]Medicine, Universidade Metropolitana de Santos (Unimes), Santos, Brazil

Background and Aims : Lipoprotein(a) has a similar structure to LDL and differs in the presence of apolipoprotein(a), which is linked to apolipoprotein B by a disulfide bridge. In some populations, lipoprotein(a) levels above 20 to 30 mg/dL increase the risk of developing cardiovascular disease. The LPA gene is responsible for encoding a serine proteinase that inhibits tissue-type plasminogen activator I activity. The encoded protein is an essential part of lipoprotein(a) and is proteolytically cleaved, resulting in fragments that bind to atherosclerotic lesions and promote thrombogenesis. Plasma concentrations of lipoprotein(a) are 75% to 95% heritable and vary between individuals. They are virtually unaltered by environmental factors and generally remain constant throughout life. The heritability of lipoprotein(a) is due single nucleotide variants (SNP) in the LPA gene and copy number variants in the kringle IV type 2 domain. Studies show that two SNPs (rs3798220 and rs10455872) are strongly associated with lipoprotein(a) concentration and risk of coronary artery disease.

Methods: Brief case report.

Results: Considering all the current evidence of the importance of lipoprotein(a) in the development of cardiovascular disease and the possibility of better prevention based on genetic predisposition, we briefly report the case of a 63-year-old male patient, nonsmoker, asymptomatic, with consistently high Lp(a) levels, who was diagnosed at a routine examination with advanced atherosclerotic disease requiring surgical intervention. Subsequently, the presence of the risk allele (C) in the SNP rs3798220 was identified.

Conclusions: Precision medicine is an expanding field. The brief report points to the analysis of molecular markers as an important tool in disease prevention.

ID:1334

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

IDENTIFICATION OF MOLECULES THAT CORRECT STRUCTURAL AND FUNCTIONAL DEFECTS OF NATURALLY-OCCURRING PATHOGENIC APOA-I MUTANTS

POSTER VIEWING SESSION

Christina Gkolfinopoulou, Angeliki Bourtsala, Angeliki Chroni
National Center For Scientific Research "demokritos, Institute of Biosciences and Applications, Athens, Greece

Background and Aims : Naturally-occurring mutations in human apolipoprotein A-I (apoA-I) have been shown to disturb protein conformation and induce functional defects that impair the levels and atheroprotective properties of HDL. One such apoA-I mutation, L178P, induces major defects in the structural integrity and functions of the protein that may underlie the reduced HDL-cholesterol and increased cardiovascular risk observed in carriers of the mutation. Here, a library of marketed drugs (~1000 compounds) was screened against apoA-I[L178P] to identify molecules that can prevent mutant apoA-I from adopting its pathological conformation.

Methods: To evaluate the effect of the drugs on the thermodynamic stability and structure of the mutant protein, we utilized the thermal stability shift assay in the presence of the fluorescent dye SYPRO Orange. As an orthogonal assay, we used the change of fluorescence intensity of 1-anilinonaphthalene-8-sulfonic acid (ANS) upon its binding on hydrophobic sites on apoA-I as a reporter of protein structural integrity.

Results: Thermal stability shift analysis identified twenty-one compounds that induce the mutant protein to undergo a melting transition similar to that of WT apoA-I. Subsequent analysis of the capacity of the twenty-one drugs to induce apoA-I[L178P] to have a similar binding capacity of ANS as WT apoA-I, narrowed the potential structure correctors to six. Functional analyses have so far identified one compound that restores the defective capacity of apoA-I[L178P] to induce ABCA1-mediated cholesterol efflux.

Conclusions: Our findings indicate that small molecules can correct defective apoA-I structure and function and may lead to novel therapeutic approaches for apoA-I-related dyslipidemias and increased cardiovascular risk.

ID:1336

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PROGRESSION OF CAROTID ARTERY STENOSES AND TARGET LEVELS OF LIPID METABOLISM IN PATIENTS FOLLOWING CORONARY ARTERY BYPASS GRAFTING

POSTER VIEWING SESSION

Irina D. Syrova, Anastasia A. Kuzmina, Anna G. Chernobai, Olga V. Gruzdeva, Olga A. Trubnikova, Olga L. Barbarash
Clinical Cardiology, Research Institute for Complex Issues of Cardiovascular Diseases, г. Кемерово, Кемеровская обл., Russian Federation

Background and Aims : Aim. To determine the progression of carotid artery stenosis (CAS) and assess its relationship with the achievement of target levels for lipid metabolism in patients following coronary artery bypass grafting (CABG) at the 5-year follow-up.

Methods: Methods. 75 male patients (the mean age of 62.5±5.5 years) were enrolled in the study. All patients underwent color duplex scanning of the brachiocephalic arteries and mapping with color-flow duplex at days 3-5 before CABG and 5 years after it.

Results: According to the results of the color duplex scanning of the brachiocephalic arteries, 28 (37.3%) patients had CAS at baseline. The number of patients with stenoses, regardless their severity, increased up to 41(54.7%) at the 5-year follow-up. In 16(39.0%) patients, stenoses were detected for the first time. 14(34.1%) patients reported the progression of the previously diagnosed stenoses. The severity of stenoses remained the same in 11(26.8%) patients. At the 5-year follow-up, the level of TC was 4.81±1.25 mmol/L, HDL-C - 1.08±0.23 mmol/L, LDL-C – 3.13±1.19 mmol/L, TG – 1.86±0.85 mmol/L. Out of 14 patients with progressed CAS, 2(14.3%) patients achieved the target levels of TC, 6 (42.9%) patients – the target HDL-C, and 5 (35.7%) patients – the target TG levels. None of the patients reached the target LDL-C levels.

Conclusions: Conclusion. At the 5-year follow-up after CABG, mild and moderate CAS progressed. Importantly, the majority of patients with CAS did not achieve the target levels for lipids.

ID:1337

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ACHIEVEMENT OF THERAPEUTIC OBJECTIVES OF SECONDARY PATIENT PREVENTION WITH ACUTE ISCHEMIC CEREBROVASCULAR STROKE.

POSTER VIEWING SESSION

Evgenia Mavrokefalou, Georgios Tomazou, Stella Ntavidi, Adamantia Chioti, Marilena Kylla, Varvara Polymniou, Dimitrios Kamarinopoulos, George Marakomichelakis
4th Clinic Of Internal Medicine, General Hospital of Athens Evaggelismos, Athens, Greece

Background and Aims : Strokes are the third most common cause of death in the general population. The aim of the study was to evaluate the achievement of therapeutic targets of secondary prevention of patients who have suffered by acute ischemic stroke (AIS).

Methods: We studied 498 patients (275 men and 223 women, with an average age of 71.6±8 years) with a confirmed AIS. Patients' compliance with medication was assessed by reviewing patients after six months.

Results: Of these, 64.55% of the patients were hypertensive, 36.8% diabetic, 55.2% active smokers and 64.9% had dyslipidemia. They were instructed to take 83% statin, 57% antihypertensive treatment, antiplatelet agent 96%, 31% antidiabetic treatment, stop smoking and lose weight in obese people. Patients were divided into two groups depending on whether or not they complied with the treatment guidelines. Of the patients, those who received antihypertensive and anti-platelet therapy, 78% and 81% respectively reported continued taking the drug. Insufficient pharmaceutical compliance was found in patients administered hypolipidemic treatment (57%). Of the patients treated with diabetes mellitus, 41% had HbA1c<6.5%. A high proportion of patients stopped smoking (84%), but not of weight loss (41%).Comparing group A that complied with the treatment guidelines with group B that did not comply, there was a 21% increase in AIS recurrence (14% in group A versus 34% in group B, $p<0.05$).

Conclusions: The achievement of therapeutic targets of secondary prevention is low after an AIS. Patients are better educated and intensive treatment regimen is administered on secondary prevention after an AIS.

ID:1340

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

EFFECT OF INCREASING DOSES OF STATINS ON THE LEVEL OF SERUM MICRORNAS INVOLVED IN REVERSE CHOLESTEROL TRANSPORT AND INFLAMMATION

POSTER VIEWING SESSION

Vasily A. Kudinov[1], Rafael I. Artyushev[1], Marina Y. Zubareva[2], Tatiana A. Rozhkova[3], Konstantin K. Baskaev[4], Julia A. Shuvalova[3], Alexander I. Kaminny[3], Igor V. Sergienko[2]
[1]Scientific Group Of Phospholipid Drugs, Institute of Biomedical Chemistry, Moscow, Russian Federation, [2]Laboratory Of Atherosclerosis Phenotypes, FSBI National medical research center of cardiology Ministry of Health of the Russian Federation, Moscow, Russian Federation, [3]Department Of Atherosclerosis, FSBI National medical research center of cardiology Ministry of Health of the Russian Federation, Moscow, Russian Federation, [4]Experimental Drug Research And Production Department, Institute of Biomedical Chemistry, Moscow, Russian Federation

Background and Aims : Circulating microRNAs as a component of such epigenetic mechanism of posttranscriptional regulation of mRNA translation may serve as blood biomarkers of CVDs, moreover, the study of circulating miRNAs may help to identify potential therapeutic targets. We investigated changes in the serum level of 4 circulated microRNAs (miR-33a, miR-33b, miR-146a, and miR-146b) in patients with coronary artery disease and disorders of carbohydrate metabolism under the influence of up-titrated doses of two widely used statins (atorvastatin and rosuvastatin).

Methods: RNA was isolated from blood plasma samples obtained from clinical trial participants (n=16; 14 males and 2 females; mean age64.25±9.19) just before and 30days after treatment. To investigate microRNAs levels, RT-qPCR analysis was performed. Exogenous cel-miR-39 was used as a reference. Changes in miRs circulating levels were evaluated, the significance level $p \leq 0.05$.

Results: All Ct's for each patient, obtained by RT-qPCR, normalized on Ct for control. Statistically significant changes in expression noted: decreasing for miR-33a($p=0.0043$) and -33b($p=0.0009$); increasing for miR-146a($p=0.0054$). For miR-146b no significant changes were observed ($p=0.5014$).

Conclusions: Our study has demonstrated that increasing doses of Rosuvastatin and Atorvastatin may influence miR-33a/b (decreasing) and miR-146a (increasing) serum levels. This data pointed that the pharmacological effect of up-titrated doses may also be explained additional pleiotropic effects on key serum miRNAs involved in the regulation of lipid metabolism and inflammation.

ID:1343

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

COMPARATIVE EFFECT OF DELAPRIL-MANIDIPINE TREATMENT VERSUS VALSARTAN-AMLODIPINE TREATMENT IN HOMA-IR, HOMA-B, HOMA-S AND QUICKI INDEXES IN PREDIABETIC HYPERTENSIVE PATIENTS.

POSTER VIEWING SESSION

Angelos Liontos[1], Sempastien Filippas-Ntekouan[1], Dimitrios Biros[1], Alexandros Papathanasiou[1], Christos Papagiannopoulos[1], Nikolaos-Gavriil Kolios[1], Cornelia Veliani[1], Lazaros Athanasiou[1], Valentini Samanidou[1], Stavros Tsourlos[1], Christiana Pappa[1], Eleni Pargana[1], Maria Nasiou[1], Athina Zarachi[2], Eirini Christaki[1], Moses Elisaf[3], Evangelos Liberopoulos[4], Haralampos Milionis[1], George Liamis[3]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]2nd Department Of Internal Medicine, University Hospital Of Ioannina, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [4]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece

Background and Aims : Introduction: Prediabetes is often present in patients with arterial hypertension. The effect of various antihypertensive drugs on the glucose homeostasis has been discussed extensively. Dual combination treatment is advised with current guidelines. We present comparative data of the effect of valsartan/amlodipine versus delapril/manidipine combination treatments, in HOMA-IR, HOMA-B, HOMA-S AND QUICKI indices before and after the 3-month treatment, in hypertensive prediabetic patients.

Methods: METHODS: Data were collected from 107 patients from the outpatient clinic for lipid metabolism, hypertension and diabetes, during the period 2014-2018. 53 patients were randomized in the delapril/manidipine group 30/10 mg per day while 54 patients had been randomized in the group of valsartan/amlodipine 160/5mg per day. All patients successfully completed the study. Baseline

characteristics are presented in **Table 1A**.

Table 1A: Baseline patients' characteristics

Characteristics/Combination of drugs	DEL/MANI	VAL/AMLO
N (Men-Women)	53(30-23)	54(33-21)
Age (Years)	58.08±11.73	64.44±11.64
Smokers (%)	12(22.6%)	14(25.9%)
Alcohol Consumers (%)	7(13.2%)	8(14.8%)
Body Weight (Kg)	83.67± 13.21	80.83±11.80
BMI (Kg/m^2)	28.73 [27.73-30.3]	1.69[1.62-1.75]
Glucose (mg/dl)	100[97-107]	104[96.25-110.75]
Insulin ($\mu IU/mL$)	8.6[6.3-11.4]	6.2[4.2-9.23]

Results: RESULTS: The results of the alternations in HOMA-IR, HOMA-B, HOMA-S AND QUICKI, before and after the 3-month treatment are presented on Table 1B

Table1B. Results of glycemic profiling tests before and after the three-month treatment

Parameter	Commencement	After 3 Months of Treatment	% change	p-value
HOMA-IR				
DEL/MANI	2.14[1.52-2.89]	2.17[1.35-2.74]	1.4 % (0.03)	0.577
VAL/AMLO	1.66[1.01-2.18]	1.87[1.05-2.83]	12.65 % (0.21)	0.072
HOMA-B (%)				
DEL/MANI	81.63[52.62-103.52]	88.24[63.91-137]	7%(6.61)	0.006
VAL/AMLO	57.95[38.3-84.82]	69.59[40.71-99.13]	17%(11.64)	0.067
HOMA-S				
DEL/MANI	0.01[0.01-0.02]	0.01[0.01-0.02]	0%(0)	0.389
VAL/AMLO	0.02[0.01-0.03]	0.01[0.01-0.03]	-33.33%(-0.01)	0.894
QUICKI				
DEL/MANI	0.34[0.33-0.36]	0.34(0.33-0.37)	0%(0)	0.177
VAL/AMLO	0.35[0.34-0.38]	0.35[0.33-0.38]	0%(0)	0.487

The data are presented as Average ± Standard Deviation, Median [25th-75th].

Conclusions: CONCLUSIONS: From the studied population, no significant differences were observed between treatment groups' comparison, for all parameters after the 3-month treatment. For the VAL/AMLO treatment group there have been noted statistically insignificant increases in HOMA-IR (+12.65%) and HOMA-B (+17%). Finally, no change has been observed in QUICKI values, while in the DEL/MANI for the HOMA-IR and QUICKI, there were no significant variance, while HOMA-B values showed a statistically significant increase (7%, p=0.006).

ID:1345

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

VULNERABLE ATHEROMATOUS PLAQUE STABILIZATION USING EXTRACORPOREAL SHOCK WAVE- MEDIATED SONOPORATION THERAPY- ASSISTED HDL AND ATORVASTATIN COMBINATION THERAPY

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : Large mature or immature lipid core (atheroma) within a thin- fibrous cap, is called vulnerable atheromatous plaque. The management of vulnerable atheromatous plaque reduces the risk of ischemic disease and its related deaths. In this study, we developed an experimental electrohydraulic shock wave generator (0–20 kv) and investigated its effectiveness on vulnerable atheromatous plaque stabilization in the golden Syrian hamster common carotid artery.

Methods: Vulnerable atheromatous plaque was induced at the right common carotid artery of golden Syrian hamsters. The animals treated by repeated electrohydraulic focused shock waves (V= 18 Kv, F= 0.1 Hz, Impulses= 120) accompanied by simultaneously atorvastatin and HDL administration. Blood volume flow and blood mean velocity were measured by color Doppler ultrasonography at the stenotic region. Moreover, wall mean thickness and percentage of luminal cross-sectional area of stenosis were measured by B-mode ultrasound and histology.

Results: from histopathology, color Doppler and B-mode ultrasonography showed a significant reduction in the mean value for blood mean velocity, wall mean thickness and the percentage of luminal cross-sectional area of stenotic region and a significant increase in the mean value for blood volume flow and plaque fibrotic content in the treatment group compared with the other groups ($P < 0.05$).

Conclusions: Sonoporation effect of shock waves, can cause to increase of lipophilic and pleiotropic effects of atorvastatin and anti-inflammatory effects of atorvastatin and HDL, resulting in a reduction in lipidic content in the atheromatous plaque and significantly increase the plaque fibrotic content and regress the atheromatous plaque.

ID:1354

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

ASSOCIATION OF MYOCARDIAL INJURY BIOMARKERS AND CARDIOVASCULAR MAGNETIC RESONANCE PARAMETERS IN STEMI PATIENTS TREATED WITH PRIMARY PCI

POSTER VIEWING SESSION

Agneta Virbickiene[1], Lina Padervinskiene[2], Rita Kreckauskiene[1], Paulius Bucius[1], Justina Jureviciute[1], Antanas Jankauskas[2], Olivija Gustiene[1], Tomas Lapinskas[1]
[1]Department Of Cardiology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania, Kaunas, Lithuania, [2]Department Of Radiology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania, Kaunas, Lithuania

Background and Aims : We tried to assess the prognostic significance of morphological LV parameters from CMR in relation with biomarkers in patients presenting with acute STEMI treated with primary percutaneous coronary intervention (PPCI).

Methods: We performed a prospective study that included 30 patients with acute STEMI. Patients underwent baseline CMR 2-5 days after myocardial infarction (n=30) and 26 patients were scanned at 6 months follow up. CMR analysis included quantification of structural and functional LV parameters and was carried out using Medis 3.2 software. Biomarkers included Brain Natriuretic Peptide (BNP), Troponin I, C-reactive protein (CRP) and high sensitivity CRP.

Results: There was significant improvement in LVEF (44.17 ± 9.61% vs. 47.52 ± 11.30%; p<0.001) and decrease of infarct size (44.40 ± 18.75% vs. 35.87 ± 16.07%; p<0.001) at follow up. Baseline MI size strongly correlated with baseline LVEF (r=-0.622; p<0.001), moderately with LVESVi (p=0.011, r=0.465). There was a moderate correlation between baseline MI size and follow-up LVEF (r=-0.526; p=0.006) as well as with LVESVi (r=0.430; p=0.028). We observed strong correlation with BNP and follow-up MI size (r=0.654; p=0.001), moderate with baseline MI size (r=0.454; p=0.028) and area at risk (AAR), (r=0.454; p=0.017). Troponin I concentration correlated with baseline (r=0.534; p=0.003) and follow-up (r=0.510; p=0.008) MI size, AAR (r=0.599; p<0.001), MVO (r=0.476; p=0.008), baseline (r=-0.432; p=0.017) and follow-up LVEF (r=-0.544; p=0.004). No significant correlation was obtained between CRP, high-sensitivity CRP.

Conclusions: Troponin I as well as BNP concentrations and reperfusion injury morphological parameters quantified by CMR possibly influence LV remodeling process in acute STEMI patients treated with PPCI.

ID:1348

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

CLINICAL IMPACT OF CIRCULATING MICRORNA-21-5P ON THE SEVERITY OF CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Md Sayed Ali Sheikh
College Of Medicine, Internal Medicine Department, Jouf University, Sakaka, Saudi Arabia

Background and Aims : To explore the clinical value of circulatory miR-21-5p as an early non-invasive biomarker for coronary artery disease (CAD) patients and the degree of coronary artery stenosis.

Methods: Invasive angiographically confirmed 87 multivessel lesion CAD, 73 double vessel lesion CAD, 35 single vessel CAD patients and 35 healthy subjects were enrolled in this study.

Results: Circulatory plasma miR-21-5p expressions were gradually and significantly elevated in single, double, and multi-vessel occluded CAD subjects as compared with healthy participants ($p<0.001$). Muti-vessel CAD (AUC: 0.962), double vessel CAD (AUC: 0.953) and single vessel CAD (AUC:0.947) patients were able to significantly differentiated from healthy subjects with remarkable specificity and sensitivity. Plasma miR-21-5p concentrations in single, double and multi-vessel geriatric (65-85 years) CAD subjects were prominently higher as compared with younger (25-45 years), (46-64 years) age groups CAD subjects($p<0.001$).

Conclusions: Elevated plasma miR-21-5p levels may be used a potential non-invasive biomarker for early detection of CAD patients and categorized the severity of coronary artery stenosis levels.

ID:1349

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

THE IMPORTANCE OF BETA-BLOCKER TREATMENT IN DIABETIC HYPERTENSIVE PATIENTS WITH DIFFERENT DIPPER PATTERNS, IN SPECIAL ON THE NOCTURNAL NON-DIPPER PROFILE.

POSTER VIEWING SESSION

Viorel Manea[1], Calin Pop[2], Lavinia Pop[3], Mircea I. Popescu[4]
[1]Upu, Emergency County Hospital, Baia Mare, Romania, [2]Faculty Of Medicine, Vasile Goldis University, Arad, Romania, [3]Cardiology, Emergency County Hospital, Baia Mare, Romania, [4]Faculty Of Medicine, University of Oradea, Oradea, Romania

Background and Aims : This study aims the effectiveness of beta-blocker treatment on nocturnal heart rate and high blood pressure (HBP) levels, especially in the non-dippers pattern, comparing mean heart rate (MHR) and mean arterial pressure (MAP).

Methods: 166 consecutive hypertensive patients with diabetes mellitus (DM) have been treated with beta-blockers (βB), angiotensin-converting enzyme inhibitors (ACEI), calcium channel blockers (CCB), angiotensin receptor blockers (ARB), and diuretics, performed 24 hours' ambulatory blood pressure monitoring (ABPM). We follow MHR, MAP, and the correlations of dipper profiles with the HBP treatment.

Results: There were: 80 non-dippers, 57 dippers, 22 reverse-dippers, and 7 extreme-dippers. Non-dippers treated with βB had lowers 24 hours MHR: 72.46 beats per minute (bpm) vs. 78.00 bpm, p=0.015, morn MHR: 73.48 vs.79.26, p=0.032, day MHR: 74.61 vs.81.50, p=0.005 and night MHR: 68.77 vs.73.26 , p=0.038, like those without βB. Non-dippers with vasodilating βB had reduced MAP/24h 90.05 mmHg vs.95.42 mmHg, p=0.030, MAP morning 93.57 vs. 99.84, p=0.023, MAP day 91.12 vs. 96.19, p=0.043 and MAP night 86.59 vs.91.84, p=0.037 compared to those without βB. Dippers treated with βB had MHR and MAP not significantly changed compared with dippers without βB.

Conclusions: The non-dippers diabetics have grown MHR and MAP compared to dippers, but non-dippers treated with βB have significantly low MHR and MAP than those without βB. Treatment of HBP with beta-blockers does not influence lowering MHR and MAP in dippers, they were mainly treated with ACEI and CCB.

ID:1350

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

COMPARATIVE EFFECT OF VALSARTAN-AMLODIPINE TREATMENT VERSUS TELMISARTAN-AMLODIPINE TREATMENT IN HOMA-IR, HOMA-B, HOMA-S AND QUICKI INDEXES IN PREDIABETIC HYPERTENSIVE PATIENTS.

POSTER VIEWING SESSION

Angelos Liontos[1], Sempastien Filippas-Ntekouan[1], Dimitrios Biros[1], Nikolaos-Gavriil Kolios[1], Christos Papagiannopoulos[1], Cornelia Veliani[1], Alexandros Papathanasiou[1], Valentini Samanidou[1], Stavros Tsourlos[1], Lazaros Athanasiou[1], Christiana Pappa[1], Eleni Pargana[1], Maria Nasiou[1], Athina Zarachi[2], Ioannis Vagias[1], Ilias Tsiakas[1], Eirini Christaki[1], Moses Elisaf[3], Evangelos Liberopoulos[4], Haralampos Milionis[1], George Liamis[3]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]2nd Department Of Internal Medicine, University Hospital Of Ioannina, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [4]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece

Background and Aims : Introduction: According to the latest ESC guidelines for hypertension treatment, it is recommended to use combination therapy of 2 antihypertensive agents as a starting point for most patients. The effect of these drugs on the glucose homeostasis has been discussed extensively. Many hypertensive patients are at risk of developing diabetes as are already in a prediabetic state. We present comparative data of the effect of valsartan/amlodipine versus telmisartan/amlodipine combination treatments, in HOMA-IR, HOMA-B, HOMA-S AND QUICKI indices before and after the 3-month treatment, in hypertensive prediabetic patients.

Methods: METHODS: Data were collected from 94 patients who visited our outpatient clinic for lipid metabolism, hypertension and diabetes, during the period 2014-2018. 54 persons were randomized in the valsartan/amlodipine group 160/5 mg per day while 51 persons had been randomized in the group of telmisartan/amlodipine 80/5mg per day. All patients successfully completed the study. Baseline characteristics are shown in **Table**

1A.

Characteristics/Combination of drugs	TEL/AMLO	VAL/AMLO
N (Men-Women)	51(35-16)	54(33-21)
Age (Years)	58.04±13. 6$$$	64.44±11.64
Smokers (%)	31(60.8%)	14(25.9%)
Alcohol Consumers (%)	16(31.4%)	8(14.8%)
Body Weight (Kg)	84.72± 12.87	80.83±11.80
BMI (Kg/m^2)	29.32 [27.37-31.65]	28.09 [26.81-29.89]
Glucose (mg/dl)	100[98-106]	104[96.25-110.75]
Insulin (*μIU/mL*)	13[9.5-14.9]	6.2[4.2-9.23]

/

Results: RESULTS: The results of the alternations in HOMA-IR, HOMA-B, HOMA-S AND QUICKI, before and after the 3-month treatment are presented

on **Table 1B**.

Table1B. Results of glycemic profiling tests before and after the three-month treatment

Parameter	Commencement	After 3 Months of Treatment	% change	p-value
HOMA-IR				
TEL/AMLO	3.06[2.27-3.91]	2.37[1.44-3.61]	-22.55 % (-0.69)	0.005*$$$
VAL/AMLO	1.66[1.01-2.18]	1.87[1.05-2.83]	12.65 % (0.21)	0.072^^^
HOMA-B (%)				
TEL/AMLO	118.33[85.23-144.66]	95.57[65.66-142.61]	-24%(22.76)	0.283
VAL/AMLO	57.95[38.3-84.82]	69.59[40.71-99.13]	17%(11.64)	0.067
HOMA-S				
TEL/AMLO	0.01[0.01-0.01]	0.01[0.01-0.02]	0%(0)	0.381
VAL/AMLO	0.02[0.01-0.03]	0.01[0.01-0.03]	-33.33%(-0.01)	0.894
QUICKI				
TEL/AMLO	0.32(0.31-0.34)	0.34(0.32-0.36)	6%(0.02)	0.002$$
VAL/AMLO	0.35[0.34-0.38]	0.35[0.33-0.38]	0%(0)	0.487^^

The data are presented as Average ± Standard Deviation, Median [25th-75th].

^p < 0.05 compared to TEL/AMLO therapy, ^^p < 0.01 compared to TEL/AMLO therapy, ^^ < 0.001 compared to TEL/AMLO therapy

$p < 0.05 compared to VAL/AMLO therapy, $$p < 0.01 compared to VAL/AMLO therapy, $$$p < 0.001 compared to VAL/AMLO therapy

Conclusions: CONCLUSIONS: Patients in the TEL/AMLO group had significantly lower insulin resistance as shown by the HOMA-IR index compared with the patients that received valsartan and amlodipine (p <0.001). Furthermore, QUICKI index was significantly increased in the TEL/AMLO group compared with the VAL/AMLO group (p<0.01).

ID:1351

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

APOLIPOPROTEIN B (APO B) AS AN ATHEROGENIC FACTOR IN PATIENTS WITH METABOLIC SYNDROME.

POSTER VIEWING SESSION

Evgenia Mavrokefalou, Georgios Tomazou, Stella Ntavidi, Adamantia Chioti, Marilena Kylla, Dimitrios Kamarinopoulos, Varvara Polymniou, George Marakomichelakis
4th Clinic Of Internal Medicine, General Hospital of Athens Evaggelismos, Athens, Greece

Background and Aims : It is known that the ratio of apolipoprotein B to apolipoprotein A1 (ApoB / ApoA1) is a strong predictor for the occurrence of cardiovascular disease. The plasma concentration of apolipoprotein B (ApoB) is associated with various cardiometabolic agents. Aim: The association of apoB levels in dyslipidemic individuals with metabolic syndrome (METS).

Methods: 548 people were studied with an average age of 62±8, of whom 230 (41.89%) were men and 318 (58.10%) women. Patients had dyslipidemia and they were divided into 2 groups depending on the presence or not of the metabolic syndrome. The METS was defined on the basis of the criteria of NCEP-ATP III. Patients were monitored annually for a total of 5 years.

Results: The prevalence of METS was 25.9%. ApoB was higher in people with METS compared to those without METS (±18 vs. ±12, p<0,001). Higher apoB was found in obese people (±15.6 vs. ±14, p=0.011), in people with blood pressure >130/85mmhg (±15 versus ±13, p<0,001), fasting glucose values >110mg/dl (± 19 vs. ±13.6, p<0.001) and triglycerides ≥150mg/dl (± 19.7 vs. ±11.8, p<0.001)..The serum level of ApoB is strongly associated with inflammatory agents and insulin resistance in people with METS and T2DM but in patients with T2DM, apoB had a high related to MetS independently of LDL-C level.

Conclusions: Increased serum ApoB levels may indicate the presence of metabolic syndrome and be an additional indicator for the onset of cardiovascular disease.

ID:1352

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

IDENTIFICATION OF FAMILIAL HYPERCHOLESTEROLAEMIA (FH) IN MALTA: AN UPDATE OF THE FH REGISTRY AND CASCADE SCREENING PROGRAMME IN MALTA

POSTER VIEWING SESSION

Myra Tilney[1,2,3], Antonio J. Vallejo-Vaz[2], Azeem Majeed[2]
[1]Primary Healthcare, Ministry for Health, Floriana, Malta, [2]Primary Care And Public Health, Imperial College London, London, United Kingdom, [3]Medicine, University of Malta, B'kara, Malta

Background and Aims : FH is a common inherited condition causing premature cardiovascular disease; early identification and implementation of available, cost-effective, lipid-lowering therapy reduces risk significantly-yet FH is underdiagnosed and undertreated. Its autosomal dominant inheritance mandates family screening - ideally using genetic testing, which is constrained by availability, resources, and unknown mutation patterns in understudied populations. Under 10% of the predicted population is included in the Malta FH Register (c. 1,715, based on prevalence 1:300). We updated Registry and cascade process information.

Methods: FH Malta commenced as a prospective observational study in 2017. Index cases (ICs) are diagnosed using DLCN clinical criteria. Relatives are invited for biochemical cascade and classified as ”Likely”, “Uncertain” and “Unlikely” FH (Starr 2008,Clin Chem Lab Med). We present registry descriptive statistics and a reflective process review.

Results: 105 ICs (76 women, 29 men) were identified, classifying as ‘definite’, ‘probable’ and ‘possible’ (6.7%,27.6%, 65.7%) FH. Mean age at registry entry was 58.9±9.6 years (women: 61.4±7.7, men 52.4±11.0, p-value women vs men 0.0003). 107 relatives were invited, with 61 (57%) attendees classified as ‘likely’,’ uncertain’ and ‘unlikely FH (19.3%,19.3%,64%). Reasons for non-attendance included: already receiving care; premature death; moved overseas, not interested. Relatives identified as ’Likely FH’ were linked to ICs uniformly classified as ‘Probable/Definite’ FH. Most ICs were identified early, with fewer

recent participants (possible pandemic impact). Some reflective points are highlighted (Table

Table 1: Features identified in cascade testing
Late identification of index patients, affecting recruitment and late treatment initiation (missing years without treatment)
Limited understanding by patients of the natural history of the condition and the risk it entails.
Reluctance to reveal hereditary condition to others in a small community
No children identified to date (expected prevalence <70 cases in Malta if prevalence 1:300).
Siblings 'grow apart' in later life - and reluctant to reveal health information.
COVID19 situation likely affecting clinic attendance, resources available and health care system priorities.
Better identification rate than the predicted 1 in every 2 first degree relatives (when comparing 'Likely/Uncertain' recruits (n=22) with those identified as 'Definite or Probable' FH- (n=36).

1).

Conclusions: The Registry has led to limited identification of FH. Improved implementation, resourcing and primary care, with consideration of points reflected in Table 1 is needed.

ID:1353

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

THE MEDITERRANEAN DIET AND GLYCEMIC REGULATION IN PATIENTS WITH DYSLIPIDEMIA AND DIABETES MELLITUS TYPE 2.

POSTER VIEWING SESSION

Evgenia Mavrokefalou, Georgios Tomazou, Marilena Kylla, Varvara Polymniou, Dimitrios Kamarinopoulos, Stella Ntavidi, George Marakomichelakis
4th Clinic Of Internal Medicine, General Hospital of Athens Evaggelismos, Athens, Greece

Background and Aims : The Mediterranean diet is considered a cornerstone in the regulation of the person with dyslipidemia and diabetes mellitus. The aim of the study is to record the eating habits of patients with dyslipidemia and type 2 diabetes mellitus and to correlate these habits with their regulation.

Methods: This study involved 686 patients (365 men and 321 women with an age of 62.6±8 years). A registration questionnaire by MedDietScore was used for them and they were reassessed with a review after six and 12 months respectively.

Results: The duration of dyslipidemia was 11.8±12.3 and DM2 was 12.6±12.3 years. The mean value of HbA1c was 6.82±2.48%, with 56.8% of patients having HbA1c **<** 7%. The BMI was 31.8±7.25 in both sexes (p=0.440). 65.6% of patients were overweight, and obese having higher in women. 84.1% of patients consume breakfast, fruits more than 7 times a week 32.1%, vegetables at least 2 times 54.8%, meat 2 times 43%, fish 1 time 45.8%, chicken 2 times 27.7% and sweets consume 18.8% of patients. A positive association with the regulation of dyslipidemia and DM2 is shown by the consumption of balanced breakfast (p=0.001) and the presence of 2 main meals (p=0.008). The high consumption of junk food (p=0.009), of soft drinks (p=0.056) and of sweets (p< 0.001) had a negative impact. The prevalence of metabolic syndrome was found to be less in those who followed the Mediterranean diet.

Conclusions: The eating habits of people with dyslipidemia and DM2 affect their regulation having a positive effect especially on glycemic regulation.

ID:1454

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

IMPACT OF COVID-19 OUTBREAK IN STEMI PATIENTS IN THE REGIONAL EMERGENCY CENTER IN SEOUL, KOREA

POSTER VIEWING SESSION

Youngduck Cho, Younghoon Yoon, Sungjun Park
Emergency Medicine, Korea University Guro Hospital, Seoul, Korea, Republic of

Background and Aims : The highly infectious character of COVID-19 demands healthcare personnel to be alert and implement special infection control measures to limit its virulence. AMI patients' prognosis depends on early diagnosis and prompt treatment. For such reasons, early transportation to the center with skilled and qualified cardiologists is critical in post AMI prognosis. However, patients who fear acquiring COVID-19 visit the hospital at a delayed time. Therefore, we presumed the COVID-19 outbreak might cause a delay in the process of STEMI patients receiving PCI in the ED. Moreover, we wanted to evaluate the outcome.

Methods: We collected data from a hospital-based registry. Our center has a cardiology team standby for 24/7 PCI, and the cardiology team is alerted by an urgent treatment processing system (UTPS). UTPS is an alert system that requires corresponding specialists to respond in priority. We set the pre-COVID 19 periods before January 1, 2020, and the COVID 19 periods after January 1, 2020. We compared data from two periods to assess the noticeable differences.

Results: During the COVID-19 period, there was a noticeable decrease in STEMI patients. After arrival, alerting cardiology specialists process time was delayed in the COVID period group. Also, puncture time after cardiologist arrival and Puncture to balloon time was significantly longer in the COVID period group. More patients suffered from MACE during the COVID-19 period without statistical significance (p=0.012). The number of patients admitted to ICU and expired were similar.

Conclusions: Early recognition of critically ill patients will lead to lower misdiagnosis rates, an increase in prompt treatments, and improving prognosis.

ID:1463

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

MACHINE LEARNING IN PREDICTION OF IN-STENT RESTENOSIS.

POSTER VIEWING SESSION

Anastasiia Y. Filatova[1], Vadim I. Vybornov[2], Ekaterina A. Pylaeva[1], Alexandra V. Potekhina[3], Tatiana I. Arefieva[1], Sergey I. Provatorov[3]
[1]Laboratory Of Cell Immunology, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation, [2]Space Research Institute, Space Research Institute, Moscow, Russian Federation, [3]Department Of Pulmonary Hypertension And Heart Diseases, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation, Moscow, Russian Federation

Background and Aims : In-stent restenosis (ISR) after coronary angioplasty and stent implantation is associated with recurrent angina symptoms, higher risk for acute coronary syndrome, and increased mortality. Current ISR risk prediction models (PRESTO-1, PRESTO-2, and EVENT) suffer from insufficient predictive power. We aimed to investigate patient outcome prediction with classification predictive modeling in Machine Learning.

Methods: In retrospective study 203 available cases of ISR and 1009 control cases were included. Twenty seven demographic, clinical, biochemical and angiographic characteristics from each patient were obtained. Such machine-learning classifiers as logistic regression, random forest and XGBoost were used. The initial dataset was randomized into training (n=1057) and test (n=155) datasets. The prediction was performed by classifying samples into low or high digital risk score (DRS) groups. The prediction of outcome in the test dataset performed by machine-learning classifiers was further compared with the human expert classification.

Results: The incidence of ISR in the test dataset was 11%. Among the used machine-learning algorithms, the XGBoost classifier demonstrated the best predictive capacity in the unbalanced dataset. The DRS classification resulted in an odds ratio of 14.57 (95% CI 2.69–84.30, p=0.01) for prediction of ISR. The accuracy (C-index) of the DRS grouping was 0.89 (95% CI 0.84–0.94), as compared to 0.75 (95% CI 0.68–0.82) for human expert prediction in the same cohort.

Conclusions: Development of machine-learning algorithms will allow to reveal patients at higher risk of ISR for the further closer monitoring ISR or consideration of alternate therapies. A prospective validation is required before this biomarker can be implemented in clinical workflows.

ID:1318

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

EVALUATION OF STABILITY OF TETRA-PRIMER ARMS PCR KIT TO DETECT PATHOGENIC FAMILIAL HYPERCHOLESTEROLAEMIA VARIANTS VIA ACCELERATED AGING METHOD

POSTER VIEWING SESSION

Norhidayah Rosman[1,2], Hapizah Nawawi[1,2], Yung An Chua[1], Alyaa Al-Khateeb[1,2], Ang Lim Chua[2]
[1]Universiti Teknologi Mara Sungai Buloh Campus, Institute of Pathology, Laboratory and Forensic Medicine (I-PPerForM), SUNGAI BULOH, Malaysia, [2]Universiti Teknologi Mara Sungai Buloh Campus, Faculty of Medicine, Sungai Buloh, Malaysia

Background and Aims : Family hypercholesterolaemia (FH) is an inherited disorder that causes elevated cholesterol levels, thus leads to premature coronary artery disease. Confirmation of FH is conducted using NGS, which is laborious, time-consuming and costly. A thermostabilised tetra-primers ARMS PCR kit was recently developed, providing ease and speed over NGS. However, the stability of this newly-developed kit is still unknown. Thus, this study aims to determine the stability of tetra-primers ARMS PCR kit to detect pathogenic FH variants via the accelerated aging method.

Methods: Twelve sets of tetra-primers ARMS PCR for pathogenic low-density lipoprotein receptor *(LDLR)* and apolipoprotein B *(APOB)* gene variants were lyophilised into a PCR plate. The kit was subjected to three storage temperatures (RT, 40ºC and 60ºC). Testing of the stability was performed on Day 1, Day 3, Day 7, Day 14, Day 30, Day 60, and Day 90 towards synthetic DNA (positive control) and non-FH patients in this study.

Results: The shelf life of lyophilised primers was ~6 months at RT but 2-3 months at 40ºC and 60ºC based on accelerated aging. Although lower concentrations of template DNA (1ng for positive control and 10ng for non-FH patient DNA) were used in this study, the accuracy of this kit remained stable over time.

Conclusions: The T-ARMS PCR kit retain accuracy and reproducibility at RT, implying they can be safely transported and stored at RT for field application if PCR equipment is available. These findings are critical for future FH research because this method is simple and effective for detecting FH patients in Malaysia.

ID:1534

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-11 Anti-inflammatory therapies*

ARGON LASER- MEDIATED THERMAL ANGIOPLASTY OF OCCLUDED ARTERY ACCOMPANIED BY COMBINED ROSE BENGAL AND RIBOFLAVIN- LOADED NANOLIPOSOMES- MEDIATED CATHETER- BASED POLARIZED GREEN LASER PHOTODYNAMIC THERAPY

POSTER VIEWING SESSION

Hossein Mehrad
Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran

Background and Aims : The atherectomy methods that are currently in use, cause to inflammation and the subsequent restenosis. The aim of this study was to evaluate the effect of combined photodynamic therapy on inflammation and intimal hyperplasia reduction after laser angioplasty.

Methods: Briefly, New Zealand white rabbits were submitted to femoral artery advanced atherosclerotic occlusion by primary perivascular severe cold injury followed by a 2% cholesterol- rich diet for fourteen weeks. Histopathology results showed the formation of advanced atherosclerotic plaque with thick-fibrous cap and collagen, lipid and neovessel - rich content, resulted in occlusion in all of the rabbits' arteries. Then treatment group underwent B- mode ultrasound- guided argon laser (488 nm) angioplasty followed by combined rose bengal (2mg/Kg) and riboflavin (5 mg/ Kg)- loaded nanoliposomes- mediated catheter- based polarized green laser (λ= 532 nm, E/A= 120 J/cm2) photodynamic therapy.

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for immune cells, foam cells and hyperplastic vascular smooth muscle cells density after angioplasty in the treatment group compared with the other groups ($p < 0.05$).

Conclusions: Photoporation and targeted drug delivery effect of laser phototherapy and enhanced cytotoxic, apoptotic and anti- inflammatory effect of photodynamic therapy, induced by combined photosensitizer- mediated photodynamic therapy, can cause to reduce the density of immune cells, foam cells and hyperplastic smooth muscle cells in the intimal layer. These findings provide the basis for developing of combined photodynamic therapy for a successful clinical application in the treatment of neointimal hyperplasia after laser angioplasty in this model.

ID:1593

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

SUBCLINICAL ATHEROSCLEROTIC LESIONS OF THE CAROTID ARTERIES IN RHEUMATOID ARTHRITIS PATIENTS WITH LOW CARDIOVASCULAR RISK

POSTER VIEWING SESSION

Elena V. Gerasimova[1], Tatiana V. Popkova[1], Daria A. Gerasimova[2], Tatiana V. Kirichenko[3]
[1]Laboratory Of Systemic Rheumatic Diseases, V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation, [2]Institute Of Pharmacy Named After A.p. Nelyubin, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation, [3]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation

Background and Aims : To evaluate the detection rate of carotid atherosclerotic plaque (ASP) (IMT≥1.2mm) in rheumatoid arthritis patients (RApts) with low cardiovascular risk (CVR) in comparison with the control group (CG).

Methods: The study included 275 RApts with low CVR (QRISK3<20%) and 100 people without autoimmune diseases (CG). The groups were comparable in terms of sex, age, traditional risk factors, and CVR value.

Results: ASP were observed more frequently in RApts (27%) than in the CG (17%),p=0.03. ASP were detected more frequently in RA men than in RA women (50% vs 24%,p<0.01). In RApts, there was a significant correlation between carotid IMT and age (R=0,48), QRISK3 (R=0,36), level of total cholesterol (R=0,28), LDL cholesterol (R=0,18), systolic (R=0,37) and diastolic blood pressure (R=0,38), p<0,05. No correlation between carotid IMT and RA biomarkers (rheumatoid factors, anti-citrullinated protein antibodies) and adhesion molecules (sVCAM, sIACAM) was found in RApts. In RApts with carotid ASP, sCD40L level was associated with carotid IMT (R=0.40,p=0.04) and cholesterol concentration (R=0.38, p=0.01).

Conclusions: Carotid ASP were observed in a quarter of RApts with low CVR and were detected at a significantly more frequent rate compared to the CG. There is an association between carotid IMT and traditional CVR factors and sCD40L level in RApts.

ID:1587

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

LDL-C CONTROL ACCORDING TO RISK: IS THERE A GENDER PARADOX?

POSTER VIEWING SESSION

Cristina Gavina[1,2], Jorge Ruivo[3,4], Anastassia Anastassopoulou[5], Élia Almeida[6], Carla Teixeira[4], Tiago Taveira-Gomes[7,8,9,10,11]
[1]Unic, Faculdade de Medicina, Universidade do Porto, Porto, Portugal, [2]Cardiology, Hospital Pedro Hispano, Matosinhos, Portugal, [3]Department Of Medicine, Lisbon Medical School, Lisbon University, Lisbon, Portugal, [4]Medical Affairs, Daiichi Sankyo Portugal Lda, Lisbon, Portugal, [5]Market Access Europe, Daiichi Sankyo Europe GmbH, Berlin, Germany, [6]Market Access, Daiichi Sankyo Portugal Lda, Porto, Portugal, [7]Departmento De Medicina Da Comunidade, Informação E Decisão Em Saúde, Faculdade de Medicina, Universidade do Porto, Porto, Portugal, [8]Faculdade De Ciências Da Saúde, Universidade Fernando Pessoa, Porto, Portugal, [9]Instituto Universitário De Ciências Da Saúde, Cooperativa de Ensino Superior Politécnico e Universitário, Porto, Portugal, [10]Centro De Investigação Em Tecnologias E Serviços De Saúde, CINTESIS, Porto, Portugal, [11]Magalhães & Taveira-gomes Sociedade Médica, MTG, Porto, Portugal

Background and Aims : Background Low density lipoprotein cholesterol (LDL-C) treatment goals used for cardiovascular disease (CVD) prevention. Sex differences in CVD have been reported and women are less likely to receive statin therapy for secondary prevention. Nevertheless, little is known about gender according to risk categories Aims
To assess the degree of LDL-C control in men vs women by CV risk levels and to report possible associations with clinical characteristics and lipid lowering therapies (LLT) in Portugal

Methods: A non-interventional, cross-sectional study of patients regularly consulted for primary/secondary CVD in Portugal (1 hospital, 14 primary care centres). Data spanned a 12-year period (01/2008-12/2020) with index date for patient identification the 31/12/2020. CVD risk assessment was done according to 2019 ESC/EAS guidelines for the management of dyslipidaemias.

Results: In our cohort of 129 764 patients with an overall median age of 53 years, 56.9% were women. 38.9% of men and 28.9% of women were classified as high/very high risk. History of previous CV hospitalization was present in 7.3% males and 5.0% females (table 1). LDL-C targets were attained more commonly in men for high and very high risk levels, although prescription of any LLT was more frequent in women (table 2). We found similar pattern in the two years prior to the COVID-19

Table 1 – Male vs Female clinical characteristics per risk category

	Male	Female
Low Risk	**N = 18 764**	**N = 38 730**
Age - P50 (IQR)	35 (18)	40 (18)
Obesity	2 530 (13.5%)	6 689 (17.3%)
Hypertension	2 260 (12.0%)	6 043 (15.6%)
Smoking	5 008 (26.7%)	6 588 (17.0%)
Moderate Risk	**N = 10 812**	**N = 13 010**
Age - P50 (IQR)	56 (9)	64 (8)
SCORE 1-5%	10 702 (98.9%)	12 894 (99.1%)
Recent T2D without CVRF	88 (0.81%)	102 (0.79%)
Recent T1D without CVRF	29 (0.27%)	21 (0.16%)
High Risk	**N = 9 874**	**N = 10 996**
Age - P50 (IQR)	69 (13)	73 (14)
eGFR 30-60 mL/min	1 083 (11.0%)	2 127 (19.3%)
T2D over 10+ years with 1 CVRF	2 376 (24.1%)	2 798 (25.5%)
Grade 3 Hypertension	47 (0.5%)	57 (0.5%)
Total Cholesterol > 310 mg/dL	205 (2.1%)	227 (2.1%)
FH without CVRF or ASCVD	11 (0.1%)	20 (0.2%)
LDL-C > 190 mg/dL	857 (8.7%)	1 060 (9.6%)
SCORE 5 - 10 %	5 295 (53.6%)	4 707 (42.3%)
Very High Risk	**N = 11 776**	**N = 10 381**
Age - P50 (IQR)	71 (16)	73 (20)
eGFR < 30 mL/min	562 (4.8%)	837 (8.1%)
ASCVD Hospitalization	5 521 (46.9%)	4 538 (43.7%)
Diabetes with Target Organ Damage	2 415 (20.5%)	2 970 (28.6%)
T2D and 3+ Major Risk Factors	1 311 (11.1%)	1 697 (16.4%)
FH with CVRF or ASCVD	204 (1.7%)	333 (3.2%)
SCORE > 10%	1 763 (15.0%)	6 (0.1%)

pandemic.

Table 2 – Male vs Female LDL-C control and LLT stratified per risk category

	Male	Female
Low Risk	**N = 18 764**	**N = 38 730**
LDL-C < 116 mg/dL	8 608 (45.9%)	17 335 (44.8%)
Lipid Lowering Therapy	1 433 (7.6%)	3 749 (9.7%)
Low Intensity Statin	95 (0.5%)	353 (0.9%)
Moderate Intensity Statin	1 083 (5.8%)	3 042 (7.9%)
High Intensity Statin	52 (0.3%)	128 (0.3%)
Ezetimibe	87 (0.5%)	16 (0.4%)
Intermediate Risk	**N = 10 812**	**N = 13 010**
LDL-C < 100 mg/dL	2 165 (20.0%)	2 813 (21.6%)
Lipid Lowering Therapy	4 684 (43.3%)	7 478 (57.5%)
Low Intensity Statin	353 (3.3%)	621 (4.8%)
Moderate Intensity Statin	3 771 (34.9%)	6 387 (49.1%)
High Intensity Statin	278 (2.6%)	326 (2.5%)
Ezetimibe	325 (3.0%)	525 (4.0%)
High Risk	**N = 9 874**	**N = 10 996**
LDL-C < 70 mg/dL	843 (8.5%)	598 (5.4%)
Lipid Lowering Therapy	6 563 (64.2%)	8 035 (71.8%)
Low Intensity Statin	537 (5.4%)	766 (7.0%)
Moderate Intensity Statin	5 410 (64.8%)	6 703 (61.0%)
High Intensity Statin	392 (4.0%)	425 (3.9%)
Ezetimibe	507 (5.1%)	656 (6.0%)
Very High Risk	**N = 11 776**	**N = 10 381**
LDL-C < 55 mg/dL	782 (6.6%)	375 (3.6%)
Lipid Lowering Therapy	9 772 (82.9%)	8 526 (82.1%)
Low Intensity Statin	594 (5.0%)	641 (6.2%)
Moderate Intensity Statin	7 647 (64.9%)	6 885 (66.3%)
High Intensity Statin	1 344 (11.4%)	867 (8.4%)
Ezetimibe	1 223 (10.4%)	941 (9.1%)

Conclusions: Women fail to achieve their LDL-C goals compared to men, although they are more frequent under LLT and have lower CV risk. The reasons and clinical associations require further research. More intensive therapies should perhaps be considered in women.

ID:1583

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

DYSLIPIDEMIA - INCIDENCE IN ONCOLOGICAL AND CANCER-FREE PATIENTS

POSTER VIEWING SESSION

Kristiyan N. Georgiev
Second Neurology Clinic, MHAT "Sveta Marina" Varna, Varna, Bulgaria

Background and Aims : Dyslipidemia as a risk factor for stroke has been well established in literature. Many publications worldwide has indicated it's incidence to be different in cacer patients as opposed to the general, cancer-free population. Our study aimed to prove the frequency of dyslipidemia in cancer patients with acute stroke, compared to stroke patients without underlying cancer.

Methods: We performed a retrospective study in the years 2007-2020 including 282 cancer patients with acute stroke to 95 cancer-free patients from the same period, comparing the frequency and occurence of stroke risk factors.

Results: Dyslipidemia was found in 97 (53,29%) of the 182 patients with established cancer diagnosis with an acute stroke. From the control group 70 (73,68%) of the 95 patients that were cancer free. After the statistics were done, this difference of 20 percent had statistical significance of p<0,001. When comparing the stroke severity in both groups, it was determined that patients with cancer and dyslipidemia had significantly higher neurological deficit, as opposed to cancer patients with stroke without dyslipidemia. Dyslipidemia in cancer patients with stroke was also linked to higher mortality rates (B value - (-)5.059, Beta - (-) 0,299, p = 0,02).

Model	Unstandardized Coefficients		Standardized Coefficients		P value
	B	Std. error	Beta	t	
Dyslipidemia	-5.059	2.241	-0.299	-2.257	0.028

	Cancer patients	Cancer-free patients
With dyslipidemia	97 (53,29%)	70 (73,68%)
Without dyslipidemia	85 (46,71%)	22 (26,23%)
Total patients	182	92

Conclusions: Even though dyslipidemia has lower frequency in cancer patients, it's strongly linked with higher neurological deficit and higher mortality rates, when compared to the cancer-free population. This shows that even with it's lower frequency in this population, dyslipidemia is still a major risk factor for stroke that should be closely managed and treated.

ID:1581

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

RELATIONSHIPS BETWEEN BIOMARKERS OF HYPOXIA AND INFLAMMATION IN ELDERLY PATIENTS WITH CHRONIC CARDIORENAL SYNDROME

POSTER VIEWING SESSION

Elena Efremova, Alexander Shutov
Department Of Therapy And Occupational Diseases, Ulyanovsk State University, Ulyanovsk, Russian Federation

Background and Aims : Multibiomarker models are promising for assessing the prognosis in chronic heart failure (CHF). The aim of this study was to investigate relationships between biomarkers of hypoxia and inflammation in elderly patients with chronic cardiorenal syndrome (CCS).

Methods: 80 elderly patients with CHF (32 males and 48 females, mean age 70.7±8.7 years) were examined. Serum levels of NT-proBNP, hypoxia-inducible factor 1-alpha (HIF-1α), endogenous erythropoietin (eEPO), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-18 (IL-18) were assessed. The follow-up period was 12 months; the primary endpoint was total mortality. Type of funding sources: The grant SP-3798.2022.4.

Results: CKD with estimated glomerular filtration rate < 60 ml/min/1.73m^2 was diagnosed in 49 (61.3%) patients with CHF. Patients with CCS had higher levels of eEPO (8.2 (IQR2.4; 16.5) and 4.9 (IQR1.9; 7.9) mIU/ml resp., p=0.02), NT-proBNP (734.3 (IQR 163.2; 1420.5) and 134.3 (IQR 134; 232.5) pg/ml, resp., p=0.002), IL-6 level (14.1 (IQR 8.4;32.9) and 8,1 (IQR 4.7;11.3) pg/ml, resp., p=0.0005). There was positive relationship between hypoxia biomarkers and NT-proBNP: HIF-1α (r=0.25, p=0.024), eEPO(r=0.36, p=0.001); between IL-6 and NT-proBNP (r=0.53, p<0.0001). We defined significant relationships between IL-6 and eEPO (r=0.47, p<0.0001) and between IL-8 and HIF-1α (r=0.37, p=0.0006). The composite index (eEPO> 16.19 mIU/mL and NT-proBN> 232.5 pg/mL) predicted annual mortality in patients with CHF (RR 15; 95% CI 3.6–62.7; p=0.0008) (sensitivity 50%, specificity 93.7% (AUC=0.72); p=0.001).

Conclusions: There were complex relationships between biomarkers of myocardial, renal dysfunction, hypoxia, and inflammation in elderly patients with CCS. The use of biomarkers combination (myocardial stress and hypoxia) to assess the prognosis in CCS is promising.

ID:1580

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

STRUCTURAL AND FUNCTIONAL FEATURES AND RHYTHM VARIABILITY IN OLDER PATIENTS WITH CARDIOVASCULAR DISEASE AND CHRONIC KIDNEY DISEASE

POSTER VIEWING SESSION

Elena Efremova[1], Alexander Shutov[1], Olga Sigitova[2]
[1]Department Of Therapy And Occupational Diseases, Ulyanovsk State University, Ulyanovsk, Russian Federation, [2]Department Of Polyclinic Therapy And General Medical Practice, Kazan State Medical University, Kazan, Russian Federation

Background and Aims : The study of cardiorenal relationships is a topical direction in the field of internal medicine. The aim of this study was to investigate structural and functional characteristics of the heart and heart rate variability in older patients with cardiovascular diseases and chronic kidney disease (CKD).

Methods: 447 older patients with stable cardiovascular disease and CKD (219 males, mean age was 69,6±7,3 years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). All patients underwent electrocardiography and transthoracic echocardiography, some patients - daily ECG monitoring.

Results: CKD with eGFR less than 60 ml / min / 1.73 m^2 was diagnosed in 277 (61.9%) patients with stable cardiovascular disease. The types of left ventricular remodeling and ejection fraction did not differ depending on the presence of CKD ($p > 0.05$). The increased left atrium index was observed more often in patients with CKD than in patients without CKD: 80 (28.9%) and 26 (15%), resp. $\chi 2 = 10.75$, $p = 0.001$. There were differences in the indicators of spectral analysis of heart rhythm in patients with CKD compared with patients without CKD: a higher centralization index (0.54 (0.32; 0.87) and 0.37 (0.24; 0 , 49), resp., $p = 0.03$) and a lower vagosympathetic interaction index (1.49 (0.86; 2.31) and 3.15 (2.11; 4.58), resp., $p = 0.0004$).

Conclusions: Older patients with cardiovascular diseases and CKD had higher left atrium index and lower vagosympathetic interaction index compared with patients without CKD.

ID:1576

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

SEQ-1 PEPTIDE A KEY COMPONENT OF NASAL THERAPEUTIC VACCINE HB-ATV-8 PROMOTES DOWNREGULATION OF PRO-FIBROTIC GENES IN THE HEPATOCYTE

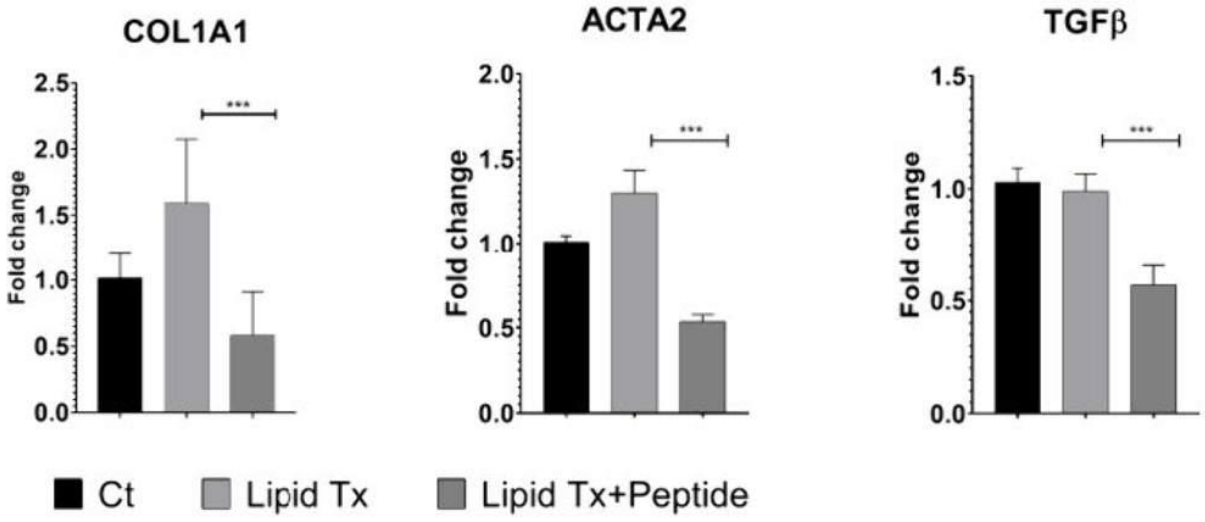
POSTER VIEWING SESSION

Jaime Mas-Oliva[1], Sandra Calixto-Tlacomulco[1], Blanca Delgado-Coello[1], Roxana Gutierrez-Vidal[2]
[1]Instituto De Fisiología Celular, Universidad Nacional Autónoma de México, Mexico City, Mexico, [2]Cinvestav, CINVESTAV, Monterrey, Mexico

Background and Aims : seq−1 peptide (CHLLVDFLQSLS) derived from the C-terminus segment of the cholesteryl-ester transfer protein (CETP), corresponds to the active component of therapeutic nasal vaccine HB-ATV-8, designed to prevent and control the processes of atherosclerosis and fatty liver disease. During our investigation, we have previously established in vivo (rabbit and pig models), the protective effect of vaccine HB- ATV-8 against the development of these two diseases.

Methods: To analyze the hepatoprotective effect of peptide seq-1 employing steatotic hepatocytes, the mRNA expression of two established pro-fibrotic markers, collagen type I (COL1A1), and *α*-smooth muscle actin (*α*-SMA), as well as cytokine TGF-*β*, was determined by quantitative RT-PCR analysis. Cell viability was assessed after treatment with lipid and/or seq-1 peptide by double staining with annexin V and 7AAD.

Results: Steatotic hepatocytes obtained by incubating HepG2 cells with a mixture of oleic acid/palmitic acid 2:1, 0.6 mM, showed an over-expression of the three transcripts studied compared to control cells. However, lipid-loaded hepatocytes when further treated with peptide seq-1 (0.01-0.1 mg/mL), show a decrease in the expression of collagen type I (p=0.001), *α*-SMA (p=0.0004), and TGF-*β* (p=0.0008). It was further determined that peptide seq-1 concentrations up to 1 mg/mL do not affect cell viability.



Conclusions: Peptide seq-1, being the active component of vaccine HB-ATV-8, independently of being the key element to produce the auto-antibody against CETP, by itself might be responsible for a direct effect upon the hepatocyte regulating extracellular matrix synthesis, and therefore the fibrotic process.

Support: UNAM-PAPIIT (IN205717); Conacyt (255778); Hamol Biosolutions LLC (development grant HB08).

ID:1572

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

ASSOCIATION BETWEEN RISK OF OBSTRUCTIVE SLEEP APNEA AND ATHEROSCLEROSIS: A REVIEW

POSTER VIEWING SESSION

Aurea M.L. Novais[1], Renan C. Castello Branco[2]
[1]Student, Bahiana School of Medicine and Public Healthy, Salvador, Brazil, [2]Biomorfofuncional Department, Bahiana School of Medicine and Public Healthy, Salvador, Brazil

Background and Aims : Obstructive sleep apnea (OSA) is a disorder characterized by airway obstruction during sleep. The relation between vasoreactivity and obstructive sleep apnea is stablished, as well as its role in vascular events; but its relation with pathogenesis of atherosclerosis and consequent events lacks information. This study reviews current knowledge about the association between atherosclerosis and OSA.

Methods: Search strategies: Pubmed and LILACS, as inclusion criteria: English language, clinical trials, published in the last 10 years, using as keywords: "atherosclerosis" and "obstructive sleep apnea"/ Exclusion criteria: articles published in other languages, involving pediatric population, studies including atherosclerosis as consequent of previous disorders, such as surgeries, or other studies that do not support the description of the clinical trial.

Results: 15 articles were found,of which 8 were primarily selected;from these,5 were excluded(they were in progress or had different outcomes evaluated).483(40%)patients were considered at high risk for OSA,with mean age of 65,and 72% were male.In two of these studies,the diagnosis of OSA was based on polysomnography and the analysis of the main outcome was the association between OSA and cardiovascular outcomes and mortality showed a significant difference.

Conclusions: Current studies demonstrate association between obstructive sleep apnea and possible mechanisms, such as endothelial dysfunction, but quantitative data and about this association is still required. The relation varies with age and the pacient's score in questionaires (Berlin, Epworth questionnaires) and presents an important role in outcomes of vascular events due to atherosclerosis. More studies are required to better define the association. This study's analyze were compromised due to different methodologies used in articles.

ID:1570

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ATHLETES HEART IN LONG DISTANCE RUNNERS: FACT OR FICTION?

POSTER VIEWING SESSION

Michiel K.B. Hartog[1,2], Louise M. Hartog[2], Jm Hartog[1]
[1]Cardiology, Diakonessenhuis, Bilthoven, Netherlands, [2]Business And Science, UU Utrecht, Bilthoven, Netherlands

Background and Aims : Since 1899 when Henschen (Sweden) described enlargement of the hearts in endurance sportsmen, there is much discussion about the effects of endurance sport on the heart. In 1959 Friedberg wrote that the athletes heart should be seen as an overloaded heart. Nowadays endurance sports like longdistance running, cycling and trathlon are very popular One of the most important questions is wether we could overload a healthy heart by extensive exercise. During extensive exercise the skeletal muscles will have een increase in bloodflow from 1 to 20 l/min. To reach this the cardiacoutput should increase from 5 to 25 l/min. ECG changes in athletes lead to false interpretations as the athletes lost weight and they had changes in sympathetic and vagal tone during there trainings program.

Methods: We performed echo measurements in 53 experienced marathon runners who were in training fort he Rotterdam Marathon. We compared their data wirh the data of 303 healthy volunteers.

Results: The marathon runners had normal end diastolic wall thickness of the left ventricle. Also the calculated end diastolic volumes of left ventrcle was similar. During rest they had a lower stroke volume. This in combination with their lower rest heartrate results in an lower cardiac output during rest. This is possible through a better oxygen extraction caused by biochemical changes by trainings effects.

Conclusions: We conclude that endurance exercise do not lead to dilated hearts. Therefore one should not be scared to do regular endurance exercise. The combined effects on health are just benificial.

ID:1562

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

HDL AND THE PATHOGENESIS OF DELAYED CEREBRAL VASOSPASM FOLLOWING SUBARACHNOID HEMORRHAGE

POSTER VIEWING SESSION

Zaida Ruiz De Azúa[1], María Rosa Pezzotti[2], Gonzalo Revilla-González[2], Joaquín Navarro-Rodríguez[1], Olivier Meilhac[3,4], Juan Ureña[2,5], Rosario Amaya Villar[1], Antonio Castellano[2,5], Lourdes M. Varela[2,5]
[1]Neurocritical Care Unit, University Hospital Virgen del Rocío, IBiS/CSIC/University of Seville, Seville, Spain, [2]Cardiovascular/respiratory And Systemic Diseases, Institute of Biomedicine of Seville, IBiS, Universitary Hospital Virgen del Rocío/CSIC/University of Seville, Seville, Spain, [3]Cyroi, UMR Inserm U1188 - Université de La Réunion Diabète athérothrombose Thérapies Réunion Océan Indien, Sainte Clotilde, Reunion Islands, [4]La Réunion, CHU de La Réunion, Saint-Denis, France, [5]Medical Physiology And Biophysics, University Of Seville, University of Seville, Seville, Spain

Background and Aims : Delayed cerebral vasospasm (DCV) is the leading cause of mortality after subarachnoid hemorrhage (SAH). There is increasing evidence that inflammation, specifically leukocyte-endothelial cell interactions, plays a role in the pathogenesis of DCV. High-density lipoproteins (HDL) are biological molecules that prevent the expression of cell adhesion molecules induced by pro-inflammatory agents in endothelial cells, thus inhibiting leukocyte adhesion. In pathological conditions, HDL undergo quantitative and qualitative changes that have been associated with loss of physiological function. However, the role of HDLs in DCV has not been studied, hence the novelty of the present work.

Methods: Plasmatic HDL were isolated from 26 patients with or without DCV, as well as 24 healthy controls. We analyzed their anti-inflammatory activity and examined the HDL-associated proteins by LC-MS-MS.

Results: We observed that SAH patients had significantly lower levels of HDL in plasma compared to controls. Furthermore, HDL isolated from patients lost the ability to prevent adhesion of THP-1 monocytes to endothelial cells (HUVEC), and the effect was more pronounced in patients with DCV. The unadjusted differential expression analysis showed eleven proteins (AGT, APOH, C3, CRP, ITIH4, LRG1, SAA1, SAA2, SAA4, SELL, SERPINA3) were overexpressed in patients, while three (APOA4, APOC2, ITIH1) were lower compared to controls. Between patients, LRG1, SAA1, and SAA2 were associated with the presence of DCV.

Conclusions: The study of HDL in the pathophysiology of DCV after SAH is needed since HDL can be considered a novel therapeutic approach to the treatment of the inflammatory response that participates in the onset of DCV after SAH.

ID:1557

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

AN UPREGULATION OF SCUBE 2 EXPRESSION IN TYPE 2 DIABETES MELLITUS WITH DYSLIPIDEMIA

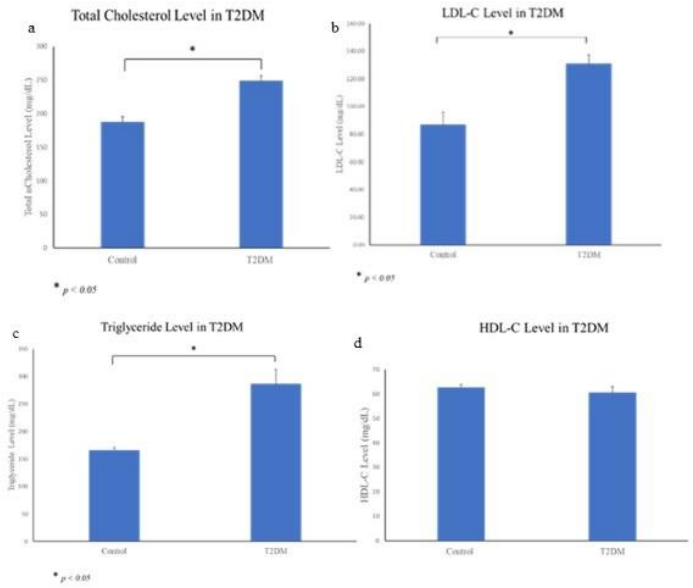
POSTER VIEWING SESSION

Hirowati Ali
Biochemistry, Faculty of Medicine, Andalas University, Padang, Indonesia

Background and Aims : Background: Type 2 Diabetes Mellitus (T2DM) reported to increase over the past 10 years. The most destructive consequence of T2DM, its long-term vascular complications. Premature atherosclerosis is one of the cardiovascular disorders in diabetes. which involving an important interactions of endothelial cells, vascular smooth muscle cells, and monocytes that lead to plaque formation. Previous study reported Signal peptide CUB-EGF like containing protein 2 (SCUBE2) gene is detected in vascular endothelial cells and affected by cytokines. Further study showed that SCUBE2 co-localized with α-SMA in intimal thickening and macrophage in advanced plaque of coronary artery, implying that this gene has a role in vascular dysfunction and inflammation. The aim of this study is to observe lipid profile and SCUBE2 gene expression in T2DM

Methods: Methods: the design of our study was cross sectional control study, recruited 25 patients diagnosed as T2DM according to American Diabetes Association (ADA) criteria which random plasma glucose (RPG) was greater than or equal to 200 mg/dL and 10 healthy control subjects

Results: our results showed that T2DM patients showed higher level of LDL cholesterol, triglycerides, and lower HDL level compared to healthy subjects (fig.1). Interestingly, we found the expression of SCUBE2 gene increased in T2DM patients with dyslipidemia
(fig.2).



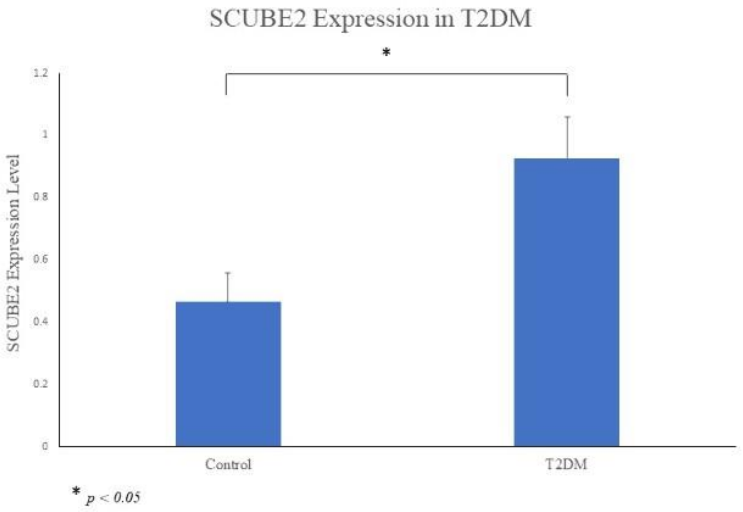


Fig.1 T2DM patients showed higher total cholesterol level, higher LDL-C level, higher triglycerides level compared to healthy controls (a, b, c). However, HDL-C showed same level in both groups (d).

Fig.2 SCUBE2 expression exhibits an upregulation in T2DM patients compared to healthy controls.

Conclusions: In conclusion, our study showed an upregulation of the expression of SCUBE2 gene in T2DM. This higher expression of this gene in concordance with the higher level of the total cholesterol, LDL-C, and triglycerides in T2DM, suggesting that SCUBE2 may be play a role in initiating premature atherosclerosis in dyslipidemic T2DM.

ID:1556

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EXPLORING FEATURE GENES FOR ISCHEMIC STROKE BASED ON BIOINFORMATICS AND MACHINE LEARNING

POSTER VIEWING SESSION

Hua Liu[1], Na Bai[1], Shenggang Liu[2], Wei Liu[3], Qiang Zhou[1], Hongwei Zhang[1]
[1]Department Of Neurology, The Affiliated Hospital of Southwest Jiaotong University, Chengdu, China, [2]Department Of Neurology, the people's hospital of Mianyang, Mianyang, China, [3]Department Of Neurology, Nanbu People's Hospital, Nanbu, China

Background and Aims : This study aims to screen the feature genes of ischemic stroke (IS) by bioinformatics and machine learning (ML) and explore the possible pathophysiological mechanism of the genes in IS.

Methods: Two RNA sequencing datasets were downloaded from NCBI Gene Expression Omnibus (GEO) database. The GSE122709 dataset with a larger sample size was used as the training set and analyzed for differentially expressed genes (DEGs), while the GSE140275 dataset was used as the test set. The DEGs were further analyzed for Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG), and Disease Ontology (DO) enrichment analyses. Then, feature genes selection was performed by two ML algorithms. The area under the receiver operating characteristic curve (AUC) was used to evaluate the performance of the ML algorithms.

Results: A total of 378 DEGs (Fold Change≥2 and *p* value≤0.05) were identified. The GO and KEGG analyses demonstrated that the majority of DEGs were associated with inflammatory response, immune regulation and COVID-19. The DO analysis revealed that the DEGs were mainly linked to demyelinating disease and cancer. The TVP23C and B3GAT1 were identified as feature genes by ML algorithms, and the AUCs of them were closer to 1 both in the training and test set. It is found that B3GAT1 may be involved in brain injury of IS by regulating AMRA glutamate receptors.

Conclusions: The integrated approach of bioinformatics and ML could be a novel approaches for screening feature genes, and the B3GAT1 gene may be a possible therapeutic target in IS.

ID:1555

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

NEW EQUATION FOR LDL-C ESTIMATION BASED ON THE RELATIONSHIPS BETWEEN EXTRAHEPATIC VLDL-C AND TOTAL TRIGLYCERIDES.

POSTER VIEWING SESSION

Victor Gurevich[1], Pavel Sadovnikov[2], Andrey Olkhovik[2]
[1]Center Of Atherosclerosis And Lipid Disorders, Saint-Petersburg State University, Saint-Petersburg, Russian Federation, [2]Data Management, Laboratory Service "HELIX, St. Petersburg, Russian Federation

Background and Aims : Friedwald formula routinely used to determine LDL-C blood levels leads to underestimated results if increased triglyceride levels take place. Proposed before alternative equations are either relatively complex for usage or are also limited by triglyceride levels.
The aim of this work was to create the calculation formula for LDL-C based on concept that the relationships between extrahepatic VLDL-C and total triglycerides are the more exact characteristic of circulating blood lipids.

Methods: 750,000 lipid tests were analyzed. Data processing was performed using the Python programming language version 3.9.2 The accuracy of the model was evaluated by the Allowable Total Error (TEa) = 11.6%.

Results: The graph of the dependence of VLDL-C levels on the content of triglycerides in all of lipoprotein fractions was constructed. The coefficients of the intermediate equations were obtained from the linear regression equation, fitted by the least squares method using the statsmodels library (0.12.0) The final formula was the following: LDL-C = nonHDL-C - (TG / 3 - 0.14). The accuracy of this equation was 96.12% on a test sample of 150,000 lipidograms. It is significantly higher than those calculated with usage Friedwald formula or alternative methods of S. Martin (2013) and M. Sampson (2020): 62.29%, 72.96% , 71.62% respectively

Conclusions: The new calculation formula for determining LDL-C proved to be a suitable tool, easy to use in any triglyceride levels. The use of this formula makes it possible to adequately compare the results of the calculated and direct assessments of LDL-C.

ID:1554

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

MICRORNA-214-3P IN CORONARY HEART DISEASE PATIENTS WITH VARIOUS VITAMIN D SUPPLIES

POSTER VIEWING SESSION

Zhanna I. Ionova, Olga A. Berkovich, Jing Du
Faculty Therapy Department, The IP Pavlov First Saint Petersburg Medical University, Saint-Petersburg, Russian Federation

Background and Aims : Recent studies show that vitamin D deficiency is a new risk factor for atherosclerosis. Vitamin D realizes protective effects through receptors in the vessel wall. Expression of the vitamin D receptor (VDR) is regulated by miRNAs, in particular, miRNA-214-3p; in this regard, the aim of the study was to study the relationship of miRNAs-214-3p with different levels of vitamin D in coronary heart disease (CHD) patients.

Methods: The content of vitamin D in blood serum was determined by enzyme immunoassay ELISA (DRG). Determination of the expression of miRNA-214-3p was carried out by reverse transcription polymerase chain reaction.

Results: The content of vitamin D was determined in 162 CHD patients and in 173 people from the comparison group. The level of vitamin D in CHD patients was lower than in the comparison group (36.96±1.30 μU/ml, 51.70±1.72 μU/ml; p=0.001). Vitamin D deficiency was detected more often in CHD patients than in the comparison group (81%, 61%; p=0.01), and sufficiency was observed more often in comparison group than in CHD patients (12%, 3% p=0.02) and was associated with a reduction of CHD risk (OR=0.31(0.11÷0.90), p=0.03). The level of microRNA-214-3p in blood plasma in CHD patients was higher than in comparison group (2.38±0.39, 1.46±0.21; p=0.04). In CHD patients with vitamin D deficiency, the miRNA-214-3p gene expression level was higher than in patients with sufficient supply (2.94±0.58, 0.92±0.27; p=0.003).

Conclusions: Vitamin D sufficiency is associated with reduction of the CHD risk. The expression level of miRNA-214-3p genes is higher in CHD patients than in the comparison group.

ID:1535

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

EFFECT OF COMBINED HIGH- INTENSITY EXERCISE AND SIMULTANEOUSLY CHOLESTEROL-RICH DIET ADMINISTRATION ON ARTERIAL MECHANICAL PARAMETERS USING A NEW ULTRASOUND IMAGE PROCESSING SOFTWARE

POSTER VIEWING SESSION

Hossein Mehrad
Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran

Background and Aims : Penetration of Low- Density Lipoproteins (LDL) into the intimal layer can cause to inflammation and resulting in lipid- rich plaque formation. In this study, we aimed to investigate the effect of combined high- intensity exercise and simultaneously cholesterol- rich diet administration on mouse healthy arterial mechanical parameters.

Methods: Treatment group underwent high- intensity exercise using a mouse treadmill (10 min/day) combined with simultaneously cholesterol- rich diet (% 5) administration for three weeks. Then, treated group underwent ultrasonography, using a new image processing software- based automatic method. In this method two algorithms, i.e. maximum gradient (radial displacement evaluation of artery walls) and block matching (longitudinal displacement evaluation of artery walls) were composed.

Results: Histopathology results showed that the combined treatment of healthy arteries, resulting in elevated reactive oxygen species (ROS), leukocytes adhesion, lipoproteins and immune cells permeability, and pro- inflammatory factors, as well as deficiency of nitric oxide (NO) bioavailability, and finally early stage atherosclerosis formation in all of the animals' major arteries of treatment group. Results from new ultrasound image processing software- based automatic method showed a significant reduction in the mean value for arterial compliance, distensibility index, longitudinal strain and radial strain in the treatment group in compared with the other groups ($P < 0.05$).

Conclusions: It is concluded that, high- intensity exercise- mediated arterial shear stress injury, accompanied by enhanced inflammatory effect of oxidized low-density lipoproteins- mediated endothelial dysfunction, induced by high cholesterol- diet administration, can cause to early stage atherosclerosis formation, resulting in imbalanced vessel wall vasodilation and vasoconstriction.

ID:1531

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

MODIFIABLE AND NON-MODIFIABLE CARDIOVASCULAR RISK FACTORS ON SENSORY DISORDER OF SMELL AND TASTE IN COVID-19 POPULATION

POSTER VIEWING SESSION

Angelos Liontos[1], Athina Zarachi[2], Orestis Milionis[1], Pezoulas Vasileios[3], Ioannis Komnos[2], Eleftherios Klouras[1], Aikaterini Lianou[2], Dimitrios Biros[1], Konstantinos Papaloukas[4], Dimitrios Fotiadis[3], Ioannis Kastanioudakis[2], Haralampos Milionis[1]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]Medical Technology And Intelligent Information Systems Unit, Department Of Materials Science, UNIVERSITY OF IOANNINA, IOANNINA, Greece, [4]Department Of Biological Applications And Technologies, UNIVERSITY OF IOANNINA, IOANNINA, Greece

Background and Aims : The purpose of this study is to investigate the role of modifiable and non-modifiable CVD risk factors in olfactory and taste functions in patients with COVID-19. Risk factors assessed were smoking, BMI, age and gender

Methods: Data were collected from 300 adults (by questionnaires), positive for SARS-COV-2 by RT-PCR. Home-quarantined were 150 patients and 150 required hospitalization. Statistical analysis was conducted on IBM-SPSS Statistics 26.0, using X^2 and Fisher's exact test.

Results: Smokers were the 14% of the population. Women represented the 35.33% while men were the 64.67% of the total sample. A total of 60.33% of patients were overweight and a total of 21.0% were obese (BMI>30). Mean age was 46.02 years, mean BMI for overweight and obese was 27.05 and 34.8, respectively. Analysis showed that smokers had a greater probability of olfactory loss (OR=1.26) especially in patients requiring hospitalization (OR=1.15) but with no statistical significance. Overweight and obese patients also had a greater risk for loss of taste or smell but no statistical significance was found. There was found a statistically significant difference regarding age and loss of smell ($p<0.001$) and taste ($p=0.013$) while the age group of 21-25 had a greater risk of sensory dysfunctions (OR=2.29, $p=0.013$). Age was also associated with a greater risk of hospital admission for all groups from 46-80 years old ($p<0.05$). no difference between genders was found.

Conclusions: these CVD risk factors could not show a possible significant association with loss of smell and taste in the studied population and further investigation is needed.

ID:1464

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

DIAGNOSTIC THE FAMILIAL HYPERCHOLESTEROLEMIA IN WEST SIBERIA USING TARGETED HIGH THROUGHPUT SEQUENCING

POSTER VIEWING SESSION

Elena Shakhtshneider, Dinara Ivanoshchuk, Sergey Semaev, Olga Timoshchenko, Mikhail Voevoda
Laboratory Of Medical Genetics, Institute of Internal and Preventive Medicine - Branch of the ICG SB RAS, Novosibirsk, Russian Federation

Background and Aims : The purpose of this study was to identify mutations in genes of lipid metabolism in the patients with familial hypercholesterolemia (FH) in West Siberia using targeted high throughput sequencing.

Methods: Definite and probable FH was identified in 82 patients (age 46±13 years) according to Dutch Lipid Clinic Network Criteria. The plasma lipid levels were determined by standard enzymatic assays. The patients were subjected to targeted sequencing of exons and adjacent splicing sites of *LDLR, APOB, PCSK9, LDLRAP1, LPL, HMGCR, NPC1L1, PPARA, MTTP, LMF1, SAR1B, ABCA1, ABCG5, ABCG8, CYP7A1, STAP1, LIPA, PNPLA5, APOA1, APOA5, APOC2, APOE, LCAT, ANGPTL3, LIPC, APOA4, APOC3, SREBF1, LMNA, PPARG, PLIN1, POLD1, LPA, LIPG* genes powered by GS Junior (Roche). In 42 patients without detectable mutations in the LDLR gene, MLPA analysis was carried out using SALSA MLPA KIT P062 (MRC-Holland, Netherlands).

Results: We identified heterozygous single nucleotide variants rs121908038, rs137853964, rs28942078, rs539080792, rs570942190, rs755757866, rs761954844, rs879254566, rs879254721, rs879254980, rs879255191, rs875989907, rs879254769 and rs875989894 in the *LDLR* and determined their pathogenicity using ClinVar and HGMD databases. The variants NM_000527.4:c.(67+1_68-1)_(1586+1_1587-1)del and NM_000527.4:c.(2140+1_2141-1)_(2311+1_2312-1)del were identified one time among all patients in the *LDLR* gene. And three unrelated patients has rs5742904 (R3500Q) in the *APOB* gene.

Conclusions: In 73% probands with FH in West Siberia were identified amino acid changes in the *LDLR* gene that may affect protein function of the LDL receptor. This study was supported RSF 22-25-00743.

ID:1503

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

THE POSSIBLE ROLE OF TYG INDEX AND TRG/HDL, CRP/HDL, NEUTROPHILS/HDL LYMPHOCYTES/HDL RATIOS IN DISEASE SEVERITY AND OUTCOMES IN COVID-19 HOSPITALIZED PATIENTS WITH ARTERIAL HYPERTENSION.

POSTER VIEWING SESSION

Angelos Liontos[1], Dimitrios Biros[1], Alexandros Papathanasiou[1], Orestis Milionis[1], Maria Nasiou[1], Eleni Pargana[1], Nikolaos-Gavriil Kolios[1], Christiana Pappa[1], Stavros Tsourlos[1], Lazaros Athanasiou[1], George Siopis[1], Athina Zarachi[2], Konstantina Tsarapatsani[3], Valentini Samanidou[1], Revekka Konstantopoulou[1], Ilias Tsiakas[1], Sempastien Filippas-Ntekouan[1], Ioannis Vagias[1], Eirini Christaki[1], Evangelos Liberopoulos[4], Haralampos Milionis[1]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]Medical Technology And Intelligent Information Systems Unit, Department Of Materials Science, UNIVERSITY OF IOANNINA, IOANNINA, Greece, [4]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece

Background and Aims : The aim of this research was to determine the possible differences and associations of the TyG index and TRG/HDL-C, CRP/HDL-C, NEUTROPHILS/HDL-C, LYMPHOCYTES/HDL-C ratios with disease progression and outcomes in COVID-19 hospitalized patients with AH.

Methods: 888 hospitalized patients in the Infections Diseases Unit of our Hospital from 03-2020 till 10-2021 were included. Variables were calculated on admission. Outcomes were defined as: patient's death, intubation and hospital length of stay (LoS). Analysis was conducted using Logistic regression and chi-square test on SPSS 26.

Results: AH was reported in 402 patients (45.2 %) in the primary sample while in those with available laboratory results AH was reported in 245 patients, with a mean value of TyG index:8.89 (SD 0.637), TRG/HDL RATIO:3.8 (SD 2.60), CRP/HDL:2.32 (SD 2.33), NEUT/HDL:162.87 (SD 113.90) and LYMPH/HDL:32.98 (SD 19.67). Logistic regression analysis of AH-group (n = 245) showed that patients with higher lymphocytes/HDL values, had a lower risk of LoS>7days (OR=0.977, p=0.008) while those with higher CRP/HDL values had an increased risk of death (OR=1.2, p=0.024). No other statistically significant difference was found in other ratios of concern or intubation. Patients with AH had higher risk of intubation compared to the non-AH group (OR=1.9198, 95%CI:1.1147-3.3064, p=0.017). Hypetensive patients also had a greater risk of LoS>7days (OR=1.6122, 95%CI:1.2151-2.1389, p=0.001) and a greater risk of death compared to the non-hypertensives (OR=1.9179, 95%CI:1.2357-2.9768, p=0.003).

Conclusions: The LYMPH/HDL and CRP/HDL ratio may play a role as a predictor of disease severity and outcome in high-risk patient populations with AH, in the COVID-19 setting of disease.

ID:1467

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

METABOLIC SYNDROME AND CARDIOVASCULAR DISEASE RISK IN END-STAGE RENAL DISEASE PATIENTS

POSTER VIEWING SESSION

Susana Coimbra[1,2], Flávio Reis[3], Sara Nunes[3], Sofia Viana[3,4], Susana Rocha[1], Maria J. Valente[1], Cristina Catarino[1], Petronila Rocha-Pereira[1,5], Elsa Bronze-Da-Rocha[1], José G. Oliveira[6], João C. Fernandes[7], José Madureira[8], Maria D.S. Faria[1,9], Vasco Miranda[10], Luís Belo[1], Alice Santos-Silva[1]
[1]Department Of Biological Sciences, Faculdade De Farmácia Da Universidade Do Porto, UCIBIO – Applied Molecular Biosciences Unit ; Associate Laboratory i4HB - Institute for Health and Bioeconomy, Porto, Portugal, [2]Toxrun-toxicology Research Unit, University Institute Of Health Sciences, CESPU, CRL, Gandra, Portugal, [3]Institute Of Pharmacology & Experimental Therapeutics, Coimbra Institute For Clinical And Biomedical Research (icbr), Faculty of Medicine, & CIBB Consortium, Coimbra, Portugal, [4]Estesc-coimbra Health School, Pharmacy, Polytechnic Institute of Coimbra, Coimbra, Portugal, [5]Health Science Research Centre, University Of Beira Interior, Health Science Research Centre, University of Beira Interior, Covilhã, Portugal, [6]Hemodialysis Clinic Of Porto (chp); Center For Health Technology And Services Research (cintesis), Faculty of Medicine, Porto, Porto, Portugal, [7]Nefroserve Hemodialysis Clinic Of Viana Do Castelo, NefroServe, Viana do Castelo, Portugal, [8]Nefroserve, Hemodialysis Clinic Of Barcelos, NefroServe, Barcelos, Portugal, [9]Hemodialysis Clinic, Hospital Agostinho Ribeiro, Felgueiras, Portugal, [10]Hemodialysis Clinic Of Gondomar, Hemodialysis Clinic of Gondomar, Gondomar, Portugal

Background and Aims : Cardiovascular disease (CVD) is one of the most common causes of morbidity and mortality in chronic kidney disease (CKD), especially in end-stage renal disease (ESRD). Metabolic syndrome (MS) is known to predispose to a higher CVD risk. It is likely that the co-existence of MS and CKD may enhance CVD risk factors. We aim to evaluate in ESRD patients on hemodialysis (HD), the impact of MS on conventional and non-conventional biomarkers of CVD risk.

Methods: We studied 308 ESRD patients on HD (2015-2019); 47 had MS according to World Health Organization classification. *We evaluated lipid profile,* HDL subfractions, adiponectin, leptin, tissue plasminogen activator (tPA), plasminogen activator inhibitor (PAI)-1, fetuin-A, asymmetric dimethylarginine (ADMA), elastase, and leukocyte and neutrophil counts.

Results: ESRD patients with MS (ESRD/MS), as compared to ESRD without MS, presented lower total cholesterol (TC) and low-density lipoprotein cholesterol (LDLc), and higher TC/HDLc ratio; lower(%) of large HDL and higher(%) of small and intermedium HDL subfractions. ESRD/MS patients also presented higher leukocyte and neutrophil counts, higher elastase, leptin, tPA, PAI-1 and ADMA levels, and lower adiponectin and fetuin-A concentrations.

Conclusions: Despite the lower cholesterol and LDLc in MS/ESRD patients**,** they showed more atherogenic changes, namely, lower large HDL%, the more atheroprotective subfraction, and higher small HDL%, the less protective subfraction; imbalance of anti- and pro-inflammatory adipokines; and, risk changes in biomarkers of inflammation, endothelial (dys)function and arterial calcification. Our data show a higher risk profile for CVD in ESRD/MS patients. Acknowledgment: UIDP/04378/2020 and UIDB/04378/2020; LA/P/0140/2020; PTDC/MEC-CAR/31322/2017; FCT/MCTES (PTDC/MEC-CAR/31322/2017) and FEDER/COMPETE 2020 (POCI-01-0145-FEDER-031322).

ID:1468

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

THE CARDIOVASCULAR RISK FACTORS PROFILE AND STRUCTURAL HEART DISEASE IN PATIENTS WITH LONG-TERM EPISODES OF PERSISTENT ATRIAL FIBRILLATION

POSTER VIEWING SESSION

Yaroslav Skybchyk[1], Kyrylo Mikhaliev[2], Oleg Zharinov[3]
[1]Cardiac Arrhythmias Department, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine, [2]Internal Medicine, SIS "RPC PCM" SAD, Kyiv, Ukraine, [3]Department Of Functional Diagnostics, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine

Background and Aims : To evaluate the cardiovascular risk factors (CVRF) profile and structural heart disease in patients with persistent atrial fibrillation (AF) and the duration of its episode <90 and ≥90 days.

Methods: We consecutively enrolled 118 persistent AF patients, with its episode lasting more than 7 days, who underwent a direct-current cardioversion. We analyzed the CVRF profile and echocardiography data. The enrolled sample was divided into groups according to AF episode duration: AF1 – 8-89 days (n = 58), and AF2 – equal or more than 90 days (n = 60).

Results: AF1 and AF2 were comparable by the major CVRF, namely the frequency of obesity, active smoking, arterial hypertension (and its degree), diabetes mellitus, as well as total serum cholesterol level and the value of estimated glomerular filtration rate by CKD-EPI equation (eGFR). About one-third of patients in both studied groups presented with eGFR decline <60 ml/min/1,73 m^2: 27,6% and 30,0% cases in AF1 and AF2, respectively. The frequency of left ventricular (LV) systolic dysfunction cases was higher in AF2, as opposed to AF1: 20,3% vs. 3,5% patients, respectively (p=0,008). The transesophageal echocardiography revealed the lower average left atrial appendage (LAA) flow velocity in AF2 (vs. AF1: 37,0 cm/s and 43,5 cm/s, respectively; p=0,020).

Conclusions: The profile of major CVRF, including the severity of kidney filtration function decline, was comparable between AF1 and AF2. Besides, AF2 was characterized by more prevalent LV systolic dysfunction cases and the worse LAA shortening function.

ID:1490

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

EFFECT OF HIGH- INTENSITY EXERCISE ON BIOMECHANICAL PARAMETERS OF HEALTHY HUMAN SUBJECTS COMMON CAROTID ARTERY USING A NEW ULTRASOUND IMAGE PROCESSING SOFTWARE- BASED AUTOMATIC METHOD

POSTER VIEWING SESSION

Hossein Mehrad[1], Alberto Foletti[2]
[1]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [2]Institute Of Translational Pharmacology Ift, Italian National Research Council, Rome, Italy

Background and Aims : Mechanical changes include thickening of arterial wall, alteration of arterial elasticity, contraction of smooth muscle, increase in sensitivity to pharmacological stimulation and increase in arterial viscoelasticity, i.e., arteriosclerosis. There is therefore interest in the application of non-invasive clinical tools to assess arterial biomechanical parameters. In this study, we aimed to investigate the effect of high- intensity exercise on biomechanical parameters of healthy human subjects'arteries.

Methods: In this study we used a new computerized analysis method for measurement of instantaneous changes in far and near arterial walls in sequential ultrasound images. In this method, two algorithms, i.e., maximum gradient and dynamic programming, were composed and implemented. Approximately 70 sequential ultrasound images spanning three cardiac cycles were analyzed from each examination to detect instantaneous changes in the far and near walls and lumen maximum, minimum, and mean diameters.

Results: from new ultrasound image processing software- based automatic method showed a significant reduction in the mean value for shear elastic modulus and a significant increase in the mean value for radial strain, compliance and distensibility index in the treatment (high intensity exercise) group compared with the other groups ($P<0.05$).

Conclusions: Nitric Oxide (NO) is considered the most important endothelial-derived vasodilation factor. It is concluded that the administration of high- intensity exercise, can cause to enhance the endothelial NO synthase, resulting in an increase in the arterial diameter and an improvement in the arterial biomechanical parameters. Furthermore, we concluded that our new computerized automatic method is reliable to accurate and repeated evaluation of arterial biomechanical parameters.

ID:1492

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

TREATMENT OF VULNERABLE PLAQUE USING COMBINED HIGH-DENSITY LIPOPROTEIN AND PENTOSTATIN- LOADED MICROBUBBLES- MEDIATED SHOCK WAVE SONOPORATION THERAPY: EVALUATION WITH POSITRON EMISSION TOMOGRAPHY IMAGING AND HISTOPATHOLOGY

POSTER VIEWING SESSION

Hossein Mehrad[1], Alberto Foletti[2]
[1]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [2]Institute Of Translational Pharmacology Ift, Italian National Research Council, Rome, Italy

Background and Aims : The rupture of vulnerable atherosclerosis and the subsequent formation of thrombi are the main factors responsible for myocardial infarctions. Macrophages are responsible for the prevalence of inflammation in atherosclerotic lesions. In the present study, we developed a shock wave sonoporation therapy system and investigated its effect on advanced atherosclerosis regression using Positron Emission Tomography (PET) imaging.

Methods: Atheromatous plaque with foam cell- rich content and thin- fibrous cap was induced via perivascular cold injury, using liquid nitrogen at the right common carotid artery of New Zealand white rabbits, before being fed a 2% cholesterol-rich diet for six weeks. Then, the lesion region treated using extracorporeal focused shock waves (V= 22 Kv, F=0.3 Hz, Impulses= 100) accompanied by intravenous combined High-density lipoprotein (HDL) (80 mg/Kg) and pentostatin (5 mg/Kg) - loaded PESDA (Perfluorocarbon- Exposed Sonicated Dextrose Albumin) microbubbles (100ml/kg, 2-5 $\times 10^5$ bubbles/ml) administration. The accumulation of 18F-FDG in plaques was evaluated.

Results: from PET imaging study and histopathology showed a significant reduction in the mean value for immune cells, lipid content and 18F- FDG accumulation in the treatment group compared with the other groups ($P< 0.05$).

Conclusions: Enhanced sonoporation effect of shock waves, induced by collapsed microbubbles and Reverse Cholesterol Transport (RCT) and anti- inflammatory effect of HDL, accompanied by cytotoxic and anti- inflammatory effect of pentostatin and anti- inflammatory effect of shock wave, can cause to reduce the inflammatin and lipid content within the plaque. Furthermore we conclude PET imaging is reliable to accurate and repeated evaluation of inflammation in this model.

ID:1498

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-11 Anti-inflammatory therapies*

SINOPORPHYRIN SODIUM (DVDMS)- LOADED NANOLIPOSOMES- MEDIATED B-MODE ULTRASOUND- GUIDED SONO- PHOTODYNAMIC COMBINATION THERAPY OF EARLY STAGE ATHEROSCLEROSIS

POSTER VIEWING SESSION

Hossein Mehrad[1], Hossein Ahmadi Noubari[2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Electrical And Computer Engineering Faculty, University of British Columbia, Vancouver, Canada

Background and Aims : Excessive lipid accumulation by macrophages plays a crucial role in atherosclerosis. Sinoporphyrin sodium (DVDMS) is a novel sensitizer and widely used in photodynamic and sonodynamic therapy. We developed an experimental sono- photodynamic combination therapy system and investigated its effectiveness on macrophages- derived foam cells density (inflammation) reduction.

Methods: Briefly, Golden Syrian hamsters underwent primary balloon dilatation injury in the abdominal aorta (approximately 0.5 cm superior to the iliac bifurcation) followed by a 1.5% cholesterol-rich diet injury for three weeks. Histopathology results showed early stage atherosclerosis formation in all of the hamsters' arteries. Then abdominal aorta of the treatment group at the lesion region, treated using intravenous DVDMS- loaded nanoliposomes (5 mg/kg) administration accompanied by extracorporeal low level focused ultrasound (F= 1.1 MHz, I= 3 W/cm^2, PW= 15 ms) and polarized red laser (λ= 632 nm, E/A= 120 J/cm^2).

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for foam cells density within the early atherosclerotic lesion in the treatment group compared with the other groups ($p < 0.05$).

Conclusions: Enhanced sonoporation and targeted drug delivery effect of ultrasound, induced by inertial collapsed nanoliposomes, accompanied by photoporation effect of laser, and enhanced anti-inflammatory and lipid effluxion effect of both sonotherapy and phototherapy, and enhanced cytotoxic and apoptotic effect of DVDMS- mediated sono- photodynamic combination therapy, can cause to reduce the foam cells density. Results from this study suggests anti-atherogenic effect of DVDMS- loaded nanoliposomes- mediated sono- photodynamic combination therapy as a potential treatment modality for the early stage atherosclerosis.

ID:1501

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-11 Plaque remodelling*

EFFECT OF HIGH- INTENSITY EXTREMELY LOW FREQUENCY MAGNETIC FIELD ON THE INTERMEDIATE STAGE ATHEROSCLEROTIC PLAQUE REMODELING: MONITORED BY HISTOPATHOLOGY AND COLOR DOPPLER ULTRASONOGRAPHY

POSTER VIEWING SESSION

Hossein Mehrad[1], Alberto Foletti[2]
[1]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [2]Institute Of Translational Pharmacology Ift, Italian National Research Council, Rome, Italy

Background and Aims : The aim of this study was to generate an experimental rabbit common carotid artery model of intermediate stage atherosclerosis and the subsequent, investigating the effect of Extremely Low Frequency (ELF) magnetic field exposure on the foam cells- rich plaque structure in this model.

Methods: Atherosclerotic plaque was induced via perivascular cold injury, using liquid nitrogen at the carotid artery of New Zealand white rabbits, before being fed a 1.5% cholesterol-rich diet for four weeks. Results from histopathology showed the progressive changes, from the foam cells and extracellular lipid droplets proliferation, up to vessel wall thickening and lumen narrowing, resulting in the formation of intermediate stage atherosclerosis with moderate stenosis (< 30%) in all of the rabbits' arteries. Then, treatment group underwent high- intensity ELF magnetic field (500 µT, 50 Hz, 30 min/day) exposure, using Helmholtz coils, for four weeks.

Results: Histopathology results showed the formation of atherosclerotic plaque with lipid- laden cells, atheroma, intraplaque neovessels and severe stenosis (>70%) in all of the rabbits' arteries in the treatment group. Results from color Doppler ultrasonography at the stenotic region showed a significant increase in the mean value for blood mean velocity, wall mean thickness, percentage of luminal cross sectional area of stenosis and significant reduction in the mean value for blood volume flow in the treatment group compared with the other groups ($P<0.05$)

Conclusions: Oxidative stress and angiogenesis effect of high intensity ELF magnetic field irradiation, can cause to increase the intraplaque neovessels and immune cells density, resulting in plaque remodeling and vulnerable plaque formation.

ID:1505

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

RELATIONSHIP OF THE DEGREE OF CORONARY LESION AND THE PRODUCTION OF PLASMINOGEN ACTIVATOR-1 INHIBITOR BY ADIPOCYTES OF CARDIAC LOCALIZATION IN CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Ekaterina Belik[1], Olga V. Gruzdeva[1], Yulia Dyleva[2], Maxim Y. Sinitsky[1], Anton V. Sotnikov[3], Olga L. Barbarash[4]
[1]Department Of Experimental Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [2]Department Of Experimental Medicine, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [3]Cardiac Surgery Department, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, Kemerovo, Russian Federation, [4]Clinical Cardiology, Research Institute for Complex Issues of Cardiovascular Diseases, г. Кемерово, Кемеровская обл., Russian Federation

Background and Aims : Determination of the characteristics of the production of plasminogen activator inhibitor-1 (PAI-1) by adipocytes of cardiac localization in relation to the plasma level and the degree of coronary lesion in patients with CAD.

Methods: Examined 86 patients with CAD: 35 with moderate atherosclerotic lesions of the coronary arteries (≤ 22 SYNTAX Score), 22 with severe (23-31), 29 with extremely severe (≥ 32). During a planned CABG, samples of subcutaneous (SAT), epicardial (EAT) and perivascular adipose tissue (PVAT) were obtained. The expression of PAI-1 was determined by qPCR using TaqManTM in a ViiA 7 Real-Time PCR system. The level of PAI-1 secretion in AT supernatants of different localization and PAI-1 concentration in blood plasma was measured PAI-1 Human ELISA. The results were analyzed using Statistica10, GraphPad Prism 8.00 for Windows.

Results: EAT is characterized by the maximum levels of PAI-1 relative to SAT and PVAT. Evaluation of PAI-1 production depending on the degree of coronary lesion according to the SYNTAX Score showed that SYNTAX Score<22 is characterized by the lowest expression, secretion of PAI-1 in all AT and plasma concentration of PAI-1. Direct correlations of PAI-1 expression, secretion in EAT and PVAT, plasma level of PAI-1 with its secretion in EAT, and plasma level of PAI-1 with its secretion in PVAT in CAD were revealed. The most significant predictors of severe/extremely severe degree of coronary lesion in CAD are PAI-1expression in EAT, plasma levels, age

Conclusions: The most significant predictors of severe/extremely severe coronary lesions in CAD are PAI-1 expression and secretion in EAT, plasma levels, age

ID:1530

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

ASSOCIATION OF CARDIOVASCULAR RISK FACTORS AND OLFACTORY OR TASTE DYSFUNCTION IN COVID-19 POPULATION. DATA FROM AN ACADEMIC CENTER IN GREECE

POSTER VIEWING SESSION

Angelos Liontos[1], Athina Zarachi[2], Orestis Milionis[1], Pezoulas Vasileios[3], Ioannis Komnos[2], Aikaterini Lianou[2], Eleftherios Klouras[1], Dimitrios Biros[1], Konstantinos Papaloukas[4], Dimitrios Fotiadis[3], Ioannis Kastanioudakis[2], Haralampos Milionis[1]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]Otorhinolaryngology, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]Medical Technology And Intelligent Information Systems Unit, Department Of Materials Science, UNIVERSITY OF IOANNINA, IOANNINA, Greece, [4]Department Of Biological Applications And Technologies, UNIVERSITY OF IOANNINA, IOANNINA, Greece

Background and Aims : The purpose of this study is to investigate the effect of SARS-COV-2 infection on the senses of smell and taste and identify potential relationship with history of diabetes mellitus (DM),arterial hypertension (AH), dyslipidemia or established CVD.

Methods: Data were collected from 300 adults (by questionnaires), positive for SARS-COV-2 by RT-PCR. 150 patients recovered at home and 150 required hospitalization in the Infectious Disease Unit of University Hospital of Ioannina. Statistical analysis was conducted on IBM-SPSS Statistics 26.0, using X^2 and Fisher's exact test.

Results: 6.33% of the population reported a medical history of DM. 11.71% reported AH, while 5.67% had dyslipidemia and 3.67% CVD. Patients with AH had lower risk of anosmia and ageusia (OR=0.40, p=0.02 and OR=0.0448, p=0.047, respectively). Patients with DM had also lower risk of anosmia and ageusia (OR=0.28, p=0.011 and OR=0.52, p=0.27). patients with dyslipidemia or established CVD history had lower risk of anosmia or ageusia but with no statistical significance. In study sub-populations (hospital or home-quarantined patients) it was found that patients at home with dyslipidemia had lower risk of ageusia (OR=0.11, p=0.04). Patients with AH, DM and CVD respectively, were more likely to require hospitalization compared to the others (OR=3.93, p=0.001, OR=20.31, p<0.001 and OR=10.64, p=0.01, respectively.

Conclusions: The tested sample did not show that DM,AH or CVD had an increased risk of olfactory and/or taste disorders. Moreover, it was shown that these patients are more prone to hospitalization. However, a larger sample of patients is required to draw concrete conclusions.

ID:1507

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

RELATIONSHIP BETWEEN EPICARDIAL AND CORONARY ADIPOSE TISSUE SIZE AND ADIPOCYTOKINE EXPRESSION IN PATIENTS WITH CORONARY HEART DISEASE

POSTER VIEWING SESSION

Yulia Dyleva[1], Olga V. Gruzdeva[1], Ekaterina Belik[1], M Sinitskiy[1], Alexander N. Stasev[2], Aleksandr Kokov[3], Olga L. Barbarash[4]
[1]Department Of Experimental Medicine, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [2]Department Of Cardiovascular Surgery - 1, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [3]Department Of Radiation Diagnostics, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian, Kemerovo, Russian Federation, [4]Director, Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian, Kemerovo, Russian Federation

Background and Aims : Purpose: to evaluate the relationship between adipocytokine gene expression in the AT of the heart of patients with CVD and morphometric parameters of AT.

Methods: This study included 150 patients with CAD. The area of abdominal, visceral AT, thickness PVAT and EAT was determined using MSCT, MRI. The SAT area was calculated mathematically. Adipocytes were isolated from subcutaneous (SAT), epicardial (EAT), and perivascular (PVAT) AT, and were cultured for 24 h. The expression of adiponectin (*ADIPOQ*), adiponectin receptor 1, 2 (*ADIPOR1, ADIPOR2*), leptin (*LEP*), leptin receptor (*LEPR*) and interleukin-6 (*IL6*) genes was determined using PCR.

Results: The thickness of the EAT LV, PVAT of the LCA trunk, the proximal third of the anterior descending artery, the proximal third of the circumflex artery, and the area of the VAT, more associated with coronary atherosclerosis. for them have been set for these parameters. EAT was characterized by the lowest level of ADIPOQ and ADIPOR1,2 expression, high level of lep expression, LEPR and IL6. The ADIPOQ expression in the EAT and PVAT, ADIPOR1,2 in the EAT, LEP in the EAT, LEPR in the EAT, IL6 in the EAT and PVAT were most associated with an increase in the size of local fat depots.

Conclusions: Increased production of leptin and IL-6 and reduced production of adiponectin in EAT and PVAT, are associated with atherosclerosis, an increase in the size of AT in the heart region and are a prognostically unfavorable sign in patients with CAD.

ID:1508

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CAROTID ENDARTERECTOMY ACCOMPANIED BY RADIUM- 224 PATCH ANGIOPLASTY-MEDIATED DIFFUSING ALPHA-EMITTERS RADIATION THERAPY (DART) FOR RESTENOSIS PREVENTION

POSTER VIEWING SESSION

Hossein Mehrad[1], Ali Sultan- Qurraie[2]
[1]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [2]Neuroscience Institute, Renton, University of Washington, Valley Medical Center, Washington, United States of America

Background and Aims : Patch angioplasty in conventional carotid endarterectomy is suggested to reduce the risk of restenosis and recurrent ipsilateral stroke compared with primary closure. Diffusing alpha-emitters radiation therapy (DaRT) is a new treatment modality, which utilizes seeds embedded with a low activity of radium- 224 (^{224}Ra). Each seed continuously emits the short-lived alpha particles, which spread over several mm around it, creating a 'apoptotic region' of high alpha-particle dose. In this study, we developed patches embedded with ^{224}Ra, and investigated its effectiveness on inflammation and intimal hyperplasia reduction after carotid endarterectomy in an animal model.

Methods: Briefly, New Zealand white rabbits were submitted to common carotid artery advanced atherosclerotic occlusion by primary perivascular severe cold injury followed by a 2% cholesterol- rich diet for fourteen weeks. Histopathology results showed the formation of advanced atherosclerosis with lipid, collagen and neovessel- rich plaque, resulted in occlusion in all of the rabbits' arteries. Then treatment group underwent endarterectomy accompanied by 5 µci ^{224}Ra patch angioplasty- mediated DaRT.

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for immune cells and intimal hyperplastic smooth muscle cells density after endarterectomy in the treatment group compared with the other groups ($p<0.05$).

Conclusions: Apoptotic and anti- inflammatory effect of DaRT in combination with anti- restenosis effect of patch angioplasty, can cause to reduce the intimal hyperplasia in this model. These findings provide the basis for developing of radium 224 patch angioplasty- mediated DaRT for a successful clinical application in the treatment of intimal hyperplasia after carotid endarterectomy.

ID:1509

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PHOTODYNAMIC THERAPY IN COMBINATION WITH PHOTOTHROMBOSIS THERAPY OF ATHEROSCLEROTIC PLAQUES WITH NEOVESSELS, USING ROSE BENGAL AND POLARIZED GREEN LASER

POSTER VIEWING SESSION

Hossein Mehrad[1], Ali Sultan- Qurraie[2]
[1]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [2]Neuroscience Institute, Renton, University of Washington, Valley Medical Center, Washington, United States of America

Background and Aims : Atherosclerotic lesions are considered to be advanced when the accumulation of lipid, immune cells, and matrix is associated with the disorganization, thickening and deformity of the arterial wall. One of the most vulnerable type of advanced atherosclerotic plaques, is neovessels- rich plaque. In this study, we investigated the effectiveness of combined photodynamic therapy and photothrombosis therapy on the intraplaque neovessels reduction, wherein a high resolution diagnostic ultrasound is adjuncted with the therapy system, with a goal of increased safety.

Methods: Briefly, New Zealand white rabbits underwent primary perivascular severe cold injury at the right common carotid artery followed by a 1.5 % cholesterol- rich diet injury for 8 weeks. Histopathology and ultrasonography results showed the formation of advanced atherosclerotic plaque with neovessels and severe stenosis (> 70%) in all of the rabbits' arteries. Then animals treated by catheter- based polarized green laser (Q- Switched Nd: YAG, λ= 532 nm, E/A= 120 J/cm^2) and intravenous rose bengal administration.

Results: from histopathology and B-mode ultrasonography showed a significant reduction in the mean value for immune cells and intraplaque neovessels density in the treatment group compared with the other groups ($p < 0.05$).

Conclusions: Thrombotic effect of rose bengal- mediated photothrombosis therapy, induced by polarized green laser phototherapy accompanied by apoptotic and anti- inflammatory effect of rose bengal-mediated photodynamic therapy, can cause to destroy the intraplaque neovessels and significantly reduce the intraplaque immune cells. This protocol may be a potential treatment to neovessels- rich plaques in comparison with conventional bypass surgery and balloon stenting.

ID:1511

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-11 Anti-inflammatory therapies*

TREATMENT OF ADVANCED ATHEROSCLEROSIS WITH CALCIFIED FIBROATHEROMA PLAQUE USING B- MODE ULTRASOUND- GUIDED HIGH- DOSE ATORVASTATIN- LOADED MICROBUBBLES- MEDIATED SHOCK WAVE THERAPY

POSTER VIEWING SESSION

Hossein Mehrad[1], Hossein Ahmadi Noubari[2]
[1]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [2]Electrical And Computer Engineering Faculty, University of British Columbia, Vancouver, Canada

Background and Aims : Atherosclerosis is the leading cause of cerebrovascular and cardiovascular diseases. The management of advanced atherosclerosis with calcification reduces the risk of stroke and myocardial infarction and their related deaths. In this study, we developed an experimental intravascular shock wave therapy system, and investigated its effectiveness on intraplaque calcium content reduction and advanced atherosclerotic plaque regression, wherein diagnostic B- mode ultrasound is combined with therapy system, with a goal of increased safety.

Methods: Briefly, New Zealand white rabbits underwent primary intravascular severe balloon injury at the right common carotid artery followed by a vitamin D_3, nicotine and cholesterol- rich diet injury for 12 weeks. Histopathology and ultrasonography results showed the formation of advanced atherosclerosis with calcified fibroatheroma plaque and severe stenosis (> 70%) in all of the rabbits' arteries. Then, animals treated by catheter- based shock waves (V= 28 Kv, F= 5 Hz, Impulses= 120) accompanied by high- dose (5mg/kg/day) atorvastatin- loaded PESDA (Perfluorocarbon- Exposed Sonicated Dextrose Albumin) microbubbles administration.

Results: from histopathology and ultrasonography showed a significant reduction in the mean value for intraplaque lipid, immune cells and calcium density in the treatment group compared with the other groups ($p < 0.05$).

Conclusions: Enhanced localized sonoporation effect of shock wave, induced by inertial collapsed microbubbles and enhanced pleiotropic, lipophilic and anti- inflammatory effect of atorvastatin, induced by high- dose administration, accompanied by intravascular shock wave lithoplasty and anti- inflammatory effect of shock wave, can cause to reduce the calcified fibroatheroma plaque content and significantly dilate the luminal cross- sectional area of stenosis.

ID:1512

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

THE RELATIONSHIPS OF MYOCARDIAL BLOOD FLOW AND RESERVE WITH LIPID LEVELS IN PATIENTS WITH NON-OBSTRUCTIVE CORONARY ARTERY DISEASE: DYNAMIC SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY STUDY

POSTER VIEWING SESSION

Alina N. Maltseva[1], Kristina V. Kopeva[2], Andrew V. Mochula[1], Elena V. Grakova[2], Konstantin V. Zavadovsky[1]
[1]Department Of Nuclear Medicine, Cardiology Research Institute, Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russian Federation, [2]Department Of Myocardial Pathology, Cardiology Research Institute, Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russian Federation

Background and Aims : More than half of patients with non-obstructive coronary artery disease (NOCAD) can suffer from microvascular dysfunction (MD). Dyslipidemia can play important role in the pathogenesis of MD. However, the available data regarding lipid levels and myocardial perfusion imaging are different and controversial. The aim of the study was to assess the relationships between myocardial blood flow (MBF) and myocardial flow reserve (MFR) derived by dynamic SPECT and lipid levels in patients with NOCAD.

Methods: Based on the data of CCTA, patients with NOCAD (stenosis <50%) were included in the study (n=26, 16 men, mean age 57,9±10,9 years). All patients underwent dynamic SPECT with the assessment of semi-quantitative indexes of myocardial perfusion (SSS, SRS, SDS) and quantitative parameters (stress/rest MBF (s/r MBF), MFR). Additionally, the blood lipid levels (TC, LDL, TG) were assessed.

Results: Based on the lipid levels study population was divided into two groups: 1. with dyslipidemia, n=13; 2. without dyslipidemia, n=13. Standard myocardial perfusion indexes and s/r MBF did not differ significantly in two groups. Dyslipidemia patients had lower MFR value in comparison to those without dyslipidemia: 1,9(0,9;2,5) vs 2,6(2,5;2,8), respectively. The Spearman correlation showed that sMBF had negative relationships with TC (ρ=-0.46), TG (ρ=-0.42) while MFR had negative relationships with TC (ρ=-0.59), LDL (ρ=-0.53). Based on the result of ROC analysis, cut-off value of MFR was 2,08 (AUC=0,84, 95% CI0,64-0,95, p=0,0001); sensitivity=61,5%, specificity=100% in determination of lipid-induced MD.

Conclusions: Dynamic SPECT derived quantitative indexes of MBF and MFR might be used for the assessment of lipid-induced microvascular dysfunction.

ID:1513

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-11 Anti-inflammatory therapies*

EFFECT OF B-MODE ULTRASOUND- GUIDED EXTRACORPOREAL LOW- LEVEL FOCUSED SONOTHERAPY ON EARLY STAGE ATHEROSCLEROSIS REGRESSION USING COLOR DOPPLER ULTRASONOGRAPHY AND HISTOPATHOLOGY

POSTER VIEWING SESSION

Hossein Mehrad[1], Hossein Ahmadi Noubari[2]
[1]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [2]Electrical And Computer Engineering Faculty, University of British Columbia, Vancouver, Canada

Background and Aims : Excessive lipid accumulation by macrophages plays a crucial role in atherosclerosis. Foam cells are generated by uncontrolled uptake of modified LDL, especially oxidized LDL. We developed an experimental sonotherapy system and investigated its effectiveness on macrophage- derived foam cells density reduction and arterial hemodynamic parameters improvement, wherein diagnostic B- mode ultrasound is combined with the therapy system, with a goal of increased safety.

Methods: Briefly, New Zealand white rabbits underwent primary balloon dilatation injury at the right common carotid artery followed by a 1.5% cholesterol-rich diet injury for three weeks. Histopathology and B- mode ultrasonography results showed the early stage atherosclerosis formation in all of the rabbits' arteries. Then, treatment group underwent extracorporeal low- level focused sonotherapy (F= 1 MHz, I= 2 w/cm^2, PD= 100 ms). Foam cells density and arterial hemodynamic parameters were evaluated in the treatment group compared with the control group using histopathology and color Doppler ultrasonography, respectively.

Results: from histopathology and color Doppler ultrasonography showed a significant reduction in the mean value for immune and foam cells density, Resistive Index (RI), Pulsatility Index (PI), Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Mean Velocity (MV) and significant increase in the mean value for volume Flow (VF) in the treatment group compared with the control group ($p < 0.05$).

Conclusions: Anti- inflammatory, lipid effluxion, reverse cholesterol transport and machrophages egress effect of sonotherapy reduces the immune and foam cells density and increase the endothelial Nitric Oxide synthase (eNOS), resulting in arterial hemodynamic parameters improvement and early stage atherosclerosis regression.

ID:1323

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

IMPACT OF THE SURFACTANT PROTEIN D AND ARTERIAL HYPERTENSION ON LIPID PROFILE IN ACUTE EXACERBATIONS OF COPD

POSTER VIEWING SESSION

Olha Shtepa
Internal Medicine 2 And Phtisiatry, Dnipro state medical university, Dnipro, Ukraine

Background and Aims : The aim of the study was to evaluate association plasma surfactant protein D (SPD) levels and lipid profile statuse in hypertensive patients (pts) with acute exacerbations of COPD (AE of COPD) during the antibacterial therapy becose dyslipidaemia and arterial hypertension (AH) are the prevalent risk factors COPD.

Methods: All pts were divided into groups: the first one (1st) - 22 hypertensive pts with AE of COPD, the second (2d) - 20 non-hypertensive pts with AE of COPD and the third (comparison group) – 12 non-hypertensive pts with COPD without AE. Plasma SPD, plasma low-density lipoprotein cholesterol (LDLc), plasma high-density lipoprotein cholesterol (HDLc), total cholesterol (Tc), triglycerides (TG) were measured on 1, 3, 10 days of admission to the hospital in addition standard diagnostic program.

Results: SPD levels in 1st and 2d groups were significantly higher on the first day than on the third day and decrease on tenth day to the 3d group ($p<0,05$). There was significant difference between SPD levels in the 1st and the 2d groups on tenth day of admission ($p<0,05$) but the 2d and the 3d groups - same levels ($p>0,05$). LDLc, HLDc, Tc, TG were significantly higher in the 1st group, but there were tendency to lower levels on the 1 day of admission ($p<0,06$). There was rank correlation between presence of hypertension and SPD levels ($R=0,57$, $p<0,05$).

Conclusions: This research has provided strong links between SPD and AH. Massive arterial SPD expression during AE COPD on the 1st day of admission and AH associated with lipid profile changes.

ID:1313

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

MODULATION OF POSTPRANDIAL PLASMA BILE ACIDS AND GLYCAEMIC CONTROL BY PROBIOTICS, APPLES AND OATS – FINDINGS FROM THE RANDOMISED CONTROLLED CABALA DIET AND HEALTH STUDY

POSTER VIEWING SESSION

Rose-Anna G. Pushpass[1], Shouq Alzoufairi[1], Camilla Pedersen[1], Andrea Manchini[2], Simone Delaiti[2], Urska Vrhovsek[2], Kieran M. Tuohy[2], Kim G. Jackson[1], Julie A. Lovegrove[1]
[1]Hugh Sinclair Unit Of Human Nutrition, Department Of Food And Nutritional Sciences, University of Reading, Reading, United Kingdom, [2]Department Of Food Quality And Nutrition, Research And Innovation Centre, Fondazione Edmund Mach, San Michele all'Adige, Italy

Background and Aims : Circulating bile acids (BAs) are proposed as mediators of dietary components which impact on the gut microbiota and have beneficial effects on cardiometabolic health. However, few studies have investigated the effects of foods during the postprandial phase. The CirculAting Bile Acids as Biomarkers of Metabolic Health - Linking microbiotA (CABALA) study aimed to determine acute effects of meals containing a probiotic, porridge oats and apples on circulating BAs and markers of cardiometabolic health.

Methods: Using a parallel design, 61 healthy volunteers were randomised to consume a high-fat (50g) breakfast drink with either 2 *Lactobacillus reuteri* capsules and 48g cornflakes or 48g cornflakes (control), 40g Jumbo whole rolled oats or 2 Renetta Canada apples, each with 2 placebo capsules after an overnight fast. Blood was collected before and after breakfast for 360 min to measure plasma BAs and cardiometabolic risk markers.

Results: Significant intervention*time interactions were evident for postprandial total, secondary, hydrophobic and unconjugated BA responses, with greater concentrations of unconjugated and hydrophobic BAs following the probiotic compared to control meal ($P<0.05$). The apple and oat meals decreased serum glucose between 40-150 minutes postprandially, with insulin and C-peptide responses also reduced after the apples than control meal ($P<0.05$). The probiotic meal had no impact on cardiometabolic disease risk markers.

Conclusions: Postprandial BAs were unrelated to changes in glycaemic control but were modulated by acute probiotic intake in healthy individuals. These results support beneficial effects of apples and oats on postprandial glycaemic control and the modulation of postprandial plasma BA profiles by *Lactobacillus reuteri*.

ID:1129

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

DISTRIBUTION OF TOTAL CHOLESTEROL (TC) AND LOW-DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) BETWEEN GENETICALLY DIAGNOSED FAMILIAL HYPERCHOLESTEROLAEMIA (FH) MEN AND WOMEN IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Žaneta Petrulionienė[1,2,3], Dovile Gabartaite[2,3], Egle Skiauteryte[3], Emilija Meskene[2,3], Juste Staigyte[2,3], Rimantė Čerkauskienė[2,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[3], Vilma Dzenkeviciute[2,3,5], Sandra Kutkiene[3], Egidija Rinkuniene[1,2,3], Jolita Badariene[1,2,3], Rasa Strupaite-Sileikiene[2,6,7], Rusne Jakaite[3], Gabriele Jaskeviciute[2]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Clinic Of Internal Diseases, Family Medicine And Oncology, Vilnius University, Faculty of Medicine, Vilnius, Lithuania, [6]Centre Of Eye Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [7]Center Of Eye Diseases, Clinic Of Ear, Nose, Throat, And Eye Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, vilnius, Lithuania

Background and Aims : to determine the distribution of TC and LDL-C between different genders with genetically confirmed FH.

Methods: Prospective observational cohort study enrolled patients (n=126) with clinically diagnosed FH according to Dutch Lipid Clinic Network (DLCN) criteria treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. Next generation sequencing was used to identify FH causing mutations. Values of serum cholesterol (TC and LDL-C) were compared in different groups. Statistical analysis was performed using R (v. 4.0.4) program package.

Results: Of 126 examined patients 54,8% (n=69) were women and 45,2% (n=57) were men. Genetic mutation of FH was confirmed in 30,2% (n=38) of the patients. The mean value of TC for genetically confirmed patients was 10.02±1,97 mmol/l, while TC in patients without determined mutation was 9,03±2.15 mmol/l (p=0,001). The mean value of LDL-C for genetically confirmed patients was 7.95±1.74 mmol/l, while LDL-C in patients without mutation was 6,73±2.04 mmol/l (p<0,001). In women with FH mutation the mean level of TC was 10,83±1,98 mmol/l, while in women without FH mutation TC was 9,31±2,61 mmol/l (p=0,001). LDL-C levels in these groups were 8,57±1,63 mmol/l and 7,15±2,54 mmol/l, respectively (p<0,001). In men with genetically diagnosed FH level of TC was 8,89±1,32 mmol/l while in men without mutation the average level of TC was 8,74±1,48 mmol/l (p=0,370). The LDL-C levels in these groups were 7,00±1,49 mmol/l and 6,25±1,09 mmol/l, respectively (p=0,044).

Conclusions: Patients (both genders) with genetically confirmed FH had statistically significant higher average levels of TC and LDL-C compared to patients without determined mutation.

ID:1178

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

LDL-C RESPONSE WITH DIFFERENT STATIN TREATMENT INTENSITIES IN FH PATIENTS: A SEX-SPECIFIC ANALYSIS

POSTER VIEWING SESSION

Michelle M. Schreuder[1], Kirsten B. Holven[2,3,4], Anja K. Johansen[3,4], Charlotte Koopal[5], M Van De Ree[5], Ben Imholz[3], Eric Boersma[6], Martin P. Bogsrud[4,7], Kjetil Retterstol[4], Frank Visseren[5], Jeanine E. Roeters Van Lennep[1]
[1]Vascular Medicine, Erasmus Medical Centre, Rotterdam, Netherlands, [2]Nutrition, University of Oslo, Oslo, Norway, [3]Department Of Nutrition, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway, [4]National Advisory Unit On Familial Hypercholesterolemia, Oslo University Hospital, Oslo, Norway, [5]Vascular Medicine, Utrecht Medical Centre, Utrecht, Netherlands, [6]Department Of Cardiology, Erasmus Mc, University Medical Centre, Rotterdam, Netherlands, [7]Unit For Cardiac And Cardiovascular Genetics,, Oslo University Hospital, Oslo, Norway

Background and Aims : Previous studies showed that women are less likely to reach LDL-C treatment targets compared to men. Our aim was to compare between men and women with Familial Hypercholesterolemia (FH) 1) untreated and on-treatment LDL-C levels 2) intensity of statins and LDL-C reduction of statin therapy 3) attainment of LDL-C target levels and 4) reasons for not reaching LDL-C treatment target.

Methods: We analyzed treatment data of statin-treated FH patients in the Netherlands and the Oslo Lipid Clinic. After a stable statin dose was reached, LDL-C reduction was analyzed in both sexes with a linear regression model.

Results: We assessed 1550 women and 1430 men with FH. Their median age was 48.7 (32.0-61.2) and 47.4 (35.8-58.1) years. Untreated LDL-C was higher in women (6.3 (IQR: 5.2-7.3) vs. 6.0 (IQR: 4.9-7.2) mmol/l, P= 0.001). Absolute and percentage LDL-C reduction were similar for women and men. Low-, moderate- and high intensity statins use was similar in both sexes. Fewer women reached LDL-C treatment targets than men (28.9% vs 29.9%, P=0.842). Women who did not reach LDL-C targets reported more statin-related side effects (21.4% vs. 12.5%) and more often discontinued statin treatment (6.2% vs. 5.5%) than men.

Conclusions: We observed that women with FH are less likely than men to achieve LDL-C treatment targets. The underlying reasons are multifactorial. As FH has an even higher impact on CVD on women it is crucial that both patients and health care providers fully understand the importance of adequate statin therapy.

ID:1236

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

EVIDENCE OF NOVEL APO B GENE COMPLEX ALLELE CAUSING FAMILIAL HYPERCHOLESTEROLAEMIA

POSTER VIEWING SESSION

Daniela Palma[1], Giovanna Cardiero[1], Carmen Flagiello[1], Unai Galicia-Garcia[2], Asier Larrea[2], Maria Donata Di Taranto[1], Cear Martin[2], Gabriella Iannuzzo[3], Matteo N.D. Di Minno[4], Antonio Pipolo[5], Giuliana Fortunato[1]
[1]Dipartimento Di Medicina Molecolare E Biotecnologie Mediche, Università degli Studi di Napoli Federico II and CEINGE S.C.a r.l. Biotecnologie Avanzate, Naples, Italy, [2]Biochemistry And Molecular Biology, Fundación Biofisika Bizkaia, LEIOA, Spain, [3]Dipartimento Di Medicina Clinica E Chirurgia, Università degli Studi di Napoli Federico II, Naples, Italy, [4]Dipartimento Di Scienze Mediche Traslazionali, Università degli Studi di Napoli Federico, Naples, Italy, [5]Dipartimento Di Cardiologia, Ospedale Universitario San Giovanni di Dio e Ruggi d'Aragona, Salerno, Italy

Background and Aims : *APOB* variants are a rare cause of familial hypercholesterolaemia (FH). Most of *APOB* variants remain of uncertain significance (VUS) for the absence of functional studies. We aim to characterize a novel *APOB* complex allele causing a severe form of heterozygous FH.

Methods: Two unrelated patients with clinical suspect of heterozygous FH were screened by next-generation sequencing (NGS). Variant confirmation and relative analysis were done by direct sequencing. Variant pathogenicity was assessed by American College of Medical Genetics and Genomics (ACMG) guidelines. Functional characterization was carried-out evaluating the proliferation of U937 cells incubated with patient or control plasma or measuring LDL uptake on a hepatoma cell line. Solid-phase immunoassay was used to evaluate the affinity of variant *APOB* for LDLR.

Results: In both patients, sequencing identified 3 rare variants at heterozygous status in the exon 21 and 26 of *APOB* gene: c.3220G>A - p.(Gly1074Arg), c.10031A>T - p.(Lys3344Ile) and c.11087T>C – (p.Ile3696Thr). Family analysis showed that 1. the variants were on the same allele; 2. relatives carrying the variants were hypercholesterolemic. The proliferation assay revealed a decreased cell growth (<65% of wild-type). Results were confirmed by decreased uptake of patient's LDL (<25% of control) and by the increased EC50 of patient's LDL for LDLR (approximately four times greater than wild-type).

Conclusions: A complex *APOB* allele was identified and functionally characterized as affecting the binding of APOB to LDLR. NGS allows to analyze all FH-causing genes improving the variant detection.

ID:1232

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

THE EFFECT OF PROBIOTIC ON ABDOMINAL AORTIC MALONDIALDEHYDE OF HYPERCHOLESTEROLEMIC RAT MODEL

POSTER VIEWING SESSION

Miranti D. Pramaningtyas[1], Alfi B.C. Dewanti[1], Rokhima Lusiantari[2]
[1]Department Of Physiology, Universitas Islam Indonesia, Sleman, Yogyakarta, Indonesia, [2]Department Of Physiology, Universitas Islam Indonesia, Yogyakarta, Indonesia

Background and Aims : *A high-fat diet is one of the risk factors for hypercholesterolemia. In the condition of hypercholesterolemia, there will be a metabolic disorder of cholesterol where the body will convert cholesterol into bile acids which in the process will produce free radicals. Probiotics are additional foods that have an antihypercholesterolemic effect. This study aims to determine the effect of probiotic administration on abdominal aortic malondialdehyde (MDA) levels in the hypercholesterolemia rat model induced by shortening.*

Methods: *A total of 19 stored biological material samples in the form of Wistar abdominal aortic organs were divided into 5 groups, namely the negative control group (C-) only received standard food, positive control group (C +) were given a high-fat diet and standard food, the T1 group was given standard food, high-fat diet, and probiotics at a dose of 1.65x cfu/kg, T2 group given standard food, high-fat diet, and probiotic dose 5.5x cfu/kg, T3 group given standard food, high-fat diet, and probiotics dose 1.65x cfu/kg. This treatment was given for 10 weeks then the data obtained were analyzed using the Kruskal Wallis test with Mann-Whitney post hoc.*

Results: *The mean of MDA levels were C- group (1.78 ± 0.11 nmol/gram), T3 group (2.20 ± 0.06 nmol/gram), T2 group (3.46 ± 0.16 nmol/gram), T1 group (4.02 ± 0.02 nmol/gram), and C + group (5.23 ± 0.51 nmol/gram). The data analysis showed a significant difference in abdominal aortic MDA levels ($p < 0.05$).*

Conclusions: *There is an effect of probiotics on MDA levels in the abdominal aorta in hypercholesterolemic rats model induced by shortening.*

ID:1231

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

STUDY OF OXIDATIVE STRESS INDICATORS IN YOUNG PEOPLE WITH CHD IN THE BACKGROUND OF ABDOMINAL OBESITY

POSTER VIEWING SESSION

Yana V. Polonskaya, Elena V. Kashtanova, Viktoriya S. Shramko, Eugeniia V. Striukova, Ekaterina M. Stakhneva, Yuliya I. Ragino
Branch Of Ic&g Sb Ras, Research Institute of Internal and Preventive Medicine – Branch of IC&G SB RAS, Novosibirsk, Russian Federation

Background and Aims : To study the parameters of oxidative stress characterizing antioxidant protection and oxidative damage in young people with coronary artery disease against the background of abdominal obesity.

Methods: The study included 49 people aged 25 – 44 years with CHD and the presence/absence of abdominal obesity. Anamnestic data, anthropometry, functional examinations were collected from the all participants. Abdominal obesity (AO) was established based on waist circumference> 80 cm in women and> 94 cm in men. All patients were divided into two groups: 1 - with the presence of CHD and AO; 2 - with the presence of CHD without AO. The level of superoxide dismutase (SOD), total antioxidant capacity, MDA of modified oxidized LDL were determined in serum.

Results: Among the studied parameters, the SOD level was statistically significantly different. In patients with the presence of AO, the SOD concentration is lower ($p < 0.001$), in comparison with patients without AO. Indicators reflecting oxidative damage such as total antioxidant capacity and MDA of modified oxidized LDL did not differ significantly in the study groups. According to the results of our studies, SOD activity negatively correlated with BMI ($r = -0.411$, $p = 0.016$). In the group of patients without AO, a relationship was found between the MDA level of modified oxidized LDL and BMI ($r = -0.507$, $p = 0.038$).

Conclusions: We have shown differences in some parameters of oxidative stress in young people with CHD, depending on the presence or absence of AO. *This study was conducted within the framework of the project RSF 21-15-00022.*

ID:1228

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

COMPARISON OF FENOFIBRATE AND REDUCED DOSE OF GEMFIBROZIL ON LIPID PROFILES AND RENAL FUNCTION

POSTER VIEWING SESSION

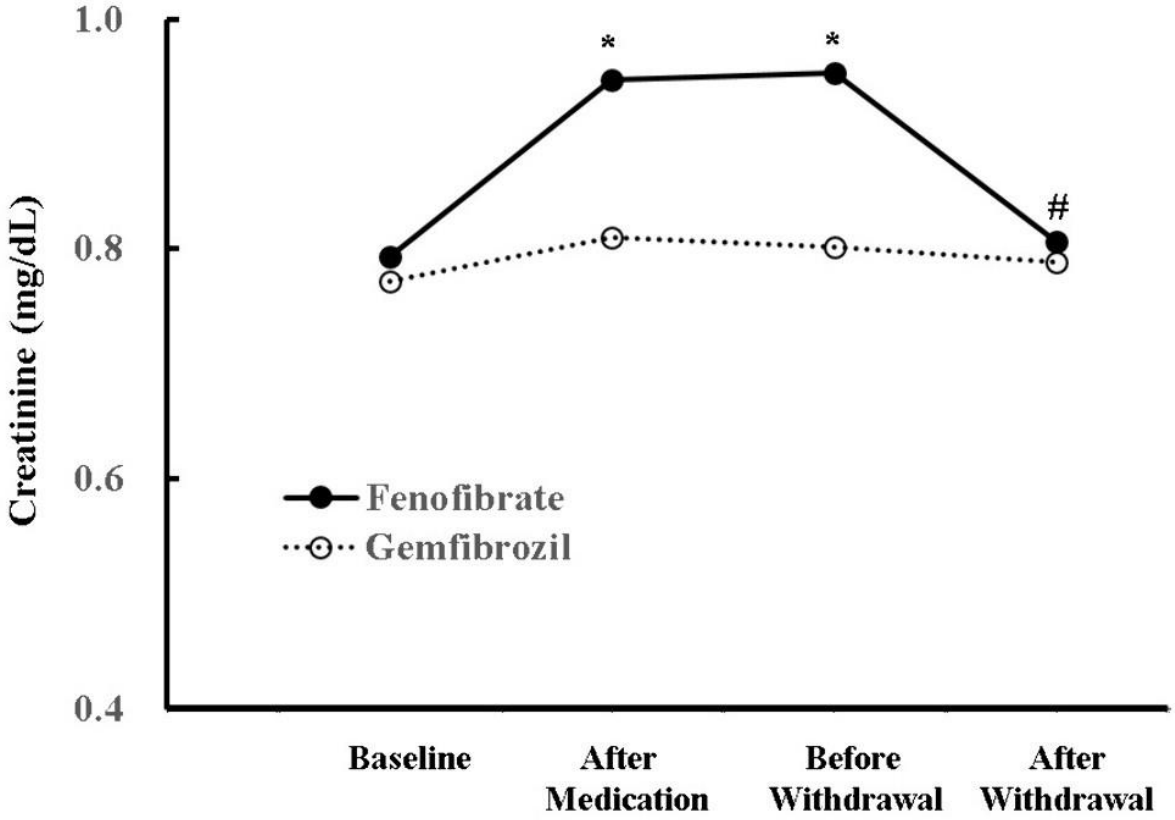
Chee Jeong Kim[1], Myung-A Kim[2]
[1]Department Of Internal Medicine, Chung-Ang University Hospital, Seoul, Korea, Republic of, [2]Internal Medicine, Seoul National University Boramae Hospital, Seoul, Korea, Republic of

Background and Aims : Fibrate is mainly used for the management of hypertriglyceridemia and deteriorates the renal function. The aims of this study are to compare the effects of different kinds of fibrates with different potencies.

Methods: Patients with triglyceride levels ≥ 200 mg and eGFR ≥ 60 ml/min/m^2 were managed with fenofibrate (160 mg QD, n=210) or gemfibrozil (200 mg BID, n=45). Fenofibrate (n=174) or gemfibrozil (n=31) was discontinued due to well-controlled triglyceride levels or adverse effects. Among them, serial changes were observed in patients with the medication for 1 year or less (n=70 and n=16). Parameters for the renal function and lipid profiles were measured at baselines and after 2 months.

Results: Creatinine levels increased both groups (17.8±12.6%, p<0.001 vs 3.9±8.0 %, p=0.008) and more in the fenofibrate group than in the gemfibrozil group (p<0.001). Changes of triglyceride levels were not different between 2 groups (-53.1±23.7% vs -53.8±21.1%, p=0.81). Percent increase of creatinine was independently associated with fenofibrate therapy (r=0.41, p<0.001) and age (r=0.25, p<0.001). The withdrawal of the medication decreased creatinine more in the fenofibrate group than in the gemfibrozil group (p<0.001). Increase of triglyceride level was similar between two groups (141.3±185.7% vs 141.0±201.8%, p=0.64). Serial changes were displayed in figure and showed similar trend. Creatinine level after withdrawal is slightly higher than baseline level without statistical significance.

Conclusions: Fibrate with lower potency has similar triglyceride lowering effect with less renal adverse effect. Renal function recovered nearly completely with the discontinuation of the medication.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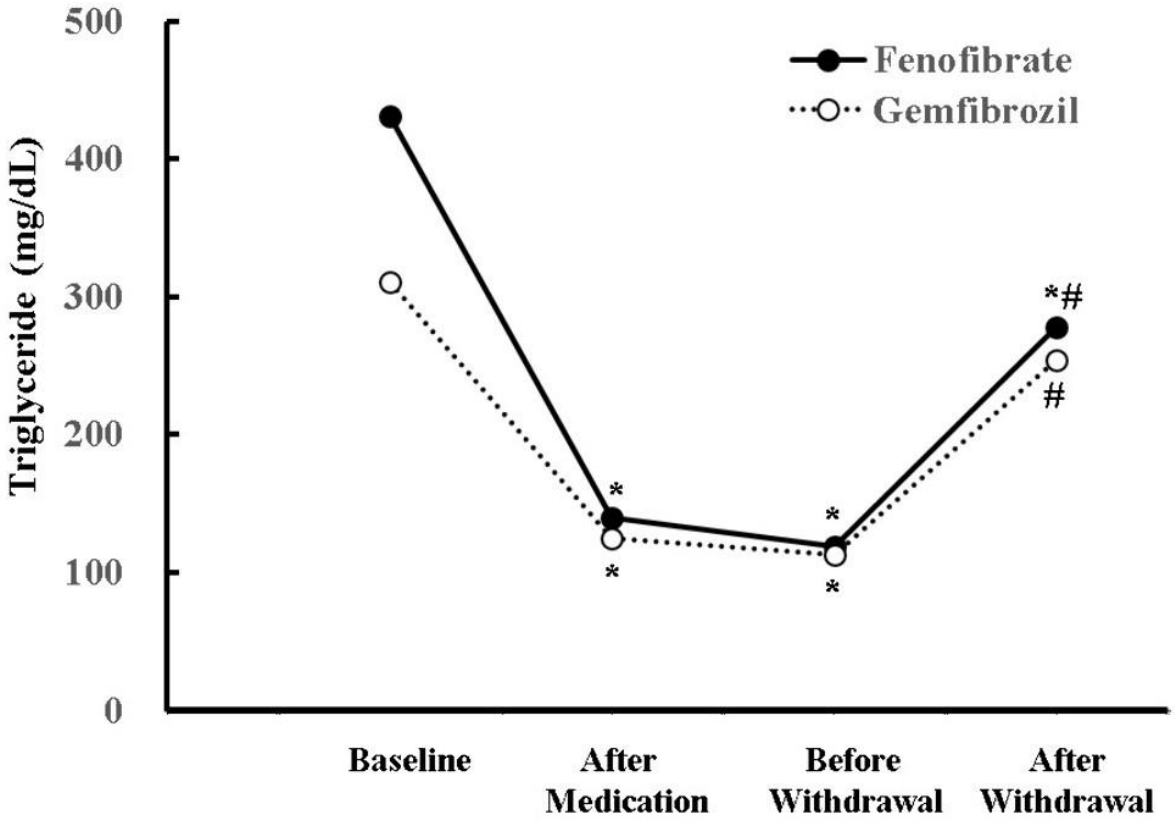
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ID:1227

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

IDENTIFICATION OF THE RISK OF IHD DEVELOPMENT IN YOUNG PEOPLE, FORMATION OF A DIAGNOSTIC MODEL

POSTER VIEWING SESSION

Yana V. Polonskaya, Elena V. Kashtanova, Ekaterina M. Stakhneva, Viktoriya S. Shramko, Eugeniia V. Striukova, Yuliya I. Ragino
Branch Of Ic&g Sb Ras, Research Institute of Internal and Preventive Medicine – Branch of IC&G SB RAS, Novosibirsk, Russian Federation

Background and Aims : To study the level of biomolecules characterizing the main pathogenetic links of coronary atherosclerosis. To develop a model for diagnosing the risk of coronary heart disease in young people based on significant biochemical parameters.

Methods: The study included 49 people with IHD and 127 people without IHD. All participants signed an Informed Consent. A survey was conducted using validated questionnaires. Anamnestic data, anthropometry, functional examinations were collected from the all participants. Total antioxidant activity, MDA-oxLDL, SOD, MCP-1, TNF-alpha, IL-1, IL-6, IL-8, total cholesterol, TG, HDL and LDL were determined in blood serum using enzyme immunoassay, multiplex assay and enzymatic method.

Results: The analysis of the data obtained revealed a difference in concentrations between the studied subgroups for the total antioxidant activity, SOD, MCP-1 and IL-6. In patients with IHD, the level of the total antioxidant activity was significantly lower by 2.9 times and MCP-1 by 1.4 times, the concentration of SOD and IL-6 was higher by 16 and 30%, respectively. For interpretation, we used a scatter diagram of the density of values - SHAP, reflecting the degree of influence of each parameter on the resulting variable. The greatest contributions to the model project were made by: the total antioxidant activity, SOD, MCP-1, IL-6 and HDL.

Conclusions: The data obtained by us can be recommended for the development of a coronary heart disease risk meter in young people, which includes the most significant laboratory parameters. *This study was conducted within the framework of the project RSF 21-15-00022.*

ID:1224

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-03 NASH and other ectopic lipid diseases*

NAFLD, PANCREATIC STEATOSIS AND ATHEROSCLEROTIC PROCESS

POSTER VIEWING SESSION

Kateryna Pivtorak, Iryna Fedzhaga, Natalia Pivtorak
Internal Medicine And Clinical Pharmacology, National Pirogov Memorial Medical University, Vinnytsia, Ukraine

Background and Aims : The atherosclerotic process is closely related to steatosis of the liver and pancreas. The aim of the study was to establish the features of lipid metabolism and carbohydrate metabolism in patients with NAFLD and pancreatic steatosis (PS).

Methods: We examined 172 patients with NAFLD with PS. All patients underwent ultrasound examination and fibroscan, determined markers of cytolysis and cholestasis, lipid metabolism, HOMA index. Correlation analysis was used to identify correlations between different indicators, calculating the correlation coefficient (d) and assessing its reliability (Pearson's test and Spearman's test).

Results: There was a frequent combination of pancreatic steatosis with hepatic steatosis, gallbladder cholesterol, gastroesophageal reflux disease and coronary heart disease. Most patients have a decrease in HDL cholesterol and an increase in LDL cholesterol. Hypertriglyceridemia was in more than 76% patients. Coefficient of atherogenicity was 3.5 units. A direct significant correlation was found between insulinemia and body mass index ($r = 0.48$; $P < 0.05$), waist circumference ($r = 0.43$; $P < 0.05$), HOMA index ($r = 0, 95$; $P < 0,05$) and serum concentration of C-peptide ($r = 0,80$; $P < 0,05$). Serum of TG concentration was directly correlated with body mass index ($r = 0.41$; $P < 0.05$), waist circumference ($r = 0.38$; $P < 0.05$), mean blood pressure ($r = 0, 40$; $P < 0.05$).

Conclusions: The most prognostic risk factors of NAFLD with pancreatic steatosis were the degree of obesity, the presence of coronary heart disease, the value of the HOMA index, total cholesterol, and triglyceride levels.

ID:1221

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

B LYMPHOCYTE-DEFICIENCY IN MICE CAUSES VASCULAR DYSFUNCTION BY INDUCING NEUTROPHILIA

POSTER VIEWING SESSION

Ning Xia[1], Solveig Hasselwander[2], Gisela Reifenberg[2], Alice Habermeier[2], Ellen Closs[2], Maximilian Mimmler[2], Rebecca Jung[3], Susanne Karbach[4], Jérémy Lagrange[4], Philip Wenzel[4], Andreas Daiber[4], Thomas Münzel[4], Nadine Hövelmeyer[3], Ari Waisman[3], Huige Li[2]
[1]Pharmacology, Johannes Gutenberg University Medical Center, Mainz, Germany, [2]Department Of Pharmacology, Johannes Gutenberg University Medical Center, Mainz, Germany, [3]Institute For Molecular Medicine, Johannes Gutenberg University Medical Center, Mainz, Germany, [4]Department Of Cardiology, Johannes Gutenberg University Medical Center, Mainz, Germany

Background and Aims : B lymphocytes have been implicated in the development of insulin resistance, athero-sclerosis and certain types of hypertension. The present study was conducted to investigate the role of B cells in regulating vascular function under physiological conditions.

Methods: Vascular function was studies in young B cell-deficient JHT mice not exposed to any known cardiovascular risk factors using a myograph system.

Results: The lack of B cells led to a massive endothelial dysfunction in the mouse aorta. The vascular dysfunction in B cell-deficient mice was associated with an increased number of neutrophils in the circulating blood. Neutrophil depletion in B cell-deficient mice resulted in a complete normalization of vascular function, indicating a causal role of neutrophilia. Moreover, vascular function in B cell-deficient mice could be restored by adoptive transfer of naive B-1 cells isolated from wild-type mice. Interestingly, B-1 cell transfer also reduced the number of neutrophils in the recipient mice, further supporting the involvement of neutrophils in the vascular pathology caused by B cell-deficiency.

Conclusions: In conclusion, the present study provides evidence for a protective effect of B lymphocytes in maintaining vascular homeostasis under physiological conditions. B cell dysregulation may represent a crucial mechanism in vascular pathology.

ID:1218

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

RACIAL DIFFERENCES IN OXIDATIVE STRESS INDEX IN DIABETES ENRICHED MULTIETHNIC POPULATION OF SINGAPORE

POSTER VIEWING SESSION

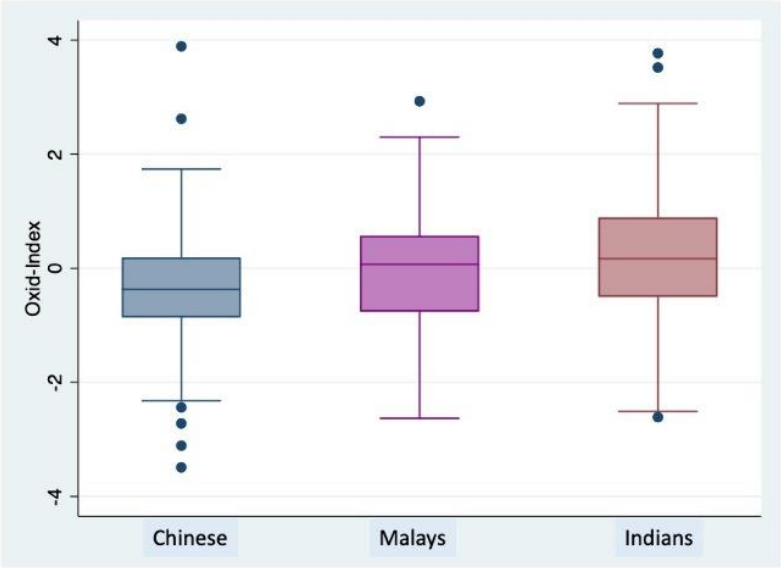
Rinkoo Dalan[1,2]
[1]Metabolic Medicine, Lee Kong Chian School of Medicine, Singapore, Singapore, [2]Endocrinology, Tan Tock Seng Hospital, Singapore, Singapore

Background and Aims : Asian Indians are at higher risk for cardiovascular disease when compared to other ethnic groups in Singapore. This study aims to determine whether oxidative index differs between the Chinese, Malays, and Indians in a diabetes enriched population.

Methods: Population: 437 type 2 diabetes individuals (Chinese: 259; Malays:53; Indians:125; mean age (SD): 50.5(13.7); Males: 201(46%) were recruited. Measurements: Demographics, BMI, blood pressure, HbA1c, glucose and lipids; Derivatives of reactive oxygen metabolites (dROMS) and total anti-oxidant status (TAC) was estimated by the automated clinical chemistry analyser (Diacron, Italy). The total oxidative index (OXY) was calculated as the difference between standardised dROMS and TAC values. Multivariate regression models were used to study the associations between oxidative stress index, dROMS , TAC and ethnicity adjusted for age, gender, BMI, systolic and diastolic blood pressure, HbA1c and LDL-C concentrations.

Results: Mean(SD) oxidative stress index :Chinese: -0.36(0.9); Malays -0.01(1.1); Indians 0.28(1.2); dROMS: Chinese: 279.1(73.2); Malays: 313.9(75.4); Indians: 343.7(100.7); TAC: Chinese: 2240.5(259.6); Malays: 2259.9(245.7); Indians: 2273.4 (345.4). Oxidative index was significantly higher in the Indians when compared to the Chinese (and this was mostly attributed to higher dROMS(. The difference in TAC was not statistically

significant(p>0.05).



Conclusions: Oxidative stress index is higher in the Indians when compared to other ethnic groups. The impact on cardiovascular health due to a higher oxidative stress index and the possible beneficial effects of antioxidants in Indian patients with diabetes needs to be studied further.

ID:1212

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

EFFECT OF HIGH- INTENSITY EXERCISE ON ENDOTHELIAL FUNCTION USING FLOW- MEDIATED DILATION PROTOCOL AND A NEW ULTRASOUND IMAGE PROCESSING SOFTWARE- BASED AUTOMATIC METHOD

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : The pathological complications of atherosclerosis, namely infarction and stroke, remain the leading cause of mortality in the world. Preceding atherosclerosis is endothelial dysfunction. There is therefore interest in the application of non-invasive clinical tools to assess endothelial function. The flow-mediated dilation (FMD) test is the standard tool used to assess endothelial function. FMD is typically expressed as the percentage increase in the artery diameter above baseline.

Methods: A pneumatic tourniquet placed around the healthy subjects' forearm, just below the elbow and inflated to a supersystolic blood pressure for 5 minutes for FMD examination. In this study we used a new computerized analysis method for measurement of instantaneous changes in far and near arterial walls in sequential ultrasound images. In this method, two algorithms, i.e., maximum gradient and dynamic programming, were composed and implemented. Approximately 70 sequential ultrasound images spanning three cardiac cycles were analyzed from each FMD examination to detect instantaneous changes in the far and near walls and lumen maximum, minimum, and mean diameters.

Results: FMD assessment and morphometric analysis of the mean value for arterial diameter in the treatment (high- intensity exercise) group showed a significant increase compared with the control group ($P < 0.05$).

Conclusions: Nitric Oxide (NO) is considered the most important endothelial-derived vasodilation factor. It is concluded that the administration of high- intensity exercise can cause to enhance the endothelial NO synthase, resulting in an increase in the arterial diameter. Furthermore, we cocluded that our new computrized automatic method is realable to accurate and repeated evaluation of FMD.

ID:1205

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

METABOLIC SYNDROME AND RISK FACTORS FOR ATHEROSCLEROTIC DISEASES IN REPRODUCTIVE AGED FEMALES

POSTER VIEWING SESSION

Tatiana Naiden[1], Svetlana Bartosh-Zelenaya[2], Nikolay Glukhov .[3], Alexandr Bartosh-Zeleniy[1]
[1]Functional Diagnostic, North-Western State Medical University named by I.I. Mechnikov, St-Petersburg, Russian Federation, [2]Functional Diagnostic, North-Western State Medical University named by I.I. Mechnikov, St.-Petersburg, Russian Federation, [3]Ultrasound Diagnostic, Center of AIDS, St.-Petersburg, Russian Federation

Background and Aims : Abdominal obesity, insulin resistance (IR), hyperinsulinemia (HI), dyslipidemia, arterial hypertension (AH), impaired glucose tolerance, hyperuricemia, polycystic ovary syndrome (POS) and hyperandrogenemia - are established cardiovascular risk factors. Purpose: to study risk factors for atherosclerotic diseases in reproductive aged women.

Methods: A total of 1786 people (598 adolescent females and 1188 reproductive aged women) with suspected MS were examined. As a result of the screening, a group of 306 people (92 adolescents and 214 reproductive women) were selected for an in-depth study for components of MS.

Results: In adolescent girls hypoalphacholesterolemia (34%), hypercholesterolemia (27%), hypertriglyceridemia (21%), overweight and obesity (59%), cystic enlarged ovaries (58%), hyperuricemia (59%) were noted. In women of reproductive age hypertriglyceridemia (58%), hypercholesterolemia (35%) and hypoalphacholesterolemia (34%), overweight and obesity (66%), AH (46%), hyperuricemia (41%) were noted. In reproductive women there was a decrease of sex hormone binding globulin (SHBG) regardless of obesity. The value of SHBG less than 60 nmol/l was observed in 79% of patients with MS. In patients of reproductive age with a sedentary lifestyle and predominance of fatty foods in the diet, the incidence of IR and HI increases, which is not a leading factor. The absence of a statistically significant effect of smoking on metabolic parameters in women with MS and POS may be due to the powerful effect of other factors, primarily genetic IR.

Conclusions: The high frequency of MS among women of reproductive age necessitates their mandatory examination for IR, HI and associated disorders, as cardiovascular risk factors. Social factors can contribute to MS manifestations.

ID:1198

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

IL-21R BLOCKADE REDUCES ATHEROSCLEROSIS DEVELOPMENT IN LDLR-/- MICE

POSTER VIEWING SESSION

Rimke J. Postel[1], Virginia Smit[2], Jill De Mol[1], Mireia N A Bernabé Kleijn[2], Maaike J.M. De Jong[1], Lucie Delfos[2], Esmeralda Hemme[2], Marie A.C. Depuydt[2], Ilze Bot[2], Johan Kuiper[2], Amanda C. Foks[2]
[1]Biotherapeutics, LACDR, Leiden, Netherlands, [2]Biotherapeutics, LACDR, Leiden University, Leiden, Netherlands

Background and Aims : Many pro-inflammatory cytokines increase during atherosclerosis and contribute to disease progression. Elevated IL-21 serum levels have been found in CAD patients, but its exact role in atherosclerosis remains unknown. IL-21 is primarily secreted by T-cells and binds to the IL-21 receptor (IL-21R), which is expressed on most lymphoid and myeloid cells. Consequently, IL-21/IL-21R signaling has pleiotropic effects and can cause activation of immune cells but can also inhibit anti-inflammatory Tregs. In this study, we aim to provide further insight into the role of IL-21 in atherosclerosis by blocking the IL-21/IL-21R axis.

Methods: First, we confirmed IL-21R expression on many immune cells within the atherosclerotic plaque of *Ldlr*$^{-/-}$ mice and carotid endarterectomy patients using flow cytometry and scRNAseq. Next, *Ldlr*$^{-/-}$ mice were fed a Western-type diet for five weeks, during which mice were treated with an IL-21R blocking antibody or an isotype control.

Results: IL-21R blockade significantly reduced atherosclerosis development by 38%. This coincided with increased atheroprotective Foxp3 expression within aortic CD4^{+} T-cells and elevated percentages of CD4^{+}Foxp3^{+} cells in lymphoid organs (spleen: αIL-21R: 14.02±0.48% vs. ctr: 12.18±0.32%, P <0.01, HLN: αIL-21R: 21.97±1.05% vs. ctr: 18.77±1.06%, P<0.05). Similarly, significantly increased anti-inflammatory IL-10 was observed in serum (αIL-21R: 617.63±156.93 vs ctr: 36.01±29.93 pg/mL, P <0.001) and culture supernatant from splenocytes (αIL-21R: 64.86±10.24 vs ctr: 38.48±5.41 pg/mL, P <0.05) of αIL-21R-treated mice.

Conclusions: Collectively, we show that IL-21R blockade reduces atherosclerosis by promoting atheroprotective regulatory T-cell immunity and elevating anti-inflammatory IL-10 production, representing a promising novel therapeutic strategy to extend health span and to combat CVD.

ID:1189

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

A REAL-LIFE CORRELATION BETWEEN METABOLIC SYNDROME AND SEVERITY OF CORONARY ARTERY DISEASE ASSESSED BY SYNTAX SCORE IN NON-DIABETIC PATIENTS UNDERGOING ELECTIVE CORONARY ANGIOGRAPHY

POSTER VIEWING SESSION

Mohamed Elfeky[1], Enora Romany Gabra[1], Mahmoud Abdelnabi[2,3], Abdallah Almaghraby[1], Mostafa Elwany[1], Mohamed Loutfi[1], Ahmed Mokhtar Abd El Azeem[1]
[1]Cardiology Department, Faculty of Medicine Alexandria University, Alexandria, Egypt, [2]Internal Medicine Department, Texas Tech University Health Science Center, Lubbock, United States of America, [3]Cardiology And Angiology Unit, Clinical And Experimental Internal Medicine Department, Medical Research Institute Alexandria University, Alexandria, Egypt

Background and Aims : The association between metabolic syndrome (MS) and coronary artery disease (CAD) severity is yet to be determined. The study aimed to determine the correlation between MS components and severity of coronary artery disease as assessed by SYNTAX score in non-diabetic patients undergoing elective coronary angiography. SYNTAX score was calculated using SYNTAX score calculator software.

Methods: A prospective study included 75 non-diabetic patients undergoing elective coronary angiography when clinically indicated were enrolled with emphasis on SYNTAX score calculation excluding patients with a previous history of PCI or CABG.

Results: The mean age of patients was 57.11 ± 7.51 years, and 57 patients (76%) were males. The correlation between MS components and SYNTAX score using Spearman correlation showed a strong correlation with correlation coefficient r = 0.837, p-value<0.001*. Table 1: Baseline patient characteristics

Sex	57 (76.0%)
Age	57.33 ± 7.41
Hypertension	69 (92.0%)
History of MI	39 (52.0%)
Smoking	35 (46.7%)
Family history of premature CAD	11 (14.7%)
Waist circumference (cm)	108.4 ± 10.64
HDL-C (mg/dL)	38.47 ± 7.37
TG (mg/dL)	173.03 ± 38.36
LDL-C (mg/dL)	121.4 ± 43.46
Total cholesterol (mg/dL)	192.8 ± 59.97
FBS (mg/dL)	82.97 ± 9.04

Table 2: Distribution of MS components according to SYNTAX score

SYNTAX score	MS components		
	2 (n= 68)	3 (n=54)	4 (n=28)

Low (1-22)	54	14	8
Intermediate (23-32)	8	23	14
High (≥33)	6	17	6

Conclusions: In non-diabetic patients with MS, components of MS had a strong positive correlation with CAD severity assessed by SYNTAX score.

ID:1187

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

REAL-WORLD, OBSERVATIONAL STUDY OF ELEVATED LP(A) AND CARDIOVASCULAR EVENTS

POSTER VIEWING SESSION

Mary P. Mcgowan, Kelly D. Myers, Katherine Wilemon, Diane E. Macdougall, Catherine D. Ahmed
Research, Family Heart Foundation, Pasadena, United States of America

Background and Aims : Lipoprotein(a) [Lp(a)] is rarely measured and the impact of inherited elevation on cardiovascular disease (CVD) is incompletely understood. This study aims to characterize Lp(a) levels and cardiovascular events in a large US dataset.

Methods: Of 301,628,074 individuals with diagnostic, procedural and prescription claims from 2012-2020, a cohort of 253,983 >/=18 years with an Lp(a) level and sufficient claims data were included in this observational cohort study. Most (93%) Lp(a) levels were reported in nmol/L. Major CVD events were tracked from time of first Lp(a) measurement to determine annual CVD event rate. Individuals having low versus high Lp(a) level were compared across 6 groups with or without Atherosclerotic Cardiovascular Disease (ASCVD) and/or diagnosed or probable Familial Hypercholesterolemia (FH) using case-controlled propensity score matching. Probable FH was determined using a validated machine learning model.

Results: Individuals were female (55%); over 60 years (58%); Black (8%), Hispanic (7%) and White (56%). Mean Lp(a) levels were 119, 81 and 87 nmol/L across Black, Hispanic and White individuals, respectively. Individuals with low (<16 nmol/L; <20th percentile) versus high (>/= 165 nmol/L; >/=80th percentile) Lp(a) were tracked for 911+/-690 and 878+/-761 days, respectively. In several risk groups, individuals with high Lp(a) levels had significantly greater annual CVD event rates. Although Blacks had higher mean Lp(a) levels, Blacks and Whites with elevated Lp(a) had similar annual CVD event rates (both 2.8%, p-

value=0.88).

	Annual CVD Event Rate				
Risk Group	**High LP(a) (n)**	**Low Lp(a) (n)**	**Absolute Difference [95% CI]**	**p-value**	**% Difference**
No ASCVD or FH	0.9% (28,977)	0.8% (28,977)	0.18 [0.08, 0.27]	**<0.001**	22.7%
ASCVD only	4.4% (10,049)	3.9% (10,049)	0.49 [0.13, 0.87]	**0.004**	13.0%
Probable FH + ASCVD	3.9% (410)	2.8% (410)	1.1	0.09	40.2%
Probable FH only	1.2% (687)	0.6% (687)	0.64 [0.03, 0.13]	**0.02**	114.3%
Diagnosed FH + ASCVD	4.7% (35)	2.5% (35)			
Diagnosed FH only	1.2% (64)	0% (65)			

Conclusions: Within a large real-world dataset, individuals with high versus low Lp(a) levels experience an increased rate of CVD events, regardless of race, during an observational follow-up period.

ID:1184

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

RELATIONSHIP BETWEEN SCLEROSTIN AND CORONARY TORTUOSITY IN POSTMENOPAUSAL FEMALES WITH NON-OBSTRUCTIVE CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Mohamed Abdelshafy M. Tabl
Cardiology, Benha university, Benha, Egypt

Background and Aims : Background: Coronary tortuosity (CT) is commonly encountered in postmenopausal females and is usually pres- ent without obstructive lesions. Circulating sclerostin levels are elevated in postmenopausal females. In view of sclerostin's vasculoprotective effect, we aimed to find possible association between circulating sclerostin and CT.

Methods: Method: We prospectively enrolled 273 consecutive postmenopausal females with non-obstructive coronary ar- tery disease diagnosed by coronary angiography. Presence and severity (by tortuosity score) of CT as well as serum sclerostin levels were assessed for each patient.

Results: Patients with CT (128, 47% of study group) were significantly older ($P < 0.001$), with higher prevalence of hypertension ($P = 0.001$) and had significantly higher levels of both sclerostin ($P < 0.001$) and hs-CRP ($P = 0.001$). Multivariate binary logistic regression revealed that the presence of CT (dependent variable) was associ- ated with high sclerostin level (OR 8.9, 95% CI: 4.9–16.2, $P < 0.001$). Using ROC curve analysis, Sclerostin at a cut- off value of >650 pg/ml was found to be associated with presence of CT (AUC 0.69, 95% CI: 0.61–0.75, $P < 0.001$) with sensitivity and specificity of 75% and 72.4%, respectively. Using Pearson's correlation analysis, significant positive correlation between sclerostin and severity of CT was found ($r = 0.29$, $P = 0.001$).

Conclusions: Conclusion: High circulating sclerostin is associated with the presence and severity of CT in postmenopausal fe- males. This may add to the literature on the incompletely understood pathogenesis of CT.

ID:1173

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

EVALUATION OF HIGH- DOSE ATORVASTATIN- MEDIATED SHOCK WAVE SONOPORATION THERAPY ON ADVANCED ATHEROSCLEROSIS WITH VULNERABLE ATHEROMATOUS PLAQUE USING MAGNETIC RESONANCE IMAGING AND HISTOPATHOLOGY

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : Mature or immature atheroma within a thin- fibrous cap accompanied by foam cells, extracellular lipid- laden cells and a low probability of calcification, is called vulnerable atheromatous plaque. In this study, we investigated the feasibility of imaging of plaque using Magnetic Resonance Imaging (MRI) technique.

Methods: Vulnerable atheromatous plaque with thin fibrous cap was induced at the right common carotid artery of White New Zealand rabbits. The animals treated by electrohydraulic focused shock waves (V= 15 Kv, F= 0.8 Hz, Impulses= 100) accompanied by high- dose atorvastatin (5 mg/kg/day)- loaded PESDA microbubbles (100 µl/kg, $2–5\times10^5$ bubbles/ml) administration. The plaque lipidic and fibrotic content were measured by MRI and histology. MRI was performed in a 1.5T system. Proton density-weighted (PDW) and T2-weighted (T2W) images were obtained.

Results: Fast spin-echo sequences for the analysis of lipid (low signal on T2W) and fibrous (high signal on T2W) were obtained. T2-weighted images showed greater contrast than proton density-weighted between these different components of the plaques. Results from histopathology and MRI showed a significant reduction in the mean value for lipidic content and significant increase in the mean value for fibrotic content in the treatment group compared with the other groups ($P < 0.05$).

Conclusions: Enhanced inertial cavitation, induced by collapsed microbubbles- mediated extracorporeal electrohydraulic pulsed low- level focused shock wave- mediated- sonoporation therapy accompanied by enhanced lipophilic and pleiotropic effects of atorvastatin, induced by high-dose administration, can significantly lead to atheromatous plaque stabilization. Furthermore, MRI technique is a reliable method for evaluation of this treatment protocol.

ID:1241

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

ASSOCIATION OF BRANCHED-CHAIN AMINO ACIDS CONSUMPTION WITH OBESITY AND DIABETES MELLITUS IN HUMAN POPULATIONS

POSTER VIEWING SESSION

Akinkunmi Okekunle[1], Rennan Feng[2], Chunlong Li[3]
[1]Department Of Food And Nutrition, Seoul National University, Seoul, Korea, Republic of, [2]Department Of Nutrition And Food Hygiene, Harbin Medical University, Harbin, China, [3]First Affiliated Hospital, Harbin Medical University, Harbin, China

Background and Aims : Branched-chain amino acids (BCAA) are essential amino acids critical for protein metabolism in the human body, but higher circulating BCAA has been linked to the risk of diabetes mellitus (DM). However, most epidemiological reports on the significance of dietary BCAA in obesity and DM risk have presented divergent conclusions. Therefore, this study sought to clarify the true association of dietary BCAA with obesity and DM in human population using a meta-analytical approach.

Methods: Eligible published reports were retrieved and screened after searching electronic scientific databases; MEDLINE, EMBASE and Cochrane Library using a predefined set of criteria. Quality evaluation of included studies was conducted using the Network of Ottawa Scale, heterogeneity of studies was determined using I^2 statistics, the strength of individual study on the overall estimate was tested using sensitivity analysis, and publication bias were determined using a funnel plot. All statistical analysis was carried out using RevMan 5.3.

Results: Out of the sixty-three articles screened, seven previously published articles on dietary BCAA consumption, obesity and DM were included in this meta-analysis. Pooled odds ratio (OR) and 95% confidence interval (CI) for higher BCAA consumption was OR: 0.6; 95%CI: 0.5, 0.8, $P < 0.001$ for obesity risk and OR: 1.3; 95% CI: 1.1, 1.5, $P < 0.001$ for DM risk. Also, no single study significantly altered the final overall pooled estimate in this meta-analysis.

Conclusions: Higher dietary consumption of BCAA was associated with lower odds of obesity but higher odds of DM in this meta-analysis. Longitudinal studies are necessary to clarify these associations.

ID:1148

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

ASSOCIATION OF COMBINED INTENSITY AND ADHERENCE TO STATIN/EZETIMIBE THERAPY WITH MAJOR ADVERSE CARDIOVASCULAR OUTCOMES IN PATIENTS WITH CORONARY HEART DISEASE

POSTER VIEWING SESSION

Faizan Mazhar[1,2], Paul Hjemdahl[3], Catherine M. Clase[4], Kristina Johnel[2], Tomas Jernberg[5], Juan J. Carrero[2]
[1]Medical Epidemiology And Biostatisitcs, Karolinska Institite, Solna, Sweden, [2]Department Of Medical Epidemiology And Biostatistics, Karolinska Institutet, Stockholm, Sweden, [3]Clinical Pharmacology Unit, Clinical Epidemiology Division, Department Of Medicine, Karolinska Institutet, Solna, Sweden, [4]Department Of Medicine And Health Research Methods, Evidence And Impact, McMaster University, Ontario, Canada, [5]Department Of Clinical Sciences, Danderyd University Hospital, Karolinska Institutet, Stockholm, Sweden

Background and Aims : Both adherence and treatment intensity can alter the effectiveness of lipid-lowering therapy (LLT). This study evaluated the association of LLT intensity, adherence and the combination of these two aspects of LLT management with the risk of major adverse cardiovascular events (MACE) in persons with coronary heart disease.

Methods: Observational study of all adults who suffered a myocardial infarction or underwent revascularisation during 2012–18 and initiated LLT in Stockholm, Sweden. Study exposures were LLT adherence (by the proportion of days (PDC)-covered), LLT intensity (based on the expected reduction in LDL-C) and the product of LLT adherence and intensity, reflecting treatment intensity after accounting for adherence. At each subsequent LLT fill, we created a rolling assessment of the average adherence and intensity during the previous 12-months. The primary outcome was 3-point MACE; secondary outcomes were the individual components of MACE, unstable angina, and heart failure. Cox models assessed associations between exposures and outcomes.

Results: We studied 20,490 patients, with mean age 68(SD, 11) years, 75% men and mean follow-up 2.6(1.1) years. As a continuous metric, every 10% increase in 1-year adherence, intensity, or intensity-adjusted adherence was associated with a 5% (HR 0.95; 95%CI 0.93–0.96), 8% (0.92; 0.88–0.96), and 9% (HR 0.91; 0.89–0.94) lower risk of MACE, respectively. Compared to adherent patients receiving a high-intensity regimen, non-adherent patients receiving a high-intensity (HR 1.16; 1.01–1.33) or low-moderate intensity (HR 1.33; 1.17–1.51) LLT had higher MACE risk.

Conclusions: Adherence to high-intensity LLT was associated with the highest benefit for secondary cardiovascular prevention of patients with coronary heart disease.

ID:1130

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

LIPID PROFILE AND ADIPOKINES LEVELS IN OVERWEIGHT AND OBESE PATIENTS

POSTER VIEWING SESSION

Yulia Prus[1], Natalia Kurochkina[1], Igor V. Sergienko[1], Anna Popova[1], Diana Nozadze[1], T Scarf[2], Valerii Masenko[2], Aleksey Ansheles[3], Maria Tkacheva[4]
[1]Laboratory Of Atherosclerosis Phenotypes, National Medical Research Center of Cardiology of the Ministry of Health of Russian Federation, Moscow, Russian Federation, [2]Department Of Neurohumoral And Immunological Research, Russian Cardiology Research Center Ministry of Health of the Russian Federation, Moscow, Russian Federation, Moscow, Russian Federation, [3]Department Of Radionuclide Diagnostics And Positron Emission Tomography, National Medical Research Center of Cardiology, Moscow, Russian Federation, [4]Endocrinology Department, Academic Clinic of Neurology and Dentistry on the basis of N.N. Burdenko Neurosurgery Research Institute "Cecil +", Москва, Russian Federation

Background and Aims : To evaluate activity of adipose tissue and lipid profile in overweight and obese patients compared to healthy volunteers.

Methods: The study included 66 patients with a BMI over 25 kg/m^2 (observation group, mean age 56±12 years) and 10 healthy volunteers (control group, mean age 49±8 years), whose levels of adipokines, lipids, glucose and glycated hemoglobin were measured.

Results: Patients' characteristic is presented in table 1. Patients from the observation group tended to be overweight ($p < 0.001$), with an increased BMI ($p < 0.001$) and increased waist circumference ($p < 0.001$). Patients with a BMI over 25 kg/m^2 more often had hypertension ($p < 0.001$), CHD ($p=0.005$), type 2 diabetes ($p=0.03$) compared to the controls. Considering the use of lipid-lowering therapy in the observation group (68.2% statins, 15.2% ezetimibe), there were no statistically significant differences in levels of TC, LDL-C compared to the controls. The TG level was significantly higher in the observation group ($p < 0.001$), and the HDL-C level was significantly higher in the control group ($p < 0.001$). In the observation group, increased glucose, glycated hemoglobin and HOMA-IR levels were more often recorded ($p < 0.05$ for all values). In patients with a BMI of more than 25 kg/m^2, an increased the leptin level were recorded as compared with the control group (30.7±12.6 ng/ml versus 12.0±12.6 ng/ml, $p=0.005$). There were no statistically significant differences in adiponectin and resistin levels compared to

the control group.

Table 1. Characteristics of patients.

Parameters	Observation group n=66	Control group n=10	p
Age, years	56±12	49±8	0,12
Weight, kg	97,5±17,9	60,8±10,3	**<0,001**
Waist circumference, cm	106,5±13,6	78,5±8,6	**<0,001**
BMI, kg/m^2	32,9±5,5	21,8±2,1	**<0,001**
Men	40 (60,6%)	4 (40%)	0,31
Smoking	16 (24,2%)	2 (20 %)	1,00
Arterial hypertension	59 (89,4%)	0 (0%)	**<0,001**
CHD	31 (46,9 %)	0 (0%)	**0,005**
Atherosclerosis of the carotid arteries	16 (24,2%)	1 (10,0%)	0,44
Type 2 diabetes	22 (33,3 %)	0 (0%)	**0,03**
Laboratory indicators			
TC, mmol/l	4,9 ±1,5	5,0 ±1,1	0,60
LDL-C, mmol/l	2,9 ±1,2	3,0±1,0	0,53
HDL-C, mmol/l	1,2±0,3	1,5±0,3	**<0,001**
TG, mmol/l	1,9±1,0	0,9±0,5	**<0,001**
Glucose, mmol/l	5,9 ±1,4	5,0±0,5	**0,04**
Glycated hemoglobin, %	6,9±1,8	4,6±0,7	**<0,001**
HOMA-IR	3,9±1,8	1,2±0,4	**<0,001**
Adiponectin, ng/ml	6,5 ±4,9	8,5 ±6,4	0,26
Leptin, ng/ml	30,7±12,6	12,0±12,6	**0,005**
Resistin, ng/ml	6,6±3,2	4,8±1,4	0,11

Conclusions: BMI of more than 25 kg/m^2 is associated with development of CVD, type 2 diabetes and an increased the leptin level.

ID:1134

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

PREVALENCE OF CORNEAL ARCUS BETWEEN GENETICALLY DIAGNOSED FH MEN AND WOMEN IN LITHUANIA

POSTER VIEWING SESSION

Urtė Aliošaitienė[1,2,3], Žaneta Petrulionienė[1,2,3], Egle Skiauteryte[3], Dovile Gabartaite[2,3], Emilija Meskene[2,3], Juste Staigyte[2,3], Rimantė Čerkauskienė[2,4], Viktoras Sutkus[4], Jurate Barysiene[1,2,3], Milda Kovaite[3], Vilma Dzenkeviciute[2,3,5], Sandra Kutkiene[3], Egidija Rinkuniene[1,2,3], Rusne Jakaite[3], Rasa Strupaite-Sileikiene[2,6,7], Goda Jackute[2], Gabriele Jaskeviciute[2]
[1]Clinic Of Cardiac And Vascular Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [5]Clinic Of Internal Diseases, Family Medicine And Oncology, Vilnius University, Faculty of Medicine, Vilnius, Lithuania, [6]Centre Of Eye Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [7]Center Of Eye Diseases, Clinic Of Ear, Nose, Throat, And Eye Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, vilnius, Lithuania

Background and Aims : to determine the prevalence of corneal arcus among men and women with genetically confirmed FH.

Methods: Prospective observational cohort study enrolled patients with clinically diagnosed FH according to Dutch Lipid Clinic Network (DLCN) criteria treated in Vilnius University Hospital Santaros Klinikos during the period of 2016-2021. Next generation sequencing was used to identify FH causing mutations. Corneal arcus was diagnosed by the opthalmologist. Data of 126 study patients were included in the analysis. Statistical analysis was performed using R (v. 4.0.4) program package.

Results: Of 126 examined patients 54,8% (n=69) were women and 45,2% (n=57) were men. Genetic mutation of FH was confirmed in 30,2% (n=38) of the patients. Corneal arcus was found in 18,4% (n=23) of our whole study population. Corneal arcus was diagnosed for 34% (n=13) of people with genetically confirmed FH and 11% (n=10) of patients with no genetic FH mutation (p=0,003). Corneal arcus was diagnosed in 52% (n=12) of women with genetically confirmed FH (mean age 44,30±13,99 years), and in 11% (n=5) of women without FH mutation (mean age 49,20±12,36 years) (<0,001). Corneal arcus was diagnosed in 7% (n=1) of men with genetically confirmed FH (mean age 37,60±17,41 years), and in 12% (n=5) of men without FH mutation (mean age 42,26±9,23 years).

Conclusions: the prevalence of corneal arcus was higher among patients (both men and women) with genetically confirmed FH compared to patients without determined genetic FH mutation.

ID:1138

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

THROMBOTIC AND THROMBOEMBOLIC EVENTS IN COVID-19 PATIENTS: ASSOCIATION WITH CLINICAL PRESENTATION, PROGRESSION AND LABORATORY FINDINGS. DATA ANALYSIS OF A 681 PATIENT COHORT

POSTER VIEWING SESSION

Angelos Liontos[1], Dimitrios Biros[1], Stavros Tsourlos[1], Lazaros Athanasiou[1], Orestis Milionis[1], Alexandros Papathanasiou[1], Cornelia Veliani[1], Nikolaos-Gavriil Kolios[1], Christiana Pappa[1], Valentini Samanidou[1], George Siopis[1], Eleni Pargana[1], Maria Nasiou[1], Stavros-Periklis Anagnostopoulos[1], Nikol-Natalia Armata[1], Aikaterini Poulopoulou[1], Sempastien Filippas-Ntekouan[1], Eleftherios Klouras[1], Maria Christaki[1], Iro Rapti[1], Maria Kosmidou[1], Aikaterini Panteli[1], Fotios Barkas[2], George Papamichael[1], Ilias Tsiakas[1], Ioannis Vagias[1], Evangelos Liberopoulos[3], Eirini Christaki[1], Haralampos Milionis[1]
[1]1st Dpt Of Internal Medicine And Infectious Diseases Unit, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [2]2nd Department Of Internal Medicine, University Hospital Of Ioannina, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, Greece, [3]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece

Background and Aims : Introduction: During the progression of the COVID-19 pandemic, SARS-CoV2 infection was positively correlated the vascular endothelium dysfunction and immunothrombosis, thus increasing the risk of thromboembolic events (TEs). The aim of this study was to determine the possible clinical presentation of such patients, as well as the laboratory findings and clinical progression.

Methods: Methods: Data of 681 hospitalized patients were collected from the University Hospital of Ioannina. The major events recorded were pulmonary embolism and vascular tree-in-bud as reported by CT angiography (upon clinical suspicion). The data were analyzed using independents samples t-test and chi-square test, on IBM SPSS Statistics 26.

Results: Results: TEs were documented in 128 patients, with a mean age of 61.6 years and BMI 30.1 kg/m^2, 69 of whom were male. The most frequent comorbidities were arterial hypertension (n=60), dyslipidemia (n=49) and obesity (n=45). The most common symptoms were fever (n=113), dry cough (n=69) and dyspnea (n=43). 19 of those patients eventually passed. Patients with peak CRP levels >100 mg/L presented higher possibility of TEs (OR= 1.61, p=0.01). Similarly, length of stay >7 days and dyspnea were associated with higher frequency of TEs (OR=2.37, p=0.004 and OR=1.51, p=0.04). Patients with TEs presented higher probability of intubation compared to the rest (OR=2.49, p=0.002). LDL/HDL ratio was higher in patients with TEs compared to the rest (2.90 vs 2.51, p=0.02).

Conclusions: Conclusion: TEs are directly associated with the inflammatory state and length of stay in COVID-19. The increased risk of intubation of these patients commands a closer follow-up during hospitalization.

ID:1139

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

UNVEILING THE ANTIATHEROGENIC ROLE OF ADVANCED LIPOPROTEIN CHARACTERISTICS IN POSTOPERATIVE SUBJECTS WITH MORBID OBESITY

POSTER VIEWING SESSION

Júlia Carmona-Maurici[1], Nuria Amigo[2], Jorge Juan Olzina Kissler[3], Juan Antonio Baena-Fustegueras[3], Josep Julve[4], Julia Peinado-Onsurbe[1], Eva Pardina[1]
[1]Biochemical And Molecular Biomedicine, Universitat de Barcelona, Barcelona, Spain, [2]Ciberdem, Biosfer Teslab SL; DEEEA, Metabolomics platform, Universitat Rovira i Virgili, IISPV, Barcelona, Spain, [3]Endocrinology Surgery Unit, Arnau de Vilanova University Hospital (UdL), Lleida, Spain, Lleida, Spain, [4]Department Of Biochemistry, CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Barcelona, Spain

Background and Aims : Nuclear magnetic resonance (1H-NMR) analysis have recently used to uncover hidden quantitative lipoprotein characteristics in cardiometabolic scenarios. The aim of this study was to assess whether bariatric surgery (BS) improved the quantitative characteristics of lipoproteins and their relationship with the presence of atherosclerotic plaque.

Methods: The number, size, and lipid content of different lipoprotein classes of 37 subjects with morbid obesity were analyzed by 1H-NMR at baseline and after one-year of BS, and in 111 non-obese volunteers.

Results: At baseline, TG, cholesterol content and number of **VLDL** were increased in the subjects with morbid obesity. Additionally, the concentrations of cholesterol, TG and number of **LDL** particles were significantly higher in those patients withobesity and atherosclerotic plaque. Conversely, subjects with obesity had lower number of **HDL** particles and had much less TG. The subjects with atherosclerotic plaque presented increased concentrations of smaller LDL and lower medium HDL particles compared with those without plaque. BS did not influence the presence of atherosclerotic plaque. However, the TG, cholesterol content and number of VLDL particles were reduced at follow-up. Moreover, the TG content, but not cholesterol, of LDL was significantly decreased, as it was the number of LDL particles, in postoperated subjects. Finally, the TG, cholesterol content and the number of HDL particles were increased after BS.

Conclusions: Excess weight loss improved the atherogenicity of the lipoprotein profile. The number of small LDL and medium HDL particles might provide an approach in subclinical atherosclerosis detection and management.

ID:1141

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

REGENERATION OF VASCULAR ENDOTHELIUM WITH EARLY PROATHEROGENIC CHANGES INDUCED BY BACTERIAL COMPONENTS IN THE PRESENCE OF HIGH FAT SUBSTANCES.

POSTER VIEWING SESSION

Agnieszka Krupa[1], Paulina Rusek-Wala[2], Przemysław Płociński[3], Magdalena Chmiela[3]
[1]Department Of Immunology And Infectious Biology,, University of Lodz, Lodz, Poland, [2]The Bio-med-chem Doctoral School Of The University Of Lodz And Lodz Institutes Of The Polish Academy Of Sciences, University of Lodz, Lodz, Poland, [3]Department Of Immunology And Infectious Biology,, Department of Immunology and Infectious Biology, University of Lodz, Lodz, Poland

Background and Aims : Endothelial dysfunction induced mostly by oxidized sterols and microbial components is one of the main causes of atherosclerotic lesion formation. Understanding the mechanisms involved in the process of development and progression of proatherogenic changes may help to find different ways to modulate the course of coronary heart disease (CHD). **Our study aimed** on analyzing the role of various sterols in the process of vessels regeneration, also in the environment of bacterial components. Also, we tried to explain the possible mechanism that is run during endothelial regeneration and differentiate it between cell migration and cell proliferation.

Methods: We employed cell line of vascular endothelial cells (HMEC-1) and performed a tube formation assay using Matrigel, wound repair test “scratch assay” and cell proliferation, as well as measured collagen production. Cells were treated with various sterols alone (involving oxidized) or together with bacterial components of *Helicobacter pylori* (*HP*).

Results: Based on results we can suggest that cholesterol has a proangiogenic potential, in the contrary components of the oxidized LDL fraction, such as 7 ketocholesterol and calcitriol, do not have any significant impact on the formation of vascular structure by endothelial cells. Based on our observation we can also suggest that bacterial components of *HP* may modulate the activity of endothelial cells and have proregenerative effect on the vascular endothelium. The study was supported by Foundation for Polish Science (POIR.04.04.00-00-16D7/18) carried out within the TEAM-NET (European Union under the European Regional Development Fund).

Conclusions: Cholesterol promotes endothelial cell migration which is not based on collagen release.

ID:1147

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

MARKERS OF CHRONIC INFLAMMATION AND ATHEROSCLEROSIS IN WOMEN AT MENOPAUSAL TRANSITION AND HISTORY OF CONFIRMED ENDOMETRIOSIS

POSTER VIEWING SESSION

Viktoriia Alieksieieva[1], Iryna Muryzina[2], Mykola Shcherbina M[2], Vitaliy Gargin[3]
[1]Department Of Otorhinolaryngology, Kharkiv National Medical Universuty, Kharkiv, Ukraine, [2]Department Of Obstetrics & Gynecology N 1, Kharkiv National Medical Universuty, Kharkiv, Ukraine, [3]Department Pathological Anatomy, Kharkiv National Medical Universuty, Kharkiv, Ukraine

Background and Aims : Recognition of high-risk population that should be screened in the first turn provides the opportunity to intervene at the reversible stage. Endometriosis is notoriously associated with chronic inflammation, which might outweigh protective influence on endothelium of almost unopposed estrogens. **Objectives.** The objectives were to test patients with confirmed endometriosis for biomarkers of inflammation and early marker of atherosclerosis during menopausal transition (MT), then to identify variables with the best predictive value with regard to subclinical atherosclerosis.

Methods: The study included 67 patients aged 45-55, with endometriosis and without a history of evident cardiovascular disease who had already experienced perimenopause-associated menstrual disorders with episode of amenorrhea 2-11 month, and 32 women matching by age and history except no records about endometriosis. They were tested for C-reactive protein (CRP), interleukine-6 (IL6), tumor necrosis factor-α (TNFα), apolipoprotein B (ApoB), fibrinogen, brachial artery dilation and cross-sectional associations were examined.

Results: It turned out that women with endometriosis showed elevated level of IL6 (1.89±0.09 pg/ml, >1.7pg/ml), CPR (5.7±0.93 mg/L, >3mg/L), slightly raised ApoB(78±2.2 mg/dL, >60 mg/dL) and TNFα (79±1.3), lower vasodilation response (7.95±0.23, <8%). Women without endometriosis showed all these variables within physiological range.

Conclusions: Chronic subclinical inflammation related to endometriosis might affect adversely endothelium and cause ED, which predisposes to alterations associated with atherosclerotic impairment of vascular network at the time of MT.

ID:1150

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-05 Extracellular matrix and calcification*

THE EFFECT OF ALPHA-KETOGLUTARATE ON PHOSPHATE AND HYPOXIA INDUCED CALCIFICATION OF VASCULAR SMOOTH MUSCLE CELLS

POSTER VIEWING SESSION

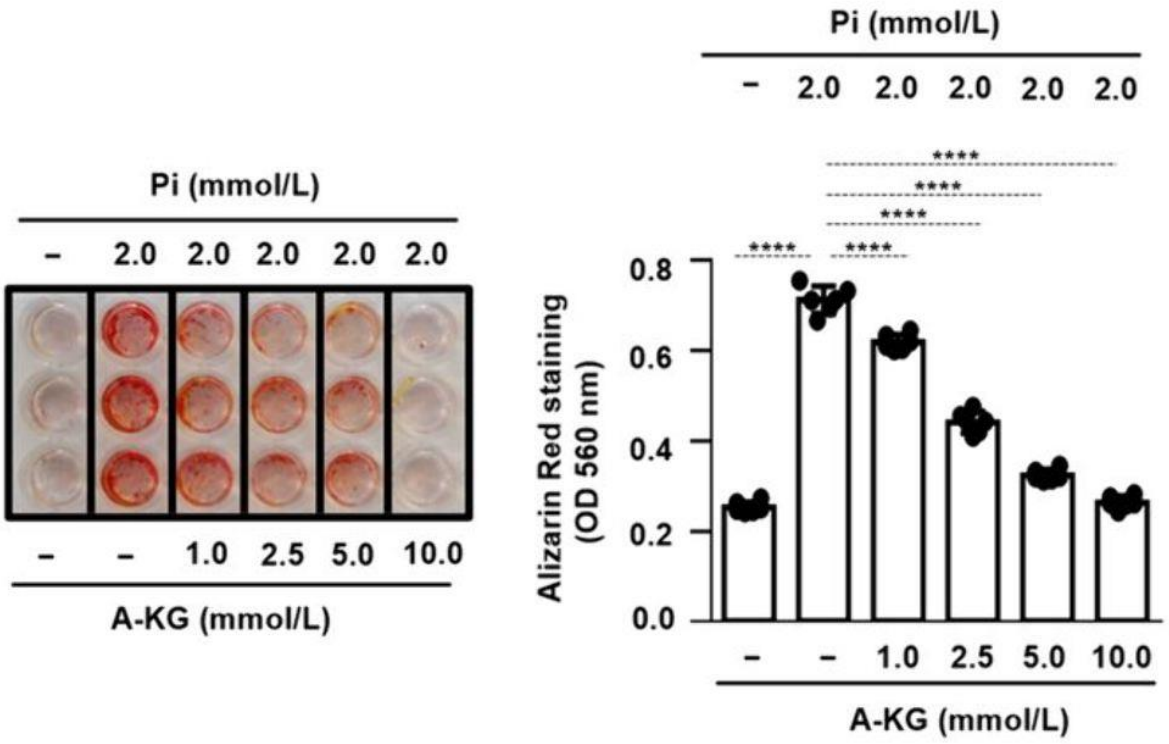
Dávid Máté Csiki, Andrea Tóth, Gréta Lente, Enikő Balogh, Viktória Jeney
Research Centre For Molecular Medicine, University of Debrecen, Debrecen, Hungary

Background and Aims : Recent studies revealed that hypoxia contributes to vascular calcification via the activation of hypoxia-inducible factor 1 (HIF-1) pathway. The alpha-ketoglutarate-dependent prolyl hydroxylase domain enzymes regulate the stability of HIF-1α in response to oxygen availability. As a rate-limiting substrate, alpha-ketoglutarate regulates the activity of prolyl hydroxylases, therefore we addressed the inhibitory effect of alpha-ketoglutarate on vascular smooth muscle cell calcification under hypoxic condition.

Methods: We induced calcification of human aortic smooth muscle cells (HAoSMCs) and mice aortic rings with elevated inorganic phosphate (Pi, 2 mmol/L) and hypoxia (1% O_2) in the presence or absence of alpha-ketoglutarate (1-10 mmol/L). Protein expressions of HIF-1α, and glucose transporter-1 (Glut-1) were evaluated by Western blot. Extracellular matrix (ECM) mineralization was assessed by Alizarin Red staining, calcium measurement and osteocalcin ELISA.

Results: Alpha-ketoglutarate dose-dependently inhibited Pi+hypoxia-induced Ca accumulation in the ECM of HAoSMCs. Osteocalcin level of Pi+hypoxia-treated HAoSMCs was largely attenuated by alpha-ketolglutarate (14.9 vs. 0.01 ng/mL). Alpha-ketoglutarate inhibited Pi+hypoxia-induced elevation of HIF-1α and Glut-1 expressions. Alpha-ketoglutarate attenuated Pi+hypoxia-induced calcification of mice aortic rings (0.2 vs. 0.03 mg Ca/mg

protein).



Conclusions: Alpha-ketoglutarate decreases Pi+hypoxia-induced osteochondrogenic transdifferentiation and ECM mineralization of HAoSMCs *in vitro* and mice aorta *rings ex vivo*. Further studies are necessary to investigate the effect of alpha-ketoglutarate on vascular calcification *in vivo*.

ID:1169

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

TETRAHYDROXYSTILBENE GLYCOSIDE ATTENUATES ENDOTHELIAL DYSFUNCTION AND OBESITY-ASSOCIATED HYPERTENSION IN OBESE RATS: THE ROLE OF OMENTIN-1

POSTER VIEWING SESSION

Haifeng Zhang, Qianqian Dong, Kaifeng Li, Tuo Zhang, Yunshu Wangsun, Wenjuan Xing
Teaching Experiment Center, Fourth Military Medical University, Xi'an, China

Background and Aims : Hypertension in obesity has become a major threat for public health. Omentin-1, a novel adipokine, is down-regulated in obesity. Tetrahydroxystilbene glycoside (TSG) is the main ingredient extracted from *Polygonum multiflorum Thunb* (PMT), a traditional Chinese medicinal herb safely used for protecting cardiovascular systems over bimillennium. This study aims to examine (i) the impact of omentin-1 downregulation on obesity-related hypertension in murine models and the underlying mechanisms; (ii) whether tetrahydroxystilbene glycoside (TSG) improved endothelial dysfunction and obesity-associated hypertension via the increase of omentin-1.

Methods: (TSG-treated) male Zucker diabetic fatty (ZDF) rats and omentin-1 knockout ($OMT^{-/-}$) mice were used. *In vitro*, human umbilical vein endothelial cells (HUVECs) and mature adipocytes differentiated from human visceral preadipocyte (HPA-v) were maintained in a co-culture system.

Results: TSG was the main active component of PMT reducing systolic blood pressure and improving endothelial vasodilation. Fortnight-TSG treatment (100 mg/kg/day) increased serum omentin-1 level, also activated Akt/eNOS signaling and enhanced NO bioactivity; decreased expression of NOX2 and $p22^{phox}$, suppressed production of superoxide and peroxynitrite anion. $OMT^{-/-}$ mice showed elevated blood pressure and impaired endothelial vasorelaxation, whereas hypotensive effect of TSG was blunted. In co-culture system, TSG incubation promoted binding of peroxisome proliferator-activated receptor-γ (PPAR-γ) and *Itln-1* promoter in adipocytes, activated Akt/eNOS/NO signaling and attenuated oxidative/nitrative stress in HUVECs. Suppression of *Itln-1* with siRNA significantly blocked the protective effect of TSG *in vitro*.

Conclusions: Down-regulation of omentin-1 partially induces endothelial dysfunction and hypertension in obesity. TSG treatment increases omentin-1 via promoting binding of PPAR-γ and *Itln-1* promoter and exerts protection on endothelial function.

ID:1153

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

ASSOCIATION BETWEEN E-CIGARETTE AND ATHEROSCLEROSIS: A REVIEW

POSTER VIEWING SESSION

Aurea M.L. Novais, Renan C. Castello Branco
Student, Bahiana School of Medicine and Public Healthy, Salvador, Brazil

Background and Aims : Smoking is responsible for 140,000 premature deaths annually from cardiovascular disease, its is already known as a risk factor for the development and worsening of atherosclerosis. Electronic cigarettes (e-cigarettes) were supposedly a healthier alternative. However, the use of e-cigarettes is still controversial because their toxicity, safety and health impact of long-term use have not been sufficiently studied. To describe the association between electronic cigarettes and the atherosclerosis process.

Methods: Material and methods: Search strategies: Pubmed, lilacs, EMBASE, as inclusion criteria: English language, clinical trials, published in the last 10 years, using as keywords: "atherosclerosis" and "electronic cigarette"; "atherosclerosis" and "vaping";"atherosclerosis" and "Vapings, nicotines"/ Exclusion criteria: articles published in other languages or other studies that do not support the description of the clinical trial.

Results: 14 articles were selected, of these, based on the exclusion criteria, a total of 3 articles were selected, where two of these addressed the use of inhaled e -cigarettes as a negative effect. Mean age 22 [19-28 years], a total of participants involving 2 studies was 33 where serum flow cytometry analyzes were performed with significant increase in the expression of extracellular vesicles of endothelial (EV) and platelet origin. And a significant increase in serum levels of endothelial progenitor cells (ECPs), especially after inhalation with nicotine.

Conclusions: Conclusion: More studies are needed on this topic of improvement approach, however, the findings of this study suggest that the increase in EVs of endothelial and platelet origin, observed after inhalation of electronic cigarette vapor, in addition to the increase (EPCs).

ID:1157

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

AGE-RELATED DIFFERENCE IN THE IMPACT OF DIABETES MELLITUS ON ALL-CAUSE MORTALITY AFTER ACUTE MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Pil-Sang Song
Division Of Cardiology, Department Of Internal Medicine, Chungnam National University Hospital, Daejeon, Korea, Republic of

Background and Aims : Little is known about the association of diabetes mellitus with clinical outcomes of post-acute myocardial infarction (AMI) in younger adults. We tested the hypothesis that the impact of diabetes on outcomes can vary by age.

Methods: A total of 12,600 AMI patients from the Korea Acute Myocardial Infarction Registry-National Institute of Health (KAMIR-NIH) between November 2011 and December 2015 was classified into young (n = 3,590 [28.5%]) and elderly (n = 9,010 [71.5%]). Those less than 55 years of age were considered young. We performed comparisons of baseline characteristics, in-hospital treatments, and clinical outcomes between patients with and without diabetes after stratification according to age group.

Results: The prevalence of diabetes mellitus was 26.5% in the young AMI group. In the multivariable-adjusted model of the entire cohort, diabetes was associated strongly with 3-year all-cause mortality (12.6% vs. 6.8%; adjusted hazard ratio [HR], 1.318; 95% confidence interval [CI], 1.138-1.526). When the entire cohort was subdivided into two age groups, young diabetic patients showed a 107.0% higher mortality rate than those without diabetes (adjusted HR, 2.070; 95% CI, 1.150-3.724). Meanwhile, elderly diabetic patients had a 25.3% higher risk of mortality than non-diabetic patients (adjusted HR, 1.253; 95% CI, 1.076-1.459). The interaction of diabetes with age was significant (adjusted *p* for interaction = 0.008).

Conclusions: Diabetes is not uncommon in younger AMI patients, and the relative risk of long-term mortality is significantly higher in young patients than in older counterparts. More aggressive treatments are needed to prevent future cardiovascular events in younger patients after AMI.

ID:1158

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-06 Gender and cardiovascular risk*

ASSOCIATION BETWEEN METABOLIC PARAMETERS AND COGNITIVE DYSFUNCTION IN DIFFERENT AGE GROUPS

POSTER VIEWING SESSION

Olga E. Zaprovalna, Olena V. Kolesnikova, Anna V. Potapenko, Anastasiia O. Radchenko
Department Of The Study Of Aging And Metabolic Associated Diseases, Government Institution "L. T. Mala National Institute of Therapy of the NAMS of Ukraine, Kharkiv, Ukraine

Background and Aims : Background: Patients with cognitive deficits have a higher cardiovascular risk, but the mechanisms are not clear. **Aims:** to determine the association between metabolic parameters and deterioration of cognitive function (DCF) in different age groups.

Methods: Methods: 151 apparently healthy people are those without established ASCVD, type 2 DM, or severe comorbidities aged 31-75 years were included after signing informed consent. We assessed clinical, biochemical, and anthropometric parameters. Cognitive function was assessed based on the results of the questionnaires: Montreal Cognitive Assessment (MoCA) and Digit Symbol Substitution Test (DSS).

Results: Results: The analyses data of the young group (aged from 31 to 45 years) indicated, that DCF was associated with blood pressure ($r=0.61$, $p<0.05$), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) ($r=0.52$, $p<0.05$). The data of the middle group (aged 45 to 60 years) indicated the association DCF with HOMA insulin resistance index, HDL-C ($r=0.38$, $p<0.05$). DCF in the old group (aged 60 to 75 years) was associated with age ($r=0.57$, $p<0.05$), HOMA insulin resistance index ($r=0.75$, $p<0.05$), creatinine ($r=0.77$, $p<0.05$) but not with lipid level. According to the data of regression analysis, DCF is independently associated with age, body mass index (BMI), waist circumference (WC) ($p = 0.001$), HOMA, HDL-C, LDL-C.

Conclusions: Conclusions: This study shows the association between metabolic parameters and cognitive dysfunction. It suggests that metabolic risk factors increased the degree of cognitive deficit and may increase the risk of developing dementia.

ID:1163

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

PHYSICAL ENVIRONMENTAL IMPACTS ON ATHEROSCLEROTIC CARDIOVASCULAR DISEASE: A REVIEW

POSTER VIEWING SESSION

Sui Yu Yau
N&hs, HKMU, HK, Hong Kong PRC

Background and Aims : Introduction: The prevalence of atherosclerotic cardiovascular disease (ACD) is alarming worldwide. In order to develop effective and timely strategies to minimize the impacts caused by ACD such as physical and psychological health of patients, financial burden due to healthcare expenses of patients and that to the society, it brings our attention on exploring the factors that prevent or lead to ACD for decades. Among all the factors, physical environmental factors is suggested to positively or negatively impacting prevalence of ACD. Objectives: The objective of this study is to review the physical environmental factors that impacts atherosclerotic cardiovascular disease based on the empirical evidences.

Methods: A systematic review was conducted using multiple databases such as Medline, PubMed, Embase. Related articles within 2016-2021 were reviewed systematically and the results were presented by thematic analysis.

Results: Results supported that physical environmental factors can positively or negatively impact the prevalence of ACD. These physical environmental factors include air pollution, global climate change, second-hand tobacco smoke were negatively impacting ACD. While for recreation facilities such as public parks and recreational facilities, good community design of land use, high walkability environment such as provision of sidewalk, were supported to be positively minimize the prevalence of ACD.

Conclusions: Conclusion: The study explored the physical environmental impacts on ACD. In order to enhance the health of individuals, interdisciplinary approach should be adopted to enhance the factors that positively contribute to the good health of cardiovascular system while at the same time eliminating those physical environmental factors lead to ACD.

ID:1164

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

EPIDEMIOLOGY OF CEREBROVASCULAR DISEASE AMONG THE ADULT POPULATION OF THE PRINCIPAL CITY: RESULTS OF A ONE-DECADE PROSPECTIVE COHORT STUDY

POSTER VIEWING SESSION

Olena Y. Fartushna[1], Maria M. Prokopiv[2], Gennadiy O. Slabkiy[3]
[1]Department Of Aviation Marine Medicine, Ukrainian Military Medical Academy, Kyiv, Ukraine, [2]Neurology, Bogomolets National Medical University, Kyiv, Ukraine, [3]Neurology, State University "Uzhhorod National University", Uzhorod, Ukraine

Background and Aims : Little to nothing is known about the epidemiology of cerebrovascular disease (CVD) among the adult population of the principal city and the capital of the largest European County, Ukraine during the last decade. We aimed to conduct a prospective analysis of the epidemiology of CVD among the adult population of Kyiv City (metro area population 2,988,000), Ukraine for the last 12 years.

Methods: During the last decade, we have prospectively collected data to identify all inpatient and outpatient adults with CVD in the capital of Ukraine, Kyiv. Multiple overlapping sources were used to analyze sectoral statistical reports of CVD in Kyiv City, Ukraine from 2009 to 2020. The statistical method and the method of systematic approach were applied.

Results: We established that during the last 12 years there was a decrease in the incidence of CVD among the adult population of Kyiv (reduction of 1.83 times ($p<0.05$) with t reliability criteria 26.89). However, the incidence remains high (476.62 per 100,000 population). At the same time, the prevalence of CVD remains stable (with small fluctuations over the years of observation and was lower than the average in Ukraine (7967, 2 in 2018)), and among the working-age population tends to increase. In the structure of morbidity traditionally in all years, women prevailed in a ratio of 1,4-1,5: 1,0 to men

Conclusions: A significant reduction in the incidence of CVD in the adult population of Kyiv during the last 12 years has been established. This might be caused by increased CVD risk factors prevention work.

ID:1167

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

INFECTIOUS AGENT AS A TRIGGER MECHANISM OF ATHEROSCLEROSIS AND CEREBROVASCULAR DISEASES

POSTER VIEWING SESSION

Olena Y. Fartushna[1], Nataliya S. Turchyna[2]
[1]Department Of Aviation Marine Medicine, Ukrainian Military Medical Academy, Kyiv, Ukraine, [2]Neurology, Bogomolets National medical University, Kyiv, Ukraine

Background and Aims : A deep understanding of the role of the infectious factor that precedes and develops atherosclerosis and cerebrovascular diseases (CVD) is important for the prevention and treatment measures. The aim is to evaluate the role of the infectious factor in the occurrence of atherosclerosis and CVD, to determine its impact on the clinical course.

Methods: Complex clinical, neurological, imaging, and laboratory examination of 43 white adults (mean age 52.7±1.4 years) with various forms of CVD, preceded by the infection (herpetic and respiratory) was provided. Based on the type of CVD and the period between the manifestations of the infection and the CVD onset, patients were divided into 4 groups.

Results: Infection associated with CVD significantly complicated the course of the disease. In the 1st and 2nd groups, there was an increase in the titer of antibodies to HVS 1 and 2 types: Ab HVS1 IgG1:3200, Ab HVS2 IgG1:1600, cytomegalovirus: Ab CMV IgG1:800. In patients of the 3rd and 4th groups, the connection between the herpes infection and the formation of progressive atherosclerosis and CVD was confirmed by clinical course, imaging, labs, an increase in the titer of antibodies Ab HVS1 IgG1:1600, Ab HVS2 IgG1:800, Ab CMV IgG1:800 in blood. Infectious factor in 12 patients was associated with the onset of arterial hypertension, in 10 - with atherosclerosis, in 5 patients with arterial hypotension.

Conclusions: Infection plays a provocative role in the development of CVD; adversely affects the clinical course of CVD; plays an important role in increasing blood viscosity and progression of atherosclerosis.

ID:1239

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

A NOVEL MISSENSE VARIANT IN CREB3L3 GENE ASSOCIATED WITH SEVERE HYPERTRIGLYCERIDEMIA

POSTER VIEWING SESSION

Giovanna Cardiero[1], Daniela Palma[1], Maria D. Di Taranto[1], Maria V. Esposito[1], Gabriella Iannuzzo[2], Matteo N.D. Di Minno[3], Carlo Molino[4], Arcangelo Iannuzzi[5], Giuliana Fortunato[1]
[1]Dipartimento Di Medicina Molecolare E Biotecnologie Mediche, Università degli Studi di Napoli Federico II and CEINGE S.C.a r.l. Biotecnologie Avanzate, NAPOLI, Italy, [2]Dipartimento Di Medicina Clinica E Chirurgia, Università degli Studi di Napoli Federico II, Naples, Italy, [3]Dipartimento Di Scienze Mediche Traslazionali, Università degli Studi di Napoli Federico, Naples, Italy, [4]Dipartimento Di Chirurgia Oncologica, A.O.R.N. "A. Cardarelli", Naples, Italy, [5]Dipartimento Medico Polispecialistico, A.O.R.N. "A. Cardarelli", Naples, Italy

Background and Aims : Severe hypertriglyceridemia (HTG) is a rare disease consisting in increased plasma triglyceride (TG) levels (>10 mmol/L). Patients can show eruptive xanthomas, lipaemia retinalis, hepatosplenomegaly and pancreatitis. For long time five genes were considered causative of the disease with autosomal recessive inheritance: Lipoprotein lipase (*LPL*), Apolipoprotein A-V (*APOA5*), Apolipoprotein C-II (*APOC2*), Glycosyl-phosphatidyl-inositol-anchored HDL-binding protein (GPIHBP1) and Lipase maturation factor-1 (*LMF1*). The introduction of next-generation sequencing (NGS) highlighted the presences of rare variant in noncanonical gene associated to dominant familial hypertriglyceridemia, such as CREB-Binding Protein 3-Like 3 (*CREB3L3*) and Glucokinase Regulator (*GCKR*).

Methods: We report the clinical, biochemical and molecular characterization of a 25 years old woman hospitalized urgently for acute pancreatitis with TG > 17 mmol/L. Patient was screened by NGS to detect variants in a large panel of 35 lipid related-genes.

Results: No know pathogenic variants of HTG were found but NGS analysis revealed the presence at heterozygous state of rare missense variant c.742C>T (p.Arg248Cys) in the exon 6 of *CREB3L3* gene. Variant was confirmed by Sanger sequencing. The variant was absent from databases of mutations (HGMD professional) and according to the ACMG guidelines can be classified as VUS. Bioinformatics predictions classified variant as damaging.

Conclusions: Severe HTG is a complex disease that can benefit from NGS to identify variants in a large number lipid-related genes that can act as phenotype modifier. Our findings support the hypothesis that rare variants in a noncanonical gene for triglyceride metabolism as *CREB3L3*, can contribute to severe hypertriglyceridemia.

ID:1245

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

COMPARISON OF CARDIOVASCULAR RISK IN IDIOPATHIC INFLAMMATORY MYOPATHY WITH GENERAL POPULATION – PRELIMINARY DATA FROM A SINGLE-CENTRE CROSS-SECTIONAL STUDY

POSTER VIEWING SESSION

Sabína Oreská[1], Hana Storkanova[1], Maja Spiritovic[2], Barbora Hermankova[3], Petr Cesak[4], Jaroslav Kudlicka[5], Vladimir Tuka[5], Ondrej Mikes[5], Martin Satny[5], Eva Chytilova[5], Zdislava Krupickova[5], Michal Vrablík[5], Karel Pavelka[1], Ladislav Senolt[1], Herman Mann[1], Jiri Vencovsky[1], Michal Tomcik[1]
[1]Department Of Rheumatology, Institute of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, [2]Department Of Rheumatology, Institute of Rheumatology, 1st Faculty of Medicine, Department of Physiotherapy, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic, [3]Department Of Physiotherapy, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic, [4]Department Of Human Movement Laboratory, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic, [5]3rd Department Of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

Background and Aims : Idiopathic inflammatory myopathies (IIM) and associated inflammation, limited mobility, glucocorticoid treatment, can have a negative impact on metabolic disease, atherogenesis, and cardiovascular risk. The aim was to assess the cardiovascular risk in IIM and healthy controls (HC) and the association with disease-specific features.

Methods: 39 IIM and 39 age-/sex-matched HC with no history of manifest cardiovascular disease were included. Disease activity (MITAX), damage (MDI), muscle involvement (MMT-8) were evaluated, comorbidities and current treatment recorded. Examination of CIMT, PWV, ABI, body composition (densitometry, bioelectric impedance), physical activity (HAP questionnaire) and the CV risk (by SCORE for European population) was performed. Data are presented as median (IQR).

Results: Baseline characteristics shows Table 1. No significant difference in blood pressure, ABI, PWV, CIMT and risk of fatal CV events (SCORE) was observed between IIM and HC. IIM had higher plaques count, significantly lower physical activity than HC (Table 2). In IIM, blood pressure (as MAP) correlated positively with age, BMI, inflammation (CRP, C3), triglycerides, atherogenic index and body fat %, negatively with albumin and HDL-C. Decreased values of ABI were associated with low HDL-C. Increased PWV was associated with age, disease duration, disease activity (MITAX), parameters of body

composition and nutritional status. CIMT and plaque thickness were associated with disease duration (Table 3).

Table 1: Baseline characteristics

	IIM (n = 39)	HC (n = 39)
Gender, n (%): female / male	32 (82) / 7 (18)	32 (82) / 7 (18)
Age (years); median (IQR)	56.0 (47.7 – 64.1)	56.0 (48.3 – 64.2)
BMI (kg/m²); median (IQR)	25.9 (23.2 – 31.1)	27.5 (23.9 – 31.7)
Disease subtype, n (%): DM / PM / IMNM	14 (36) / 18 (46) / 7 (18)	
Disease duration (years); median (IQR)	4.84 (1.96 – 8.31)	
Disease activity (MITAX); median (IQR)	0.13 (0.06 – 0.29)	
Disease damage (MDI); median (IQR)	0.05 (0.03 – 0.08)	
MMT-8; median (IQR)	64 (54 – 70)	
CRP (mg/L); median (IQR)	3.0 (1.4 – 5.0)	
ESR (mm/h); median (IQR)	13 (8 – 25)	
CK (µkat/L); median (IQR)	3.0 (1.3 – 9.4)	
LD (µkat/L); median (IQR)	3.7 (3.4 – 5.2)	
Myoglobin (µg/L); median (IQR)	93.6 (60.4 – 250.2)	
Glycaemia (mmol/L); median (IQR)	5.2 (4.8 –5.8)	
Current dose of GC - prednisolone equivalent dose (mg/day); median (IQR)	6.5 (3.75 – 15)	
IIM-associated clinical manifestations, n (%): MW / OD / SR / MH / RP / A / ILD / CI	35 (88) / 7 (18) / 5 (13) / 8 (21) / 10 (26) / 5 (13) / 16 (41) / 3 (8)	
Autoantibodies (positive), n (%): ANA / Mi-2 / TIF-1γ / CADM-140 / SAE / p140 / SRP / Jo-1 / PM-Scl / RNP / Ku / Ro / HMGCR	24 (62) / 3 (8) / 3 (8) / 0 (0) / 0 (0) / 0 (0) / 3 (8) / 10 (26) / 5 (13) / 5 (13) / 0 (0) / 16 (41) / 3 (8) / 2 (5)	
Treatment, n (%): GC / MTX / AZA / CSA / CPA / LEF / MMF	36 (92) / 11 (28) / 8 (21) / 5 (13) / 2 (5) / 2 (5) / 1 (3)	
Arterial hypertension (treated), n (%)	15 (38)	
Diabetes mellitus, n (%): Untreated / PAD / Insulin treatment	3 (8) / 1 (3) / 1 (3)	
Statin use, n (%): Current / Previous / Other current hypolipidemic drugs	0 (0) / 4 (10) / 1 (3)	
Smoking (current), n (%)	0 (0)	

Acronyms: IIM, idiopathic inflammatory myopathies; DM, dermatomyositis; PM, polymyositis; IMNM, immune mediated necrotizing myopathy; HC, healthy controls; MITAX, Myositis Intention to Treat Activity Index; MMT-8, manual Muscle Testing-8; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; CK, creatine kinase; LD, lactate dehydrogenase; MW, muscle weakness; OD, oesophageal motility disorder; SR, skin rash; MH, mechanic's hands; RP, Raynaud's phenomenon; A, arthritis; ILD, interstitial lung disease; CI, cardiac involvement; ANA, antinuclear antibodies; Mi-2, anti-nuclear helicase 218/240 kDa; p155 140, anti TIF1 (transcription factor 1); CADM 140, anti MDA5 (antigen associated with melanoma differentiation); SAE, anti-SUMO1 (small ubiquitin-like activating enzyme); p140, anti NXP2 (nuclear matrix protein); SRP, anti-signal recognition particles; Jo-1, anti-histidyl tRNA synthetases; PM-Scl, anti-PM-Scl (anti-core complex 11-16 proteins); RNP, anti-ribonucleoprotein; Ku, anti-Ku (against the nuclear DNA-protein kinase subunit); Ro, anti-Ro (52 / 60kDa, against cytoplasmic RNA and associated peptides); GC, glucocorticoids; MTX, methotrexate; AZA, azathioprine; CSA, cyclosporin A; CPA, cyclophosphamide; LEF, leflunomide; MFF, mycophenolate mofetil; PAD, per oral antidiabetic drugs

Table 2: Cardiovascular (CV) parameters in patients with idiopathic inflammatory myopathies (IIM) and healthy controls (HC)

Parameters of CV risk	IIM (n = 39)	HC (n = 39)	p-value
MAP (mmHg): median (IQR)	**95** (86 - 103)	**97.7** (89.3 - 107)	0.497
ABI; median (IQR)	**0.995** (0.92 – 1.06)	**1.05** (0,89 – 1.10)	0.265
PWV (m/s); median (IQR)	**8.0** (6.05 – 9.40)	**8.0** (7.05 – 9.38)	0.484
CIMT (mm) ; median (IQR)	**0.7** (0.6 – 0.8)	**0.7** (0.6 – 0.8)	0.356
Plaque: n (%)	**14** (35.9)	**10** (25.6)	0.462
Plaque thickness (mm); median (IQR)	**1.4** (1.3 – 1.8)	**1.6** (1.2 – 2)	0.978
BMI (kg/m²); median (IQR)	**25.9** (23.2 – 31.1)	**27.5** (23.9 – 31.7)	0.893
HAP; median (IQR)	**58.3** (47.8 – 69.8)	**83** (79 – 90.8)	**<0.001**
SCORE (%); median (IQR)	**2** (1 – 5)	**3** (1 – 5)	0.990

Acronyms: MAP, mean arterial pressure; ABI – ankle-brachial index; PWV – pulse wave velocity; CIMT – carotid intima-media thickness; BMI – body mass index; HAP, human activity profile questionnaire; SCORE, systematic Coronary risk evaluation – risk of fatal cardiovascular event in 10 years (%)

Table 3: Correlation of cardiovascular parameters and disease-specific features in all IIM patients (n=39)

Correlated parameters	Spearman's r	p-value
MAP: Age; BMI CRP; albumin; C3; TG; HDL-C; AI BF (%, DXA); VF (kg, DXA), BF (%, BIA)	0.567; 0.346; 0.324; -0.452; 0.451; 0.518; -0.418; 0.466 0.521; 0.512; 0.402	<0.001; 0.042; 0.044; 0.014; 0.014; 0.004; 0,024; 0.011; 0.002; 0.002; 0.012
ABI: HDL-C	0.106	0.024
PWV: Age; disease duration; MITAX; albumin; Phase angle (BIA); ECM/BCM (BIA); Cell quota % (BIA)	0.793; 0.368; -0.430; -0.430; -0.420; 0.793; -0.125	<0.001; 0.049; 0.046; 0.010; 0.023; 0.023; 0.037
CIMT: disease duration	0.377	0.020
Plaque thickness: disease duration	0.438	0.029

Acronyms: MAP, mean arterial pressure; ABI – ankle-brachial index; PWV – pulse wave velocity; CIMT – carotid intima-media thickness; BMI – body mass index; CRP, C-reactive protein; C3, complement 3; TG, triglycerides; HDL-C, high-density lipoprotein; AI, atherogenic index of plasma = log(TG/ HDL-C);BF, body fat; VF, visceral fat; DXA, dual X-ray absorptiometry; BIA, bioelectrical impedance; MITAX, Myositis Intention to Treat Activity Index; ECM/BCM, extracellular mass/body cell mass index

Conclusions: No significant differences in cardiovascular risk between our IIM and HC were detected. In IIM, cardiovascular risk factors were associated with age, disease duration, glucocorticoids dose,

lipidogram and body composition. No association with decreased physical activity was observed.
Acknowledgement: AZV-NV18-01-00161A, MHCR-00023728, SVV-260373

ID:1308

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EFFECT OF PCSK9 INHIBITORS ON CARDIO-ANKLE VASCULAR INDEX IN FAMILIAL HYPERCHOLESTEROLEMIA SUBJECTS

POSTER VIEWING SESSION

Arman S. Postadzhiyan[1], Ivailo Tzvetkov[2], Lora Andreeva[2], Bojidar Finkov[2], Vassil Velchev[2]
[1]Saint Anna University Hospital, Cardiology Departement, Medical University of Sofia, Sofia, Bulgaria, [2]Cardiology, Saint Anna University Hospital, Cardiology Departement, Sofia, Bulgaria

Background and Aims : Subjects with familial hypercholesterolemia (FH) are characterized by an increased amount of LDL-C that promotes a development of early atherosclerosis. Our aim was to evaluate the effect of PCSK9-i on atherosclerosis damage analyzed by cardio-ankle vascular index (CAVI) in a cohort of FH subjects.

Methods: In this prospective observational study, we included 54 FH subjects on moderate or high-intensity statins with or without ezetimibe. All subjects were placed on PCSK9-i therapy (Evolocumab 140 mg SC q2weeks) and biochemical analysis as well as CAVI evaluation at baseline and after twelve months of PCSK9-i therapy was obtained.

Results: The mean age of the patients was 52.5±1.69 with DCLN of 7.98±0.3 and 70.3% with previous myocardial infarction or proven coronary disease. After 12 months there were a significant reduction of LDL-C (-3.21 mmol/l, 95% CI -2.49 to -3.92 mmol/l) and non HDL-C (-4.43 mmol/l, 95% CI -3.04 to -5.83 mmol/l). The proportion of patients reaching the target LDL levels according to the 2016 and 2019 ESC / EAS guidelines were 62.5% and 45% respectively. In the group taking double lipid lowering therapy (high intensity statin with PCSK9-i, n=30, 55.6%) and triple LLT (with ezetimibe, n=15, 27.8%) we noticed a profound improvement of CAVI which was more pronounced in the latest group (- 14.5% and 20.4%, $p < 0.05$).

Conclusions: In addition to the reduction in atherogenic lipids and better achievment of targets, we also found a significant improvement in arterial stiffness among high-risk patients with FH. The observed effect depends on the intensity of lipid-lowering therapy.

ID:1282

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

HEMATOPORPHYRIN- MEDIATED FOCUSED ULTRASOUND SONODYNAMIC THERAPY COMBINED WITH CATHETER- BASED RHENIUM-186 BRACHYTHERAPY AFTER B- MODE ULTRASOUND- GUIDED BALLOON ANGIOPLASTY OF OCCLUDED ARTERY

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : Three mechanisms are responsible for the development of restenosis: elastic recoil, intimal hyperplasia and late vascular constriction, all grouped under the catch phrase “negative remodeling”. Neointimal hyperplasia is usually defined in an artery as thickening of the intimal layer after an injury such as balloon angioplasty methods. The aim of this study was to evaluate the effect of combined ultrasound sonodynamic therapy and catheter- based ^{186}Re-mediated beta radiation (β^-) brachytherapy on restenosis reduction after balloon angioplasty.

Methods: Briefly, golden Syrian hamsters were submitted to common carotid artery advanced atherosclerotic occlusion by primary perivascular Co2 laser-mediated far-infrared injury followed by a 2% cholesterol-rich diet for six weeks. Histopathology results showed the formation of a thick- cap fibroatheromatic plaque, resulted to occlusion in all of the hamsters’ arteries. Then treatment group (n=10) underwent B-mode ultrasound- guided balloon angioplasty followed by sonosensitizer hematoporphyrin- loaded PESDA (Perfluorocarbon Exposed Sonicated Dextrose Albumin) microbubbles (100ml/kg, 2–5×10^5 bubbles/ml)- mediated pulsed low level focused ultrasound (F=450 KHz, I=5.5 W/cm2, PD=120 ms) sonodynamic therapy and catheter- based β^- brachytherapy (^{186}Re −, 28 Gy).

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for macrophages and hyperplastic vascular smooth muscle cells density after balloon angioplasty in the treated group compared with the other groups ($p<0.05$).

Conclusions: Enhanced anti-inflammatory effect of hematoporphyrin- mediated sonodynamic therapy, induced by collapsed microbubbles- mediated enhanced ultrasound sonoporation therapy accompanied by apoptotic effect of rhenium-186- mediated β- brachytherapy, can cause to reduce the neointima hyperplasia.

ID:1305

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

A SUITABLE SEQUENCE OF BIOINFORMATICS TOOLS FOR NGS DIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Ales Horinek[1,2], Kateřina Hirschfeldová[1,2], Lena Obeidova[1], Eva Pazourková[1], Veronika Todorovova[2], Michal Vrablík[2], Martin Satny[2]
[1]Institute Of Biology And Medical Genetics, First Faculty of Medicine Charles University, Prague, Czech Republic, [2]3rd Department Of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

Background and Aims : Familial hypercholesterolemia (FH) is the most common monogenic congenital metabolic disease with an estimated frequency of 1: 200 - 500 in the population. Aberrations of the LDL receptor gene (*LDLR*) or mutation in his ligand apolipoprotein B100 (*FDB*) are the most common cause of FH. To date, over 2000 different mutations have been described in the *LDLR*. More rarely the pathology could be detected in other genes (*APOB, LDLRAP , PCSK9*, etc.). Early diagnosis using molecular genetic methods enables appropriate treatment and belongs to the basic pillars of routine practise. Considering various types of possible mutations, next - generation sequencing (NGS) method using hybridization-based enriched libraries can provide a potent solution for required multilevel genetic analysis. Each level of data analysis requires specific bioinformatic tool although the sensitivity to detect certain types of variants may partially overlap.

Methods: We present three bioinformatic tools (FreeBayes, Manta and CNVkit) as an example of suitable unique combination of optimal NGS data analysis pipeline - specifically for the custom Hyperlipoproteinemia 1 (HLP) SureSelect library panel (Agilent Technologies) covering 53 HLP genes and 55 SNPs.

Results: The spectrum of causal mutations detected in our FH and HLP patients cohort were as follows: 81% of single-nucleotide variants, 5% of minor and 14% of gross (two and more exons) intragenic rearrangements. Mutations in *LDLR* covered 74,4% of causal variants, 11,6% of mutations were in *APOB* and 14% in another genes from the HLP panel.

Conclusions: The presented combination of bioinformatic tools represents effective diagnostic algorithm with increase diagnostic yield.

This work was supported by the Cooperatio Program, research area "Metabolic Diseases* **207037"

ID:1304

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

INCREASED VALUES IN TOTAL CHOLESTEROL AND LDL CHOLESTEROL IN "PREDIABETIC" MIDDLE-AGED AND ELDERLY ADULTS WITH A1C BETWEEN 5.7 AND 6.4%

POSTER VIEWING SESSION

Regina Helena M. Pereira[1], Rodrigo Tallada Iborra[2], Raphael D.S. Pinto[3], Marisa Passarelli[4,5], Adriana Machado-Lima[4,6]
[1]Ppgce, Universidade Sao Judas Tadeu, São Paulo, Brazil, [2]Ppgef, Universidade Sao Judas Tadeu, Sao Paulo, Brazil, [3]Biomedicina, Universidade Santa Cecília, Santos, Brazil, [4]Laboratorio De Lipides (lim-10), Faculdade de Medicina da USP, Sao Paulo, Brazil, [5]Programa De Pós-graduação Em Medicina, Universidade Nove de Julho, São Paulo, Brazil, [6]Ppgce, Universidade Sao Judas Tadeu, Sao Pulo, Brazil

Background and Aims : Patients with "prediabetes" are defined by the presence of Impaired Fasting Glucose and/or Impaired Glucose Tolerance and/or HbA1c 5.7-6.4%. Although prediabetes should not be seen as a clinical entity per se, the risk of diabetes and cardiovascular disease (CVD) may be increased in this condition. The aim of this study was to evaluate whether slight changes in glycated hemoglobin may interfere with the cholesterol profile

Methods: Twenty-two individuals without diabetes with a mean age of 56 years (SD±9.8) were classified into two groups, LH group with HbA1c < 5.5% and MH group with HbA1c between 5.7 and 6.2%. Waist circumference, body mass index, fasting glucose, glycated haemoglobin, skin autofluorescence, dietary intake of AGEs, total plasma cholesterol, LDCc and HDLc were measured.

Results: The LH and MH groups did not differ in age (55.3±10 and 55±8 years, respectively), WC (92.3±8 and 95.5 ±12 cm, respectively), BMI (27.1±1 and 28.9±1, respectively), fasting blood glucose (92.6±7.8 and 91.1±6.6 mg/dL, respectively), dietary intake of AGEs (20626±5367 and 17689±7189 AGE KU/day, respectively and skin autofluorescence (2.88±0.7 and 2.66±0.6 AU, respectively). When we observed plasma lipids, the LH group had lower LDLc (93±8 mg/dL) and total cholesterol (173±9mg/dL) compared to the MH group, LDLc (119±8mg/dL) and total cholesterol (206±9mg/dL) p=0.0386 and p=0.0215, respectively.

Conclusions: We can conclude that even in the absence of other components of metabolic syndrome, elevated HbA1c values that would already indicate a prediabetic state seem to negatively interfere with plasma total cholesterol and LDLc values.

ID:1299

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

INNFLAMMATION-, APOPTOSIS- AND MITOPHAGY-RELATED GENE EXPRESSION IN ANEURISMATIC AND NOB-AFFECTED MEDIAL LAYER OF HUMAN THORACIC AORTA

POSTER VIEWING SESSION

Igor A. Sobenin[1,2], Petr V. Chumachenko[3], Zukhra B. Khasanova[1], Anton Y. Postnov[4]
[1]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [2]Central Pathologoanatomic Laboratory, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [3]Laboratory Of Pathomorphology Of Cardiovascular Diseaeses, National Medical Research Center of Cardiology, Moscow, Russian Federation, [4]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation

Background and Aims : Aortic aneurysm is one of the main causes of cardiovascular surgery. An inflammatory etiology is emerged increasingly as a pathologic background for aortic aneurysms dissection. This study was undertaken to reveal association between thoracic aneurism, inflammation, apoptosis and mitophagy at the gene expression level.

Methods: RNA was isolated from 20 intraoperative samples of medial layer of the thoracic aortic aneurysm and adjacent intact areas, followed by reverse transcription. The expression of several genes associated with apoptosis (CASP3, CASP9, ENO1, NTN1, NTN4, and UNC5A), inflammation (TNF, CCL18, CD14, IL1B, CASP1, and APAF1), and mitophagy (BECN1, LAMP1 LAMP2, MAP1LC3B, VSP18, PINK1, PARK2 and CTSD) was measured by qPCR.

Results: The expression of inflammation-related genes was increased in aneurysmal samples compared to unaffected tissue. Thus, in the aneurismal aortic media, the expression of TNF, CCL18, CD14, IL1B, and CASP1 genes was significantly increased. The expression of all apoptosis-related genes seemed to be somehow increased in aneurysmal media, but the differences reached statistical significance only for the CASP3 and UNC5A genes expression. Finally, none of the genes mitophagy-related genes were overexpressed in the medial aneurysmal regions.

Conclusions: Based on the data obtained, it should be assumed that in the aneurysm of the thoracic aorta, a pronounced inflammatory reaction develops in the medial layer; activation of apoptosis may be regarded as a secondary phenomenon, and minimal changes in mitophagy are not of a systemic nature and, most likely, not associated with the development of aneurysmal lesions. This study was supported by Russian Science Foundation, grant 20-45-08002.

ID:1298

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

REGRESSION OF ADVANCED ATHEROSCLEROSIS WITH NEOVESSELS USING INERTIAL CAVITATION EFFECT OF COLLAPSED MICROBUBBLES- MEDIATED PULSED- FOCUSED ULTRASOUND ANTIVASCULAR THERAPY

POSTER VIEWING SESSION

Hossein Mehrad[1,2], Alberto Foletti[3]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [3]Institute Of Translational Pharmacology Ift, Italian National Research Council, Rome, Italy

Background and Aims : Atherosclerosis is the leading cause of infarction. Atherosclerotic lesions are considered to be advanced when the accumulation of lipid is associated with the disorganization and deformity of the arterial wall. In this study, we investigated focused ultrasound effectiveness on destruction of neovessles in advanced atherosclerotic plaque.

Methods: Briefly, New Zealand white rabbits underwent primary perivascular severe cold injury at the right common carotid artery followed by a 1.5 % cholesterol- rich diet injury for 8 weeks. Histopathology and ultrasonography results showed the formation of advanced atherosclerosis with neovessel- rich plaque and severe stenosis (> 70%) in all of the rabbits' arteries. The animals treated by PESDA (Perfluorocarbon- Exposed Sonicated Dextrose Albumin) microbubbles (100 ml/kg, 2- 5 × 10^5 bubbles/ml)- mediated pulsed- focused ultrasound (I= 60 W/cm^2, F= 750 KHz, PD= 50 ms) therapy.

Results: from histopathology, B-mode and color Doppler ultrasonography showed a significant reduction in the mean value for blood mean velocity, intraplaque neovessels density, wall mean thickness and percentage of luminal cross- sectional area of stenosis and significant increase in the mean value for blood volume flow at the stenotic region in the treatment group compared with the other groups ($p < 0.05$).

Conclusions: Enhanced inertial cavitation effect of high- intensity pulsed focused ultrasound, induced by collapsed PESDA microbubbles within the intraplaque neovessels, can cause to destroy the neovessels and significantly dilate the luminal cross- sectional area of stenosis. This protocol may be a potential treatment to advanced atherosclerosis with neovascularization in comparison with conventional bypass surgery and stenting.

ID:1296

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

IMPACT OF THE DURATION OF PROGRAM HEMODIALYSIS AND HEART FAILURE ON THE PATTERN OF LIPID PROFILE IN PATIENTS WITH END-STAGE CHRONIC KIDNEY DISEASE

POSTER VIEWING SESSION

Olha Shtepa[1], Olexandr Kuryata[1], Olha Halushchak[2]
[1]Internal Medicine 2 And Phtisiatry, Dnipro state medical university, Dnipro, Ukraine, [2]Dialysis Department, Dnipropetrovsk Regional Clinical Hospital named after I.I. Mechnikov", Dnipro, Ukraine

Background and Aims : Patients with chronic kidney disease often have multiple comorbidities and the high cardiovascular mortality. Dyslipidemia is one of the possible risk factors associated with uremia and an increased risk of cardiovascular disease. The aim of our study was to evaluate the influence of the duration of program hemodialysis and presence of heart failure (HF) in patients with end-stage chronic kidney disease on the pattern of lipid profile.

Methods: All patients were divided into groups: I group included 20 patients with end-stage chronic kidney disease (ESCKD) on hemodialysis (duration - 5 years),II group - 20 patients with ESCKD (over 10 years), III group - 16 patients with ESCKD on hemodialysis with HF (over 10 years). Control group – 12 healthy persons. Laboratory blood tests of lipid profile (Triglycerides (TG), Total Cholesterol, High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL)), C Reactive Protein (CRP) were analyzed in addition to standard diagnostic program.

Results: The pattern of lipid profile is characterized by increased plasma TG ($p<0.05$) second and third groups due to elevated VLDL and decreased HDL compared to the control group. There were a significant difference ($p<0.05$) in patients of the first and the third groups between of the lipid profile. We observed positive correlation of dyslipidemia with CRP ($p<0.05$). Dyslipidemia is associated with uremia.

Conclusions: ESCKD patients have increased risk of CVD. A higher prevalence of dyslipidemia is common among patients with ESCKD on the program hemodialysis. HF is associated with lipoprotein abnormalities and cardiovascular mortality.

ID:1295

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-10 Anti-thrombotic therapies*

B- MODE ULTRASOUND- GUIDED HEPARIN- LOADED MICROBUBBLES- MEDIATED SHOCK WAVE THROMBOLYTIC THERAPY OF EMBOLIC ARTERY

POSTER VIEWING SESSION

Hossein Mehrad[1,2], Ali Sultan- Qurraie[3]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran, [3]Neuroscience Institute, Renton, University of Washington, Valley Medical Center, Washington, United States of America

Background and Aims : A plaque may rupture with high risk of subsequent thrombus- mediated acute clinical events such as myocardial infarction and stroke. Catheter-based thrombectomy systems have been extensively studied as effective methods to treat thrombosis. The aim of this study was to generate a rabbit model of femoral artery thromboembolism occlusion and the subsequent investigating the feasibility of B- mode ultrasound- guided shock wave thrombolytic therapy accompanied by simultaneously intravenous heparin- loaded microbubbles administration in this model.

Methods: Briefly, New Zealand White rabbits were submitted to thromboembolism occlusion by injecting autologous blood clots through femoral artery. Then treatment group underwent low- level electrohydraulic pulsed- focused shock wave (V=15 Kv, F=0.2 Hz, Impulses= 200) thrombolytic therapy accompanied by simultaneously intravenous heparin (25000 Units/kg)- loaded PESDA (Perfluorocarbon-Exposed Sonicated Dextrose Albumin) microbubbles (100ml/kg, 2-5 $\times 10^5$ bubbles/ml) administration, wherein diagnostic B- mode ultrasound is combined with therapy system, with a goal of increased safety.

Results: from B-mode ultrasonography and histopathology, showed a significant reduction in the mean value for thrombus content at the embolic region in the treatment group compared with the other groups ($P< 0.05$).

Conclusions: Enhanced thrombolytic effect of heparin therapy, induced by inertial cavitation effect of collapsed PESDA microbubbles- mediated low level electrohydraulic pulsed focused shock wave sonoporation therapy, can cause to reduce the thrombus content and significantly dilate the luminal cross-sectional area at the embolic region and lower treatment time.

ID:1294

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

DECREASING GPLD 1-LEVELS IN PATIENTS AFTER ST-ELEVATED MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Aenne Kruse[1], Erik Bischof[1], Dorette Raaz-Schrauder[2], Stephan Achenbach[1], Barbara Dietel[3], Miyuki Tauchi[1], Katharina Urschel[1]
[1]Department Of Cardiology And Angiology, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany, [2]Cardiology, Pneumology, Nephrology And Internal Intensive Care, Klinikum Aschaffenburg-Alzenau, Aschaffenburg, Germany, [3]Department Of Cardiology And Angiology, University Hospital Erlangen, Erlangen, Germany

Background and Aims : Recently, higher levels of phosphatidyl-inositol-glycan specific phospholipase D (GPLD1) were associated with an impaired glucose tolerance and diabetes mellitus, factors of the metabolic syndrome, being a risk factor for myocardial infarctions. A previous study already showed higher serum GPLD1-levels in stroke patients compared with a healthy control group. Our pilot study analyzed the serum concentration of GPLD1 in patients with ST-elevated myocardial infarction (STEMI) at two different time points.

Methods: To date, 24 STEMI patients (33% women) were included in preliminary analyses. Blood was drawn at admission to hospital (time point A) and in average 5:54 hours (±60 min) later (time point B). GPLD1 serum concentration was determined by ELISA.

Results: We observed a significant decrease in GPLD1 serum concentration at time point B ($p<0.001$) compared to time point A, with a strong positive correlation between both samples ($r=0.848$, $p<0.001$). We observed a negative correlation between BMI and age ($r=-0.495$; $p=0.014$) and a trend for a positive correlation of age and GPLD1-levels at time point A ($r=0.359$; $p=0.085$). When stratified by sex, the decrease of GPLD1 was seen in both men and women ($p_{male}<0.001$, $p_{female}=0.008$). No significant correlations were found in men between GPLD1 serum levels and cardiovascular risk factors, while women interestingly showed a negative correlation between BMI and GPLD1 at time A ($r=-0.730$; $p=0.04$).

Conclusions: These preliminary data give a first indication, that GPLD1 serum levels might be influenced in STEMI patients. Raising patient's numbers and a non-STEMI control cohort will be analyzed as well as further markers influenced by GPLD1.

ID:1293

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

FABP2 GENE POLYMORPHISM (ALA54THR) AND ANTHROPOMETRIC, LIPID AND GLUCOMETABOLIC PARAMETERS DURING EXERCISE EXPANSION

POSTER VIEWING SESSION

Iryna Komir[1], Natalya Y. Emelianova[2], Maryna M. Vovchenko[2]
[1]Complex Risk Reduction Of Chronic Non-communicable Diseases, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Ukraine, Ukraine, [2]Department Of Complex Reduction Of The Risk Of Chronic Non-infectious Diseases, Government Institution “L.T.Malaya Therapy National Institute of, Kharkiv, Ukraine

Background and Aims : To study the influence of polymorphic variants of the FABP2 gene (Ala54Thr) on the change of anthropometric parameters, indicators of carbohydrate and lipid metabolism in persons with different physical activity.

Methods: 192 patients, average age 59.39±1.09 years with moderate and high cardiovascular risk were examined. Genotyping of the Thr54Ala163G>A, rs179988346A>G polymorphism was performed by real-time polymerase chain reaction. Body mass index (BMI), fat to the muscular ratio (bioimpedance method, Body Composition Monitor BF511,Omron), blood lipids, glucose, and HbA1c levels were assessed. Physical activity was assessed by the IPAQ questionnaire. Muscle strength was assessed using a CAMRY dynamometer. The training program included: warm-up, a basic aerobic program, stretching, and breathing exercises. SPSSIBM version 17.0 was used for statistical analysis.

Results: there was a tendency in the group with variant AA to lower BMI, the proportion of adipose tissue and greater strength ($p>0.05$) and had higher total cholesterol ($p=0.02$). There was no difference in fasting glucose levels, HvA1c% ($p>0.05$). After 12 weeks of follow-up, a significant difference in the decrease in BMI,% adipose tissue, increase in muscle strength in each group. In carriers of polymorphic variant AA, glucose reduction was significant ($p=0.04$).In the estimates of the distribution by groups of polymorphic variants of the FABP2 gene (Ala54Thr), no differences in gene loci were found.

Conclusions: Carriers of the GG variant had a higher BMI throughout the study period compared to AA carriers, but the association of weight loss with genotypes of the polymorphic locus FABP2 (Ala54Thr) on the background of physical activity was not established.

ID:1292

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-10 Anti-thrombotic therapies*

EFFECT OF WARFARIN COMBINED WITH B- MODE ULTRASOUND- GUIDED PHOTOMECHANICAL THROMBOLYTIC THERAPY ON ATHEROTHROMBOTIC STENOSIS

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : Thrombus formation on a disrupted atherosclerotic plaque is a key event that leads to atherothrombosis. The aim of this study was to generate a hamster model of abdominal aorta atherothrombotic stenosis with morphological similarities to the human disease and the subsequent assessment of the reliability of B- mode ultrasound- guided laser photomechanical thrombolytic therapy accompanied by warfarin administration in this model.

Methods: Briefly, Golden Syrian hamsters were submitted to abdominal aorta atherothrombotic stenosis by primary balloon injury followed by a 1.5% cholesterol- rich diet injury for 12 weeks and finally perivascularly severe cold injury. Then treatment group underwent catheter- based Q-switched Nd: YAG laser (F= 532 nm, P= 25 W, PD= 15 ns)- mediated inertial cavitation therapy accompanied by simultaneously intravenous warfarin (25000 Units/kg) administration, wherein a precise diagnostic B-mode ultrasound is combined with therapy system, with a goal of increased safety.

Results: from color Doppler and B-mode ultrasonography and histopathology, showed a significant reduction in the mean value for blood mean velocity and the percentage of luminal cross-sectional area of stenosis and a significant increase in the mean value for blood volume flow at the stenotic region in the treatment group compared with the other groups ($p< 0.05$).

Conclusions: Enhanced thrombolytic effect of warfarin, induced by inertial cavitation effect of Q-switched Nd: YAG laser, can cause to significantly reduce the thrombus content in the stenotic region and significantly dilate the luminal cross- sectional area of stenosis.

ID:1289

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

LASER- MEDIATED THERMAL ANGIOPLASTY OF OCCLUDED ARTERY ACCOMPANIED BY DISULPHONATED ALUMINUM PHTHALOCYANINE - MEDIATED PHOTODYNAMIC THERAPY COMBINED WITH CATHETER- BASED RUTHENIUM-106 BRACHYTHERAPY

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : The laser atherectomy methods that are currently in use, cause to inflammation and subsequent restenosis. The aim of this study was to evaluate the effect of photodynamic therapy and brachytherapy on inflammation and intimal hyperplasia reduction after laser angioplasty of the animal occluded femoral artery, wherein diagnostic ultrasound is adjuncted with angioplasty and combination therapy system, with a goal of increased safety.

Methods: Briefly, New Zealand white rabbits were submitted to femoral artery advanced atherosclerotic occlusion by primary perivascular severe cold injury followed by a 2% cholesterol- rich diet for fourteen weeks. Histopathology results showed the formation of stable advanced atherosclerosis with lipid and neovessel - rich plaque, resulted in occlusion in all of the rabbits' arteries. Then treatment group underwent B- mode ultrasound- guided argon laser (488 nm) angioplasty followed by catheter- based β^- brachytherapy (^{106}Ru, 15 Gy) in combination with photodynamic therapy with red diode laser (WL= 635 nm, E/A= 120 J/cm^2) accompanied by photosensitizer disulfonated aluminum phthalocyanine (AlS2Pc) administration and simultaneously ultrasound imaging.

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for immune cells and hyperplastic vascular smooth muscle cells density after angioplasty in the treatment group compared with the other groups ($p<0.05$).

Conclusions: Apoptotic effect of ruthenium-106- mediated beta radiation (β^-) brachytherapy in combination with anti- inflammatory effect of disulfonated aluminum phthalocyanine (AlS2Pc)- mediated red laser- assisted photodynamic therapy can cause to reduce the density of macrophage cells and hyperplastic vascular smooth muscle cells in the intimal layer.

ID:1288

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

TOTUM-070 PREVENTS DIET-INDUCED HYPERCHOLESTEROLEMIA IN WESTERN DIET FED MICE

POSTER VIEWING SESSION

Cédric Langhi[1], Yolanda F Otero[1], Florian Le Joubioux[2], Bruno Guigas[3], Sébastien Peltier[2], Pascal Sirvent[1]
[1]Preclinical Research Center, Valbiotis, RIOM, France, [2]Périgny Center, Valbiotis, PERIGNY, France, [3]Department Of Parasitology, Leiden University Medical Center, Leiden, Netherlands

Background and Aims : TOTUM-070 (T070) is a clinical stage substance composed by the association of 5 plant extracts. We assessed the hypothesis that administration of T070 prevents hypercholesterolemia in mice and explored the potential mechanisms involved.

Methods: C57BL/6 mice were fed either a normal diet (ND) or western diet (WD) for 6 weeks and received either vehicle or T070 (1g/kg or 3g/kg) daily by gavage (n=14 mice per group).

Results: At the end of the study, body weight in WD-fed mice was increased to 28.3 ± 0.8 g compared to the ND group (24.5 ± 0.4 g, $p<0.001$). A significant ($p<0.01$) 29% reduction in body weight gain was observed in the T070 3g/kg group compared to the WD group at the end of the study. Total-cholesterol was reduced in mice supplemented by T070 in a dose dependent manner (276 ± 9 mg/dl T070 1g/kg, ($p=0.19$) and 265 ± 8 mg/dl T070 3g/kg, $p<0.05$ vs. 298 ± 8 mg/dl WD). There was no change in triglyceridemia among the groups compared to the ND mice. However, hepatic steatosis induced by the WD was reduced by 73% ($p<0.001$) in the T070 3g/kg group. A significant increase in feces production was observed in mice supplemented with T070 3 g/kg compared to the mice fed with WD alone (234 ± 7 mg/day WD+T070 3g/kg *vs* 207 ± 6 mg/day WD, $p<0.01$), probably contributing to the beneficial phenotype induced by T070 administration.

Conclusions: This study highlights the interest of using TOTUM-070 for management of mild hypercholesterolemia.

ID:1286

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

TOTUM-070 PREVENTS DIET-INDUCED HYPERLIPIDEMIA IN HIGH FAT HIGH CHOLESTEROL FED HAMSTERS

POSTER VIEWING SESSION

Cédric Langhi[1], Yolanda F Otero[1], Florian Le Joubioux[2], Bruno Guigas[3], Sébastien Peltier[2], Pascal Sirvent[1]
[1]Preclinical Research Center, Valbiotis, RIOM, France, [2]Périgny Center, Valbiotis, PERIGNY, France, [3]Department Of Parasitology, Leiden University Medical Center, Leiden, Netherlands

Background and Aims : TOTUM-070 (T070) is a clinical stage patented blend of biomolecules extracted from 5 plant extracts. We tested the hypothesis that T070 administration prevents hyperlipidemia in hamsters and explored the potential mechanisms involved.

Methods: Syrian hamsters were fed either normal diet (ND) or high fat high cholesterol diet (HFHCD) with or without T070 mixed at 3.5%, 4.25% and 5% in the diet for 12 weeks (n=16 per group).

Results: HFHCD feeding led to a 5-fold increase in blood total cholesterol compared to ND (1141± 49mg/dl vs 221.4 ± 8.8 mg/dl, respectively, $p<0.0001$), and a 13-fold increase in non-HDL Cholesterol compared to ND (866 ± 43 mg/dl *vs* 65 ± 9 mg/dl, respectively, $p<0.0001$). The 3 groups supplemented with T070 at 3.5%, 4.25% and 5% exhibited a dose-dependent decrease in total-Cholesterol (788 ± 61 mg/dl, n.s; 678 ± 41 mg/dl, $p<0.01$ and 667 ± 37 mg/dl, $p<0.01$, respectively) and non-HDL Cholesterol (542 ± 61 mg/dl, $p<0.05$; 455 ± 37 mg/dl, $p<0.01$ and 455 ± 33 mg/dl, $p<0.01$, respectively) compared to the HFHC group. The HFHCD induced an increase in serum TG levels (1018 ± 103 mg/dl vs (256 ± 24 mg/dl ND). T070 had a dose-dependent effect on serum TG levels reduction (709 ± 91 mg/dl T070 3.5%, $p<0.05$; 605 ± 56 mg/dl T070 4.25%, $p<0.001$; and 547 ± 57 mg/dl T070 5%, $p<0.001$) in comparison to the HFHCD group.

Conclusions: Collectively, our results highlight the beneficial effect of T070 in the management of moderate cholesterol levels.

ID:1284

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

PREVALENCE AND PROGNOSTIC IMPACT OF LIPID GOAL ATTAINMENT AND PATIENT ADHERENCE TO LOWERING LIPID TREATMENT: DATA FROM COMMUNITY ITALIAN SETTING

POSTER VIEWING SESSION

Chiara Cappelletto[1], Agnese Garavaglia[2], Simone Poli[2], Elena Peruzzi[2], Arjuna Scagnetto[1], Giulia Barbati[3], Andrea Di Lenarda[1]
[1]Cardiovascular Center, University Hospital and Health Services of Trieste, TRIESTE, Italy, [2]Medical Department, Novartis Farma S.p.A., Origgio, Italy, [3]Department Of Medical Sciences, Biostatistics Unit, Trieste, Italy

Background and Aims : The aim is to provide real-world data on low-density lipoprotein cholesterol (LDL-C) goal achievement at the time of current 2019 ESC/EAS Guidelines,treatment patterns and patient adherence to lowering lipid treatment (LLT).

Methods: This community-based study identified patients with at least one LDL-C measurement and cardiological evaluation from Jan-2016 to Dec-2018. Risk stratification and LDL-C target achievement were assessed according to 2019 EAS/ESC guidelines.

Results: To identify the proportion of patients at LDL-C target, only patients with an available LDL-C evaluation after 1 year from baseline were considered (7317 patients, 51% of initial cohort 14317 pts). Of those,492 pts (7%) presented LDL-C at target. 187 were at very high risk (4% of very high risk subgroup) and 47 at high risk (3% of high risk subgroup).Statin intolerance was reported in 7,5% of patients.The adherence evaluation was performed in patients having 1-year of follow-up and at least one statin purchase.It was estimated through the Proportion of Days Covered, defining as adherent patients with a value ≥75%. 8332 (58% of initial cohort 14317 pts) met the selection criteria for PDC calculation.Of those,3346 (40%) patients resulted as adherent (46% and 22% at very high and high CV risk categories).In a multivariable Cox regression model, adjusted for age, sex, risk factors and comorbidities,patients adherence emerged as a protective factor (HR 0.62; 95% CI 0.43-0.89; p=0,010).

Conclusions: In a real-world setting, the achievement of LDL-C target and patient adherence was suboptimal across different CV risk categories. In a full adjusted survival model,patient adherence was independently associated with a prognosis improvement.

ID:1283

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MIDTERM GENERAL MORTALITY IN PATIENTS WITH PERIPROCEDURAL HYPOTENSION DURING CAROTID STENTING

POSTER VIEWING SESSION

Teodora Yaneva-Sirakova[1], Galina Zlatancheva[1], Kiril Karamfiloff[1], Anastas Dimov[2], Dobrin Vassilev[3]
[1]Department Of Internal Medicine, Medical University Sofia, Sofia, Bulgaria, [2]Department Of Statistics And Econometrics, University of National and World Economy, Sofia, Sofia, Bulgaria, [3]Department Of Health Care, University of Ruse "Angel Kanchev", Sofia, Bulgaria

Background and Aims : Carotid stenting may be correlated with significant bradycardia and/or hypotension. They can potentially lead to hypoperfusion, new neurological symptoms and higher death rate. Our aim was to assess the midterm general mortality rate in patients with carotid stenting.

Methods: A hundred and thirty eight consecutive patients were included for a period of 4.5 years before mid 2019 year. Mean age - 67.41±10.70 years. The mean follow-up period was 31 months/922 days. Patients' hemodynamics was monitored periprocedurally. Every patient received intraprocedural volume expansion and vasopressors if needed. Statistical data was managed with SPSS IBM19, p=0.05, CI 95%.

Results: The males were 94(68%). The number of patients with periprocedural hypotension was 55(42%). The mean values of blood pressure were: 135/83 mmHg before, 116/76 mmHg during and 121/73 mmHg postprocedure. Neider Kaplan-Maier analysis, nor cox regression analysis showed any significant difference in the mid-term general mortality rate between patients with and without transitory hypotension. There wasn't any difference in the postprocedure neurological outcome also.

Conclusions: Hypotension during carotid stenting was not associated with elevation in mid-term all-cause mortality. The finding can be due to the relatively short period of hypotension and to the quick administration of vasopressors and volume substitution.

ID:1278

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

SONO- SHOCK WAVE COMBINATION ANGIOGENIC THERAPY FOR CARDIAC FUNCTION IMPROVEMENT IN THE HYPERCHOLESTEROLEMIC HAMSTERS WITH MYOCARDIAL ISCHEMIA

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : Cardiac shockwave therapy is a novel, noninvasive approach that has been shown to ameliorate the myocardial ischemia and improve cardiac function. Cardiac shockwave therapy is a potential and effective remedy to promote revascularization in the ischemic myocardium of patients with refractory coronary heart disease. The technique is both safe and non-invasive.; however, the underlying molecular mechanism remains unclear. In this study, we developed an sono- shock wave combination therapy system and investigated its effectiveness on myocardial angiogenesis in the hamsters accompanied by PESDA (Perfluorocarbon- Exposed Sonicated Dextrose Albumin) microbubbles administration.

Methods: Briefly, hamsters underwent 2 % cholesterol- rich diet injury for twelve weeks. Histopathology results showed the formation of soft atherosclerotic plaques with moderate stenosis in all of the hamsters' coronary arteries. The animals treated by pulsed focused ultrasound (F= 1.1 MHz, P= 24 w) combined with electrohydraulic low- level pulsed shock waves (10Kv, 0.5 Hz, 200 pulse), accompanied by PESDA (100 ml/kg, 2- 5 × 10^5 bubbls/ml) microbubbles administration .

Results: from histopathology showed a significant increase in the mean value for myocardial neovessels density in the treatment group compared with the control group ($p < 0.05$).

Conclusions: Enhanced inertial cavitation, induced by collapsed microbubbles- mediated angiogenesis, accompanied by angiogenic effect of shock wave and ultrasound, can cause to induce VEGF, interleukin-8 (IL-8), stromal cell-derived factor 1 (SDF-1) and matrix metalloproteinase 9 (MMP-9) secretion in the hypercholesterolemic rabbits' arteries, and increase proliferation, differentiation and recruitment of endothelial progenitor cells (EPCs) and promote revascularization in the ischemic myocardium and improve cardiac function.

ID:1246

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-08 Platelets, thrombosis and atherosclerosis*

INVESTIGATING MECHANISMS OF TMA PRODUCTION FROM CHOLINE, L-CARNITINE AND RELATED PRECURSORS BY THE HUMAN GUT MICROBIOTA USING OF AN IN-VITRO BATCH FERMENTATION (HUMAN COLON) MODEL

POSTER VIEWING SESSION

Priscilla Day-Walsh, Emad Shehata, Shikha Saha, George M. Savva, Barbora Nemeckova, Jasmine Speranza, Arjan Narbad, Paul A. Kroon
Food Innovation And Heath Programme, Quadram Institute, NR UQ, United Kingdom

Background and Aims : High levels of plasma trimethylamine-N-oxide (TMAO) have been shown to correlate with increased risk of cardio-metabolic diseases including cardiovascular diseases and adverse events after heart failure. TMAO is formed via oxidation of TMA catalysed by flavin-dependent monooxygenases (FMOs) in the human liver, mainly by FMO3. The vast majority of trimethylamine (TMA) is produced by the action of the gut microbiota that produce TMA from dietary substrates including choline, carnitine, and betaine. Reducing microbial TMA production is the most promising sustainable approach to reducing TMAO burden in those at risk.

Methods: TMA production from choline, L-carnitine, betaine and γ-butyrobetaine was studied over 24–48 h using an *in-vitro* human colon model with metabolite quantification performed using LC–MS.

Results: Choline was metabolised via the direct choline TMA-lyase route but not the indirect choline–betaine-TMA route, conversion of L-carnitine to TMA was slower than that of choline and involved the formation of the intermediate γ-BB, whereas the Rieske-type monooxygenase/reductase pathway for L-carnitine metabolism to TMA was negligible. The rate of TMA production from precursors was choline > carnitine > betaine > γ-BB. 3,3-Dimethyl-1-butanol (DMB) had no effect on the conversion of choline to TMA.

Conclusions: Here we demonstrate that the *in-vitro* human colon model authentically replicates the metabolic pathways demonstrated in humans *in-vivo* and to some extent in animal models except that we did not observe betaine as an intermediate in either choline or l-carnitine metabolism. This model will be useful for screening suitable drug targets that may alter the microbiome in order to reduce the burden of TMAO in those at risk.

ID:1260

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

PREVALENCE OF HIGH LIPOPROTEIN (A) AMONGST HIGH CARDIOVASCULAR RISK POPULATION IN NORTH WALES, UNITED KINGDOM

POSTER VIEWING SESSION

Suchitra Balasubramanian[1], Malarmannann K Balasubramanian[2], Robert Gingell[3], Yee Ping Teoh[4]
[1]General Medicine, Wrexham Maelor Hospital, WREXHAM, United Kingdom, [2]Emergency Medicine, Caxton Place, Wrexham, United Kingdom, [3]All Wales Fh Service, Betsi Cadwaladr University Health Board, Conwy, United Kingdom, [4]Clinical Biochemistry, Wrexham Maelor Hospital, WREXHAM, United Kingdom

Background and Aims : Lipoprotein(a) (Lp(a)) is an established risk factor for cardiovascular disease and concentrations are predominantly (90%) determined by genetic factors. In the Copenhagen City Heart Study, it was found that 20% of the general population has Lp(a) >50mg /dL. We attempted to retrospectively review Lp (a) data amongst North Wales (United Kingdom) patients who have been referred to the Lipid / Cardiovascular Risk / Familial Hypercholesterolaemia clinics over the past 6 years.

Methods: In the period between 2015 and 2020, a total of 379 patients were referred from both primary and secondary care to the clinics. Of them, 368 patients had their baseline Lp (a) performed using Roche-Cobas Lp(a) assay which is a particle enhanced immunoturbidimetric assay. The study population was further divided into high and low cardiovascular risk based on any previous cardiovascular event(s). Results were analysed.

Results: Of the 368 patients, 121 **(32.9 %)** have Lp(a) levels >50mg/dL. The baseline Lp(a) range varies from <3.1 mg/L to 299 mg/dL. It was also found that 59 **(43.4%)** of high risk group (those with previous cardiovascular event(s)) had Lp(a)

>50mg/dl.

Table 1

Total Patients referred during the study period			Lipoprotein (a) levels					
	Females	Males						
368 (100%)	171 **(46.5%)**	197 **(53.5%)**	**Normal <=50mg/dl**	247	**67.1%**	Females	110	44.5%
						Males	137	55.5%
			Elevated >50mg/dl	121	**32.9%**	Females	61	50.4%
						Males	60	49.6%

Table 2

CVD Risk	High	136	Lp(a) Normal	77	56.6%
			Lp(a) Elevated	59	**43.4%**
	Low	232	Lp(a) Normal	170	73.3%
			Lp(a) Elevated	62	**26.7%**

Conclusions: Lp(a) is significantly elevated in high cardiovascular risk group, more than double the proposed 20% in the general population in the Copenhagen City Heart Study. With the availability of PCSK9 inhibitor drugs and also potential antisense oligonucleotide Lp (a), measurements of this important lipoprotein in high risk patients will allow further early risk stratification in their management.

ID:1247

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

TRANSLATING NOVEL EVIDENCE INTO PRACTICE: CONSENSUS FOR INTENSIVE THERAPY WITH HIGH DOSE POTENT STATIN TO IMPROVE OUTCOMES IN ACUTE CORONARY SYNDROME

POSTER VIEWING SESSION

Jc Mohan[1], Ashwani Mehta[2], Praveen Chandra[3], Padhinhare Mohanan[4], Jabir Abdullakutty[5], Abraham Oomman[6], Sanjay Porwal[7], Kamal Sharma[8], Mahantesh Charantimath[9], Suvro Banerjee[10], Soumitra Kumar[11], Group Novel[12]
[1]Cardiology, Jaipur Golden, Delhi, India, [2]Department Of Cardiology, Sir Ganga Ram hospital, New delhi, India, [3]Cardiology, Medanta Medicity, Gurgaon, India, [4]Cardiology, Westfort Hi-Tech Hospital, Thrissur, India, [5]Cardiology, Lisie Hospital, Cochin, India, [6]Cardiology, Apollo Hospitals, Chennai, India, [7]Cardiology, KLE Society's Dr. Prabhakar Kore Hospital & Research Centre, Belagavi, India, [8]Cardiology, U.N.Mehta Institute Of Cardiology, Ahmedabad, India, [9]Cardiology, Tathagat Heart Care Centre & Hospital, Bangalore, India, [10]Cardiology, Apollo Gleneagles Hospital, Kolkata, India, [11]Cardiology, Fortis Hospital, Kolkata, India, [12]Cardiology, NOVEL GROUP, Mumbai, India

Background and Aims : We aimed to determine the level of consensus for the clinical utility of high potency statin including Rosuvastatin in Acute Coronary Syndrome (ACS)

Methods: 160 leading cardiologists (NOVEL working Group), with individual clinical experience of at least two decades, across India, deliberated virtually. 10 questions were interspersed, with contemporary evidence published during 2019 -2021, of which seven were 5-point Likert scale (1 = strongly disagree, 5 = strongly agree)

Results: The mean cumulative responses per statement was 63 (SD ± 6.7, 95% CI 58 to 67). Total cumulative responses were 627 (44.7% responder rate). Mean duration of meeting was 120 minutes (SD ± 26, 95% CI 104 to 135). Consensus was agreed-strongly agreed for benefits of Rosuvastatin during ACS; for reduction of high CV risk (87.8%, n=65/74), for novel mechanistic insights implicated for clinical benefits (83.3%, n=50/60), property of high potency is beneficial in young ACS (77.6%, n=52/67). ACS patients when started Rosuvastatin, more than 50%, achieve LDL-C goals within a month, was opined by (53.2, n=33/62). 57.1% (n=32/56) strongly agreed, that patient education at discharge post ACS, yields high compliance, to prescribed statin dose. Effective LDL-C goal (52.2% n=35/67) attainment followed by rapid LDL-C lowering (34.3% n=23/67) were key attributes of Rosuvastatin in ACS. Initiative like ACS

Lipid EuroPath would be useful to improve lipid management in ACS in Indian setting (81.4% n=53/65)

Table : Detailed description of the responses

Q No	Question	Agree	Disagree	Neither agree nor disagree	Strongly Agree	Strongly Disagree	Total responses
1	Results for dissimilarities in ACS across gender and younger age patients, are similar to what you experience in the day to day practice in the real world setting	45	0	1	8	4	58
2	Tool similar to the ACS Lipid EuroPath, would be useful for Indian setting	38	4	7	15	1	65
3	Patient educational intervention at the time of discharge post ACS, would yield better compliance to the prescribed dose of statin	16	1	1	32	6	56
4	Rosuvastatin at the time of ACS reduces the high CV risk beyond LDL-C lowering	30	0	2	35	7	74
5	Novel mechanistic insights for Rosuvastatin are clinically meaningful, especially for management of ACS	39	1	9	11	0	60
6	Rosuvastatin for its high potency is well suited for management of younger patients with ACS	39	2	11	13	2	67
7	Contemporary evidence for rosuvastatin, are relevant in practice for delivering efficiency in clinical care in the real world setting	35	0	0	15	1	51
8	In your practice, % of patients with ACS, at one month, attain lipid goals with Rosuvastatin (Total)						62
	<25%						4
	25-50%						25
	50-75%						23
	>75%						10
9	The most important characteristic of Rosuvastatin at the time of ACS and beyond, that delivers the clinical efficiency (Total)						67
	Rapid LDL- lowering						23
	Effective LDL-C goal attainment						35
	Durability of the LDL- C lowering effect						9
10	Post ACS, at what time point, is the intervention necessary to reinforce adherence to high dose (Total)						67
	At discharge						43
	At next follow up visit						8
	At 6 -12 months						5
	At 3-6 months						11

(Table)

Conclusions: The results highlight that the contemporary evidence, for potent statin like Rosuvastatin enable to adopt evidence-based medicine for clinical decision making for managing patients with ACS

ID:1252

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

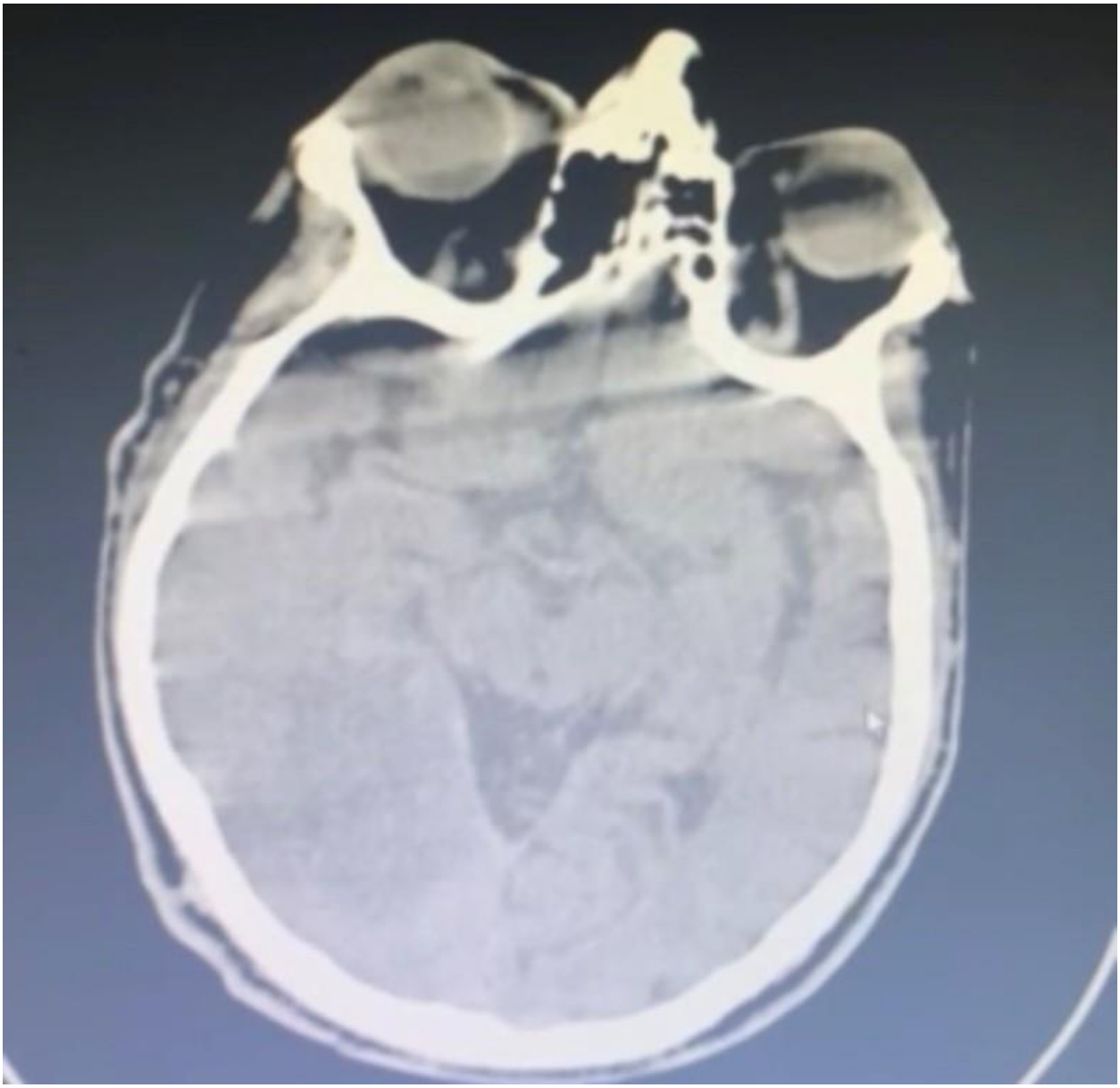
ACUTE ISCHEMIC STROKE DUE TO MASSIVE ARTERIOVENOUS MALFORMATION: A CASE REPORT

POSTER VIEWING SESSION

Georgios Filippidis, Margarita Triantafyllou, Ioanna Kiriakouli, Alexandros Nakis, Alexandros Samis, Rea Saiti, Georgios Giannakopoulos, Danae Kavvada, Matina Gkliati, Christos Zafeiriadis, Timos Karousos, Katerina Trachana, Meropi Mousdi, Sofia Pegka, Myrto Skouteli, Stefanos Varvaresos, Georgios Chatzis, Panagiotis Nikolinakos, Sofoklis Bakidis
Internal Medicine, General hospital of Lakonia, Molaoi, Greece

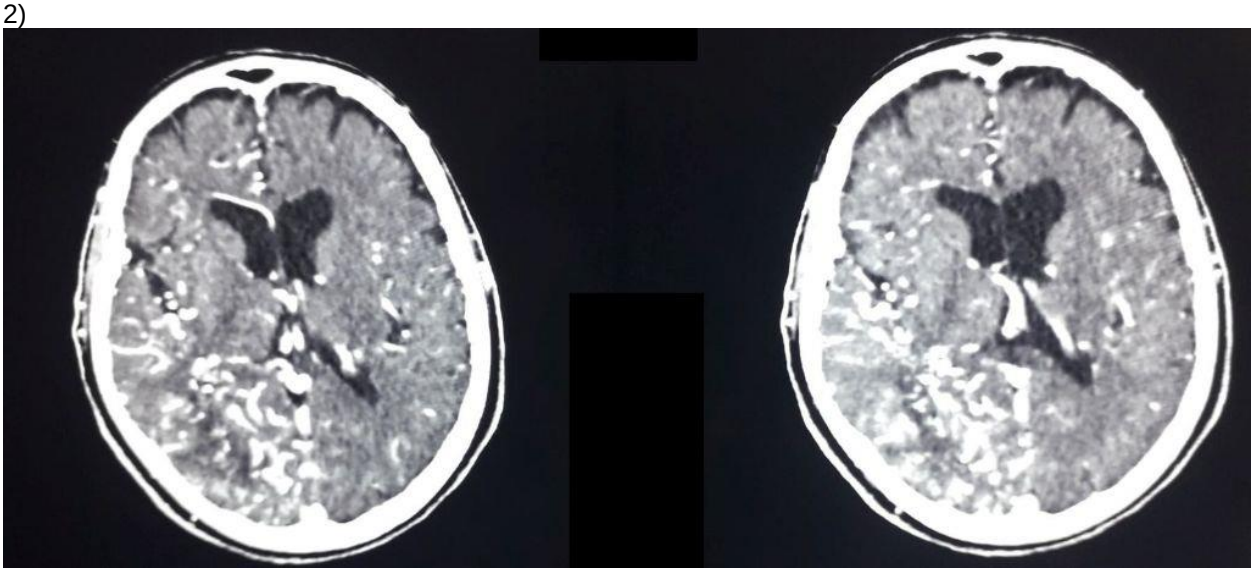
Background and Aims : We report a case of a 76-year-old patient with ischemic stroke presentation, where cerebral imaging led to the diagnosis of a massive arteriovenous malformation (AVM) of the whole left hemisphere. We suggest considering AVM as a differential diagnosis in patients with symptoms of acute stroke despite age and, in the absence of contraindications, in this setting to obtain MRI or CT angiography of the brain.

Methods: A 76-year-old μαλε patient was assigned to our emergency department with acute onset aphasia, tonic clonic seisure, and reduced strength in the left arm and leg, Clinical examination showed a left sided hemiparesis and hemihypesthesia, and dysarthria. The tendon reflexes were brisk. Furthermore, orientation was impaired.in time, not in space .Suspected diagnosis was ischemic stroke with possible epileptic component.His medical history revealed hypertension and spondylopathy Emergency CT brain scan revealed large subdense are in the right temporal lobe and hematoma in the right thalamus (fig1)



Due to the suspicious imaging result, CT brain angiography was performed, showing unexpected, in consideration of the patient's age, massive AVM of the right hemisphere (fig

2)



Results: An anti-epileptic therapy with levetiracetam was started and subsequently sensory as well as motor deficits and aphasia disappeared. Patient was discharged with anti-epileptic therapy

Conclusions: There are several descriptions of first diagnosis of AVM in younger patients. Surprisingly, in our case the patient did not show any symptoms until an advanced age despite the huge size of AVM. To our knowledge, the age of our patient combined with the expanse of the AVM are unique

ID:1253

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

DIAGNOSTIC ROLE OF SORTILIN AND INFLAMMATION MARKERS IN ATHEROGENESIS OF CORONARY ARTERIES IN PATIENTS WITH ARTERIAL HYPERTENSION

POSTER VIEWING SESSION

Irina Sharafutdinova, Irina Gubareva, Yulia Vukolova
Department Of Internal Diseases, Samara State Medical University, Samara, Russian Federation

Background and Aims : To study the associations of pro-inflammatory interleukin IL-8 and anti-inflammatory IL-10 in blood serum and sortilin levels in patients with arterial hypertension(AH),with varying degrees of atherosclerotic lesions of the coronary arteries.

Methods: 83 male patients aged from 30 to 66 years old with AH of I-III stages.The patients were divided into groups depending: group I consisted of patients with unchanged coronary arteries (CA), (n = 10); group II – patients with CA tortuosity (n = 20); group III – patients with coronary artery lesion less than 50% (n = 19); group IV included patients with coronary artery lesion more than 50% (n = 24). The control group consisted of practically healthy individuals (n = 10). The subjects were assessed: IL-8, IL-10 (pg/ml), sortilin (ng/ml) of blood serum.

Results: In the first three groups of patients high numbers of sortilin activity were recorded (124.02±16.6; 161±19.1; 123.2±21.1; 65.13±10.1, respectively) compared with group IV and control one ($p < 0.05$). A high level of sortilin was combined with an increase in the concentration of pro-inflammatory IL-8 in groups I-III (55.15±5.1; 56.98±3.5; 45.1±0.1; 33.24±1.4), while the greatest increase took place in groups I and II. The concentration of IL-10 in group IV group was 70% higher than the control(33.10±2.6; 36.85±2.8; 22.34±1.83; 48.61±4.8).

Conclusions: A high level of sortilin is associated with an increase of pro-inflammatory cytokines II-III groups and of CA damage which confirms the role of inflammatory reactions in the initiation and progression of atherosclerotic lesions. In group IV processes initiated by anti-inflammatory cytokines prevailed.

ID:1257

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

HDL CHOLESTEROL DYNAMICS AFTER STEMI DETERMINES THE TENDENCY TO RECURRENT CORONARY EVENTS

POSTER VIEWING SESSION

Dmytro Bilyi, Alexander Parkhomenko, Oleg Irkin, Yaroslav Lutai, Serhiy Kushnir, Olena Dovhan, Anton Stepura
Intensive Care Unit, NSC “Institure of cardiology n.a. M.D.Strazhesko” NMAS of Ukraine, Kyiv, Ukraine

Background and Aims : The aim of the study was to evaluate the effects of HDL dynamics after STEMI on the development of events after hospital discharge.

Methods: The study involved 96 STEMI patients hospitalized during the first 12 hours (4.7±1.0 hours) after symptoms onset and treated by primary PCI. Lipid-lowering-therapy included atorvastatin 40 or 80mg, or combination of atorvastatin-40mg and ezetimibe-10mg. All patients were divided into 2 groups depending on the increasing or decreasing of the HDL level during the FU-period (90days) - group1 and group2 accordingly.

Results: The target level of LDL (<1,4mmol/l) on day 90 was achieved in 32% of patients. The mean level of HDL at admission did not differ significantly between groups. The mean level of the HDL on day 90 in group 1 was significantly higher than in group2 (1.5mmol/l vs 1.17mmol/l, p<0,05). Patients of the first group were more often treated by the combination of atorvastatin and ezetimibe. During 90 days of FU recurrent PCI due to UA were more often done in group2 (6.25% vs 0%, p<0.05)

	Group1	Group2	p
Number of patients	32	64	
Atorvastatin40+ezetimibe10	16(50%)	18(28,1%)	<0,05
The average dose of atorvastatin,mg	43	40	NS
Ezetimibe,%	62,5	53	NS
HDL 1day,mmol/l	1,2±0,06	1,46±0,07	NS
HDL 90days,mmol/l	1,5±0,09	1,17±0,05	<0,05
Repeated myocardial revascularization,%	0(0%)	4(6,25%)	<0,05

Conclusions: Destabilization of the CAD registered more often in patients with decreasing of HDL level on the 90th day after STEMI and leads to the new revascularization procedures. Patients with increasing of HDL level more frequently received combination of atorvastatin with ezetemibe.

ID:1258

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

DIABETIC MACROVASCULAR COMPLICATIONS OF THE LOWER EXTREMITIES: ULTRASOUND DOPPLEROGRAPHY AND MORPHOLOGICAL DIAGNOSTICS

POSTER VIEWING SESSION

Liliya Volos[1], Tetyana Mykhaylichenko[2]
[1]Pathological Anatomy, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine, [2]Department Of Internal Medicine N2, Donetsk National Medical University, Kramatorsk, Ukraine

Background and Aims : The main cause of disability and mortality in patients with diabetes mellitus is late vascular complications, including diabetic micro- and macroangiopathy of the lower extremities. Timely diagnosis of and adequate treatment can prevent the development of diabetic foot syndrome. The aim of the work was to investigate the Doppler ultrasonographic manifestations and morphological changes of lower extremity vessels in patients with diabetes.

Methods: The patency of arterial vessels lower extremities 37 patients with severe diabetes was analyzed. The ultrasonographic findings of lower extremity arterial lesions were evaluated according to location, type, and length. The histological examination of the lower extremities' tissues of 7 cases in diabetic gangrene was carried out.

Results: The ultrasound examination of the arteries of the lower extremities and use the Fontaine-Leriche classification showed presents widespread heterogeneous concentric atherosclerotic plaques, with asymmetry and a deficit of blood flow on the affected side. More than 10 cm occlusion lesion was the main manifestation in crural artery. In diabetic gangrene skin defects of various depths and areas are determined with microcirculatory disorders, stasis, thrombus formation, wall hyalinosis, accumulation of purulent exudate and tissue detritus in the interstitial tissue.

Conclusions: Crural artery was the mainly involved location (33/37; 89,2%), with occlusion more than 10 cm (28/37; 75,7%). Pathomorphological criteria for the viability of the lower extremity tissues in diabetic foot and gangrene are the patency of large vessels, the integrity and clear differentiation of tissue structures, the arterioles wall thickness in the range 18,5±1,5 μm, the diameter - 29,7±0,8 μm, Kernogan index - 0,67±0,08.

ID:1259

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-09 Aortic valve stenosis*

GENETIC EXPRESSION AND IMMUNOFLUORESCENCE MAPPING OF NAV1 HIGHLIGHT POTENTIAL THERAPEUTIC TARGETS IN ANTI-INFLAMMATORY TREATMENT OF AORTIC VALVES STENOSIS.

POSTER VIEWING SESSION

David Hupin, Magnus Bäck
K2 Medicine Solna, karolinska Institutet, Stockholm, Sweden

Background and Aims : Aortic valve stenosis (AVS) is the most prevalent heart valve disease worldwide. Despite better interventional treatment strategies, AVS is associated with a high morbidity and mortality. The aortic valve is innervated, but the neural regulation of these AVS processes is unknown. Recently, a genome wide analysis study (GWAS) associated neuron navigator 1 (NAV1) with AVS. Since NAV1 is a microtubule-associated protein involved in developmental neural migration, the aim of the study was to establish the relation of NAV1 expression to AVS disease stages and AVS pathophysiological pathways, and to map the neural NAV1 to demonstrate its possible role in guiding the valvular anti-inflammatory cholinergic pathway.

Methods: Human aortic valves were obtained from patients undergoing surgical aortic valve replacement at Karolinska University Hospital in Stockholm (Sweden). The valves were used for (1) RNA extraction and (2) for immunohistochemistry. Gene expression was determined by Affymetrix Human Transcriptome Arrays 2.0 and analysed the statistical software Qlucore (Sweden). NAV1 protein expression was localized and quantified by computerized image analysis from the Light Sheet Microscope (LSM, Scotland).

Results: In 74 stenotic aortic valves, NAV1 mRNA expression was significantly gradually decreased when disease stages progressed from healthy through intermediate to calcified aortic valve tissue. Immunofluorescence NAV1 staining was in contrast visualized with LSM only in calcified valve tissue.

Conclusions: These results identified differential valvular NAV1 expression patterns with decreased mRNA and increased protein expression in calcified aortic valve tissue. These results point to NAV1 as a local valvular potential therapeutic target for future studies.

ID:1262

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

CARDIOVASCULAR RISK CLASSIFICATION AND LIPID LOWERING TREATMENT PRESCRIPTIONS IN A REAL-WORLD: INSIGHT FROM ITALIAN COMMUNITY COHORT

POSTER VIEWING SESSION

Chiara Cappelletto[1], Agnese Garavaglia[2], Simone Poli[2], Elena Peruzzi[2], Arjuna Scagnetto[1], Giulia Barbati[3], Andrea Di Lenarda[1]
[1]Cardiovascular Center, University Hospital and Health Services of Trieste, TRIESTE, Italy, [2]Medical Department, Novartis Farma S.p.A., Origgio, Italy, [3]Department Of Medical Sciences, Biostatistics Unit, Trieste, Italy

Background and Aims : Lipid lowering treatment (LLT) and LDL-C target across CV risk categories might prompt consideration on further lower LDL-C levels advocated by EAS/ESC guidelines.The aim was to provide prevalence, clinical characteristics,LLT across different CV risk classes at the time of publication of current ESC/EAS Guidelines.

Methods: The study enrolled 6851 patients with LDL-C measurement and cardiological evaluation from Jan-2018 until Dec-2018. Of those, 67% patients were at very high risk,22% at high risk,6% at moderate risk,and 5% at low risk according to EAS/ESC 2019 guidelines.

Results: Dyslipidemia was present in three quarter of patients, and 57% received LLT.High efficacy (LDL-C reduction ≥50%) LLT was prescribed in 21% of patients (23% and 10% in very high and high risk categories).There was a statistically significant difference between CV categories with respect to demographic, CV risk factors and comorbidities.Patients at very high risk were older and more likely affected by atherosclerotic CVD.9% patients at very high risk and 7% patients at high risk presented LDL-C at target.Among very high risk patients, 10% were treated with ezetimibe.At 24 months, death occurred in 8% patients.In adjusted survival curves,an increased risk of death and CV hospitalization was confirmed in the high risk and very high risk categories.Similar trend was confirmed considering the composite endpoint of myocardial infarction/stroke.

Conclusions: In a contemporary population the strategy to achieve the ambitious LDL-C target of current Guidelines continue to be largely suboptimal and LLT is widely underused. This underlines the huge unmet need when assessed more aggressive LDL-C target advocated in current EAS/ESC guidelines.

ID:1276

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

IDENTIFYING MOLECULAR DEFECTS IN SWEDISH PATIENTS WITH FH: NO INFLUENCE OF POLYGENIC LDL CHOLESTEROL SNP-SCORE

POSTER VIEWING SESSION

Peter Benedek[1], Hong Jiao[2], Päivi Kiviluoma[3], Juha Kere[3], Mats Eriksson[1], Bo Angelin[4]
[1]Dep. Of Internal Medicine And Endocrinology, Karolinska Instiutet, Huddinge, Sweden, [2]Biosciences And Nutrition, Karolinska Institutet, Huddinge, Sweden, [3]Clinical Research Center, Karolinska Institutet, Huddinge, Sweden, [4]Dep. Of Internal Medicine And Endocrinology, Karolinska Instiutet, HUDDINGE, Sweden

Background and Aims : Even in well characterized patients with a clinical diagnosis of autosomal dominant familial hypercholesterolemia (FH), mutations in the classical FH-related genes *(LDLR*, *APOB*, or *PCSK9*) are not identified in ~20% of those examined genetically. This indicates that the FH phenotype can be caused by additional inherited abnormalities such as heterozygous mutations in still unknown genes, or epigenetic mechanisms. An alternative hypothesis has been proposed by Talmud et al. [Lancet 2013; 381:1293] who suggest that a substantial fraction of such “mutation-negative” (M-) FH cases could be explained by polygenic inheritance. The validity of this concept is still unclear, however, with differing results in several international cohorts.

Methods: The potential polygenic influence was investigated in 88 unrelated (M-) Swedish patients with probable or definite FH (DLCN-score 6 or higher). This was done by calculating the weighted 12-SNP-scores for LDL-cholesterol described by Talmud et al. and comparing them to those seen in 57 (M+) Swedish FH patients and in their reference cohort.

Results: Although the mean SNP-score was somewhat higher in the (M-) patients, there was no correlation between the SNP-score and the LDL-cholesterol level in either group of FH patients.

Conclusions: We conclude that polygenic inheritance is not a likely explanation to the phenotype in Swedish FH (M-) patients, nor does it modify the lipoprotein pattern in FH (M+) individuals. Our finding instead supports the continued search for novel mono- or oligogenic mechanisms in Swedish families with FH (M-), and also strengthens maintaining the recommendation to perform cascade screening of plasma lipids in such kindreds.

ID:1266

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

ATHEROSCLEROSIS IN BRAZIL: AN ECOLOGICAL STUDY

POSTER VIEWING SESSION

Mariana S.T.C. Guelli, Lorena A.S. Dias, Leticia M.L.D. Costa, Daniela B.D.A. Zampier, Isabella Maria Silva, Thais B.C. Ibañez, Sergio I. Nunes
Faculty Of Medicine, University Center of Volta Redonda, Volta Redonda, Brazil

Background and Aims : Atherosclerosis is a subclinical chronic inflammatory disease. It is a multifactorial and complex process with fatty plaques, calcium and other elements appearing in the intimal layer of vessels that precedes clinical manifestations of cardiovascular diseases. Physical activity is an important protective factor for its prevention.The aim of this study is to analyse the epidemiological profile of patients with atherosclerosis in Brazil in the last 10 years.

Methods: Ecological study was performed.Data were obtained from the Informatics Department of the Unified Health System (DATASUS) from October 2011 to October 2021. A descriptive analysis, was performed, including region, sex, ethnicity and age group.

Results: 469,875,283 cases of atherosclerosis were registered in Brazil, with an annual average of 46,987,528 cases. Between the five Brazilian regions, the most prominent was the Southeast region with 207,885,906 cases (44.24%), followed by the South region 136,974,119 (29.15%), Northeast region 91,397,124 (19.45 %), central-west region 26,190.241 (5.57%) and north region 7,427,890 (1.59%). Male patients represented 267,775,647 (56.98%) cases. Most of white ethnicity: 219,236,164 (46.65%). The most affected age group was 60 to 69 years old with 160,624,111 (34.18%) cases, followed by the 70 to 79 year old group with 131,784,337 (28.04%) cases.

Conclusions: A high number of patients with atherosclerosis was observed, mainly in the Southeast region of Brazil. In addition, most were male, white and aged between 60 and 69 years. Thus, the need for greater visibility of this public health problem is highlighted, as well as more educational and preventive public policies.

ID:1269

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE ASSOCIATION BETWEEN PERIOPERATIVE FACTORS AND NEUROCHEMICAL MARKERS AND INDICATORS OF COGNITIVE FUNCTIONS IN PATIENTS UNDERGOING SIMULTANEOUS CORONARY ARTERY BYPASS GRAFTING AND CAROTID ENDARTERECTOMY

POSTER VIEWING SESSION

Olga Maleva
Department Of Clinical Cardiology, Federal State Budgetary Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Background and Aims : To identify the association between perioperative factors and markers of traumatic brain injury and cognitive functions in patients undergoing simultaneous coronary artery bypass grafting (CABG) and carotid endarterectomy (CEA).

Methods: The study included 56 men with hemodynamically significant coronary and precerebral artery stenosis scheduled for simultaneous CABG and CEA, the mean age was 64.8±7.05 years. The assessment of cognitive function indicators was performed on the Status-PF software-hardware complex. Neurochemical markers were determined. SPSS 26 Statistics software package was used for statistical analysis of the obtained data.

Results: An inverse correlation was found between the coronary artery bypass grafting factor and the attention volume (r = -0.518; p=0.031), the sustained attention (r=-0.545; p=0.05), the reaction time (r=0.476; p=0.04) and the number of mistakes made in the Bourdon-Wiersma test (r=0.449; p=0.03). Another correlation was revealed between the neurochemical factor and the number of letters processed in a minute (r=-0.642; p=0.01), and the total number of processed letters while doing the Bourdon-Wiersma test (r=-0.617; p=0.01). The simultaneous factor was associated with the reaction time (r=0.609; p=0.041), the number of letters processed in the first (r=-0.538; p=0.05) and the fourth minute (r=-0.490; p=0.017), and the total number of letters processed while doing the Bourdon-Wiersma test (r=-0.334; p=0.006).

Conclusions: The coronary artery bypass grafting factor and the simultaneous factor are associated with lower levels of attention and memory, the neurochemistry factor is associated with the attention deterioration in the early postoperative period.

ID:1271

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

GENOTOXIC STRESS IN ENDOTHELIOCYTES LEADS TO ENDOTHELIAL DYSFUNCTION: RESULTS OF GENE EXPRESSION ANALYSIS

POSTER VIEWING SESSION

Maxim Y. Sinitsky[1], Anna V. Sinitskaya[1], Anton G. Kutikhin[2], Daria K. Shishkova[2], Anastasia V. Ponasenko[1]
[1]Laboratory Of Genome Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [2]Laboratory Of Molecular, Translational, And Clinical Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Background and Aims : To study the gene expression signature in endothelial cells exposed to alkylating mutagen mitomycin C (MMC).

Methods: Primary human coronary- (HCAEC) and internal thoracic artery endothelial cells (HITAEC) exposed to 500 ng/mL MMC (experimental group) and 0.9% NaCl (control) was used. Expression of leukocyte adhesion (*VCAM1*, *ICAM1*, *SELE*, *SELP*), endothelial mechanotransduction (*KLF4*), endothelial differentiation (*PECAM1*, *CDH5*, *CD34*, *NOS3*), endothelial-to-mesenchymal transition (*SNAI1*, *SNAI2*, *TWIST1*, *GATA4*, *ZEB1*, *CDH2*), scavenger-receptors (*LOX1*, *SCARF1*, *CD36*, *LDLR*, *VLDR*), antioxidant system (*PXDN*, *CAT*, *SOD1*) and transcription factor (*HEY2*) genes was evaluated by RT-qPCR after 6 hours of incubation with mutagen and 24 hours after elimination of MMC from cultures.

Results: After 6 hours of MMC exposure, a decreased expression of almost all studied genes was noted in the experimental group; the only *SNAI2* demonstrated a 4-fold increased expression compared to the unexposed control. Elimination of MMC from the both cell cultures was accompanied by increased expression of *VCAM1*, *ICAM1*, *SELE*, *SNAI2*, *KLF4* genes and decreased expression of *PECAM1*, *CDH5*, *CD34*, *ZEB1*, *CAT*, *PXDN* genes. HITAEC cells were characterized by decreased expression of *SOD1*, *SCARF1*, *CD36* genes and an increased expression of *SNAI1* and *TWIST1* genes; in HCAEC, increased expression of *LDLR* and *VLDLR* genes was noted.

Conclusions: The MMC-induced genotoxic stress is associated with the endothelial dysfunction, manifested by the altered gene expression profile of the endothelial cell cultivated under conditions of the genotoxic load. This work was supported by a grant from the President of the Russian Federation for young scientists – candidates of science МК-1228.2021.1.4.

ID:1272

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

MONOCYTE CHEMOATTRACTANT PROTEIN-1 SERUM LEVELS IN DEPENDING ON HISTORY OF PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH CORONARY ARTERY DISEASE WITH TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Nataliia Mavrycheva, Serhii Serik
Department Of Ischemic Heart Disease And Metabolic Disorders, Government Institution "L.T. Malaya Therapy National Institute of The National Academy of Medical Sciences of Ukraine", Kharkiv, Ukraine

Background and Aims : Monocyte chemoattractant protein-1 (MCP-1) is a proinflammatory chemokine, which plays a key role in the pathophysiology of both atherosclerosis and diabetes. MCP-1 is involved in the development of neoatherosclerosis after percutaneous coronary intervention (PCI). Investigate serum MCP-1 levels in patients with coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) depending on the previous history of PCI.

Methods: Serum MCP-1 levels were measured in 31 patients with CAD with T2DM, 26 non-diabetic patients with CAD, and 15 control group persons.

Results: MCP-1 level in CAD patients with T2DM was higher than in the control group ((355,77 [278,01; 399,25]) pg/ml, vs. (244,64 [182,67; 297,77]) pg/ml, p=0,0007) and non-diabetic patients with CAD ((289,28 [204,17; 329,17]) pg/ml, p=0,039). The elevation of MCP-1 level in non-diabetic patients was insignificant. MCP-1 levels did not differ significantly in patients with and without a history of the previous myocardial infarction both in non-diabetic patients and in patients with T2DM. CAD patients with T2DM after PCI more than 1 year previously have higher MCP-1 levels than CAD patients with T2DM without a history of PCI ((399,25 [355,77; 443,14]) pg/ml vs. (317,31 [244,12; 371,15]) pg/ml, p=0,038). In non-diabetic patients with CAD with the same history of PCI MCP-1 decreased compared to non-diabetic patients without previous PCI ((199,715 [179,68; 296,93]) pg/ml vs. (294,95 [240,10; 348,66]) pg/ml, p=0,030).

Conclusions: In patients with CAD and T2DM MCP-1 level increased in comparison with the controls and CAD patients without T2DM. CAD patients with T2DM with a history of PCI have the highest MCP-1 level.

ID:1273

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EFFECT OF TALAPORFIN SODIUM- MEDIATE RED LASER- ASSISTED PHOTODYNAMIC THERAPY ON ARTERIAL BIOMECHANICAL PARAMETERS IN THE RABBIT CAROTID ARTERY MODEL OF NEOINTIMAL HYPERPLASIA

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : Smooth muscle cell proliferation and migration from the medial layer into the intima, following an intravascular damage like angioplasty, causes neointimal hyperplasia. There exists a range of treatment protocols for neointimal which can be divided into two main groups: invasive and non-invasive. In this study, we aimed to introduce a novel non-invasive treatment (Photodynamic therapy) for neointimal hyperplasia reduction, for which the evaluation procedure (a new computerized ultrasound image processing) is be based on a non-invasive method.

Methods: In the current study, we first induced neointimal hyperplasia in the common carotid artery of New Zealand white rabbits by arterial injury following balloon angioplasty for two minutes. After four weeks, pathology results confirmed the induction of neointimal hyperplasia in all the rabbits´ arteries. At the end of four weeks, we performed extracorporeal red laser (ƛ= 664 nm, P= 150 mw) irradiation for 20 minutes, accompanied by photosensitive drug, talaporfin sodium (6mg/Kg) administration (Photodynamic therapy) at the injury site of treatment group. Next, the rabbits were care given for two weeks. Arterial biomechanical parameters at the site of injury to be evaluated by a new computer based image processing and ultrasound were: resistance index, pulse index, radial strain and longitudinal strain.

Results: Our findings suggest the statistically meaningful decrease of resistance and pulse indexes and elevated radial and longitudinal strain of the treatment group in comparison with the other groups ($p < 0.05$).

Conclusions: Photodynamic therapy recovers arterial biomechanical parameters by ameliorating of inflammation and suppressing of hyperplasia in smooth muscle cells at the injury site.

ID:1274

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EFFECT OF HDL- LOADED PESDA MICROBUBBLES- MEDIATED FOCUSED SHOCK WAVE SONOPORATION THERAPY ON BIOMECHANICAL PARAMETERS IN AN EXPERIMENTAL ANIMAL MODEL OF ABDOMINAL AORTA FIBROATHEROMATIC PLAQUE

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : It is known that high- fat diet, induce hypercholesterolemia, deterioration of arterial wall, both morphologically and mechanically. Mechanical changes include thickening of arterial wall, alteration of arterial elasticity, contraction of smooth muscle, increase in sensitivity to pharmacological stimulation and increase in arterial viscoelasticity, i.e., arteriosclerosis. In this study, we developed an shock wave generator system (0– 20 kv), and investigated its effectiveness on plaque regression in the hamster abdominal aorta, wherein diagnostic B- mode ultrasound is combined with shock wave therapy system, with a goal of increased safety.

Methods: Thick-cap fibroatheromatic plaque with severe stenosis (>80%) was induced at the right common carotid artery of Golden Syrian Hamsters. The animals treated by repeated electrohydraulic focused shock waves (V = 12 Kv, F = 0.1 Hz, Impulses = 100) accompanied by HDL- loaded PESDA microbubbles (100 µl/kg, 2– 5×10^5 bubbles/ml) administration. Arterial biomechanical parameters were evaluated in the different groups using B-mode ultrasound images.

Results: from ultrasound images analysis showed a significant reduction in the mean value for shear elastic modulus, resistive index and a significant increase in the mean value for radial strain, compliance and distensibility index in the treatment group compared with the other groups ($P < 0.05$).

Conclusions: Enhanced inertial cavitation, induced by collapsed microbubbles- mediated enhanced HDL shock wave sonoporation therapy, accompanied by anti-inflammatory effect of shock waves, can cause to reduce the atheroma content in the plaque and significantly dilate the luminal cross- sectional area of stenosis. These features can cause to improve the arterial biomechanical parameters.

ID:622

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

CARDIOVASCULAR OUTCOMES OF COVID-19 DISEASE AT THE ELDERLY

POSTER VIEWING SESSION

Ana Capisizu[1], Ruxandra Mihalache[1], Alexandru Capisizu[2], Mihaela Roman[1], Sorina M. Aurelian[1]
[1]Geriatrics, University "Carol Davila" Bucharest Romania, Bucharest, Romania, [2]Neurology, University "Carol Davila" Bucharest Romania, Bucharest, Romania

Background and Aims : Covid-19 disease can cause multiple organ damages. Male gender, advanced age, chronic lung, kidney and cardiovascular diseases have been identified as risk factors for severity of the disease. The persisting alterations of the heart for more than four weeks is framed in post-Covid-19 syndrome. Cardiovascular system is affected by direct effect of Sars-Cov-2, as well as by preexistent frailty.

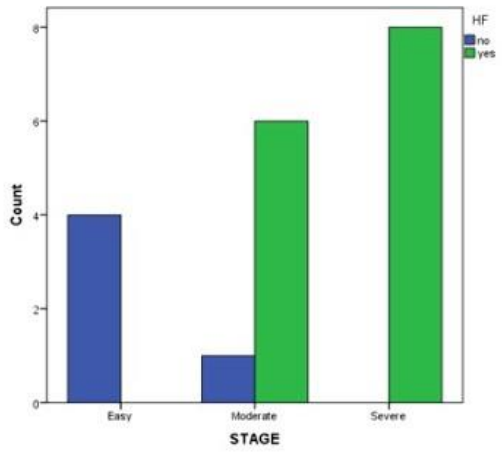
Methods: Retrospective study on 19 inpatients postCovid-19, 63.2% females; mean-age 79.84y.o.[66,90](SD:5.83), in Geriatric “Sf. Luca” hospital, Bucharest, Romania. All patients were assessed by Fried Scale(score>2points =“frail”). We analyzed the relationship between post-Covid cardiovascular effects(heart failure/HF; atrial fibrillation/AF) and: vaccination, frailty, days of recovery. Data statistical analysis: IBM SPSS Statistics20.

Results: Age-group 75-84y.o. is most numerous(68.4%); Average fragility score: 2.84[2,5](SD:0.765); Average recovery days: 15.32d.[0,30](SD:7.86); 42.1% of patients had severe stage of Covid-19; 57.9% of patients were vaccinated. *Correlation statistic data:* 85.7% of moderate-stage and all severe-stage covid-patients had HF, differences between groups(HF/non-HF) in terms of stage being statistically significant(p=*0.001)*. 80% of patients with 21 recovery days were in severe stage(p=*0.019*). 62.5% of unvaccinated patients had 21 recovery days(p=*0.002*), compared to those vaccinated. 87.5% of patients with AF had severe frailty(p=*0.036*). 37.5% of patients with AF died(p=*0.027*). All deaths (15.8%) were

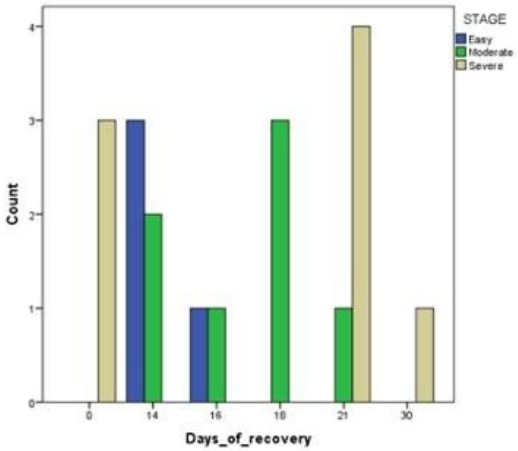
among unvaccinated patients(p=*0.027*) **(Fig.)**

Figures

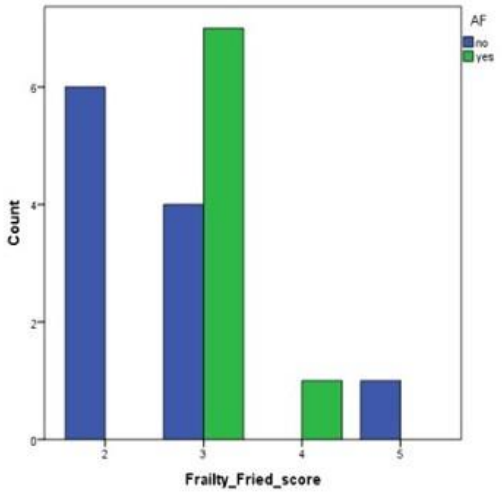
1. Relationship between HF and Covid-19 stages



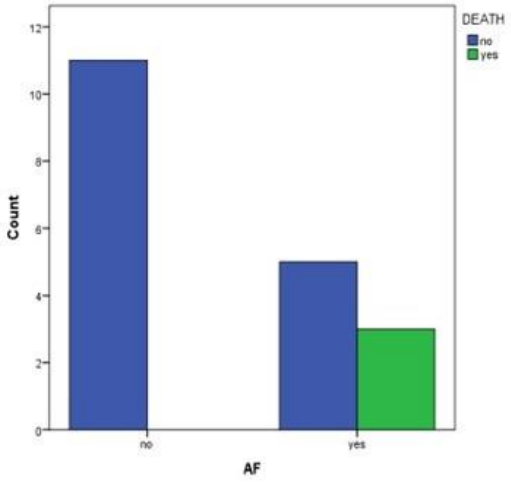
2. Relationship between days of recovery and Covid-19 stages



3. Relationship between AF and frailty score



4. Relationship between AF and death



Conclusions: The severity of Covid-19 in the elderly is dependent on vaccination and frailty score. Cardiovascular diseases such as heart failure are risk factors of Covid severity, increasing the number of recovery days. Atrial fibrillation is associated with frailty in the elderly being correlated with Covid-19 deaths.

ID:835

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

GIANT MULTINUCLEATED ENDOTHELIAL CELLS ARE ASSOCIATED WITH LOCAL ACCUMULATION OF LDL AND CD45+ LYMPHOCYTES IN THE INTIMA OF HUMAN AORTA

POSTER VIEWING SESSION

Nikita Nikiforov[1,2,3], D Zlenko[4], Alexander N. Orekhov[1]
[1]Laboratory Of Angiopathology, Institute Of General Pathology And Pathophysiology, Moscow, Russian Federation, [2]Institute Of Experimental Cardiology, National Medical Research Center of Cardiology, Moscow, Russian Federation, [3]Russian Academy Of Sciences, Institute of Gene Biology, Moscow, Russian Federation, [4]Russian Academy Of Sciences, N.N. Semenov Federal Research Center for Chemical Physics, Moscow, Russian Federation

Background and Aims : At the early stages of atherogenesis, low-density lipoprotein (LDL) particles and immune cells penetrate into the intimal layer of the arterial wall through the endothelium. In adult humans, the luminal surface of the arterial wall is a heterogeneous monolayer of cells with varying morphology, including typical endothelial cells (ECs) and multinucleated variant endothelial cells (MVECs). We hypothesized that distribution of MVECs in the endothelial monolayer can explain the distribution pattern of early atherosclerotic lesions.

Methods: To test our hypothesis we obtained en face preparations of intact adult (22-59 years old) aortic wall sections. We compared the distribution of MVECs in the endothelial monolayer with the localization of LDL aggregates and CD45+ lymphocytes in subendothelial intima.

Results: In primary culture, MVECs demonstrated increased phagocytic activity as compared to mononuclear ECs. We have shown that unaffected aortic intima contains associates of LDL particles that are non-randomly distributed. That indicated that MVECs may be involved in the accumulation of LDL in the subendothelial layer through increased transcytosis. Study of unaffected aortic intima revealed non-random distribution of leukocytes in the subendothelial layer and increased localization of CD45+ leukocytes in the subendothelial layer adjacent to MVECs.

Conclusions: In this study, we revealed a relationship between the localization of MVECs in the endothelial layer and clusters of leukocytes in the adjacent subendothelial layer of human aortic intima. Therefore, MVEC formation can serve as a trigger of early atherogenesis events. Supported by RSF (Grant # 20-65-46021).

ID:613

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

THROMBOEMBOLIC COMPLICATIONS IN COVID-19 CLINICAL CASE

POSTER VIEWING SESSION

Ana Capisizu[1], Sorina A. Capisizu[2], Dragos Cuzino[2], Andreea Zamfirescu[1]
[1]Geriatrics, University "Carol Davila" Bucharest Romania, Bucharest, Romania, [2]Radiology, University "Carol Davila" Bucharest Romania, Bucharest, Romania

Background and Aims : In patients with Covid-19, vascular occlusion occurs, leading to territorial infarction and poor prognosis. From the first days of the disease there is an overproduction of cytokines that depends on the viral replication and the patient's proinflammatory immune response. Microangiopathy and arterial thromboembolism are associated with Covid19.

Methods: We present a clinical case of a female, 50 years old, with no comorbidities, positive SARS-CoV2, unvaccinated, mild respiratory symptoms (cough, dyspnea, low fever), treated at home for 7 days; On the 8th day of her debut, she was hospitalized with neurological symptoms (confusion, headache) and right hemi body neuromotor disorders.

Results: *Laboratory:* inflammatory syndrome and prothrombotic status (**Tabel1**). *Cerebral MRI* with gadolinium paramagnetic contrast agent - Ischemic round-oval lesions recently formed in the middle cerebral artery (MCA) territory on the left side (precentral gyrus, postcental and radiated corona) and posterior occipital by the occipital horn. The lesions have hypo signal T1, hyper signal T2, FLAIR, more obvious peripheral contrast uptake and diffusion restriction. There are also squeals ischemic lesions with microangiopathic substrate in the frontal and parietal lobes and enlarged Virchow-Robin per vascular spaces. *Diagnosis*: MCA Stroke post Covid-19 infection; *Evolution:* post covid recovery in 68 days, with right brachial hemiparesis sequels.

Table 1 – Laboratory outcomes at admission

RT-PCR	+++	Glucose	**120 mg/dl**
Leukocyte	**10.000 µL**	Aspartate Aminotransferase	**47.22 U/L**
Neutrophil/Lymphocyte Ratio	2.98	Alanine aminotransferase	**57.66 U/L**
Platelets	**103000 µL**	D-dimer	**0.99 µg/ml FEU**
ESR	**48 mm/h**	Ferritin	173 ng/ml
C-reactive protein	**26.10 mg/L**	Urea	**99.53 mg/dl**
Procalcitonin	0.35 ng/mL	Creatinine	0.96 mg/dl
Creatine phosphokinase	34.90 U/L	Uric acid	**8.30 mg/dl**

Conclusions: Covid-19 infection can be considered an *independent risk factor* for stroke. The pattern of large vessel occlusion suggests that cerebral thrombosis and/or thromboembolism could be possible causative pathways attributed to a proinflammatory and prothrombotic condition.

ID:345

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

PATHOLOGICAL NEWBORN BODY WEIGHT AS PREDICTOR OF METABOLIC DISORDERS AND REDUCED EXERCISE TOLERANCE IN YOUNG FEMALE

POSTER VIEWING SESSION

Tatiana Naiden[1], Svetlana Bartosh-Zelenaya[2], Alexandr Bartosh-Zeleny[1], Nikolay Glukhov .[3]
[1]Functional Diagnostic, North-Western State Medical University named by I.I. Mechnikov, St-Petersburg, Russian Federation, [2]Functional Diagnostic, North-Western State Medical University named by I.I. Mechnikov, St.-Petersburg, Russian Federation, [3]Ultrasound Diagnostic, Center of AIDS, St.-Petersburg, Russian Federation

Background and Aims : Background: Metabolic syndrome (MS) is a claster of metabolic disorders associated with insulin resistance and abdominal obesity, associated with an increased risk of type 2 diabetes mellitus (DM) and cardiovascular disease (CVD). Due to the high prevalence of MS (20-40%), and especially in young people of working age, its early detection has undoubtedly great importance for the timely initiation of prevention of complications (heart attack, stroke, diabetes, etc.). **Purpose:** assessment of newborn body influence on subsequent metabolic disorders and exercise intolerance in young females during adolescence.

Methods: The total number of patients was 92 aged18-21 years. Metabolic syndrome (MS) was diagnosed according to the following "summary" criteria: WHO criteria, 1999 (impaired glucose tolerance), modified WHO criteria (fasting plasma insulin level more than its upper quartile in this population) and IDF criteria (2005, 2009, 2014). Exclusion criteria: active physical activity and/or sports.

Results: 48 patients (52.7%) had abnormal body weight at birth: low (<2800 g) - in 23 people (25.3% - group 1); high (>4000 g) - in 25 people (27.5% - group 2). Group 1 showed the highest values of total and LDL cholesterol (p=0.006), group 2 - hypercholesterolemia, hypertriglyceridemia (p=0,05) and hypoalphacholesterolemia (p=0.05). The last had increased basal glycemia (p=0.004), insulin (p=0.05) and C-peptide (p=0.006), while patients of group 1 had an increase in postprandial glucose (p=0.009) and insulin (p=0.05). In patients of group 2 were mentioned cardiac remodeling, reduced exercise tolerance.

Conclusions: Abnormal fetal body weight may be a predictor of MS and low exercise tolerance in adolescent females.

ID:387

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

ASSOCIATIONS BETWEEN SERUM AND DIETARY OMEGA-3 FATTY ACID AND COGNITIVE FUNCTION IN A POPULATION OF COMMUNITY-DWELLING JAPANESE - TANUSHIMARU STUDY -

POSTER VIEWING SESSION

Ako Fukami[1], Hiromi Sato[1], Maki Yamamoto[1], Nagisa Morikawa[1], Mika Enomoto[1], Hisashi Adachi[2], Yoshihiro Fukumoto[1]
[1]Division Of Cardiovascular Medicine, Department Of Internal Medicine, Kurume Univiersity School of Medicine, Kurume, Fukuoka, Japan, [2]Cardiology, Keikokai, Hara Hospital, Fukuoka, Japan

Background and Aims : Previous studies indicate that dietary omega-3 polyunsaturated fatty acids (PUFA) are modifiable risk factors for CVD and cognitive decline. To investigate the association between serum and dietary omega-3 PUFA and cognitive function were measured in a general population.

Methods: A total of 976 residents (381 males, 595 females, mean age 62.6 years) underwent a physical examination, a nutrition survey and the mini-mental state examination as an evaluation of cognitive function in 2009 and 2018.

Results: The serum omega-3/omega-6 ratio were significantly associated with age ($p < 0.0001$), sex (male, $p < 0.0001$), MMSE ($p < 0.0001$), LDL-c (inversely, $p < 0.01$), and salt intake ($p < 0.05$), using by multiple stepwise regression analysis. The dietary intake of proteins from fish ($p < 0.0001$), trace elements, ($p < 0.01$), vitamin D, B6, B12 ($p < 0.0001$), and salt ($p < 0.0001$) showed dose dependent relationships with the serum omega-3/omega-6 ratio using analysis of covariance. Subjects were divided into 4 groups according to their progression of cognitive decline in 10 years. Serum omega-3 levels of group with normal cognitive function (NC) were significantly higher than those of group with cognitive decline (CD) ($p < 0.05$). However, dietary intakes of omega-3 and omega-6 PUFA were not significant. Interestingly, salt intakes in group with CD were higher than those in group with NC ($p < 0.05$).

Conclusions: The present study demonstrated that omega-3 PUFA may preserve a cognitive function and excessive intakes of salt may have an adverse effect on cognitive function

ID:383

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

CARDIOVASCULAR RISK FACTORS IN YOUNG PATIENTS PRESENTING WITH STEMI IN A CITY OF SOUTH EUROPE

POSTER VIEWING SESSION

Diego Félix Arroyo Moñino, Carlos Barea González, Marta Pelaz Sánchez, Néstor García González, Juan Carlos García Rubira
Cardiology, Hospital Universitario Virgen Macarena, Sevilla, Spain

Background and Aims : The presence of ischaemic heart disease and Acute Coronary Syndromes (ACS) in young patients are becoming more frequent in our society nowadays. However, there is little information published about this population, especially in the area of South Europe, where we cannot find large series of young patients. Furthermore, there are socio-demographic differences between North and South Europe, which may have an influence over the prevalence of risk factors in this population. Our aim is to describe the prevalence of risk factors in one population of young patients admitted to our hospital with the diagnosis of ST elevation myocardial infarction (STEMI).

Methods: Retrospective, descriptive, unicentric and observational registry of young patients (<45 years old) admitted to one Coronary Critical Care Unit (CCCU) with the diagnosis of STEMI between January 2.010 and April 2.021. The follow-up of these patients was performed using the electronic platform of Andalusian Health Security System.

Results: A total number of 181 patients were included, with a mean age of 41 years old, being 157 male (86,7%). The most prevalent risk factor in this population was active smoking (143 patients – 79%). We found a low prevalence of classic risk factors in this population: dyslipemia (70 patients - 38,7%); hypertension (51 patients - 28,2%), diabetes (16 patients - 8,8%), obesity (42 patients - 23,2%). Only 15 patients (8,3%) had consumed previously.

Conclusions: In our pouplation, smoking was the most prevalent risk factor in young patients admitted due to STEMI, with a low prevalence of classic risk factors.

ID:379

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

CURRENT CAUSES OF DEATH IN FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Victoria Marco-Benedí[1], Ana Maria Bea[2], Ana Cenarro[3], Estibaliz Jarauta[1], Martin Laclaustra[1], Fernando Civeira[1]
[1]Universidad De Zaragoza, Hospital Universitario Miguel Servet, IIS Aragón, CIBERCV, Zaragoza, Spain, [2]Iis Aragón, Cibercv, Hospital Universitario Miguel Servet, Zaragoza, Spain, [3]Instituto Aragonés De Ciencias De La Salud (iacs), Cibercv, Hospital Universitario Miguel Servet, Zaragoza, Spain

Background and Aims : Familial hypercholesterolemia (FH) is a codominant autosomal disease characterized by high low-density lipoprotein cholesterol (LDLc) and high risk of premature cardiovascular disease (CVD). The molecular bases have been well defined and effective lipid-lowering is possible. This analysis aimed to study the current major causes of death of genetically defined heFH.

Methods: Case-control study designed to analyze life-long mortality in a group of heFH and control families. Data of first-degree family members of cases and controls (non-consanguineous cohabitants), including deceased relatives, were collected from a questionnaire and review of medical records. Mortality was compared among heFH, non-heFH, and non-consanguineous family members.

Results: We analyzed 813 family members, 26.4% of them, deceased. Among deceased, mean age of death was 69.3 years in heFH, 73.5 years in non-heFH, and 73.2 years in non-consanguineous, differences that were not statistically significant. Among them, CVD cause of death was 59.7% in heFH, 37.7.% in non-heFH, and 37.4% in non-consanguineous (*P*=0.012). These differences were greater restricting the analyses to parents' mortality. The hazard ratio of dying from CVD was 3.02 times higher (95% CI, 1.90-4.79) in heFH members in comparison with the other two groups (non-FH and non-consanguineous), who did not differ in their risk.

Conclusions: Current CVD mortality in heFH is lower and occurs later than that described in the last century but still higher than in non-FH. This better prognosis in CVD risk is not associated with changes in non-CVD mortality.

ID:374

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 Cholesterol efflux and reverse cholesterol transport*

AUTOPHAGY IS DIFFERENTIALLY REGULATED IN LEUKOCYTE AND NONLEUKOCYTE FOAM CELLS DURING ATHEROSCLEROSIS

POSTER VIEWING SESSION

Sabrina Robichaud[1,2], Adil Rasheed[1], Antonietta Pietangelo[1], Anne Doyoung Kim[1], Dominique Boucher[2], Christina Emerton[1], Viyashini Vijithakumar[1,2], Lara Gharibeh[1], Garrett Fairman[1,2], Esther Mak[1], My-Anh Nguyen[1], Michèle Geoffrion[1], Robert Wirka[3], Katey Rayner[1,2], Mireille Ouimet[1,2]
[1]Research, University of Ottawa Heart Institute, Ottawa, Canada, [2]Biochemistry, Microbiology And Immunology, University of Ottawa, Ottawa, Canada, [3]School Of Medicine, University of North Carolina, Chapel Hill, United States of America

Background and Aims : Atherosclerosis is characterized by an accumulation of foam cells within the arterial wall, resulting from excess cholesterol uptake and buildup of cytosolic lipid droplets (LDs). Autophagy promotes LD clearance by freeing stored cholesterol for efflux, a process that has been shown to be atheroprotective. While the role of autophagy in LD catabolism has been studied in macrophage (Mϕ)-derived foam cells, this has remained unexplored in vascular smooth muscle cell (VSMC)-derived foam cells.

Methods: We performed a comparative analysis of autophagy flux in lipid-rich aortic intimal populations to determine whether VSMC-derived foam cells metabolize LDs similarly to their Mϕ counterparts.

Results: Atherosclerosis was induced in GFP-LC3 transgenic mice by PCSK9-AAV injection and Western diet feeding. Using flow cytometry of aortic digests, we observed a significant increase in dysfunctional autophagy of VSMC-derived foam cells during atherogenesis relative to Mϕ-derived foam cells. Using cell culture models of lipid-loaded VSMC and Mϕ, we show that autophagy-mediated cholesterol efflux from VSMC foam cells was poor relative to Mϕ foam cells, and largely occurs when HDL is used as a cholesterol acceptor, as opposed to apoA-1.

Conclusions: These data demonstrate that VSMC and Mϕ foam cells perform cholesterol efflux by distinct mechanisms and that autophagy flux is highly impaired in VSMC foam cells.

ID:370

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

VERIFICATION OF SECONDARY DYSLIPIDEMIA AMONG "PSEUDO-POSSIBLE" FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

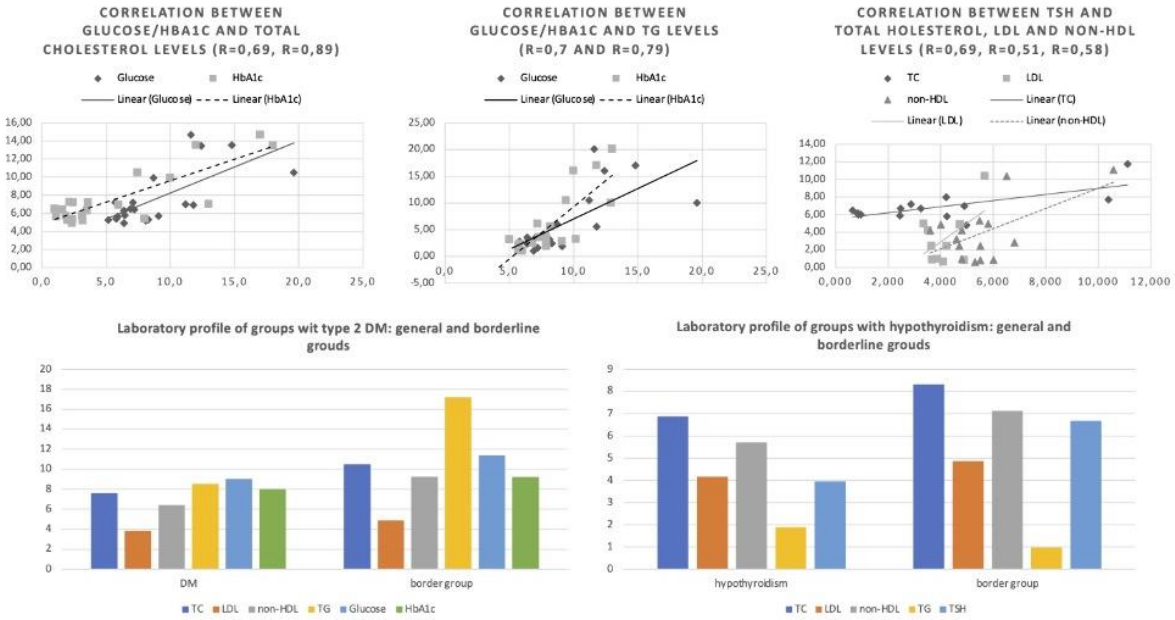
Kateryna Timokhova, Olena Mitchenko, Vadym Romanov, Nataliia Chulaievska
Endocrine Cardiology And Dyslipidemia, STATE INSTITUTION NATIONAL SCIENTIFIC CENTER «THE M.D. STRAZHESKO INSTITUTE OF CARDIOLOGY NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE», Kyiv, Ukraine

Background and Aims : Secondary dyslipidemia (SD) may appear as a high-grade or "borderline" hypercholesterolemia (LDL-cholesterol≥5 mmmol/l) and mimic a possible familial hypercholesterolemia (FH). The aim was to investigate the heterogeneity of "borderline" patients.

Methods: 75 patients with SD caused by type 2 diabetes, hypothyroidism and grade II-III obesity were divided into 3 groups. Patients with non-HDL≥5.8 mmol/l revealed in each goup formed the subgroups, called "borderline". Methods: clinical, laboratory, statistical: t-test, correlation analyses

Results: Patients in diabetes group had hypertriglyceridemia, increased LDL and non-HDL. Correlations between glycemic and lipid profiles: a positive relationship between glucose/HbA1c and TG /non-HDL levels. In "borderline" subgroup the level of LDL-cholesterol was 44% higher compared to general diabetes group. Greater atherogenic profile correlated with destabilization of diabetes (significantly higher glucose, HbA1c levels). Characteristics of dyslipidemia in hypothyroidism group: increased levels of TC, LDL, non-HDL. There was a positive correlation between TSH and cholesterol, LDL and non-HDL. In the "borderline" subgroup, the level of LDL was 24% higher than in general group with hypothyroidism in combination with significantly higher TSH level. In group with obesity combined dyslipidemia and metabolic syndrome were observed. Prediabetes detected in 63%. In the "borderline" subgroup, the level of LDL was 25% higher compared to general group with

obesity.



Conclusions: It's necessary to distinguish the "borderline" group among patients with SD with lipid profile that imitates "possible" FH. The final establishment diagnosis of "possible" FH should be conducted after stabilization of comorbid pathology. Elimination of the secondary cause of hypercholesterolemia should be a component of intensive lipid-lowering therapy.

ID:362

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-09 Epidemiology of socioeconomic and psychosocial risk factors*

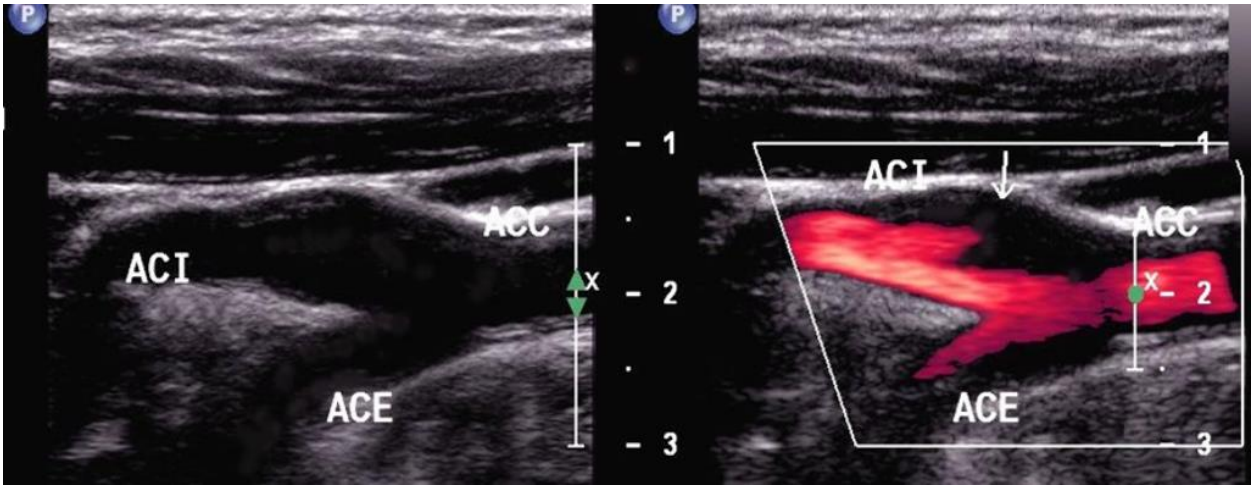
ASSESSMENT OF ATHEROSCLEROTIC LESIONS OF THE CAROTID ARTERIES DEPENDING ON THE SMOKING INDEX IN PATIENTS WITH CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Muborakhon Zokirova, Surayo Shukurdjanova, Maksuda Zubaydullaeva, Nigora Nuritdinova
Internal Disease, Tashkent Medical Academy, Tashkent, Uzbekistan

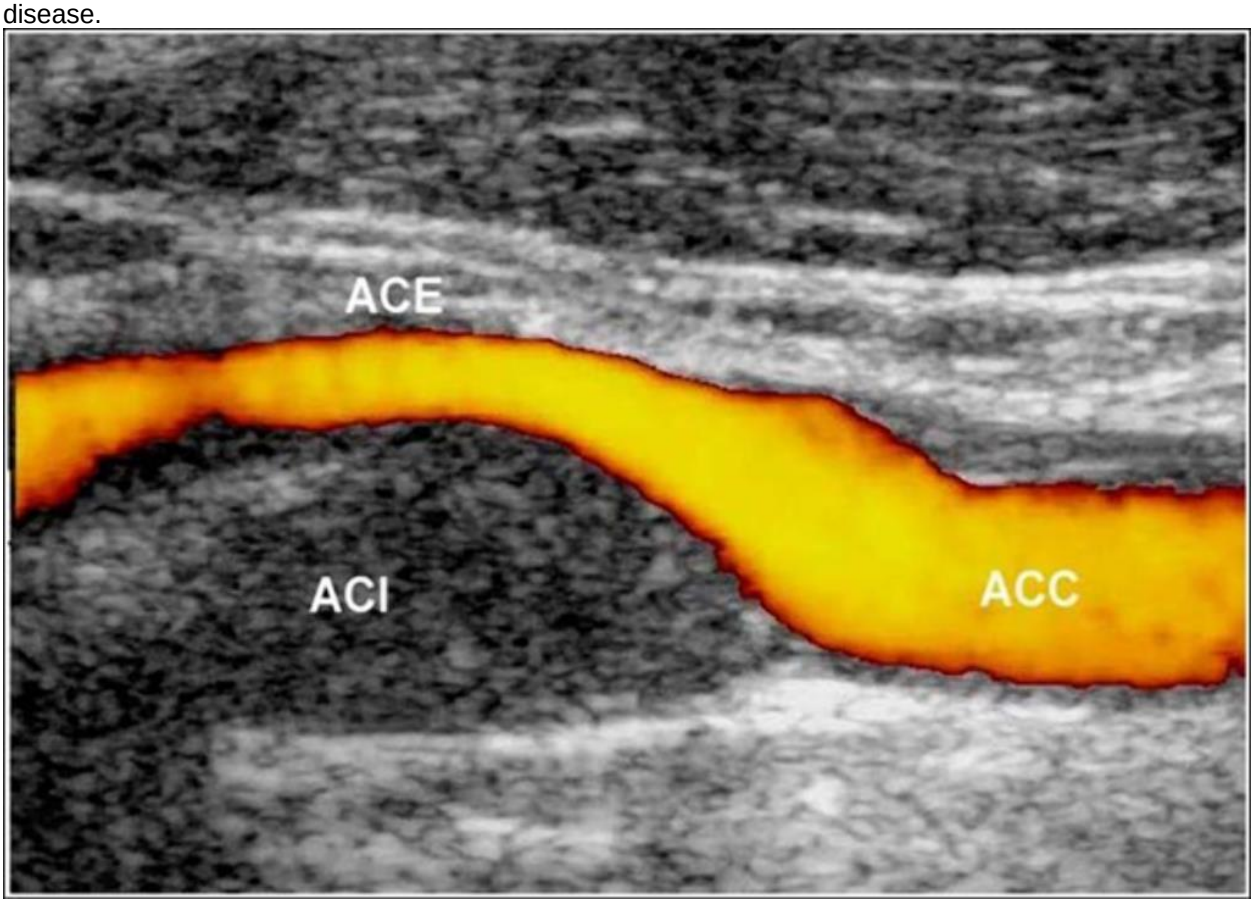
Background and Aims : Aims. Determine the severity of atherosclerotic lesions of the walls of the carotid arteries, depending on the smoking index in patients with coronary artery disease.

Methods:



Methods. The study included 60 male patients aged 40-72 years with a diagnosis of coronary artery

disease.



Results: According to duplex scanning of the common carotid arteries , the average thickness of the IMC in the smoking group was 0.94 ± 0.22 mm, in the CG - 0.80 ± 0.19 mm. Atherosclerotic plaques of varying severity in the main group were diagnosed in 24 (70.59%) of the subjects. In the CG, they were found in 8 (30.77%) of the subjects. A close correlation between the IMC and the number of smoked, SI was also revealed: with IR = 10-15 pack / years, was 0.86±0.11 mm, with IR = 15-20 pack / year - 0.98±0.10 mm, with IR = 10-15 pack / year - 1.20±0.14 mm. Analysis of data by age groups showed that in smokers the increase in the IMC with age occurs faster, than non-smokers.

Index	Core group, n=34
thickness of the intima-media complex, mm(IMC)	0,94 ± 0,22*

in both groups, atherogenic fractions of the blood lipid profile were elevated, and most patients had type IIa dyslipidemia.

Conclusions: In patients with CAD, a direct correlation was found between structural changes in the walls of the common carotid arteries in the form of an increase in the thickness of the IMC and the number of cigarettes smoked, smoking experience, and the smoking index.

ID:358

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

ANALYSIS OF MICRORNA BIOMARKERS IN INFLAMMATORY PATHWAYS REGULATION OF PRE-MATURED ATHEROSCLEROSIS IN RATS MODEL

POSTER VIEWING SESSION

Zulhabri Othman[1], Christianus Rustin[2], Irfan Sazali Kamaruddin[2], Lilik Herawati[3], Norwahidah Abdul Karim[4], Marim A. Fatima[5]
[1]Faculty Of Health & Life Sciences, MANAGEMENT & SCIENCE UNIVERSITY, SHAH ALAM, Malaysia, [2]School Of Graduate Studies, MANAGEMENT & SCIENCE UNIVERSITY, SHAH ALAM, Malaysia, [3]Faculty Of Medicine, AIRLANGGA UNIVERSITY, SURABAYA, Indonesia, [4]Faculty Of Medicine, UNIVERSITI KEBANGSAAN MALAYSIA, KUALA LUMPUR, Malaysia, [5]Research Management Centre, MANAGEMENT & SCIENCE UNIVERSITY, SHAH ALAM, Malaysia

Background and Aims : MicroRNAs are highly up-regulated within atherosclerotic plaque complex indicating their heavy involvement in inflammatory genes regulation in atherosclerosis pathways. Hence, microRNA considered as a promising biomarker for the aforementioned disease. This study aims to investigate the changes in inflammatory microRNA expression in pre-matured atherosclerosis Sprague Dawley (SD) rats induced with high-fat diet.

Methods: Rats (n=10) were randomly divided into High Fat Diet (HFD) and normal diet (ND) groups. Blood was collected for biochemistry analysis of lipid profiling, histology assessment of tunica intima on aorta by Haematoxylin and Eosin (H&E) staining and microRNAs analysis conducted in week 6 and week 12 using Real-Time PCR.

Results: Biochemistry analysis shown significant correlation between HFD and ND and Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), Triglyceride (TG) and Total Cholesterol (TC) level from week 0 to 12, $p<0.05$. MicroRNA analysis revealed that, rno-miR-17-1-3p, rno-miR-210-5p, rno-miR-181a-2-3p and rno-miR-155-5p was expressed in both HFD and ND. There was significantly higher ($p<0.05$; $t=11.80$) expression of microRNAs in HFD group (27.15±8.90) compared to ND group (30.82±1.72). [z1] [z2] Microscopic analysis reveals the thickening on tunica intima of aorta due to inflammation activities in HFD (152.497±7.518 µm) compared to ND (148. 408±1.94 µm).

Conclusions: High calorie diet influenced the expression pattern of the inflammatory microRNA biomarkers. The microRNA may play important role in the regulations of inflammatory gene in the development of pre-mature atherosclerosis.

ID:350

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

CLINICAL AND GENETIC DATA OF THAI SUBJECTS WITH FAMILIAL HYPERCHOLESTEROLEMIA FROM THE THAI FH REGISTRY

POSTER VIEWING SESSION

Poranee Ganokroj[1,2], Suwanna Muanpetch[3], Nuntakorn Thongtang[4], Rungroj Krittayaphong[5], Kanya Suphapeetiporn[6,7], Vorasuk Shotelersuk[6,7], Weerapan Khovidhunkit[1,3,8]
[1]Division Of Endocrinology And Metabolism, Department Of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [2]Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [3]Excellence Center For Diabetes, Hormone, And Metabolism, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand, [4]Division Of Endocrinology And Metabolism, Department Of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [5]Division Of Cardiology, Department Of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [6]Excellence Center For Genomics And Precision Medicine, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand, [7]Center Of Excellence For Medical Genomics, Department Of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [8]Hormonal And Metabolic Disorders Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Background and Aims : Thai Familial Hypercholesterolemia (FH) registry has been established to characterize Thai FH subjects, identify treatment gaps, and raise awareness of the disease.

Methods: Subjects with clinical diagnosis of FH by the Dutch Lipid Clinic Network (DLCN) criteria were recruited and clinical data were collected. Blood specimens were obtained for whole exome sequencing (WES).

Results:

Genetic results of Thai subjects with Familial Hypercholesterolemia by whole exome sequencing

	ALL (N = 27)	PROBABLE FH (N = 10)	DEFINITE FH (N = 17)
DLCN score		6-8	>8
Number of subjects with mutations found, n (%)	8 (30)	1 (10)	7 (41)
LDLR mutations	5	p.Asn428Lys	p.Glu208Ter p.Asn428Lys p.Leu568Val c.695-1G>A
APOB mutations	2	-	p.Arg3527Trp
PCSK9 mutations	1	-	p.Arg93Cys

As of June 2021, 154 subjects with probable or definite FH (DLCN score ≥6) were recruited. The mean age was 51 years old and 63% were women. Mean LDL-C was 4.07 mmol/L. Only 7% had history of premature coronary artery disease (CAD) and 19% had family history of premature CAD. Around 49% were given lipid-lowering medications. Among 27 subjects who underwent WES, eight (30%) were found to harbour six pathogenic variants. Four variants in the *LDLR* gene (c.622G>T, c.695-1G>A, c.1284C>G, and c.1702C>G) were found in five subjects. A missense variant in the *APOB* gene (c.10579C>T, p.Arg3527Trp) was identified in two cases and a missense variant in the *PCSK9* gene (c.277C>T, p.Arg93Cys) was also found.

Conclusions: Our first preliminary report of the Thai FH registry showed that history of premature CAD was less prevalent than that of the regional or global data. Only half currently received lipid-lowering medications, allowing us to identify treatment gaps in care of these subjects. Majority of patients did not carry pathogenic variants in coding regions of genes known to cause FH.

ID:349

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

A NOVEL COMPOUND MOUSE MODEL OF DIABETES, ATHEROSCLEROSIS AND FATTY LIVER USING AAV8-PCSK9 INJECTION IN DB/DB MICE

POSTER VIEWING SESSION

Mengyun Xu[1], Xiumei Wu[2], Zhenghong Liu[1], Suowen Xu[1], Jianping Weng[1]
[1]Institute Of Endocrine And Metabolic Diseases, The First Affiliated Hospital Of Ustc, Division Of Life Sciences And Medicine, University Of Science And Technology Of China, Laboratory of Metabolics and Cardiovascular Diseases, hefei, China, [2]Department Of Endocrinology And Metabolism, Guangdong Provincial Key Laboratory Of Diabetology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background and Aims : Preclinical mouse models are lacked in predicting the pathomechanisms of cardiometabolic diseases and explore new therapeutic agents. Using double-knockouts in ApoE−/− or LDLR−/− background mice are impractical due to the extensive amount of breeding required and substantial costly. Recently reports indicated that overexpression of PCSK9 (AAV8-PCSK9) can induced spontaneous hyperlipidemia which mediated by adeno-associated-virus-8 (AAV8). The purpose of our research was to assess the injection of AAV-PCSK9 vectors in db/db mice as a novel compound mouse model of diabetes, atherosclerosis and fatty liver to study the cardiometabolic diseases and complications.

Methods: Db/db mice were injected with AAV8-PCSK9 (n=3) or AAV8-control (n=3) and high-cholesterol containing diets for 8 weeks. We have detected serum TG, TC and PCSK9 levels. Pathological staining and image analysis were used to determine the plaque morphology.Data were analyzed using unpaired and paired t tests, $p < 0.05$. Results are presented as mean ± SEM.

Results: TC and TG levels were significantly elevated in AAV8-PCSK9-injected mice compared to the controls. AAV8-PCSK9 led to increased serum PCSK9, serious liver steatosis, hypercholesterolemia and quickly formed atherosclerosis plaque as determined by aortic arch/roots plaque imaging and pathological staining, e.g., Oil-Red-O, masson-trichrome and hematoxylin-eosin. RNA sequencing and bioinformatics was used to assessed the global gene expression in liver tissue.

Conclusions: We conclude that AAV8-PCSK9 injection in db/db mice is a promising and time-efficient approach to induce atherosclerosis within a short time. This model is fit perfectly to quickly investigating the etiology and evaluation of drug treatment on cardiometabolic diseases.

ID:341

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

ANTIDIABETIC TREATMENT IN ELDERLY PATIENTS WITH LOW PERFORMANCE STATUS ADMITTED TO INTERNAL MEDICINE WARD

POSTER VIEWING SESSION

Ioanna Papakitsou, Emmanouil Petrakis, Georgios Vougiouklakis, Vasiliki Mavrikaki, Despoina Spentzouri, Sotirios Tzalis, Marios Bargodakis, Kuriakos Vasilopoulos, Alexandros Tsiavos, Anastasios Zagaliotis, Petros Ioannou, Theodosios Filippatos
Internal Medicine, UNIVERSITY HOSPITAL OF HERAKLION, CRETE, GREECE, HERAKLION, Greece

Background and Aims : The prevalence of diabetes mellitus (DM) increases with age. According to the 2021 American Diabetes Association (ADA) guidelines, elderly patients with multiple comorbidities may have less stringent glycemic targets. The aim of this study was to record the medication and the glycemic regulation of patients with DM admitted to the Internal Medicine Department of the University Hospital of Heraklion, Crete.

Methods: Elderly patients (>65 years old) with DM admitted to the Internal Medicine department were consecutively enrolled. This preliminary analysis concerns the first 70 patients.

Results: Patients had an average age of 82 ± 6 years (54.4% men), a body mass index (BMI) of 27±3.8 kg/m^2, while 26.9% of them were bedridden and 35.8% had advanced dementia. Additionally, 41.8% of patients had Katz index=0-2 (poor performance status based on the last 6 months), while 94.1% of patients had Charlson Comorbidity Index (CCI) ≥5 and 58.3% CCI ≥7. Regarding antidiabetic treatment, 22.4% of patients received sulphonylureas, 25.4% basal insulin and 16.4% regimens with fast-acting insulin. Patients with Katz index 0-2 received sulphonylureas (25%), basal insulin (25.6%) and regimens with fast-acting insulin (14.3%), while they exhibited glycosylated hemoglobin values of 5.5±0.7, indicating a stringent DM regulation.

Conclusions: The present analysis outlines a rather stringent treatment of elderly patients with DM with drugs predisposing to hypoglycemia, without taking into account coexisting chronic illnesses, cognitive function and functional status.

ID:393

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

CROSS-SECTIONAL STUDY OF ABDOMINAL OBESITY AS THE LEADING RISK FACTOR FOR THERAPEUTIC DISEASES IN 25-44 YOUNG PEOPLE IN SIBERIA

POSTER VIEWING SESSION

Yuliya I. Ragino[1], Alyona Khudyakova[1], Eugeniia V. Striukova[2], Diana V. Denisova[1], Liliya Shcherbakova[1]
[1]Branch Of Ic&g Sb Ras, Research Institute of Internal and Preventive Medicine – Branch of IC&G SB RAS, Novosibirsk, Russian Federation, [2]Branch Of Ic&g Sb Ras, Research Institute of Internal and Preventive Medicine, Novosibirsk, Russian Federation

Background and Aims : The study is about the prevalence of abdominal obesity (AO) in the 25-44 years population of Novosibirsk, as well as the prevalence of therapeutic diseases and pathological conditions in individuals with AO.

Methods: We conducted a cross-sectional population study of the 25-44-year-old population of Novosibirsk (Russia). At the screening, we examined 1,415 people, including 670 men and 745 women. For all subjects, we evaluated the presence of such conditions as AO, arterial hypertension (AH), increased BMI, ischemic heart disease, diabetes mellitus (DM), reduced glomerular filtration rate (GFR), chronic bronchitis (CB), increased blood levels of total cholesterol and cholesterol-LDL.

Results: The prevalence of AO in the 25-44 years population of Novosibirsk was 42.4%, in men-42.7%, in women-42.1%. We found that AO has a significant direct effect on the development of AH, CB, hypercholesterolemia, hyper-LDL-cholesterolemia, and the reverse effect on the reduced GFR. In the male population under 45 years of age, AO has a significant direct effect on the development of AH, CB, hypercholesterolemia, and hyper-LDL-cholesterolemia. In the female population under the age of 45, AO has a significant direct effect on the development of DM, AH, CB, hyper-LDL-cholesterolemia, and a reverse effect on the reduced GFR development.

Conclusions: Thus, in the young Siberian population under the age of 45, abdominal obesity is associated with the development of common therapeutic diseases and pathological conditions. This work was supported by the grant of the Russian Science Foundation No. 21-15-00022.

ID:340

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

LIPID LOWERING THERAPY IN ELDERLY PATIENTS WITH POOR PERFORMANCE STATUS

POSTER VIEWING SESSION

Ioanna Papakitsou, Emmanouil Petrakis, Vasiliki Mavrikaki, Georgios Vougiouklakis, Despoina Spentzouri, Sotirios Tzalis, Angelos Matheakakis, Alexandros Tsiavos, Kuriakos Vasilopoulos, Marios Bargodakis, Ioannis Akoumianakis, Petros Ioannou, Theodosios Filippatos
Internal Medicine, UNIVERSITY HOSPITAL OF HERAKLION, CRETE, GREECE, HERAKLION, Greece

Background and Aims : Lipid lowering agents are the cornerstone of primary prophylaxis in patients with increased cardiovascular disease (CVD) risk. However, their beneficial effects in elderly patients with poor performance status/high comorbidity and reduced life expectancy are not yet elucidated.

Methods: Patients aged >65 years admitted to the Internal Medicine department were consecutively enrolled. The Katz index and Charlson Comorbidity Index (CCI) were used for assessment of functionality (calculations performed based on the usual operational status in the last 6 months) and comorbidity, respectively.

Results: A sample of 201 patients [age 83±8 years (50% men)] with a body mass index (BMI) of 25±4kg/m^2 were enrolled. Among the study population, 42.6% of the patients had decreased functionality (Katz index=0-2), while 40.7% had advanced dementia. In terms of comorbidity, 77.9% of patients had CCI ≥5, while 28.9% of the sample had CCI ≥7. Regarding lipid lowering therapy, 27.9% of the patients received a stain, while 2.5% were on combination therapy with statin/ezetimibe. A subgroup analysis of patients with poor performance status showed that 23% of patients with Katz index=0-2 were on statins, while 2.3% on combination therapy. Importantly, only 13% of patients with Katz index=0-2 had a history of established CVD.

Conclusions: Almost 10% of patients with poor performance status were on lipid lowering therapy as primary prevention. Lipid-lowering therapy as primary prevention should be individualized in elderly individuals based on the general performance status, life expectancy and the increased risk of polypharmacy-related side effects.

ID:336

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

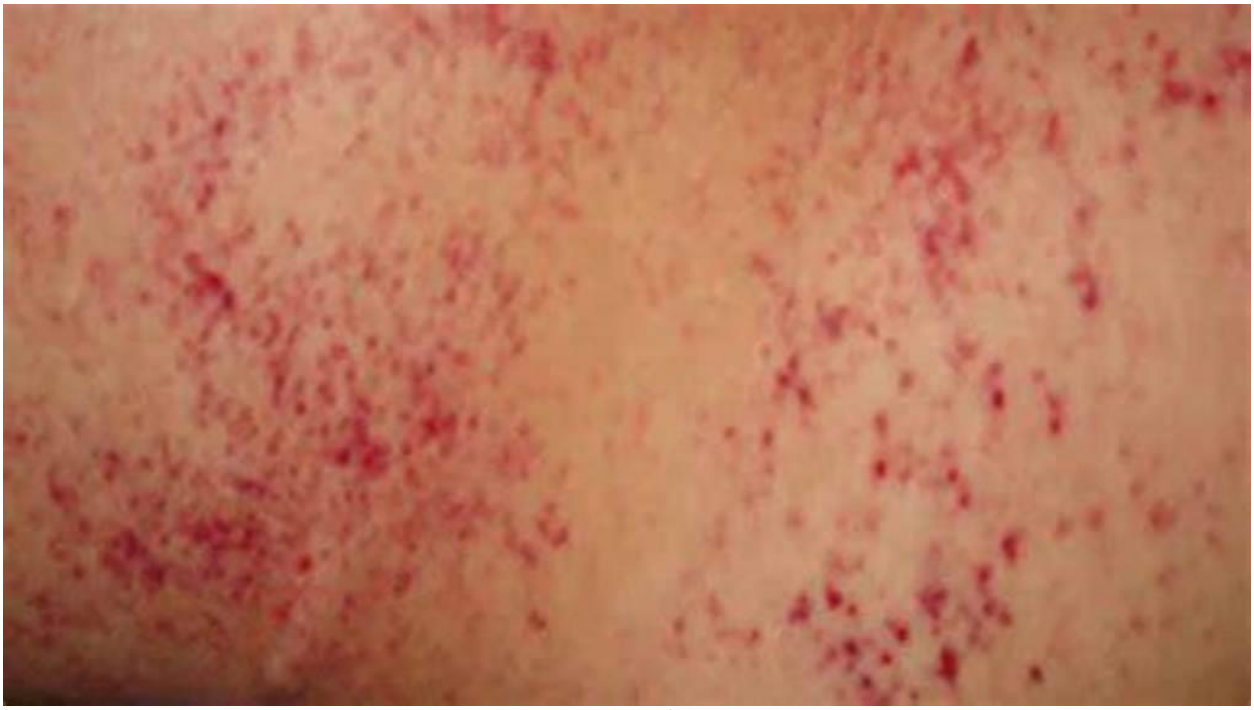
COVID-19 VACCINATION ASSOCIATED SEVERE IMMUNE THROMBOCYTOPENIA: A CASE REPORT

POSTER VIEWING SESSION

Meropi Mousdi, Sofia Pegka, Myrto Skouteli, Katerina Trachana, Georgios Chatzis, Sofoklis Bakidis
Internal Medicine, General Hospital of Molaoi, Lakonia, Molaoi, Greece

Background and Aims : Coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has emerged as a deadliest global pandemic after its identification in December 2019 in Wuhan, China resulting in more than five million deaths worldwide. Until now, only vaccination is known to prevent its morbidity and mortality. Most commonly used is the Pfizer-BioNTech COVID-19 vaccine We report one case of severe immune thrombocytopenia (ITP) following COVID-19 vaccination and their clinical course.

Methods: Case report: 24 year old male with no past medical history came to emergency department reporting hemorragic skin rush at inner thgh area 36 hours after the second dose of Pfizer-BioNTech COVID-19
vaccine.



A complete blood test showed a platelet count of 1×10^9/L. Patient did not have a prior history of thrombocytopenia, except a lab result of platetet count 135×10^9/L 45 days ago, . and other causes of thrombocytopenia were ruled out by history and pertinent lab data. No signs of thormbosis were found and D- dimers were at normal range

Results: He received 14 units of platelets, two doses of intravenous immunoglobulin and oral dexamethasone for 4 days resulting in normalization of platelet counts.

Conclusions: COVID-19 vaccination induced ITP has been recently acknowledged. However, given very few cases and limited data, currently there are no guidelines for management of ITP caused by COVID-19 vaccine as well as vaccination of people with predisposing conditions. furthemore, there has to be a differential diagnosis from Vaccine Induced Thrombotic Thrombocytopenia (VITT), at the onset of clinical manifestation

ID:328

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

BASELINE HIGH-DENSITY LIPOPROTEIN LEVEL IS ASSOCIATED WITH COVID-19 PNEUMONIA SEVERITY IN HEMODIALYSIS PATIENTS

POSTER VIEWING SESSION

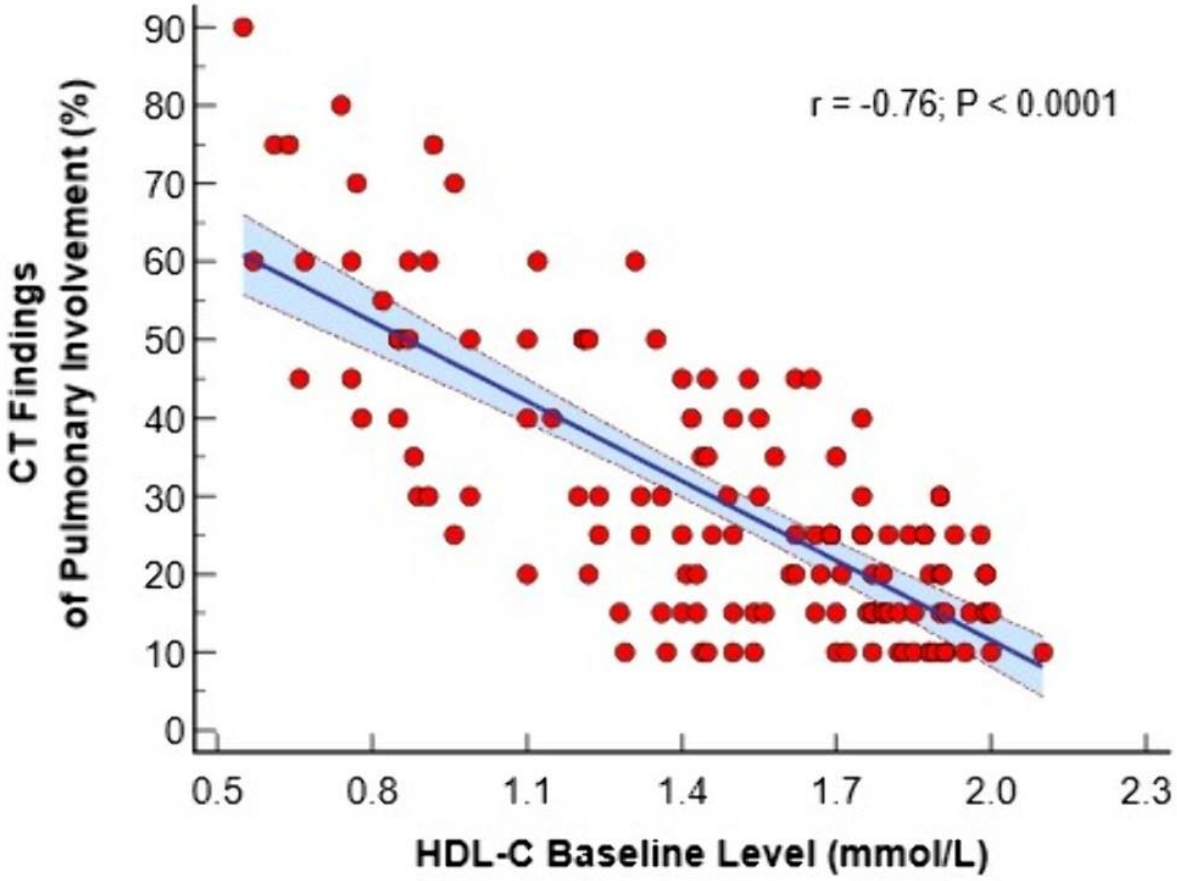
Natalia Stepanova[1,2], Andriy Rysyev[3], Oksana Rusyn[4], Tetyana Ostapenko[5], Lyudmila Snisar[1,2], Serhiy Rusanov[2]
[1]Nephrology And Dialysis, State Institution “Institute of Nephrology National Academy of Medical Science of Ukraine, Kyiv, Ukraine, [2]Nephrology, Dialysis Medical Center LLC “Nephrocenter”, Kyiv, Ukraine, [3]Nephrology, Dialysis Medical Center LLC “Link-Medital”, Odesa, Ukraine, [4]Nephrology, Dialysis Medical Center LLC “Nephrocenter”, Lviv, Ukraine, [5]Nephrology, Dialysis Medical Center LLC “Nephrocenter”, Zaporizhzhia, Ukraine

Background and Aims : A decline in high-density lipoprotein cholesterol (HDL) has been observed in the general population of COVID-19 patients. However, there is a general lack of data on the association between the baseline HDL level and COVID-19 outcomes in HD patients. The present study aimed to assess the association between baseline HDL levels and COVID-19 pneumonia severity in HD patients.

Methods: A total of 428 HD patients aged 55 **(**44-64) years and a dialysis vintage of 44 (21-76.6) months were enrolled in this multicenter retrospective cohort study. Baseline HDL levels were obtained from the electronic health records of the patients. Severe COVID-19-associated pneumonia was estimated based on chest CT findings of pulmonary involvement. The Mann-Whitney test, the Spearmen correlation test, and the Cox regression analysis were used for the statistical analysis.

Results: Among 428 enrolled HD patients, there were 142 (33.2%) patients infected with COVID-19 and 286 (66.8 %) non-infected patients. Forty (28%) of 142 COVID-19 positive patients were hospitalized, 34 patients (24%) needed oxygen supplements and 16 patients (11.3%) died. The baseline HDL level was significantly lower in the COVID-19 patients compared with the non-infected patients ($p = 0.011$). Moreover, the baseline HDL level was significantly negatively associated with CT findings of pulmonary involvement (Fig. 1). In the Cox regression analysis adjusted for age, diabetes and dialysis vintage, low HDL level (<1.22 mmol/L) was found to be associated with COVID-19-related mortality in the HD patients (HR 0.57, 95% CI 0.37;

0.89).



Conclusions: Baseline low HDL level was independently associated with severe COVID-19 pneumonia in HD patients.

ID:322

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

DYNAMICS OF THE QUALITY OF LIFE AFTER CABG IN PATIENTS WITH STABLE ISCHEMIC CORONARY DISEASE

POSTER VIEWING SESSION

Yuliia Borkhalenko[1], Olga Yepanchintseva[1], Borys Todurov[2], Oleg Zharinov[3]
[1]Department Of Diagnostics Of Pathology Of The Heart And Great Vessels, The Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine, [2]Department Of Surgical And Minimally Invasive Treatment, The Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine, [3]Department Of Functional Diagnostic, Shupyk National Healthcare Univercity of Ukraine, Kyiv, Ukraine

Background and Aims : To evaluate QOL, LV diastolic function parameters and brain natriuretic peptide (BNP) in patients with CAD and preserved or mid-range LVEF before and 6 months after CABG.

Methods: The cross-sectional single-center retrospective study included data from clinical and instrumental examination of 71 patients with CAD and preserved or mid-range systolic function (LVEF 40 >%), consecutively selected for CABG. Among them, there were 60 men and 11 women,middle age (64±4) years. 11 (17%) patients had signs of stable angina II FC, 44 (69%) had III FC, 9 (14%) had IV FC. We analyzed FC of angina, QOL parameters by using SF-36, SAQ, MLHFQ, the echocardiographic parameters and the BNP level before and 6 months after CABG

Results: Six months after CABG a significant improvement of QOL was registered by questionnaires MLHFQ, SF-36 and SAQ, compared to base[1]line(p <0,001). The angina symptoms significantly decreased: there were no angina attacks in 59% patients, and I-II FC were observed in 39% patients (p <0,001). Six months after surgery, there was a significant improvement in LV diastolic function, namely reduction of DT from median 262 to 250 ms (p <0,001), IVRT from 118 to 112 ms (p = 0,021), and increase of E/A from 0,82 to 0,92 (p = 0,043). The BNP level decreased from 115,4 to 52,4 pg/ml (p <0,001).

Conclusions: Reducing angina pectoris and improving parameters of QOL 6 months after CABG is associated with positive changes of LV diastolic function parameters and decrease of BNP

ID:317

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

LONG-TERM CHANGES IN COGNITIVE STATUS OF CARDIAC SURGERY PATIENTS WITH TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Irina V. Tarasova, Anastasia S. Sosnina, Olga A. Trubnikova, Irina D. Syrova, Olga L. Barbarash
Clinical Cardiology, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Background and Aims : There are insufficient data about the long-term cognitive trajectory in patients with type 2 diabetes mellitus (DM) who underwent coronary artery bypass grafting (CABG). The study aimed to evaluate the long-term changes of the cognitive status in patients with type 2 diabetes at 5-7 years after CABG.

Methods: The study included 47 male CABG patients. All participants provided written informed consent and underwent cognitive screening using the Mini-Mental State Examination (MMSE) scale, general medical, neurological, and instrumental examinations. The extended neuropsychological testing (psychomotor and executive function, attention, short-term memory) was also carried out. Based on the preoperative examination results the patients were divided into two groups: with type 2 DM (n = 21) and without (n = 26).

Results: It was found that DM patients had the cognitive status decrease measured by the MMSE scale at 5-7 years after CABG in comparison to the preoperative level (28.1 ± 1.3 and 27.0 ± 1.46, p = 0.04). The relative risk of mild cognitive impairment in type 2 DM patients was 1.92 (95% CI = 1.09-3.37; Z = 2.26, p = 0.02). Patients with type 2 DM had the worst indicators of psychomotor and executive functions both at baseline and 5-7 years after CABG ($p \leq 0.05$). At 5-7 years CABG the higher glycated hemoglobin (HbA1c) blood level was associated with the worst executive functions and short-term memory only in patients with type 2 DM.

Conclusions: Type 2 DM patients demonstrated negative changes of psychomotor and executive functions associated with HbA1c level in the CABG long-term period.

ID:309

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-15 Gene-Environment interactions*

ASSOCIATION OF ANGIOTENSIN-CONVERTING ENZYME INSERTION/DELETION GENE POLYMORPHISM WITH CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Duy C. Tran[1], Linh G.H. Le[2], Minh D. Do[2], Truc T. Thai[3], Sy V. Hoang[1], Binh Q. Truong[1]
[1]Department Of Internal Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam, [2]Center For Molecular Biomedicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam, [3]Faculty Of Public Health, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam

Background and Aims : Recent advances in molecular biology have identified several gene variants of the renin-angiotensin-aldosterone system, which play an important role in the pathogenesis mechanism and prognosis of myocardial infarction (MI). This study was conducted to assess the association of angiotensin-converting enzyme (ACE) insertion/deletion (I/D) gene polymorphism with cardiovascular risk factors in patients with MI.

Methods: This was a prospective cohort study among acute MI patients admitted to Cho Ray Hospital, Viet Nam between January 2020 to June 2020. Genotypes of the ACE I/D variant were tested at the Center for Molecular Biomedicine, University of Medicine and Pharmacy at Ho Chi Minh City.

Results: A total of 130 patients with acute MI (mean age 64.9 ± 11.6; 69.4% men) were enrolled in the study. The frequency of II, ID, and DD genotypes of ACE I/D polymorphism were 44.4%, 42.6%, and 13.0% respectively. Patients with the DD genotype had higher mean serum LDL-C concentrations than patients with ID or II genotypes (137.9±56.8 vs 107.0±39.9 mg/dL; P=0.016). The DD genotype was associated with serum triglyceride levels ≥150 mg/dL (OR=0.165; 95% CI 0.035–0.792; P=0.024) and overweight and obesity status (OR=0.206; 95 % CI 0.044–0.973; P=0.046). The ACE I/D gene variant was not significantly associated with age, gender, hypertension, diabetes, and smoking.

Conclusions: In patients with acute MI, the ACE I/D gene polymorphism was associated with dyslipidemia, overweight, and obesity, but was not associated with other classic cardiovascular risk factors.

ID:305

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ALPHA LIPOIC ACID PRESERVES LONG-TERM PATENCY AND FUNCTIONAL PERFORMANCE OF THE HUMAN SAPHENOUS VEIN GRAFT BY PREVENTING VASOSPASM

POSTER VIEWING SESSION

Taskin Kalkan[1], Buket Reel[2], Caglar Bintepe[1], Ismail Yurekli[3], Nevin Ersoy[4], Alper Bagriyanik[4,5]
[1]Department Of Pharmacology, Ege University Faculty of Pharmacy, Izmir, Turkey, [2]Department Of Clinical Pharmacy, Ege University Faculty of Pharmacy, Izmir, Turkey, [3]Department Of Cardiovascular Surgery, Izmir Katip Celebi University, Ataturk Education and Research Hospital, Izmir, Turkey, [4]Department Of Histology And Embryology, Dokuz Eylul University School of Medicine, Izmir, Turkey, [5]., Izmir Biomedicine and Genome Center, Izmir, Turkey

Background and Aims : Graft vasospasm due to inflammation and oxidative stress in human saphenous vein (HSV) grafts during or after coronary artery bypass grafting (CABG) operation is an important complication that limits long-term graft patency and functions. In our previous study, we showed that alpha lipoic acid (ALA) decreased ROS levels and MMP-2 expression/activity and α-smooth muscle actin expression in Tumor Necrosis Factor-α (TNF-α)-induced HSV grafts. The aim of the present study was to investigate the effect of ALA on vascular functional responses in TNF-α-induced HSV grafts.

Methods: HSV grafts (n=7) obtained from patients undergoing CABG operation were separated into 4 rings after the endothelium was gently removed. The rings were incubated in RPMI containing 20 ng/ml TNF-α and/or 2 mM ALA for 24 hrs. Untreated rings were called as control. Concentration-response curves to potassium chloride (KCl), noradrenaline (NA), serotonin (5-HT), prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and papaverine were performed by using organ bath system to evaluate vascular function.

Results: TNF-α induced vascular injury and inhibited the contractile responses to KCl, NA, 5-HT and $PGF_{2\alpha}$ compared to the control group. ALA exerted vasodilatory effect and significantly decreased all contractile responses. However, relaxant effect of ALA was masked in TNF-α+ALA group. Papaverine relaxation was changed by neither TNF-α nor ALA. Sensitivity to contractile agents was not affected by either TNF-α or ALA.

Conclusions: ALA may contribute to the preservation of long-term patency and functional performance of the graft by preventing vasospasm, despite inflammatory conditions and endothelial damage in patients undergoing CABG surgery.

ID:303

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

THE ASSOCIATION OF CHOLESTEROL, BLOOD METHEMOGLOBIN LEVELS AND SERUM ANTIOXIDANT ACTIVITY.

POSTER VIEWING SESSION

Irina Starodubtseva[1], Konstantin Boev[2], Dmitry Vasilenko[2]
[1]Internal Diseases, NN Burdenko Voronezh State Medical University, Voronezh, Russian Federation, [2]Clinical Laboratory Diagnostics, NN Burdenko Voronezh State Medical University, VORONEZH, Russian Federation

Background and Aims : The aim of the study is to reveal the relationship between the level of blood methemoglobin and the antioxidant activity of serum, depending on the concentration of cholesterol

Methods: Venous blood of healthy men (n= 65) and patients (males) with CAD (n=40) was used. Methemoglobin (MetHb) concentration and the antioxidant activity of serum were determined spectrophotometrically.The antioxidant activity of serum was determined by the degree of inhibition of adrenaline autooxidation in an alkaline medium.

Results: When the concentration of cholesterol in healthy was up to 5.0 mmol / L (4.3±0.65), the concentration of MetHb was 2.9±0.15 g /L. At a cholesterol concentration of 7.1±0.85 mmol /L ($p < 0.01$), the MetHb concentration was 4.6±0.28 g / L ($p < 0.01$) in comparison with normal level 2.8 g /L. In patients with CAD it was found that an increase in cholesterol concentration was accompanied by an increase in blood MetHb: 4.7 ± 0.7 mmol /L cholesterol and 3.1±0.3 g /L MetHb, 6.7±0.76 mmol /L cholesterol and 4.8±0.22 g /L MetHb ($p < 0.01$). The degree of inhibition of adrenaline autooxidation was 62.0±7.0% at a cholesterol concentration of 4.7 mmol /L, MetHb 3.1 g /L and 38.2±4.6% at a cholesterol concentration of 6.7 mmol /L, MetHb 4.8 g /L ($p<0.01$). A relationship was found between an increased level of MetHb and antioxidant activity of blood serum against the background of an increase in cholesterol levels ($r = -0.7$)

Conclusions: Elevated cholesterol levels are associated with an increase in blood MetHb concentration and a decrease in serum antioxidant activity.

ID:300

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

AWARENESS OF POSITIVE GENETIC TESTING FOR FAMILIAL HYPERCHOLESTEROLEMIA ENCOURAGES BETTER ADHERENCE TO TRIPLE-COMBINED LIPID-LOWERING THERAPY

POSTER VIEWING SESSION

Anastasia Blokhina[1], Alexandra Ershova[1], Alena Limonova[1], Oxana Kopylova[1], Stepan Smetnev[2], Anna Kiseleva[2], Vladimir Kutsenko[3], Irina Efimova[4], Alexey Meshkov[2], Oxana Drapkina[5]
[1]The Laboratory Of Clinomics, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [2]The Laboratory Of Molecular Genetics, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [3]Epidemiology Of Non-communicable Diseases, Laboratory Of Biostatistics, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [4]Bank Of Biological Material, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [5]Fundamental And Applied Aspects Of Obesity, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation

Background and Aims : To assess the impact of awareness of genetic testing for familial hypercholesterolemia (FH) on the adherence to the lipid-lowering therapy (LLT).

Methods: Patients ≥18 y.o. with “probable” or “definite” FH according to the DLCN criteria were included (n=82). The study consists of three visits (follow-up is 6 months) with a block randomization with a 2:1 allocation ratio (with: without genetic testing). The results of genetic testing were reported at the second visit. Patients were divided into 3 groups: I - with "positive" genetic testing (n=38); II - with "negative" genetic testing (n=19); III - without genetic testing (n=25). Fisher's test was used for statistical analysis. The study was registered on ClinicalTrials (NCT04656028).

Results: Individuals with FH variants knew more often their LDL-C target level (61.1% at visit 3 vs 26.3% at visit 2; p=0.004) and comparing with group II (17.6%) by visit 3 (p=0.006). There was no difference in the proportion of patients taking combined LLT (statin+ezetimibe+PCSK9i) at the first visit (5.3% at groups I and II, 12.0% at group III; p=0.556) and in the frequencies of its prescribing at the second visit (70.3% at group I, 52.6% at group II and 56.0% at group III; p=0.326). Only patients with FH variants began to take the combined LLT significantly more often by visit 3 (43.2% vs 5.3% at visit 1 (p <0.001)).

Conclusions: Knowledge of positive genetic testing for FH contributes to a better knowing of the LDL-C target level and better adherence to the triple-combined LLT.

ID:288

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

VASCULAR EHLERS-DANLOS SYNDROME (SACK- BARABAS SYNDROME) – MULTIORGANOMULTIVASCULAR DISEASE

POSTER VIEWING SESSION

Gabriela Gubo[1], Peter Gavorník[2,3], Andrej Dukát[3,4], Ludovít Gašpar[3,5]
[1]General Practice, Havering Health, London, United Kingdom, [2]Faculty Of Medicine, Comenius University in Bratislava, Bratislava, Slovak Republic, [3]Angiology Section Of Slovak Medical Chamber, Slovak Medical Chamber, Bratislava, Slovak Republic, [4]Ministry Of Health, Ministry of Health of the Slovak Republic, Bratislava, Slovak Republic, [5]Faculty Of Health Sciences, University of Ss. Cyril and Methodius in Trnava, Pieštany, Slovak Republic

Background and Aims : Ehlers-Danlos syndromes (EDS) are a group of rare connective tissue disorders that can be inherited and are varied both in how they affect the body and in their genetic causes. They are generally characterized by joint hypermobility, skin hyperextensibility, and tissue fragility. The aim of this review article is to raise awareness about the vascular subtype of Ehlers-Danlos syndrome (subtype 4) - an orphan disease which is prognostically the most serious subtype of this group of disorders.

Methods: This presentation summarizes the classification, clinical manifestation, diagnosis, differential diagnosis and management of Sack-Barabas syndrome, based on systematic review of specialist literature dealing with this topic.

Results: Ehlers-Danlos syndromes are currently classified in a system of thirteen subtypes. Each EDS subtype has a set of clinical criteria that help guide diagnosis. Vascular Ehlers-Danlos syndrome (VEDS; EDS subtype 4; EDS IV; Sack-Barabas syndrome) is rare genetic connective tissue disorder of blood-vessels typically characterized by the association of unexpected vascular and organovascular fragility (arterial/ microvascular/ bowel/ gravid uterine rupture) with inconstant physical features as thin, translucent skin, easy bruising and acrogeric traits.

Conclusions: Awareness about this rare condition is essential for early recognition and therefore for the initiation of management and prevention of complications, often requiring treatment in a specialized vascular centre.

ID:388

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

ASSOCIATION OF COGNITIVE FUNCTION WITH OXYTOCIN AS A SOCIAL HORMONE IN A COMMUNITY DWELLING JAPANESE WOMEN; UKU STUDY

POSTER VIEWING SESSION

Mika Enomoto[1], Ako Fukami[1], Nagisa Morikawa[1], Maki Yamamoto[1], Hiromi Sato[1], Hisashi Adachi[2], Yoshihiro Fukumoto[1]
[1]Division Of Cardiovascular Medicine, Department Of Internal Medicine, Kurume Univiersity School of Medicine, Kurume, Fukuoka, Japan, [2]Cardiology, Keikokai, Hara Hospital, Fukuoka, Japan

Background and Aims : Cognitive impairment leads to loss independence in daily activities. Maintain of cognitive function keeps daily high living activity. Oxytocin is an essential hormone for mammalian labor and lactation. The relationship between oxytocin and social cognition is supported by impairment of social recognition, which is associated with learning and memory integrity, in animal study. We investigated whether oxytocin levels are associated with cognitive function.

Methods: Subjects were 219 residents (90 men and 129 women) who participated in a health check-up examination in Uku Town in Sasebo city in 2016. Oxytocin concentrations were measured in 129 women and using radioimmunoassay. Cognitive function was assessed by Mimi-Mental State Examination (MMSE).

Results: Cognitive dysfunction was defined as smaller than 26 MMSE scores. Mean plasma oxytocin levels were 7.3(3.0-69.5) μU/ml. Mean MMSE scores were 28.2 ±2.3 points. The subjects with normal cognition were 110, and those with cognitive dysfunction were 17. Mean oxytocin levels in 17 subjects with cognitive dysfunction were much higher than in 110 subjects with normal cognitive function (8.0μU/ml) (p=0.67). In the linear regression analysis, MMSE was related to age (p=0.001; inversely) whereas; MMSE was not related to oxytocin (p=0.223). In the multiple regression analysis after adjustment for age, MMSE was not associated with oxytocin (p=0.357).

Conclusions: This study demonstrated that cognitive dysfunction was not associated with oxytocin levels in women. A prospective study is needed to examine the causal relationship between cognitive dysfunction and oxytocin including men.

ID:402

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

IMPLEMENTATION OF A DASHBOARD FOR MONITORING HEALTH DATA AT REGIONAL LEVEL IN ITALY

POSTER VIEWING SESSION

Ottavio Gallo[1], Paolo Francesconi[2], Francesco Profili[2], Edoardo Mannucci[3]
[1]Crm, Novartis Farma, Varese, Italy, [2]Osservatorio Di Epidemiologia, Agenzia Regionale di Sanità della Toscana, Firenze, Italy, [3]Scienze Biomediche, Sperimentali E Cliniche, Università di Firenze, Firenze, Italy

Background and Aims : Collection of epidemiological data and information on related healthcare is crucial to monitoring healthcare appropriateness and the fulfillment of clinical needs. This project aimed to implement a dashboard for epidemiological data collection, with a focus on patients with hypercholesterolemia.

Methods: A linkage was created between health administrative data and laboratory tests results by the Regional Health Agency of Tuscany (Italy) to collect data from Local Health Districts on patients with hypercholesterolemia. Coexistence of type 2 diabetes (T2D), history of major adverse cardiac and cerebrovascular events (MACE) and/or peripheral arterial disease (PAD), and prescription/use of anti-hypercholesterolemic agents were monitored.

Results: As of 2020, data from 7 Local Health Districts identified a cohort of 864,396 individuals. Overall, 11.0% of individuals had T2D and 11.1% experienced MACE and/or PAD. From 864.396 individuals, LDL cholesterol (LDL-C) data were available for 301.138 patients (34.8%). Less than one fifth (16.1%) of the cohort were on statins and/or ezetimibe. Untreated patients accounted for 37.5% of T2D-MACE and 50.7% of non-T2D-MACE patients, respectively. One% of patients received combinations of any statin + ezetimibe for at least 75% of treatment days. Among patients with LDL-C data, 87.2% with history of MACE didn’t achieved target LDL-C levels, which underlines an unmet clinical need in this very high-risk population.

Conclusions: The implementation of a dashboard facilitated the collection of epidemiological and outcome data that are crucial to highlighting unmet clinical needs and implementing proactive and specific population health initiatives.

ID:284

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

HEPARIN BINDING TRIGGERS VLDL REMODELING BY CIRCULATING LIPOPROTEIN LIPASE: RELEVANCE TO VLDL FUNCTIONALITY IN HEALTH AND DISEASE

POSTER VIEWING SESSION

Shobini Jayaraman[1], Antonio Pérez[2], Inka Miñambres[3], Jose Luis Sánchez Quesada[2], Olga Gursky[1]
[1]Physiology & Biophysics, Boston University School of Medicine, Boston, United States of America, [2]Cardiovascular Biochemistry Group, Research Institute of the Hospital de Sant Pau (IIB Sant Pau), Barcelona, Spain, [3]Endocrinology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background and Aims : Hydrolysis of VLDL triacylglycerol (TG) by lipoprotein lipase (LpL) is a major step in energy metabolism and VLDL-to-LDL maturation. Most functional LpL is anchored to the vascular endothelium, yet a small amount circulates on TG-rich lipoproteins. As circulating LpL has low catalytic activity, its role in VLDL remodeling is unclear.

Methods: We used pre-heparin plasma and heparin-sepharose affinity chromatography to isolate VLDL fractions from normolipidemic, hypertriglyceridemic, or type-2 diabetic subjects. VLDL remodeling and functionality were assessed by size-exclusion chromatography and enzymatic assays.

Results: LpL was detected only in the heparin-bound fraction. Our results showed that transient binding to heparin activates this VLDL-associated LpL, which hydrolyses TG, leading to gradual VLDL remodeling into IDL/LDL and HDL-size particles. The products and the timeframe of this remodeling closely resemble VLDL-to-LDL maturation *in vivo.* Importantly, the VLDL fraction that does not bind heparin is not remodeled. This fraction shows impaired functionality as a substrate for the exogenous LpL or CETP, and likely has prolonged residence time in blood, which is expected to promote atherogenesis. This non-bound VLDL fraction increases in hypertriglyceridemia and in type-2 diabetes but decreases upon diabetes treatment that restores the glycemic control.

Conclusions: Collectively, the results reveal that binding to glycosaminoglycans initiates VLDL remodeling by circulating LpL, and suggest heparin binding as a marker of VLDL functionality and a readout for treatment of metabolic disorders.

ID:462

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

PREDICTORS OF INCREASED CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH DIABETES TYPE 2 AND CHRONIC KIDNEY DISEASE

POSTER VIEWING SESSION

Volha Vasilkova[1], Tatsiana Mokhort[2], Yana Borovets[1], Yulia Yarets[3], Ludmila Korotaeva[3], Ivan Pchelin[4]
[1]Endocrinology, Gomel State Medical University, Gomel, Belarus, [2]Endocrinology, Belarusian State Medical University, Minsk, Belarus, [3]Laboratory, The Republican Research Centre Radiation Medicine and Human Ecology, Gomel, Belarus, [4]Internal Medicine, Saint Petersburg State University, Saint Petersburg, Russian Federation

Background and Aims : The aim of our study was to find predictors for increases of carotid intima-media thickness (cIMT) in patients with diabetes type (DT2) and CKD.

Methods: We examined at baseline 316 patients with DT2 and CKD and various degrees of renal impairment who were aged between 25 and 65 years. The development of a prognostic model for the probability of a binary outcome was carried out using logistic regression. Nagelkerke R^2 was used as a measure of the model performance. ROC analysis was used to assess the diagnostic performance of quantitative variables in predicting a categorical outcome. The optimal cut-off value of the quantitative variable at was estimated using the Youden's J statistic.

Results: A predictive model was developed to estimate the probability for increases of cIMT using binary logistic regression. Asignificant relationship of homocysteine level, CKD 3-5 stages and presence of proteinuria with the probability for increases of cIMT were established. When evaluating the dependence of the probability for increases of cIMT on the Value of logistic function P using the ROC analysis. The cut-off value of logistic function P was 0.712. If of logistic function P was greater than or equal to this value, increases of cIMT was predicted.

Conclusions: A multimarker approach should be used to recognize patients with the highest risk for cardiovascular events. In the future, more attention should be given to the decrease in prevalence of DM and prevention of CKD development in diabetic patients.

ID:500

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

SPECKLE-TRACKING TRANSESOPHAGEAL ECHOCARDIOGRAPHY IN THE MODERATE DILATATION AND ANEURYSM OF THE ASCENDING AORTA: PRELIMINARY RESULTS FROM PROSPECTIVE STUDY

POSTER VIEWING SESSION

Dmitri Panfilov[1], Alexander Vrublevsky[2], Victor Saushkin[3], Eugene Lilik[1], Yulia Chernykh[1], Svetlana Sazonova[3], Boris Kozlov[1]
[1]Cardiovascular, Research Institute for Cardiology, Tomsk, Russian Federation, [2]Atherosclerosis And Coronary Artery Disease Department, Research Institute for Cardiology, Tomsk, Russian Federation, [3]Cardiac Imaging Department, Research Institute for Cardiology, Tomsk, Russian Federation

Background and Aims : The aortic size alone is insufficient predictor of the aortic-related events. In this regard, aortic wall stiffness also need to be evaluated for clearer understanding on the contributors of aortic-related complications. We compared global circumferential strain (GCS) and global circumferential strain/pulse pressure (GCS/PP) and fraction area change (FAC) in moderated dilated and aneurysmal ascending aorta (AA).

Methods: Twenty patients were enrolled in the prospective study. Of these, 9 patients (Dilatation group) presented with AA dilatation (45-50 mm) and 11 patients (Aneurismal group) had AA aneurysm (>50 mm). Mean age of the participants was 65±9 years. All of the patients were candidates for AA surgery. Aortic wall stiffness parameters such as GCS, GCS/PP and FAC were assessed at 4 levels of the thoracic aorta by 2D speckle-tracking transesophageal echocardiography. Variables were compared using Student t-test.

Results: Mean aortic size at the mid-ascending aorta was 46.7±2.2 mm in Dilatation group and 55.6±8.5 mm ($p<0.01$) in Aneurismal group. GCS, GCS/PP and FAC were 3.9±2.8% versus 1.5±3.9% ($p=0.14$), 6.1±4.7 versus 2.6±7.8 ($p=0.26$) and 8.2±4.4% versus 5.9±2.5% ($p=0.16$) in Dilatation and Aneurismal groups, respectively.

Conclusions: Aortic wall stiffness parameters did not differ between moderate dilatation and aneurysm of the AA. According to these data, AA surgery seems to be reasonable in moderate dilatation for prevention aortic-related events. This study was supported by a grant from the Russian Science Foundation № 21-15-00160

ID:499

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

AGE-ASSOCIATED CHANGES IN THE VASCULAR WALL IN PATIENTS WITH ARTERIAL HYPERTENSION WITH SUBCLINICAL HYPOTHYROIDISM

POSTER VIEWING SESSION

Olena V. Kolesnikova, Anastasiia O. Radchenko, Olga E. Zaprovalna, Anna V. Potapenko
Department Of The Study Of Aging And Metabolic Associated Diseases, Government Institution "L. T. Mala National Institute of Therapy of the NAMS of Ukraine, Kharkiv, Ukraine

Background and Aims : Background and Aims. Subclinical hypothyroidism (SH) may affect vascular aging, especially in patients with arterial hypertension (AH). The purpose of our study was to study changes in the structure and function of arteries depending on the telomere length (TL) in patients with AH and SH.

Methods: Materials and methods. The study included 98 patients with AH and SH without clinical manifestations of cardiovascular diseases and 40 patients without SH (comparison group). We assessed the carotid intima-media thickness (CIMT), carotid-femoral pulse wave velocity (PWV), the presence of atherosclerotic plaques and TL in peripheral blood lymphocytes in all patients.

Results: Results. Vascular changes were more pronounced in patients with AH and SH. TL in these patients was shorter than in comparison group (p=0.03). Significant differences in the state of the vascular wall depending on the TL were found in patients with AH and SH, namely lower PWV (p=0.01), lower CIMT (p=0.004) in individuals with "long" telomeres compared to "short" ones. No significant differences were found in the structure of arteries between groups with "long" telomeres. However significant differences were revealed between groups with "short" telomeres in PWV (p=0.015) and CIMT (p=0.05).

Conclusions: Conclusion. Markers of vascular aging were more pronounced in patients with AH and SH. However, despite the presence of SH, vascular changes were minimal in patients with "long" telomeres and are comparable to the state of the vascular wall in healthy people. The TL may have a protective effect on the vascular wall by preventing damaging effects of metabolic factors.

ID:496

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

JENA AUF ZIEL – JAZ" - A PROSPECTIVE COHORT STUDY AIMING TO GET ALL PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION ON ESC/EAS LDL-C TARGETS

POSTER VIEWING SESSION

Umidakhon Makhmudova, Beasat Samadifar, Aurel Maloku, Pellumb Haxhikadrija, Sylvia Otto, P.Christian Schulze, Oliver Weingärtner
Internal Medicine I, Jena University Hospital, Jena, Germany

Background and Aims : Low-density lipoprotein cholesterol (LDL-C) reduction is an essential part of the 2019 ESC/EAS dyslipidemia guidelines. "Jena auf Ziel – JaZ" is the first prospective study that aims at LDL-C target attainment in all patients with ST-elevation myocardial infarction (STEMI) and determination of reasons for failed target attainment.

Methods: All patients with STEMI were started on atorvastatin 80 mg and ezetimibe 10 mg on admission. LDL-C levels were monitored during the hospital stay and a 12 months follow-up period. Patients were educated about cardiovascular risk factor optimization with attention to LDL-C target attainment and provided with individual patient cards for LDL-C level documentation.

Results: In first 52 consecutive patients, LDL-C levels were 3.39±1.23 mmol/L on admission, 1.84±0.86 mmol/L on discharge and 1.30±0.65 mmol/L during the first follow-up visit (6-8 weeks). Fourteen out of 50 patients (28%) reached the LDL-C goal on discharge, 36 out of 50 patients (72%) achieved the target after 6-8 weeks. All other patients reached the LDL-C targets after the addition of either bempedoic acid or PCSK9-inhibitors. Only two patients reported myalgias and one had elevated liver enzymes, which could be resolved after switching to a lower statin dose.

Conclusions: One out three patients with STEMI reach LDL-C target during the initial hospital stay on atorvastatin 80 mg and ezetimibe 10 mg. An addition of further lipid-lowering agents results in LDL-C goal attainment in all STEMI patients during follow-up. LDL-C target attainment is feasible and well-tolerated in empowered, well-educated patients. We highly recommend implementing this approach in patients with STEMI.

ID:495

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

IMPARED METABOLISM OF VEGF-A, HGF, IGF-1, G-CSF AND GM-CSF IN THE PROGRESSION OF OBESITY IN PATIENTS WITH GOUT

POSTER VIEWING SESSION

Tatyana A. Medvedeva[1], Marina Y. Mishko[2], Eugenia V. Radaeva[1]
[1]Therapy, City clinical hospital №40 of the Moscow Department of the health, Russia, Moscow, Russian Federation, [2]Internal Diseases, Chita State Medical Academy, () --, Russian Federation

Background and Aims : To study the plasma levels VEGF-A, HGF, IGF-1,G-CSF and GM-CSF in gouty patients with obesity and establish the relationship between arterial stiffness and circulating growth factors of new vessels.

Methods: The study involved 215 men with gout. Daily monitoring of blood pressure was carried out by the BPLab device. Vascular growth factors concentrations were measured by multiplex immunological fluorescent analysis in plasma collected from 93 men and 122 overweight and obese subjects after an overnight fast.

Results: Plasma levels of VEGF-A and IGF-1 but not HGF were elevated in group with overweight and obese subjects (p<0,001). Patients with severe obesity had elevated serum levels of HGF and VEGF, while IGF-1 was slightly increased in patients with BMI>35 kg/m2 (P=0.017). The plasma level of G-CSF, GM-CSFdid not differ between all the groups, but was slightly higher than the control group by in 1.3 times for GM-CSF in patients with obesity (p=0,002). In univariate analysis, VEGF-A had positive correlations with BMI (p<0.001), HGF (p=0.012) and IGF-1 (p=0.042). Plasma levels of HGF had correlations with VEGF-A, hsCRP (p=0,001), cystatin C (p=0,015), uric acid (p=0,024) and negatively with eGFR by CKD-EPIcreatinin-cystatinC formula (P=0.028). In a multivariate analysis between all study parametrs only HGF was independent determinant of higher PWV.

Conclusions: Increased levels of vascular growth factors are present in overweight and obese subjects and may contribute to previously increased risk of metabolic disorders in gouty subjects with obesity. Circulating levels of HGF may be a new marker of cardiovascular damage in patients with gout.

ID:480

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

ANTIBODIES TO HERPES SIMPLEX VIRUS TYPE 1 IN PATIENTS WITH CORONARY HEART DISEASE

POSTER VIEWING SESSION

Yulia Kotova
Polyclinic Therapy, Voronezh state medical university named after N.N. Burdenko, Voronezh, Russian Federation

Background and Aims : Atherosclerosis is a chronic inflammatory disease and metabolic disorder that can manifest itself as myocardial infarction (MI), ischemic stroke (AI) or other conditions caused by artery stenosis. Despite significant advances in prevention and treatment, coronary heart disease (CHD) remain the leading causes of morbidity worldwide, accounting for about a third of all deaths. **The aim of the study is** to determine antibodies to herpes virus 1 (HSV-1) in patients with CHD who have undergone MI as a possible marker of the course of the disease.

Methods: The study involved 76 patients with diagnosis of coronary heart disease. The patients were divided into 2 groups: group 1 - 42 patients with MI, group 2 - 34 patients without MI. The level of IgG HSV-1 antibodies was measured using commercial ELISA kit. Antibody levels were expressed as antibody concentration indices (antibody index = sample optical density/cut-off average serum optical density).

Results: In the group of patients who underwent MI, we noted higher values of IgG antibodies: their level was 9.5 [7.7; 13.1]. In the group of patients without MI, the level of antibodies was 8.2 [5.2; 10.2]. A significant difference was determined between the groups. (p=0.002). During the correlation analysis, statistically significant indicators were established between IgG antibodies and the level of troponin I (r=0.657, p=0.001), CPK-MV (r=0.461, p=0.003), as well as total cholesterol (r=0.362 p=0.001) and LDL cholesterol (r=0.412 p=0.0001).

Conclusions: We came to the conclusion that HSV-1 may play a role in the development of atherosclerosis, which requires further careful study.

ID:474

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

THE ASSOCIATION BETWEEN GENETIC MARKERS FROM GWAS AND ESSENTIAL HYPERTENSION IN A CASE-CONTROL STUDY (SIBERIAN POPULATION)

POSTER VIEWING SESSION

Ekaterina V. Mazdorova, Andrew Ryabikov, Vladimir N. Maximov, Pavel S. Orlov, Sofia Malyutina
Laboratory Of Internal Medicine, Institute of Internal and Preventive Medicine - Branch of Institute of Cytology and Genetics SB RAS, Novosibirsk, Russian Federation

Background and Aims : Hypertension is a major risk factor for atherosclerosis-related cardiovascular diseases (ACVD) and a multifactorial condition with genetic susceptibility. In a case-control study we investigated the association between essential hypertension (HT) and blood pressure (BP) and a number of single nucleotide polymorphisms (SNPs) identified in GWAS.

Methods: In a case-control design we recruited the samples of hypertensives and normotensives (n=514, men/women, 45-69, Novosibirsk population). We assessed the association of HT and BP phenotypes with 16 SNPs (rs11646213, rs17367504, rs11191548, rs12946454, rs16998073, rs1530440, rs653178, rs1378942, rs1004467, rs381815, rs2681492, rs2681472, rs3184504, rs2384550, rs6495122, rs6773957).

Results: Among tested SNPs, rs1378942 (cytoplasmic tyrosine kinase; CSK), was associated with HT (p=0.030) and DBP (p=0.042, women); in heterozygous OR for HT was 1.65 (p=0.013) independent from age- and sex and modulated by body mass index (BMI). AA genotype was protective against HT (OR = 0.62; p=0.027). Rs653178 (ataxin2; ATXN2) was associated with HT (GG vs. AA/AG; OR=0.61; p=0.022) regardless of age and BMI, this association was realized by impact from men (p=0.027). Rs6773957 (adiponectin; ADIPOQ) was related to HT in women (GG vs. AA/AG; OR=0.29 p=0.001) regardless of age. Rs 2384550 (T-box transcription factor 3; TBX3) was related to SBP in men (p=0,043).

Conclusions: In case-control sample in Novosibirsk we found the association between 4 SNPs (rs1378942, rs653178, rs6773957, rs2384550) and HT or BP phenotypes with context-dependency on sex. These replications in newly studied Caucasian population support the search of genetic variation at identified or close loci in relation to mechanisms of HT susceptibility. Supported RAS (AAAA-A17-117112850280-2).

ID:470

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

ELUCIDATING THE DIFFERENTIAL EFFECTS OF STATINS ON METABOLISM IN PANCREATIC B-CELLS CULTURED UNDER HIGH AND LOW GLUCOSE

POSTER VIEWING SESSION

James A. Hamilton[1], Abhi Shah[2], Grace D. Tasik[2], Keanu Sao[2], Sunni C. Lin[3], Nasi Huang[1], Barbara Corkey[2], Jude Deeney[2], David P. Hajjar[4], Antonio M. Gotto[5], Craig Sponseller[6]
[1]Physiology And Biophysics, Boston University School of Medicine, Boston, United States of America, [2]Endocrinology - Diabetes & Nutrition, Boston University School of Medicine, Boston, United States of America, [3]Biomedical Engineering, Boston University College of Engineering, Boston, United States of America, [4]Pathology, Weill Cornel Medicine, New York, United States of America, [5]Pathology, Weill Cornell Medicine, New York, United States of America, [6]Chief Medical Officer, Kowa Pharmaceuticals America - Inc., Montgomery, United States of America

Background and Aims : Statins are effective for lipid lowering, but some statins increase risk for early onset of type 2 diabetes (T2D). Continuing reports with this conclusion have led to uncertainty among clinicians about discontinuing or limiting statin therapy. In this study, we extended our β-cell studies to further elucidate differences between simvastatin (SVA) and pitavastatin (PVA) based on quantitative measurements of glucose-induced insulin secretion (GSIS).

Methods: Clonal pancreatic β-cells were chronically cultured at low glucose (4G, mM) and exposed to SVA and PVA at a physiologically relevant concentration (**50 nM**). We compared GSIS in the cells after exposure to the statins for 10 and 17 days at acute exposure to different glucose concentrations. Insulin secretion and content were measured using immunoassays, and intracellular Ca2+ oscillations were measured using Ca2+ indicator fura-2.

Results: SVA, but not PVA, increased insulin secretion after a 10-day incubation at both basal (**3 mM**) and high glucose (**12 mM**) (**Fig 1**). After extending the incubation time to 17 days, SVA but not PVA caused basal hypersecretion in cells at basal glucose (**3 mM**) and impairment of GSIS at high glucose (**Fig 2**). PVA-treated cells did not increase insulin secretion at low concentration but showed reduced GSIS at high glucose.

Conclusions: The left-shift glucose influx caused by SVA correlates with the calcium left-shift in **Fig 3**. Thus, an important difference between pitavastatin and simvastatin could be attributed to differences in calcium influx into INS-1 cells, a possible cellular mechanism for the clinical observations that certain statins increase pre-diabetes.

Figure 1. Percent insulin released from INS-1 cells chronically cultured with 4G and 50 nM statin for 10 days after correction for insulin content. Simvastatin, but not pitavastatin, caused an increase in percent insulin release in cells acutely exposed to **12 mM** glucose. Cells acutely exposed to **3 mM** glucose were not affected by either statin.

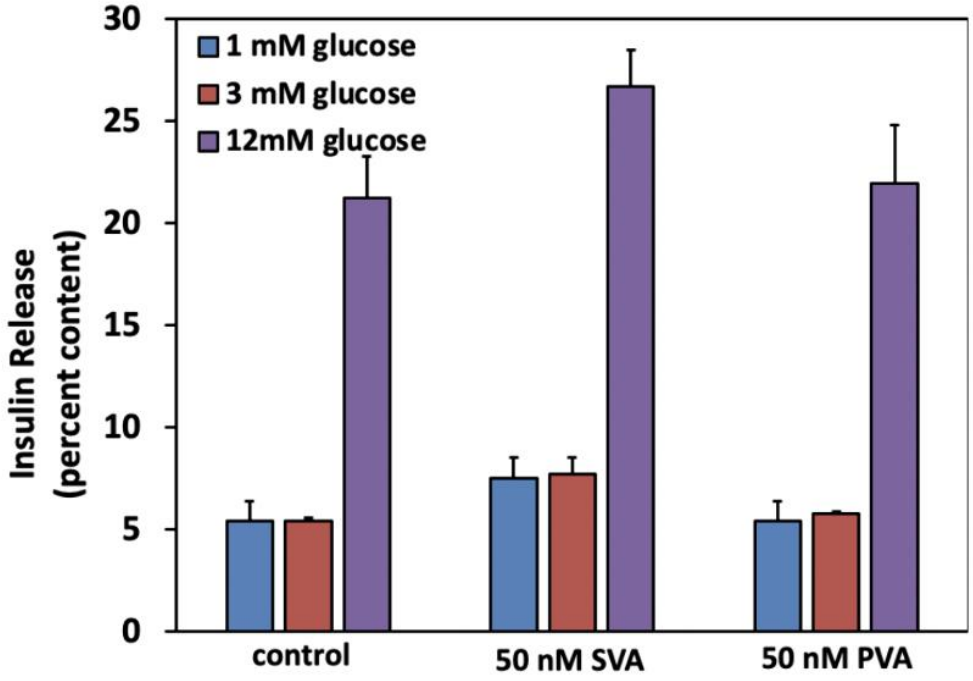


Figure 2. Insulin secreted from INS-1 cells chronically cultured with 4G and 50 nM statin for 17 days. Simvastatin, but not pitavastatin, caused hypersecretion at **3 m M** glucose.

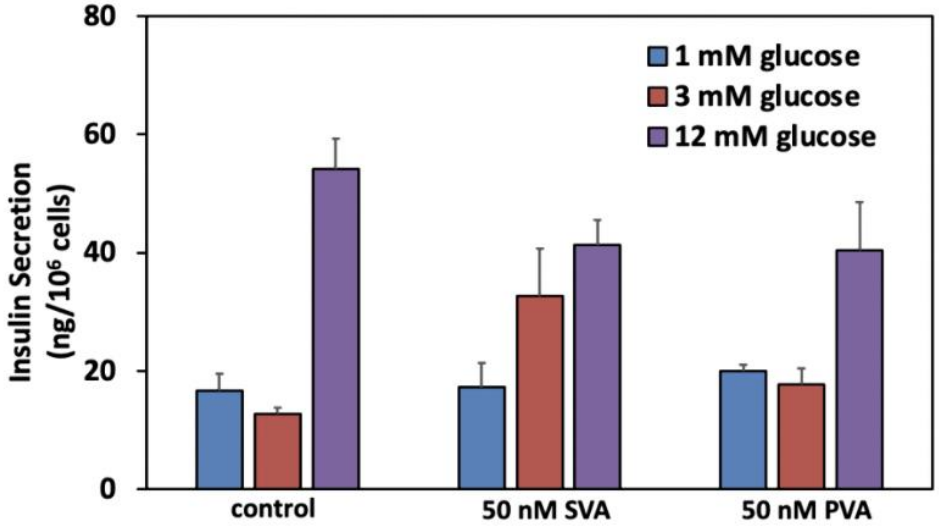
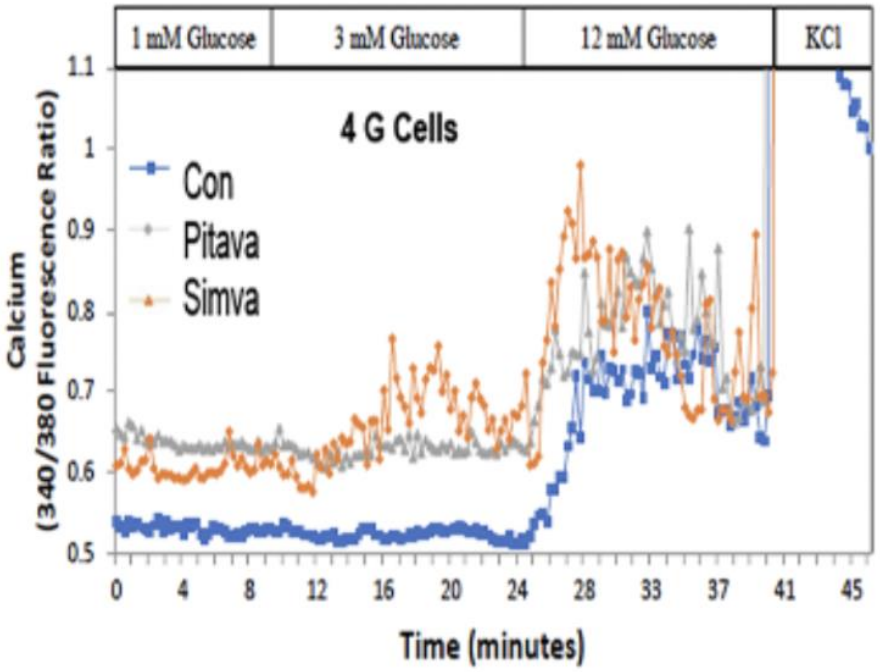


Fig 3. Simvastatin left-shifted glucose-induced Ca^{2+} influx in ß-cells cultured at low glucose (4 mM) and acutely exposed to 3 mM glucose. Simvastatin increased glucose secretion from cells at **3 mM** glucose, while pitavastatin did not have this effect.



ID:468

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

THE RELATIONSHIP BETWEEN EPIGENETIC AGE AND MYOCARDIAL INFARCTION IN A POPULATION BASED CASE-CONTROL STUDY

POSTER VIEWING SESSION

Sofia Malyutina[1], Olga Chervova[2], Taavi Tillmann[3], Vladimir N. Maksimov[4], Valery Gafarov[5], Andrew Ryabikov[1], Jaroslav Hubacek[6], Hynek Pikhart[7], Stephan Beck[2], Martin Bobak[7]
[1]Laboratory Of Internal Medicine, Institute of Internal and Preventive Medicine - Branch of Institute of Cytology and Genetics SB RAS, Novosibirsk, Russian Federation, [2]Ucl Cancer Institute, University College London, London, United Kingdom, [3]Institute For Global Health, University College London, London, United Kingdom, [4]Laboratory Of Molecular Genetic Investigation Of Internal Diseases, Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics, Novosibirsk, Russian Federation, [5]Collaborative Laboratory Of Cardiovascular Diseases Epidemiology, Institute of Internal and Preventive Medicine – branch of Institute of Cytology and Genetics RAS, Novosibirsk, Russian Federation, [6]Experimental Medicine Centre, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [7]Institute Of Epidemiology And Health Care, University College London, London, United Kingdom

Background and Aims : Epigenetic modifications such as DNA methylation (DNAm) have been shown to be the most accurate molecular readout of ageing. We investigated the relationship between ‘epigenetic age’ (EA) derived from DNAm and myocardial infarction (MI) /acute coronary syndrome (ACS).

Methods: A random population sample was examined in 2003/2005 (n=9360, 45–69, HAPIEE project) and followed up for 15 years. From this cohort, incident MI/ACS (cases, n=129) and age- and sex-stratified controls (n=177) were selected for a nested case-control study. Baseline EA (Horvath, Hannum, PhenoAge, Skin and Blood) and the differences between EA and chronological age (CA) were calculated (ΔDAHr, ΔAHn, ΔAPh, ΔASB).

Results: EA by Horvath’s, Hannum’s, Skin and Blood were close to CA (median absolute difference, MAD, of 1.08, -1.91 and -2.03 years); PhenoAge has MAD -9.29 years vs CA. The age-sex-adjusted odds ratios (ORs) of MI/ACS for highest vs. lowest tertile of ΔAHr and ΔAHn were 1.14 (95% CI 0.59–2.22) and 1.26 (0.61–2.60). For ΔAPh, the corresponding ORs were 2.09 (1.11–3.94) independent of age and 1.84 (0.99–3.52) independent of age and sex; this association was partly explained by smoking and metabolic factors. There was no association with ΔASB.

Conclusions: In conclusion, this case-control study nested in a prospective population-based cohort found a borderline association between accelerated epigenetic age and increased risk of MI/ACS. Supported by clinical data and in silico analysis, metabolic modulation may be the likely mechanism of this association. Supported by RSF (20-15-00371); WT (064947, 106554/Z/14/Z); NIA (1RO1AG23522).

ID:467

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

RELATIONSHIP BETWEEN LOW DENSITY LIPOPROTEIN CHOLESTEROL AND LEFT VENTRICULAR HYPERTROPHY IN PATIENTS WITH ARTERIAL HYPERTENSION

POSTER VIEWING SESSION

Olha M. Chernatska
Internal Medicine, Sumy State University, Sumy, Ukraine

Background and Aims : Aim is the determination of the relationship between low density lipoprotein cholesterol and left ventricular mass index in patients with arterial hypertension (AH).

Methods: We examined 25 patients with AH. Their middle age is 65 years old. The systolic blood pressure was 153,9 ± 0,43 mmHg, diastolic – 101,1 ± 0,02 mmHg, duration of AH – 9 years. The lipid profile was determined by biochemical method. The level of low density lipoprotein cholesterol (LDL-CH) was 2,78 ± 0,02 mmol/l. All patients were analyzed using M-Mode echocardiography with determination of ejection fraction (EF), left ventricular posterior wall thickness (LVPW), intraventricular septal wall thickness (IVST) wall thickness, internal wall thickness (IWT) and left ventricular mass index (LVMI), calculated by ASE formula.The results were analyzed statistically by Microsoft Excel with using of Pearson criteria for observation of relationship between indicators.

Results: The relationship between low density lipoprotein cholesterol and echocardiography data

Indicators
LDL-CH and EF
LDL-CH and LV PW
LDL-CH and IV ST
LDL-CH and LVMI
LDL-CH and LV IWT

Conclusions: The positive correlation between low density lipoprotein cholesterol and left ventricular mass index in hypertensive patients is associated with significant role of lipid profile disorders in left ventricular hypertrophy progression.

ID:461

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

A NEW ANIMAL FEMORAL ARTERY MODEL OF LOCALIZED INTERMEDIATE STAGE OF ATHEROSCLEROSIS USING FOCUSED ULTRASOUND- MEDIATED INERTIAL CAVITATION-INDUCED INJURY AND HIGH- CHOLESTEROL DIET INJURY

POSTER VIEWING SESSION

Hossein Mehrad[1,2]
[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims : The use of animal models in atherosclerotic lesions has improved our understanding of atherosclerosis pathophysiology. We sought to develop an easily reproducible and inexpensive experimental rabbit femoral artery model of intermediate stage atherosclerosis with moderate stenosis (< 40%).

Methods: Intermediate stage atherosclerosis was induced at the right femoral artery in White New Zealand rabbits using B- mode ultrasound- guided extracorporeal high intensity pulsed focused ultrasound (F= 750 KHz, I= 120 W/cm^2)- mediated cavitation- induced injury combined with a 1% cholesterol-rich diet injury in five weeks. Ultrasonography and histopathology was evaluated after five weeks.

Results: Histopathologic evaluation revealed progressive smooth muscle cells and extracellular lipid droplets proliferation in the intimal layer, resulting in the formation of intermediate stage of atherosclerosis. Percentage of luminal- cross sectional area of stenosis was 34 ± 5.31 compared with the other groups ($P < 0.05$). Results from ultrasonography and histopathology showed a significant increase in the mean value for arterial Wall Thickness (WT),Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Mean Velocity (MV), Resistance Index (RI), Pulsatility Index (PI) and significant reduction in the mean value for arterial Lumen Diameter (LD), blood Volume Flow (VF) at the stenotic region in the atherosclerotic group compared with the other groups ($p < 0.05$).

Conclusions: We successfully produced an easily reproducible and inexpensive experimental rabbit femoral artery model of intermediate stage atherosclerosis with moderate stenosis using B- mode ultrasound- guided high intensity pulsed focused ultrasound, similar to the condition seen in human subjects. This condition in rabbits can be properly assessed by ultrasonography.

ID:405

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-11 Plaque remodelling*

SUBCLINICAL CAROTID ATHEROSCLEROSIS IN THE CONDITIONS OF ROTATIONAL SHIFT WORK IN THE ARCTIC: DATA OF PREVENTIVE EXAMINATION

POSTER VIEWING SESSION

Nina P. Shurkevich, Alexander Vetoshkin, Lyudmila Gapon, Ani Simonyan, Maria Kareva
Department Of Arterial Hypertension And Coronary Insufficiency, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Science, Tomsk, Tyumen, Russia, Russian Federation

Background and Aims : To study subclinical carotid atherosclerosis (SCA) in the relationship of EchoCG, treadmill test (TT), ABPM results

Methods: In Yamburg polar settlement (68 N) 743 males (M) and 213 females (F) with mean age of 49.9±7.6 years (p=0.709) with arterial hypertension (400 individuals), office blood pressure (BP) 145.9±10.0/94.9±6.9 mmHg in M and F (p=0.224/0.587) and normotensive individuals were examined.

Results: SCA in CA in M were associated with age (p<0.01), years of rotational shift work (p<0.01), left ventricular (LV) remodeling (p<0.01), type of daily BP profile (p<0.01); in W - with age (15.6%). In M AP were more often located in CA (p=0.0001). ABPM determined normotension in 34.9% of M and 42.1% of F (p=0.208). SCA were detected in M with daily BP profile "non dipper" and "night peaker". While concentric hypertrophy (p=0.0001) and concentric LV remodeling in M (p=0.046). SCA were registered more often in individuals with concentric LV hypertrophy regardless of BP level. Negative TT was obtained in 82.6% of M and 87.2% of F (p=0.393). In 79.5% of M with SCA there was revealed negative TT, in 10.6% - doubtful, in 9.9% - positive.

Conclusions: Under the conditions of rotational shift work in the Arctic, subclinical carotid atherosclerosis was detected twice more often in M compared to F. It was equally dependent on age, years of rotational shift work, daily BP profile,and to a lesser extent on office and average daily BP. It correlated with concentric hypertrophy and concentric LV remodeling in M and was associated with negative treadmill test result.

ID:454

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-10 Clonal Haematopoiesis*

DEPICTION OF SOMATIC STRUCTURAL VARIATIONS IN ATHEROSCLEROTIC PLAQUE THROUGH WHOLE-EXOME SEQUENCING

POSTER VIEWING SESSION

Alexei A. Sleptcov, Alexei Zarubin, Maria Nazarenko
Research Institute Of Medical Genetics, Tomsk National Research Medical Center of Russian Academy of Sciences, Tomsk, Russian Federation

Background and Aims : Studies of DNA damage and mutagenesis in atherosclerotic lesions have provided primary evidence for a role for somatic mutations in atherogenesis. The present study aims for somatic events by comparing blood and atherosclerotic plaques from the same patients using whole-exome sequencing.

Methods: An advanced carotid atherosclerotic plaque and white blood cells were collected simultaneously from each patient (eight Slavic males, aged 67 ± 3.8 years [mean ± SD]) to assess the spectrum of germline and somatic genetic variants. Exome sequencing of DNA from the samples was performed with the SureSelect Clinical Research Exome Enrichment Kit (Agilent Technologies) and HiSeq 1500 (Illumina). Our collected data of WES available in NCBI BioProject PRJNA758796. The search for somatic single nucleotide variants (SNV) and indels was performed using GATK, VarScan, Strelka, MuTect2, and IGV tools.

Results: It has been identified that, on average, 56 somatic events occur in a human atherosclerotic plaque. A total of 449 SNVs / indels were identified in exomes, of which 3 somatic variants were shared at most between two individuals. Most of the somatic variants are SNVs (98%). Somatic loss of function mutations, an average of 3.6 in patients, was found.

Conclusions: In the present study, many somatic events have been identified that indicate the features of such events, mainly, similarly to neoplastic processes, different from person to person, and some of the events may lead to, some emanate from atherogenesis. Nevertheless, our data indicate the potential for detecting the most common somatic variants in atherosclerosis in studies using larger cohorts.

ID:453

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MEDICAL CARE TO PATIENTS WITH ACUTE MYOCARDIAL INFARCTION DURING COVID-19 PANDEMIC

POSTER VIEWING SESSION

Natalia A. Koriagina, Vladimir S. Koriagin, Kirill V. Prokhorov, Grigorii N. Spasenkov
Polyclinic Department, Perm state medical university, Perm, Russian Federation

Background and Aims : The aim of the study is to determine there are delays in the provision of medical services for acute myocardial infarction during the COVID-19 pandemic compared to the same period in 2019.

Methods: In this one-center retrospective study, we evaluated patients admitted with ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI) during the COVID-19 pandemic (10/01/2020 - 11/30/2020) versus patients admitted in the same period a year earlier.

Results: 30 and 62 patients presented with STEMI in 2020 and 2019. The median pain-to-door delivery time was significantly longer during the pandemic (1885 (880, 5732) vs 606 (388, 944) min, $p<0.0001$). In 2020, there was a significant delay in door-to-door reperfusion time, 332 (182, 581) vs 194 (92, 329) min ($p=0.0371$). There were 24 (80%) and 25 (42%) patients who presented 12 hours after the onset of pain in the pandemic and pre-pandemic eras ($p=0.0006$). There were 47 and 60 patients with NSTEMI during the pandemic and before the pandemic, respectively. The average delivery time from pain to door during a pandemic is longer (620 (255, 1500) vs 349 (146, 659) min, $p=0.0141$). There were 22 (47%) and 14 (24%) patients. who turned 12 hours after the onset of pain in the pandemic and pre-pandemic eras ($p=0.0127$). There was no significant delay in door-to-reperfusion time ($p=0.9833$).

Conclusions: patients waited significantly longer during the pandemic to seek medical attention. There is a 3-fold increase in the time from the onset of symptoms to revascularization.

ID:452

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CHARACTERISTIC OF PATIENTS WITH COVID-19 AND MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Natalia A. Koriagina, Vladimir S. Koriagin, Kirill V. Prokhorov, Grigorii N. Spasenkov
Polyclinic Department, Perm state medical university, Perm, Russian Federation

Background and Aims : Limited information is available on the clinical characteristics and outcomes of SARS-CoV-2 (COVID-19) patients with acute myocardial infarction.

Methods: In a one-center retrospective study, we examined a group of patients with acute myocardial infarction and COVID-19 who were admitted to the vascular center from October 01, 2020 to November 30, 2020. A total of 28 patients, 19 (67.8%) men, average age 65 [58, 71] years. There was a high burden of comorbidities, atrial fibrillation in 42%, and diabetes mellitus in 56%.

Results: All patients with myocardial infarction and COVID-19 had pneumonia with 50-75% lung involvement. During hospitalization, 14 (50%) developed acute respiratory distress syndrome, and 8 (28%) required mechanical ventilation. 23 (82%) patients received primary percutaneous coronary intervention (PCI), and 4 (14.2%) received fibrinolytic therapy. 8 (28%) patients required cardiac resuscitation during hospitalization, and 6 (21.4%) died. In 3 (75%), initially receiving fibrinolytic therapy, fibrinolysis was successful. Stent thrombosis occurred in 8 (34.7%) patients after PCI.

Conclusions: We analyzed a series of COVID-19 infections in patients with myocardial infarction. Found a high incidence of stent thrombosis, which indicates a possible need to adapt the treatment of acute myocardial infarction in patients with COVID-19. Every fifth patient with COVID-19 in combination with myocardial infarction died in a hospital.

ID:441

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

C-13 NMR SPECTROSCOPIC CHARACTERIZATION AND DISTINCTION OF EPA AND DHA IN LIPID EMULSIONS

POSTER VIEWING SESSION

James A. Hamilton[1], Nasi Huang[1], Jesse Ng[1], Troy Gubler[2], Raisa Khuda[3], Richard J. Deckelbaum[4], Chuchun L. Chang[4]
[1]Physiology And Biophysics, Boston University School of Medicine, Boston, United States of America, [2]Nutrition & Metabolism, Boston University School of Medicine, Boston, United States of America, [3]Sargent College Of Health & Rehabilitation Sciences, Boston University, Boston, United States of America, [4]Pediatrics, Columbia University Irving Medical Center, New York, United States of America

Background and Aims : Omega-3 polyunsaturated fatty acids (n-3 PUFA) in fish oils (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA) are metabolized to molecules (resolvins) that mitigate high chronic systemic inflammation. Supplementation of dietary sources with n-3 PUFA fish oil capsules has been shown to decrease risk of CVD and MI, but there is considerable disagreement regarding whether EPA alone is more effective than DHA or a combination of both EPA and DHA.

Methods: We obtained natural abundance spectra at 38°C of aqueous dispersions of phospholipids and triglycerides with omega-3 fatty acid chains (tri-EPA, and tri-DHA). Peak linewidths, intensities, and chemical shifts were compared for samples prepared by sonication of egg PC with 0-40 mol% of tri-EPA, tri-DHA, or triglyceride mixtures.

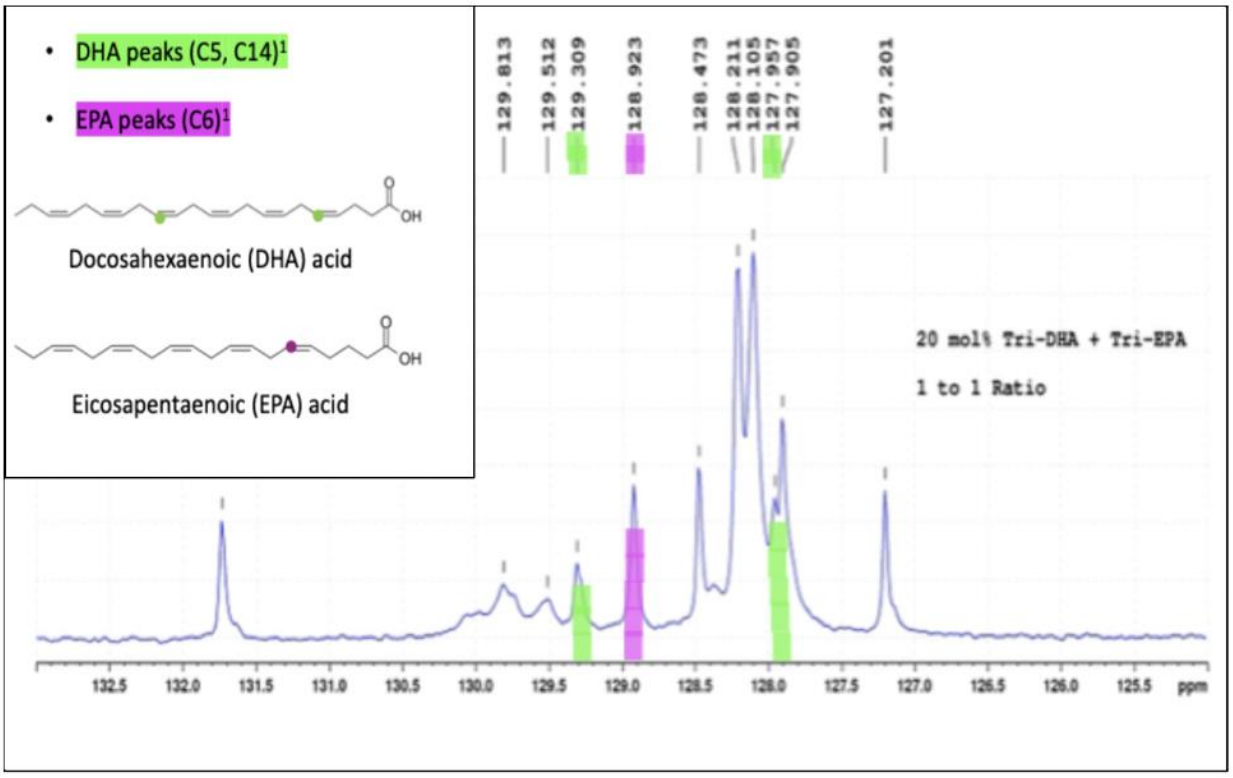
Results: C-13 NMR characterized the physical state and fluidity of the n-PUFA in both environments. Tri-DHA and tri-EPA were incorporated into the phospholipid membrane without altering the bilayer structure or mobility, and formed emulsion droplets when bilayer incorporation was exceeded. DHA and EPA were identified by unique chemical shifts (Fig 1).

Conclusions: We have shown that C-13 NMR of the lipid dispersions provides biophysical characterizations of emulsions that will aid designing and optimizing acute therapy. The spectra exhibited narrow, well-resolved peaks representing all carbons in the constituent lipids. For future therapeutic applications, the olefinic spectral region can reliably identify EPA and DHA and monitor their entry into cells and their local fluidity. Optimizing the ratio of EPA to DHA could increase the potency for healing acute ischemic damage from stroke, CVD, and

MI.

Figure 1. Detailed Olefinic Spectral Region Expanded

Figure 1 shows the expanded olefinic region in the NMR spectrum with exceptional details because of the narrow line widths. Chemical shift analysis revealed a unique peak at 128.923 ppm for EPA and two unique peaks for DHA (129.309 and 127.957). These peaks serve as markers for the presence of the specific fatty acid and will allow differentiation of fatty acids in emulsions consisting of EPA and DHA.



ID:435

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-09 Epidemiology of socioeconomic and psychosocial risk factors*

SOME SOCIAL AND CLINICAL CHARACTERISTICS OF PATIENTS ON IPCSK9 THERAPY IN KARELIA REPUBLIC

POSTER VIEWING SESSION

Victoria A. Korneva, Tatiana Kuznetsova, Natalya Vezikova
Faculty Therapy, Petrozavodsk State University, PETROZAVODSK, Russian Federation

Background and Aims : to evaluate some characteristics in patients, who received iPCSK9 in Karelia Republic

Methods: we analyzed the data from Karelian registry about 55 patients, who received iPCSK9 (28 alirocumab, 27 evolocumab). We had developed special questionnaire, it included age, gender, smoking, diabetes mellitus, body mass index (BMI), lipid profile before and after treatment, data about education, marital status, adherence to therapy. Mean age of patients was 46.3±2.7 y.o., 65% male, 47 patients had ischemic heart disease, 32 patients had myocardial infarction, 25 had revascularization procedures.

Results: Eleven (20%) patients younger 40 y.o., 14 (25%) patients older 60 y.o., 39 (71%) patients had high education; 47 (85.7%) patients lived in the city. More often specialties: 21 (38%) engineer, 6 (11%) has medical education, 5 (9%) teachers. Five (9%) patients live in own house, 3 (5.5%) rent a flat, and others 47 (85.7%) lives in own flats, 49 (89% patients) did not smoke, 8 (14%) patients had diabetes mellitus, 13 (24%) patients had BMI 25-29.9 kg/m2, 14 (25.4%) had obesity. It was 45 (82%) patients, who had achieved the target LDL-cholesterol level. Adherence to statin therapy was 3.5±0.3 balls and adherence to iPCSK9 was 3.99±0.01, it did not depend on availability of cardiovascular disease and age.

Conclusions: Patients who received iPCSK9 in Karelia characterized by high education (85.7%), living on own flats (87.5%), 89% of them did not smoke. Adherence to iPCSK9 was higher than to statin and did not depend on availability of cardiovascular disease and age.

ID:434

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

THE REAL EXPERIENCE OF REACHING AN EXTREMELY LOW LDL-C LEVEL IN HIGH RISK PATIENTS

POSTER VIEWING SESSION

Victoria A. Korneva, Tatiana Kuznetsova
Faculty Therapy, Petrozavodsk State University, PETROZAVODSK, Russian Federation

Background and Aims : to evaluate the safety of extremely low LDL-C (low density cholesterol) concentration on iPCSK9 therapy.

Methods: we investigated 64 patients (32 with alirocumab, 32 evolocumab), mean age 46.1, male 39 (61%). All patients were in very high risk group (88% with coronary heart disease, 53% with familial hypercholesterolemia (FH)). The main indications for iPCSK9 therapy were inefficiency of target LDL-C achievement by standard hypolipidemic therapy (56%), statin intolerance (36%) and high Lp(a) level (9.4%). We performed clinical examination, ECG, lipid spectrum and coagulation activity every three months in the first year of therapy and one time per six months later. We performed mini-cog test before and every year on iPCSK9 therapy. Observation period was three years.

Results: Target LDL-C levels were achieved in 82.8% patients (in FH in 62%). The mean LDL-C concentration had changed on iPCSK9 therapy from 3.9±0.05 to 1.68±0.03 mmol/L. LDL-C less than one mmol/L was in 10.9% patients, and less than 0.5 mmol/L in 7.8% patients. Two patients had LDL-C concentration ≤ 0.3 mmol/L, in one of them 0.1 mmol/L. We did not find the destabilization of coronary artery disease or new ischemic and hemorrhagic stroke in patients during this period, including patients with LDL-C less than 0.3 mmol/L. The results of mini–cog test did not differ significantly in patients with different achieved LDL-level, there was not impair of it results on iPCSK9 therapy.

Conclusions: extremely low LDL-C concentration on iPCSK9 therapy was in 10.9% patients, it was safely during three years follow up

ID:432

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

EFFICACY OF A MULTISPECIALTY, MULTIDISCIPLINARY STRATEGY TO IMPROVE THE LEVEL OF AWARENESS AND CONTROL OF CARDIOVASCULAR RISK FACTORS AFTER LIVER TRANSPLANTATION

POSTER VIEWING SESSION

Clara Viñals[1], Lydia Sastre[2,3], Raquel Garcia[2], Antonio J. Amor[1], Gema Yago[1], Alicia Hervas[2], Lorena Sanchez[1], Joan Trabal[1], Judit Molero[1], Laia Escude[2], Giulia Pagano[2], Miqual Blasco[4], Rosa Gelabert[5], Pablo Ruiz[2,6,7], Jordi Colmenero[2,6,7,8], Miquel Navasa[2,6,7,8], Gonzalo Crespo[2,6,7,8], Emilio Ortega[1,6,9]
[1]Endocrinology And Nutrition, Hospital Clínic Barcelona, Barcelona, Spain, [2]Liver Transplant And Hepatology Unit, Hospital Clínic de Barcelona, Barcelona, Spain, [3]Gastroenterology And Hepatology, Hospital Son Espases, Palma de Mallorca, Spain, [4]Nephrology, Hospital Clínic Barcelona, Barcelona, Spain, [5]Radiology, Hospital Clínic Barcelona, Barcelona, Spain, [6]Idibaps, Institut d'Investigacions Biomèdiques August Pi I Sunyer, Barcelona, Spain, [7]Cibrehd, Centro de Investigación Biomédica en Red-Enfermedades Hepáticas y Digestivas, Madrid, Spain, [8]Ub, Universitat de Barcelona, Barcelona, Spain, [9]Ciberobn, Centro de Investigación Biomédica en Red-Fisiopatología de la Obesidad y Nutrición, Madrid, Spain

Background and Aims : Although liver transplant (LT) recipients are at high cardiovascular risk, the management of cardiovascular risk factors (CVRF) after LT is far from optimal. We designed a multi-professional, multidisciplinary protocol to improve our grade of awareness and control of CVRF after LT.

Methods: A multidisciplinary protocol was developed in 2017 to standardize the risk stratification, CVRF management and targets of therapy during the first post-LT year. The post-intervention cohort consisted in patients who underwent LT between 2018-2020(n=150). The grade of awareness and control of CVRF 12 months after LT were compared to those of patients who underwent LT between July 2015 and December 2016 (control cohort,n=100).

Results: Before LT, the prevalence of NASH as the indication of LT and the presence of obesity were significantly higher in the post-intervention cohort, while the prevalence of other CVRF and renal dysfunction tended to be higher. Twelve months after LT, the proportion of patients with measured blood pressure (88%vs.56%), HbA1C (96%vs.72%) and HDL/LDL-cholesterol (67%vs.33%) was higher in the post-intervention than in the control cohort (all p<0.001). In addition, blood pressure and HbA1c were at target levels in more individuals with hypertension (64%vs.36%, p=0.02) and diabetes (85%vs.70%, p=0.01) in the post-intervention than in the control cohort. Total cholesterol levels in patients with dyslipidemia were lower in the post-intervention (184[160-210])mg/dl than in the control cohort (212[186-240]),p=0.02.

Conclusions: A multidisciplinary, multi-professional strategy can achieve higher awareness and better control of post-LT CVRF despite a worse metabolic profile of LT recipients and may result in improved long-term outcomes.

ID:417

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

URINARY EXTRACELLULAR VESICLES SHOW EARLY CARDIORENAL RISK WITHIN THE STRATIFIED NORMOALBUMINURIA CONDITION

POSTER VIEWING SESSION

Miriam Anfaiha Sánchez[1], Aranzazu Santiago-Hernandez[1], Juan A. Lopez[2], Fernando De La Cuesta[3], Ariadna Martin-Blazquez[1], Jesus Vazquez[2], Gema Ruiz-Hurtado[4], Maria G Barderas[5], Julian Segura[4], Luis M. Ruilope[4], Marta Martin-Lorenzo[1], Gloria Alvarez-Llamas[1]
[1]Immunology, FIIS- Fundación Jiménez Díaz, Madrid, Spain, [2]Cardiovascular Proteomics, CNIC, Madrid, Spain, [3]Pharmacology And Therapeutics, Autónoma University, Madrid, Spain, [4]Cardiorenal Translational Laboratory, Hospital 12 de Octubre, Madrid, Spain, [5]Vascular Physiopathology, Hospital Nacional de Parapléjicos, Toledo, Spain

Background and Aims : High albuminuria is an indicator of cardiovascular risk. Despite clinical evidences of early cardiorenal risk in normoalbuminuric subjects (ACR<30mg/g), they are out of therapy targets. By stratifying the normoalbuminuria condition, we aimed to identify alterations in urinary extracellular vesicles (uEVs) which may aid in assessing individual cardiovascular risk while revealing pathophysiological processes behind early albuminuria development.

Methods: Hypertensive patients under RAS suppression were classified based on their ACR values as control (C) (ACR <10 mg/g) and High-normal (HN) (ACR =10-30 mg/g) (n=10). uEVs were isolated by ultracentrifugation and characterized by Western blot, nanoparticle tracking analysis and electron microscopy. uEVs proteins involved in albuminuria development were analyzed by isobaric-labeling (TMT) and liquid chromatography with mass spectrometry. Systems biology analysis was carried out, coordinated protein responses were evaluated and functional categories were identified, being considered significant if p-value<0.05. Protein variations here identified in uEVs were compared with previous data from our laboratory when analyzed in urine from the same cohort [Santiago-Hernandez A, et al. 10.1097/HJH.0000000000002936].

Results: A total of 6275 proteins and 3204 functional categories were identified, from which 480 and 263 varied significantly in HN vs. C, respectively. A subset of 49 exosomal proteins, previously detected in urine but without showing a differential profile, showed significantly altered abundance in uEVs from HN subjects reflecting altered homeostasis, coagulation cascade and lipids metabolism together with tubular and glomerular damage.

Conclusions: uEVs evidenced early cardiorenal damage within the normoalbuminuria condition, paving the way towards a personalized medicine in the control of cardiovascular risk.

ID:412

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-02 Smooth muscle cell biology*

PROTEIN ALTERATIONS IN VSMCS REVEAL A DEFECTIVE REPAIRMENT CAPACITY IN THORACIC AORTIC ANEURYSM ASSOCIATED TO BAV

POSTER VIEWING SESSION

Ariadna Martin-Blazquez[1], Marta Martin-Lorenzo[1], Aranzazu Santiago-Hernandez[1], Juan A. Lopez[2], Angeles Heredero[3], Alicia Donado[3], Miriam Anfaiha Sánchez[1], Vanesa Esteban[1], Jesus Vazquez[2], Gonzalo Aldamiz-Echevarria[3], Gloria Alvarez-Llamas[1]
[1]Immunology, IIS-Fundacion Jimenez Diaz, Madrid, Spain, [2]Cardiovascular Proteomics, CNIC, Madrid, Spain, [3]Cardiac Surgery, Fundación Jiménez Díaz, Madrid, Spain

Background and Aims : Thoracic aortic aneurysm (TAA) is caused by the progressive dilatation of the aortic wall. Its prevalence is significantly higher in subjects with bicuspid aortic valve (BAV) for unknown reasons. Considering that vascular smooth muscle cells (VSMCs) are essential for maintenance of the aortic wall structural integrity, we aimed to identify pathophysiological changes occurring in VSMCs from TAA subjects with BAV.

Methods: VSMCs were isolated of aortic tissue from 9 TAA subjects. A minimum of $8x10^6$ cells from tricuspid aortic valve (TAV-TAA) and BAV subjects (BAV-TAA) were analyzed by untargeted proteomics to identify molecular changes and by systems biology analysis to reveal the biological processes associated. Proteins were localized within the cell and a translational analysis of the extracellular secreted proteins most significantly altered was performed in 61 plasma samples from TAA (BAV-TAA and TAV-TAA) and control subjects (BAV-C).

Results: The VSMC proteome of TAA was composed by 8796 proteins, pointing to a proliferating phenotype of VSMCs with differential stress response in BAV subjects. Processes involved in DNA replication were found decreased and cell adhesion, differentiation and migration were found increased. C1QT5 and ceruloplasmin showed altered abundance in plasma from BAV-TAA vs TAV-TAA subjects. C1QT5 also showed lower levels in TAA vs C in BAV subjects, evidencing their translational potential.

Conclusions: Changes identified in VSMCs reveal novel action routes pointing to a defective repairment capacity of the aortic wall in BAV subjects, which may be essential in the development of TAA. C1QT5 may be used as TAA diagnostic marker in BAV patients.

ID:407

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

JNK AFFECTS ON NEUTRAL LIPIDS ACCUMULATION IN THE LIVER OF DIFFERENT AGE INSULIN RESISTANT RATS

POSTER VIEWING SESSION

Ganna B. Kravchenko, Oksana A. Krasilnikova
Biological Chemistry, National University of Pharmacy, Kharkiv, Ukraine

Background and Aims : JNK activation is one of the important stages in development of resistance to insulin and could be mediated by oxidative stress and neutral lipids accumulation, the processes which are associated with eldering. The purpose of the experiment was to compare the importance of liver JNK under IR development in young and old rats.

Methods: Experiment was conducted on 3- and 24-month old male Wistar rats (24 and 64 animals, respectively). IR was induced by keeping animals on a high-fructose diet (HFD) during 7 weeks, beginning from the 5th week young and old animals were administered intraperitoneally JNK inhibitor SP600125 50 mg/kg (groups HFD_sp_3, HFD_sp_24), additionally old animals were administered intragastrically resveratrol 100 mg/kg and intraperitoneally carnitine 200 mg/kg (HFD_sp_rc_24). For this part of experiment in liver homogenate were determined fatty acids (FA), diacylglycerols (DG), triacylglycerols (TG) levels by TLCh, JNK (total and phosphorylated) content by ELISA kit. Statistical analysis was performed using Statisica 12.

Results: Keeping animals on HFD led to significant DG, TG, FA accumulation and was accompanied by increased pJNK content in both age groups; however, initial level of studied indices was higher in old rats (Tab. 1). SP600125 administration ameliorated harmful changes in HFD_sp_3 group, but not in 24-month old rats. Nevertheless, in group HDF_sp_rc_24 effect sp600125 was modified by complex administration of resveratrol and carnitine.

Table 1. Neutral lipids and JNK in the liver homogenate in different age insulin resistant rats

Groups / Idices	3-month old			24-month old			
	Control_3	HFD_3	HFD_sp_3	Control_24	HFD_24	HFD_sp_24	HFD_sp_rc_24
FA, mmol/mg pr	102±12	117±19[b]	93±8[d]	135±12[a]	187±17[c]	180±19	145±14[e]
DG, mmol/mg pr	137±12	187±13[b]	111±9[d]	264±16[a]	305±24[c]	301±33	253±21[e]
TG, mmol/mg pr	264±25	325±32[b]	275±19[d]	331±23[a]	493±39[c]	501±46	353±27[e]
Total JNK, mmol/mg pr	119±12	127±9	121±14	271±21[a]	264±19	258±32	261±19
p-JNK, mmol/mg pr	73±5	108±11[b]	87±7[d]	143±9[a]	187±15[c]	153±12[e]	150±11[e]

[a]P<0.05 (control_24 compared to control_3); [b]P<0.05 (HFD_3 compared to control_3);
[c]P<0.05 (FHD_24 compared to control_24); [d]P<0.05 (HFD_sp_3 compared to to HFD_3);
[e]P<0.05 (HFD_sp_24 and HFD_sp_rc_24 compared to to HFD_24)

Conclusions: Thus, neutral lipid accumulation in young animal's liver mediated by JNK activation. We supposed that JNK signal pathway functioning is reduced with eldering.

ID:286

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

EFFECT OF EXERCISE TRAINING ON THE CAPACITY OF HDL TO RECEIVE UNESTERIFIED AND ESTERIFIED CHOLESTEROL AND ON PARAOXONASE 1 ACTIVITY IN AGED INDIVIDUALS

POSTER VIEWING SESSION

Pedro Gabriel Senger Braga[1], Thauany M. Tavoni[1], Roberta V. Baroni[1], Fatima R. Freitas[1], Maria Carolina Guido[1], Maria Janieire Nazaré N. Alves[2], Gislene A. Rocha[3], André Luis L. Bachi[3], Carlos Eduardo Negrão[2], Mauro Walter Vaisberg[3], Raul C. Maranhão[1]
[1]Lipid And Metabolism Laboratory Of Heart Institute, Heart Institute (InCor) of the Medical School Hospital, University of São Paulo, Brazil., Sao Paulo, Brazil, [2]Cardiovascular Rehabilitation And Exercise Physiology, Heart Institute (InCor) of the Medical School Hospital, University of São Paulo, Brazil., Sao Paulo, Brazil, [3]Sports Medicine, Federal University of São Paulo, Sao Paulo, Brazil

Background and Aims : Aim: To investigate influence of exercise training on cholesterol transfer to HDL and paraoxonase 1 (PON1) activity in aged individuals.

Methods: 43 aged individuals were enrolled in two groups according their self-reported exercise training history: 22 exercised (13 males, 67 ± 6 yrs) and 21 non-exercised (9 males, 68 ± 5 yrs). PON1 activity was measured by p-nitrophenol consumption method. Cholesterol transfer to HDL was performed by incubating plasma with a donor lipoprotein-like nanoparticle containing radioactively labeled unesterified (UC) and esterified cholesterol (EC), followed by chemical precipitation and radioactive count. All subjects performed cardiopulmonary test to determine VO_2 peak.

Results: Body-mass index (28.1 ± 4.8 kg/m² vs. 24.7 ± 2.8 kg/m²; p=0.0072) and waist circumference (95 ± 10 cm vs. 87 ± 10 cm; p=0.0135) were lower and VO_2 peak was higher in the exercised (27.3 ± 5.9 ml/kg/min vs. 32.7 ±5.0 ml/kg/min; p=0.0024) than in non-exercised group. HDL-C (51 ± 14 mg/dL vs. 68 ±14 mg/dL; p=0.0002), apo A-I (1.5 ± 0.3 g/L vs. 1.7 ± 0.2 g/L; p= 0.0420), PON1 activity (65 ± 48 U/L vs. 84 ± 33 U/L; p=0.0477) were also higher in exercised group. In respect to cholesterol transfer, both EC (4.2 (3.2:5.9) % vs. 4.7 (3.6:5.5) %; p=0.0477) and UC (5.5 (3.8:8.2) % vs. 6.4 (4.8:8.9) %; p=0.0026) were greater in the exercised than in non-exercised.

Conclusions: Conclusion: Exercise training not only increased HDL-C but also improved protective HDL functions such as capacity to receive both forms of cholesterol and HDL-associated PON1 activity.

ID:282

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

MITOCHONDRIAL HETEROPLASMY VARIANTS ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS

POSTER VIEWING SESSION

Tatiana V. Kirichenko[1], Saule J. Urazalina[2], Alexander N. Orekhov[3], Igor A. Sobenin[1], Sergey Kozlov[4]
[1]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [2]Department Of Cardiology, JSK Scientific-Research Institute of Cardiology and Internal diseases, Almaty, Kazakhstan, [3]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [4]Laboratory Of Problems Of Atherosclerosis, National Medical Research Center of Cardiology, Moscow, Russian Federation

Background and Aims : The level of mitochondrial heteroplasmy increases with age and may play an important role in the development of atherosclerotic lesions. Previously we determined several variants of mitochondrial heteroplasmy associated with atherosclerotic lesions in aortal intima and carotid intima-media thickness (cIMT) in Russian population. In present study, these variants of mitochondrial heteroplasmy were analysed in Kazakh subjects with subclinical atherosclerosis.

Methods: The study included 70 participants free of cardiovascular disease aged 50-70 years old. DNA was isolated from blood leukocytes by phenol-chloroform extraction. Mitochondrial heteroplasmy levels were determined by pyrosequencing of mtDNA PCR-amplificated fragments. B-mode ultrasound scanning of carotid arteries was performed to measure cIMT. Statistical analysis was performed by SPSS ver.27.0.

Results: The mean age of study participants was 62.0(4.5) years old, the mean cIMT – 0.806(0.097) mm. The following levels of pro-atherosclerotic mitochondrial heteroplasmy variants were determined: 13513G>A – 11.7(6.4)%; 12315G>A – 29.3(6.2)%; 5178C>A – 22.5(8.2)%; 14459G>A – 13.2(11.2)%; 14846G>A – 18.9(4.9)%. The significant association of cIMT with mitochondrial heteroplasmy variants m.13513G>A and m.12315G>A was found. Mitochondrial heteroplasmy 13513G>A correlated negatively with cIMT (r=-0.526, p=0.036); 12315G>A correlated positively with cIMT (r=0.696, p=0.025).

Conclusions: Thus, atherosclerosis-related variants of mitochondrial heteroplasmy were found in subjects from Kazakh population, however, further search in larger cohorts of genetically diverse populations is needed to estimate the role of mitochondrial heteroplasmy in atherosclerosis development.
This work was supported by the Russian Science Foundation (Grant #22-15-00134).

ID:507

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

SNPS AND HAPLOTYPES IN THE CETP GENE AND THEIR EFFECTS ON CARDIOVASCULAR RISK ESTIMATED BY FRS AND SCORE IN THE HUNGARIAN GENERAL AND ROMA POPULATIONS

POSTER VIEWING SESSION

Peter Piko[1], Zsigmond Kosa[2], Janos Sandor[3], Ildiko Seres[4], Gyorgy Paragh[4], Roza Adany[1]
[1]Department Of Public Health And Epidemiology, Mta-de Public Health Research Group, University of Debrecen, Faculty of Medicine, Debrecen, Hungary, [2]Department Of Health Methodology And Public Health, University of Debrecen, Faculty of Health, Nyíregyháza, Hungary, [3]Department Of Public Health And Epidemiology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary, [4]Institute Of Internal Medicine, University of Debrecen, Faculty of Medicine, Debrecen, Hungary

Background and Aims : Cholesteryl ester transfer protein (CETP) is known to reduce high-density lipoprotein cholesterol (HDL-C) levels and, as a result, increase cardiovascular risk. Serum levels of CETP are genetically determined, therefore the polymorphisms influencing it are also suspected to influence cardiovascular risk. This study aims to explore the association between 5 single nucleotide polymorphisms (SNPs) and their haplotypes (H) in *CETP* genes and the 10-year cardiovascular risk estimated by the Framingham Risk Score for hard coronary heart disease (FRS_{CHD}) and for cardiovascular disease in general (FRS_{CVD}), and the Systematic Coronary Risk Evaluation (SCORE) among the Hungarian general (HG) and Roma populations.

Methods: The study involved 150 people from the Roma and 127 people from the HG population. Frequencies of variables were statistically compared by using the chi-squared test. For association tests, linear and logistic regression analyses were applied, and Bonferroni adjusted $p<0.01$ were considered as significant one.

Results: From the five SNPs studied, the A allele of rs5882 as recessive and the T allele of rs7499892 as codominant inheritance showed significant association with elevated cardiovascular risk estimated by FRSs. Ten haplotypes were identified, three of which significantly increased cardiovascular risk (H2: CAGTA, H7: CGGTG, and H9: AAACA) compared to the reference one (H1: AGACG). The H2 and H7 are significantly more common in the Roma population compared to the Hungarian general one.

Conclusions: Polymorphisms in the *CETP* gene and their haplotypes significantly increase cardiovascular risk estimated by FRSs and SCORE and may contribute to the higher cardiovascular risk generally present among the Roma.

ID:130

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PROTECTIVE GENES AND EVOLUTION REDUCES THE ATHEROSCLEROTIC PROCESS IN HISPANICS (PUERTO RICO) WHEN COMPARED WITH THE U.S.A. MAINLAND

POSTER VIEWING SESSION

Pablo I. Altieri[1,2], Nelson Escobales[1], Luis E. Barreto[1], Hector L. Banchs[1], Nicole Villar[1], Francisco J. Colón[1]
[1]Medicine And Physiology, University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico, [2]Cardiology, Cardiovascular Center of Puerto Rico and the Caribbean, San Juan, Puerto Rico

Background and Aims : Atherosclerosis (A.) is a complicated process produced by many factors, including genetic factors, diabetes mellitus, hypertension and others. In Puerto Rico (P.R.) and possibly other Hispanic countries, especially genes, which we call “protective genes” (P.G.) controls the degree of this A. process. It is the purpose to describe these mechanisms.

Methods: These genes, whose origins are Europeans, African and Amerindians, described by Duconge and colleagues at the University of Puerto Rico. The most important genes reducing this inflammatory process are an admixture of: *CYP_2C9, VXORC1 and* V*KORC1-1639>A allele in sector 1. These genes are homogeneous in the full Puerto Rican culture. Another factor is a reduction of monocytes transformation to macrophage producing sub endothelial accumulation in the union of the A pub by blocking Angiotensin II and cytokines-mechanisms, especially by Losartan. The most frequent antihypertensive drug used in P.R. This will reduce the endothelial damage which will produce plaques, foam cells and organ ischemia.*

Results: *We think the P.G. are crucial in these mechanisms reducing the origin and progression of the atherosclerotic process, more in P.R. (30%), U.S.A. Island, than in the U.S.A., because they don’t have these anti-inflammatory P.G.*

Conclusions: *The reduction of damage to the endothelial lining, reducing plaque formation and foam cells, the prelude of severe damage to the endothelium and myocardial damage. Probably the main factor is gene induced by the P.G. Evolution has a big role.*

ID:172

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

SERUM INDOXYL SULFATE LEVEL PREDICTS ATHEROGENIC DYSLIPIDEMIA IN DIALYSIS PATIENTS

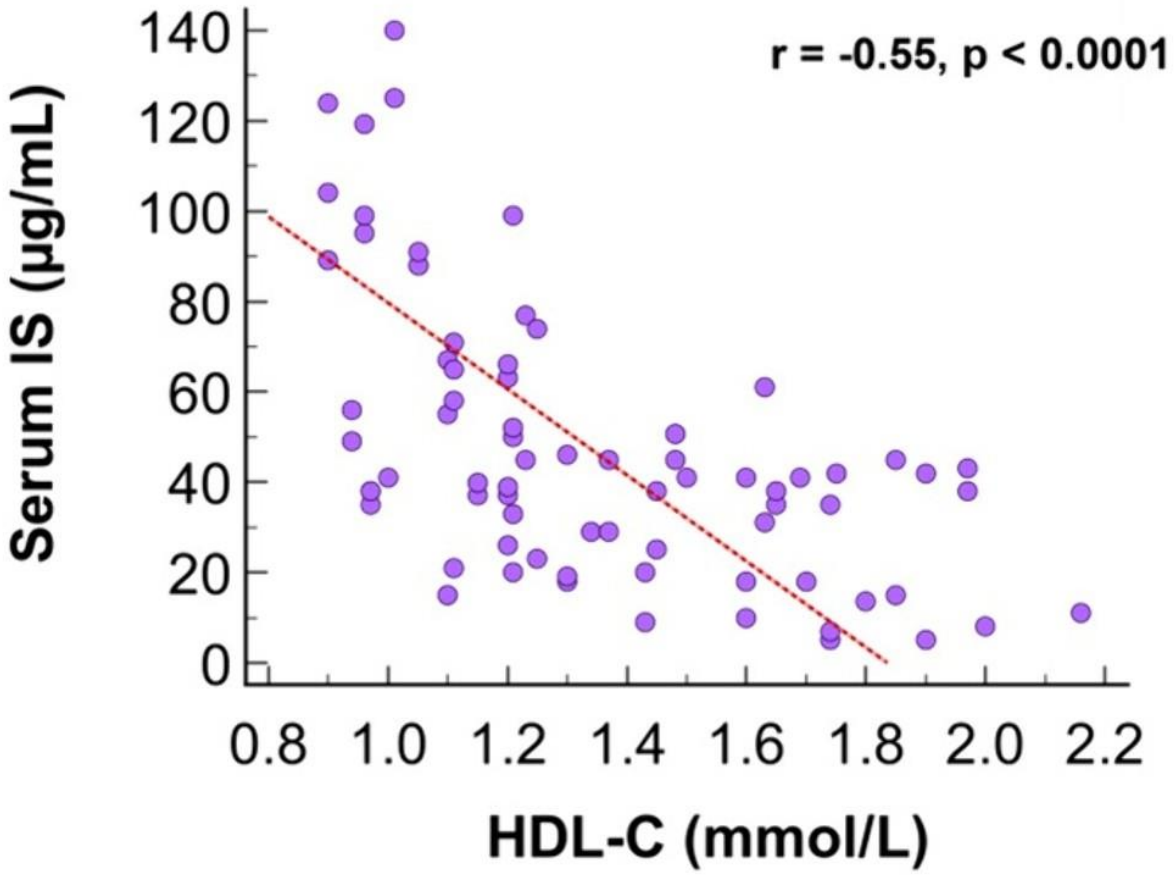
POSTER VIEWING SESSION

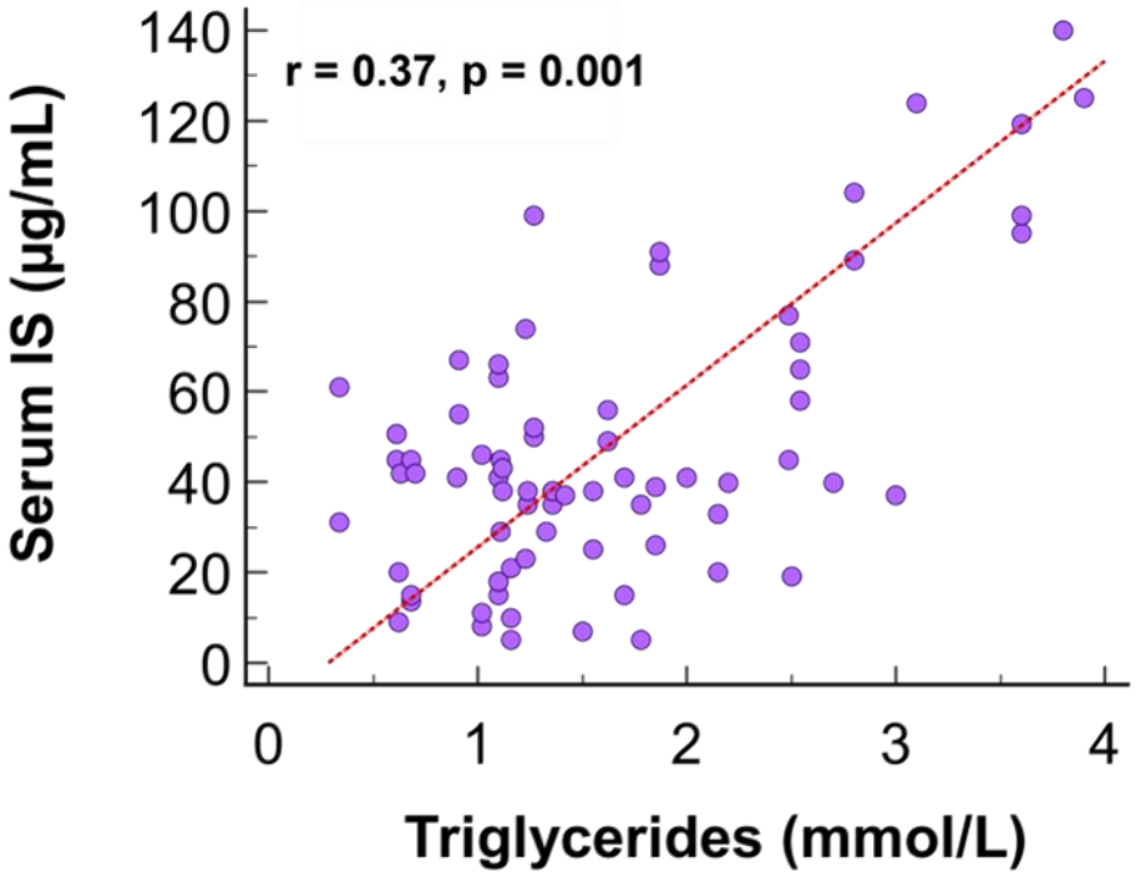
Natalia Stepanova, Lesya Korol, Olena Burdeyna, Lyudmila Snisar, Larysa Lebid, Olga Kompaniets
Nephrology And Dialysis, State Institution “Institute of Nephrology National Academy of Medical Science of Ukraine", Kyiv, Ukraine

Background and Aims : It is suggested that both high level of indoxyl sulfate (IS) and atherogenic dyslipidemia are associated with CVD in dialysis patients. However, it remains unanswered whether serum IS affects lipid profile in dialysis patients. This study was designed to explore the potential association between IS and atherogenic dyslipidemia in the dialysis population.

Methods: A total of 78 ESKD patients aged 49 (40-56.7) years and with a dialysis vintage of 30 (18.5-88) months were enrolled in this cross-sectional study. Among them, were 33 (42.3%) patients treated with peritoneal dialysis (PD) and 45 (57.7%) hemodialysis (HD) patients. HDL-C and triglyceride levels were used to define atherogenic dyslipidemia. Serum IS was measured spectrophotometrically. The data were presented as Me (Q25-Q75) and compared using the Kruskal-Wallis test. The Spearmen correlation test and the logistic regression analysis were performed to assess the association between IS and dyslipidemia.

Results: Serum IS level was statistically higher in the hemodialysis patients compared with the peritoneal dialysis patients: 47.5 (30.5-83.0) vs 37.5 (18.5-43.5) µg/mL, p = 0.03. Serum IS was negatively associated with HDL-C level (Fig. 1) and had a direct correlation with triglycerides concentration (Fig. 2).


r = -0.55, p < 0.0001
Serum IS (μg/mL)
140
120
100
80
60
40
20
0
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
HDL-C (mmol/L)



The logistic regression analysis demonstrated that elevated serum IS level (≥52 µg/mL) was an independent risk factor for atherogenic dyslipidemia even after adjustment for potential confounders (age, sex, body mass index and dialysis modality), OR = 1.3, 95% CI: 1.01-2.19, p = 0.01).

Conclusions: The results of this study indicate that elevated serum IS is an independent risk factor for atherogenic dyslipidemia in dialysis patients.

ID:169

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-08 Platelets, thrombosis and atherosclerosis*

INFLUENCE OF PSYCHOLOGICAL STRESS TO PLATELET ACTIVATION AND FATTY ACID COMPOSITION IN PLATELET PHOSPHOLIPID MEMBRANE

POSTER VIEWING SESSION

Inga Bikulčienė[1], Monika Pošiūnaitė[1], Aušra Linkevičiūtė-Dumčė[1,2], Aušra Janiulionienė[2], Rėda Matuzevičienė[1,2], Dovilė Karčiauskaitė[1,2], Arvydas Kaminskas[1]
[1]Institute Of Biomedical Sciences, Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [2]Center Of Laboratory Medicine, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Background and Aims : Platelet membrane is susceptible to oxidative stress. Prolonged stress and platelet-granulocyte aggregates (PGAs) have a synergistic effect on developing cardiovascular lesions. So the aim of this study was to evaluate the interface between platelet membrane fatty acids (FAs) composition and formation of PGAs under psychological stress.

Methods: 30 Wistar rats were divided into 3 groups for a month. First group was on a diet of extra omega (ω) 3/ω6 FAs without stress. Second group had extra ω9 FAs and stress and third group had extra ω3/ω6 FAs along with stress. FA methyl esters of platelet membrane were identified by GC/MS while PGAs were analyzed by whole blood flow cytometry. The concentration of malondialdehyde (MDA) in blood serum was determined by HPLC. The composition of platelet membrane FAs was compared to MDA concentration (μg/l) and the percentage of PGA formation among these groups.

Results: The levels of C20:5ω3 FA and C22:6ω3 FA were higher in platelet membrane of ω3/ω6 FAs stress-free group compared to stress group with ω3/ω6 FAs (med. 0.6700 vs med. 0.2550, p=0.07813; med. 0.835 vs med. 0.2050, p=0.007813). MDA concentration was higher in stress group with ω3/ω6 FAs than in ω3/ω6 FAs stress-free group (med. 563.7 vs 493.4, p=0.04883). The percentage of PGAs formation was also higher in stress group with ω3/ω6 FAs compared to ω9 with stress group (med. 5.90 vs 2.95, p= 0.03711).

Conclusions: Psychological stress promotes oxidation of polyunsaturated FAs in platelet membrane, thereby activating platelets, which may lead to the development of cardiovascular diseases in the future.

ID:166

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

THE BLOOD PROTEO-GENOMIC ARCHITECTURE OF VENOUS THROMBOEMBOLISM

POSTER VIEWING SESSION

Arnaud Girard[1], Erik Abner[2], Hasanga D. Manikpurage[1], Eloi Gagnon[1], Émilie Gobeil[1], Christian Couture[1], Patrick Mathieu[1,3], Tonu Esko[2], Benoit J. Arsenault[1,4]
[1]Cardiology, Quebec Heart and Lung Institute, Québec, Canada, [2]Estonian Genome Center, Uniersity of Tartu, Tartu, Estonia, [3]Department Of Surgery, Université Laval, Québec, Canada, [4]Département De Médecine, Université Laval, Québec, Canada

Background and Aims : Genome-wide association studies (GWAS) have identified dozens of genetic loci associated with venous thromboembolism (VTE) susceptibility. The functional impact of these genetic variants is not completely characterized. We hypothesized that VTE susceptibility loci have an important influence on the human blood proteome.

Methods: We performed two new GWAS in the Estonian Biobank (12,569 cases and 164,827 controls) and in the UK Biobank (13,722 cases and 393,364 controls) and used GWAS summary statistics from FinnGen (9176 cases and 209,616 controls) to perform a genome-wide association meta-analysis of these three cohorts totaling 35,467 cases and 766,807 controls. Using a Bayesian genetic colocalization method, we mapped genome-wide significant hits at 26 loci from that GWAS meta-analysis and from previously published GWAS to blood proteins using GWAS summary statistics on 2925 blood proteins from 3301 participants of the INTERVAL cohort. Genetic variants with a posterior probability of genetic colocalization (PPH4)>0.80 were considered as colocalized.

Results: When taking into consideration trans-pQTL, this method identified 382 blood proteins (313 blood proteins after excluding the ABO locus) that colocalized with at least one VTE variant. A total of 32 VTE variants were transacting only, while 4 variants had both cis and trans effects (31 trans-acting only and 2 cis and trans-acting after exclusion of the ABO locus).

Conclusions: We mapped 26 VTE susceptibility loci to hundreds of blood proteins. Most of these associations were driven by trans-acting SNPs, thereby highlighting the complexity of the genetic architecture of VTE.

ID:153

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

LIPOPROTEIN(A) CHOLESTEROL CONTRIBUTION TO “LDL-C” LOWERS THE ABILITY OF A STATIN TO REDUCE “LDL-C”

POSTER VIEWING SESSION

Christian Schrock
Lipidology Research, Lp(a) CARE Foundation, Hopkins, United States of America

Background and Aims : In patients with high levels of Lp(a), the Lp(a)-Cholesterol is a significant component of the “LDL-C”. This affects the ability of a statin to lower “LDL-C” because statins cannot lower this Lp(a)-Cholesterol component. We provide a method to calculate this effect.

Methods: Lp(a)-Cholesterol(mg/dL) equals Lp(a)(nmoles/L) divided by 7.5 based on accepted conversion factors. With Lp(a)-Cholesterol calculated the % of Lp(a)-Cholesterol in the "LDL-C" can be calculated. Then the % of actual LDL-C in the "LDL-C" is known. The % reduction of “LDL-C” by statin therapy is linearly proportional to the % of actual LDL in the “LDL-C” . For example if 20% of "LDL-C" is Lp(a)-Cholesterol then 80% is actual LDL-C. Thus the 50% lowering of "LDL-C" expected with a high intensity statin would be only 80% of 50% which is 40%

Results:

Reduction of the 50% expected lowering of "LDL-C" by High Intensity Statin Therapy in a patient with "LDL-C" of 110mg/dL (113 mg/dL is the mean "LDL-C" in the US) at different levels of Lp(a)

Lp(a) Level nmoles/L (mg/dL)	Lp(a)-C mg/dL	%Lp(a)-C of "LDL-C"	%actual LDL-C of "LDL-C"	%Reduction of "LDL-C of "LDL-C"
25 (10)	3.3	3%	97%	48.5%
125 (50)	16.7	15%	85%	42,5%
175 (70)	23.3	21%	79%	39.5%
250 (100)	33.3	30%	70%	35.0%
300 (120)	40,0	36%	64%	32.0%

Conclusions: If a Lp(a) level is determined before statin therapy, this method allows the actual percentage reduction expected with statin therapy to be determined. The appropriate level of intensity can thus be chosen.

Early repeating of Lp(a) and "LDL-C" may be indicated.

ID:152

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-11 Anti-inflammatory therapies*

THE IMPACT OF HIGH INTENSITY STATINS LONG TREATMENT FOR RECURRENCE OF ATRIAL FIBRILLATION AFTER SUCCESSFUL CARDIOVERSION.

POSTER VIEWING SESSION

Svetlana V. Grigoryan, Lusine G. Hazarapetyan, Parunak H. Zelveian
Arrhythmia, Research Institute of Cardiology, Yerevan, Armenia

Background and Aims : Background: Atrial fibrillation (AF) is the frequent arrhythmia found in clinical practice and. s associated with atrial structural changes that may have an inflammatory basis. Whereas the pleiotropic effect of statines, we **aimed** to assess the influence of high intensity statins on recurrence AF after successful cardioversion.

Methods: Methods: 126 patients with non-valvular persistent AF (mean age 64.6 ± 9.7) where enrolled in this study and followed up during 24 weeks. .The echocardiography examination and 24-hour ambulatory Holter monitoring ECG were registered in each patient. Blood samples were tested on the serum levels of hs-CRP and IL-6. All patients were divided in to two groups. The first group was treated by Atorvastatin 40mg or Rosuvastatine 10mg; the second group has administrated placebo (P). Prophylactic drug therapy with Amiodarone (200-300 mg daily) was administered to all patients.

Results: Results: The obtained results have shown that the basis data of hs-CRP and of IL-6 levels in patients with persistent AF were increased (0.82±0.32 mg/dL and 22±11 pg/ml accordingly). After 24 weeks treatment in first group these indices were significantly reduced (0.48±0.11 mg/dL, $p < 0.001$ and 12.1±4.9 pg/ml, $p<0.001$ accordingly vs. second group with P; 0.76± 0.32 mg/dL, 18.1± 3.9 pg/ml,). The follow-up during 24 weeks has shown that primary end-point in first group reduces AF recurrence to 4.6% compared 19% in the placebo group.

Conclusions: Conclusion: High intensity statins have been effective in the prevention of AF recurrence after successful cardioversion.

ID:150

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

CRYPTOGENIC STROKE: THE RIDDLE WITH POSSIBLE SOLUTION

POSTER VIEWING SESSION

Olga Germanova[1], Giuseppe Galati[2], Andrey Germanov[3]
[1]International Centre For Education And Research In Cardiovascular Pathology And Cardiovisualization, Samara state medical university, Samara, Russian Federation, [2]Cardiology, Ospedale San Raffaele, Milan, Italy, [3]Propedeutical Therapy, Samara state medical university, Samara, Russian Federation

Background and Aims : By AHA/ASA 2021 Guidelines, up to 45% of stroke are classified as cryptogenic. Aim. To study the possible reasons of stroke in patients with permanent atrial fibrillation (AF) without intra-heart thrombus.

Methods: . We studied 88 patients with permanent AF. Mediana age - 68±4,6 y.o. All patients were performed 24-hours ECG monitoring, transesophageal and transthoracic echocardiography, Doppler ultrasound of brachiocephalic arteries. We excluded intra-heart thrombus in all cases. All patients regularly took warfarin of NOACs. We used CHADS-2Vasc: 0 points - 0 (0%) patients, 1 point - 2 (2,2%), 2 points - 12 (13,6%), 3 points - 21 (23,9%), 7 points - 18 (20,4%), 9 points - 20 (22,7%), 11 points - 15 (17,2%). Most of patients – 58 (64,8%) had atherosclerotic plaques of internal carotid artery. In 41 (46,6%) plaques were non-stable (heterogenic structure, rough surface). We valued the arterial wall kinetic parameters with sphygmography: speed, acceleration, power, work.

Results: .
1. If longer was the pause between cardiocycles in AF than more increase of kinetic parameters was observed.
2. The secondary hemodynamic arterial hypertension at the moments after long pause between cardiocycles.
3. In patients with stenosis ~70% of internal carotid artery the speed after the long pause in AF rising up to 4-4,6m/s (2,3 m/s in sinus rhythm). This can cause non-stable plaque damage.
4. Increased arterial wall deformation: additional, stand waves.
5. Stroke appeared in 21 (23,8%) patients in 1 year of investigation despite of anticoagulant therapy.

Conclusions: Conclusion. The source of stroke in AF can be non-stable plaques in patients with multi-focus atherosclerosis.

ID:148

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-11 Plaque remodelling*

MODELING OF HEMODYNAMICALLY SIGNIFICANT ATHEROSCLEROTIC STENOSIS OF MAIN ARTERIES IN EXPERIMENTAL CARDIOLOGY

POSTER VIEWING SESSION

Olga Germanova[1], Giuseppe Galati[2], Andrey Germanov[3]
[1]International Centre For Education And Research In Cardiovascular Pathology And Cardiovisualization, Samara state medical university, Samara, Russian Federation, [2]Cardiology, Ospedale San Raffaele, Milan, Italy, [3]Propedeutical Therapy, Samara state medical university, Samara, Russian Federation

Background and Aims : Aim. To perform the modeling of hemodynamically significant atherosclerotic stenosis of main arteries using the original device for modeling of intra-arterial circulation.

Methods: . We used the device for modeling of intra-arterial circulation (№ RU 202780 U1). It has rotameter glass tube. An aqueous solution of glycerin is introduced inside closed system with the viscosity as blood. Electric pump has various modes (imitation of pulse waves in regular rhythm (RR), atrial fibrillation (AF)), connected into closed system with rotameter by silicone tubes. Plastic diaphragms 15 mm with hemodynamically significant stenosis of 70%, 90% were hermetically put inside. The hemodynamics was studied by intravascular piezoelectric crystal pressure sensor connected to an oscillograph, silk thread, clerical ink.

Results: . In AF imitation, after the long pause the speed of fluid flow increased: if longer was the pause than more speed increased. With 70% stenosis: the speed with a RR was 3.24m/s, with AF after the pause<1s-3.96m/s, AF after the pause>1,<2s-5.87m/s, AF after the pause>2s-7.83m/s; with 90% the speed at RR 8.96m/s, with AF after the pause <1s-9.46m/s, AF after the pause>1,<2s -11.17m/s, AF after the pause>2s -13.45m/s. We observed the appearance of reflected, standing waves in the edge zones of the diaphragms and turbulent fluid flow. The pressure inside increased proportionally to the speed.

Conclusions: Conclusion. We propose the concept of "hydraulic shock" of hemodynamic changes inside the arterial vessels. Intense additional mechanical effect of the pressure waves after the long pauses in AF in the edge zones of the diaphragm can lead to the further growth of plaques and progression of atherosclerosis.

ID:134

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

HIGH PREVALENCE OF ATHEROSCLEROSIS COMORBIDITY AND HIS RISK FACTORS IN PATIENTS WITH PSORIATIC ARTHRITIS COMPARED TO PSORIASIS WITHOUT ARTHRITIS: A RETROSPECTIVE DERMATOLOGICAL CLINIC-BASED STUDY.

POSTER VIEWING SESSION

Nadezhda Batkaeva[1], Tatiana Korotaeva[2]
[1]Dermatology And Cosmetology, RUDN University, Moscow, Russian Federation, [2]Rheumatology, Research Institute of Rheumatology n.a. V. A. Nasonova, Moscow, Russian Federation

Background and Aims : An association between atherosclerosis **and** psoriasis (PsO) has still limited data. **Objectives:** to evaluate the prevalence of atherosclerosis comorbidity and his risk factors in patients (pts) with psoriatic arthritis (PsA) compared to PsO without arthritis in a dermatological hospital cohort.

Methods: 765 pts (Male-439/Female-326) with moderate-to-severy plaque PsO, age PSO pts 52.4±15,6 years were included. 274 out of 765 pts (35.8%) had PsA and 491 out of 765 pts (64.2%) had PsO alone. PsA pts were older then PsO pts – 55.3±13.7 and 50.4±17,6 ($p<0.001$).

Results: Atherosclerosis coding as I 70 were registered often in PsA pts compared to PsO pts – in 40 out of 274 pts (14.6%) and in 35 out of 491 pts (7.3%) accordingly ($p<0.001$). Smoking patients was found often in PsO pts compare to PsA pts – in 230 out of 491 pts (46.9%) and in 101 out of 274 pts (36.9%) accordingly ($p<0.05$). In PsA pts AH coding as I 10 - I 15 was found in more cases than in PsO pts - in 260 out of 491 PsO pts (52.8%) and in 187 out of 274 PsA pts (68.2%) accordingly ($p<0.001$). Obesity coding as E65-E68 was identify in 102 out of 765 pts (13.3%). Obesity were found in more cases in PsA pts - in 53 out of 491 PsO pts (10.9%) and in 49 out of 274 PsA pts (17.9%) accordingly ($p<0.001$).

Conclusions: Atherosclerosis found increased frequency in PsA than PsO due to share inflammation pathways between atherosclerosis and PsA.

ID:131

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

GENETICS IS MORE IMPORTANT IN THE HISPANIC SOCIETY THAN THE COMPLEX OF ANGIOTENSIN II-MONOCYTES-MACROPHAGES AXIS IN THE ORIGIN OF THE ATHEROSCLEROTIC PROCESS

POSTER VIEWING SESSION

Luis E. Barreto[1], Pablo I. Altieri[1,2], José E. Muñoz[1], Nelson Escobales[1], Hector L. Banchs[1], Nicole Villar[1], Francisco J. Colón[1]
[1]Medicine And Physiology, University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico, [2]Cardiology, Cardiovascular Center of Puerto Rico and the Caribbean, San Juan, Puerto Rico

Background and Aims : Atherosclerosis (A.) is a complicated process produced by many factors, including genetic factors, diabetes mellitus, hypertension and others. In Puerto Rico (P.R.) and possibly other Hispanic countries, especially genes which we call “protective genes” (P.G.) controls the incidence and degree of this A. process.

Methods: *We review the data reported in the U.S.A. health services and the P.R. Department of Health. A comparison was done.*

Results: These genes whose origins are Europeans, African and Amerindians, described by Duconge and colleges at the University of Puerto Rico, probably are protective in our population. The most important genes reducing this inflammatory process are an admixture of: *CYP_2C9, VXORC1 and VKORC1-1639>A allele in sector 1. These genes are homogeneous in the full Puerto Rican culture. We think the protective genes are crucial in these mechanism reducing the origin and progression of the atherosclerotic process, more in P.R. (30%) (U.S.A. island) than in the U.S.A. (20%). The U.S.A. population don’t have these protective genes, which will reduce the oxidative stress of the endothelial lining, reducing plaque formation and foam cells. We think now with the increase in admixture of the American society with the Hispanic population there will be a reduction of the A. process in the U.S.A. population.*

Conclusions: *We think the protective genes are crucial in these mechanisms reducing the origin and progression of the atherosclerotic process, more in P.R. (30%), U.S.A. Island, than in the U.S.A.*

ID:129

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CORONAVIRUS AT THE HEART CENTER OF PUERTO RICO INCIDENCE-DEATH: THE ROLE OF GENETICS

POSTER VIEWING SESSION

Claudia M. Diaz[1], Luis E. Barreto[1], Pablo I. Altieri[1,2], Hector L. Banchs[1], Nicole Villar[1], Francisco J. Colón[1]
[1]Medicine And Physiology, University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico, [2]Cardiology, Cardiovascular Center of Puerto Rico and the Caribbean, San Juan, Puerto Rico

Background and Aims : Coronavirus disease mostly affects the respiratory system. Since it is a novel disease, little is known about the connection between heart involvement and COVID-19.

Methods: In total, 50 patient records with positive PCR for SARS-CoV-2 were analyzed from the Heart Center Hospital. Within the medication section, our prime focus was to find whether these P. were currently taking or took Losartan in the past, because this drug reduces the penetration intracellularly of the virus.

Results: All of the 50 P. were from Puerto Rico (P.R.), a Hispanic population. None of the P. was taking Losartan. According to the records 96% had severe health problems previously to being contaminated by the virus. Ten percent of these P. died; cause of death was not a result of a clear correlation between COVID-19 and other comorbidities. These P. were chronically ill. The CFR was .005, while the total CFR of the Puerto Rican population with the virus was .1. Probably, this increase is due an aged population (age >65 years) and comorbidities.

Conclusions: In P.R., and possibly other Hispanic countries, there are genes which we call “protective genes” (P.G.) (*CYP_2C9, VXORC1 and VKORC1-1639>A allele in sector 1)* that control the incidence and degree of heart disease. In addition, since none of the 50 P. took Losartan, we think this is a factor which will increase the incidence of the disease.

ID:179

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

THE CURRENT STATUS OF LIPID CONTROL IN ELDERLY HIGH-RISK PATIENTS WITH DYSLIPIDEMIA IN TAIWAN

POSTER VIEWING SESSION

Chih-Hung Liang[1], Ya-Hui Chang[2], Chia-Ling Tsai[3], Jen-Yu Chuang[1], Chih-Chung Hsiao[3], Yi-Hong Zeng[4], Yi-Han Chen[5], Hung-I Yeh[3,6], Chao-Feng Lin[3,6]
[1]Department Of Medical Education, MacKay Memorial Hospital, Taipei, Taiwan, [2]Department Of Pharmacy, MacKay Memorial Hospital, Taipei, Taiwan, [3]Department Of Cardiology, MacKay Memorial Hospital, Taipei, Taiwan, [4]Department Of Endocrinology, MacKay Memorial Hospital, Taipei, Taiwan, [5]School Of Public Health, College Of Public Health, Taipei Medical University, Taipei, Taiwan, [6]Department Of Medicine, MacKay Medical College, New Taipei City, Taiwan

Background and Aims : The elderly people have a higher prevalence of dyslipidemia and more cardiovascular risks compared with young people. Here we aimed to investigate the current status of lipid control, including the prescription rates of high-intensity statin (HIS)/ezetimibe and the goal attainment rates of low-density lipoprotein cholesterol (LDL-C), in elderly high-risk patients in a tertiary medical center in Taiwan.

Methods: Between July 2018 and August 2019, 208 high-risk patients with a suboptimal serum LDL-C level were enrolled, including 70 elderly patients (age ≥65 years) and 138 non-elderly patients (age <65 years). Each patient received lipid-lowering therapy according to the current lipid guidelines' recommendations. The target serum LDL-C levels in high-risk patients with CAD and high-risk patients without CAD were respectively <70 mg/dL and <100 mg/dL irrespective of age. The prescription rates of HIS/ezetimibe, and the goal attainment rates of LDL-C among high-risk patients were compared between elderly and non-elderly patients at 12-month follow-up.

Results: There is no significant differences in LDL-C levels between the elderly and non-elderly high-risk patients at baseline and 12-month follow-up. The percentages of reduction in serum LDL-C level were similar between the elderly and non-elderly high-risk patients during follow-ups. The elderly and non-elderly high-risk patients have similar goal attainment rates of LDL-C in the present study.

Conclusions: Despite a higher cardiovascular risk, the elderly high-risk patients received similar lipid-lowering therapy and had similar goal attainment rates of LDL-C compared with non-elderly high-risk patients. Our findings highlight that we implemented an aggressive strategy for management of dyslipidemia in Taiwan.

ID:112

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EFFICACY AND SAFETY OF EVOLOCUMAB IN CHINESE PATIENTS WITH PRIMARY HYPERCHOLESTEROLEMIA AND MIXED DYSLIPIDEMIA: PRIMARY RESULTS OF THE HUA TUO _ CLINICAL TRIAL

POSTER VIEWING SESSION

Hong Tan[1], Weimin Li[2], Zhouqing Huang[3], Yajun Han[4], Xuecheng Huang[5], Dongye Li[6], Xiaochun Xing[7], Maria Laura Monsalvo[8], You Wu[9], Jackie Mao[10], Lily Xin[10], Jiyan Chen[10]
[1]Cardiology, Guangdong Provincial People's Hospital, Guangzhou, China, [2]Cardiology, The First Affiliated Hospital of Harbin Medical University, Harbin, China, [3]Cardiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, [4]Cardiology, Inner Mongolia Autonomous Region People's Hospital, Hohhot, China, [5]Cardiology, The Second Nanning People's Hospital, Nanning, China, [6]Cardiology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, China, [7]Cardiology, Tianjin Forth Central Hospital, Tianjin, China, [8]Global Clinical Development, Amgen, Thousand Oaks, United States of America, [9]Global Biostatistical Science, Amgen, Thousand Oaks, United States of America, [10]Clinical Development, Amgen, Shanghai, China

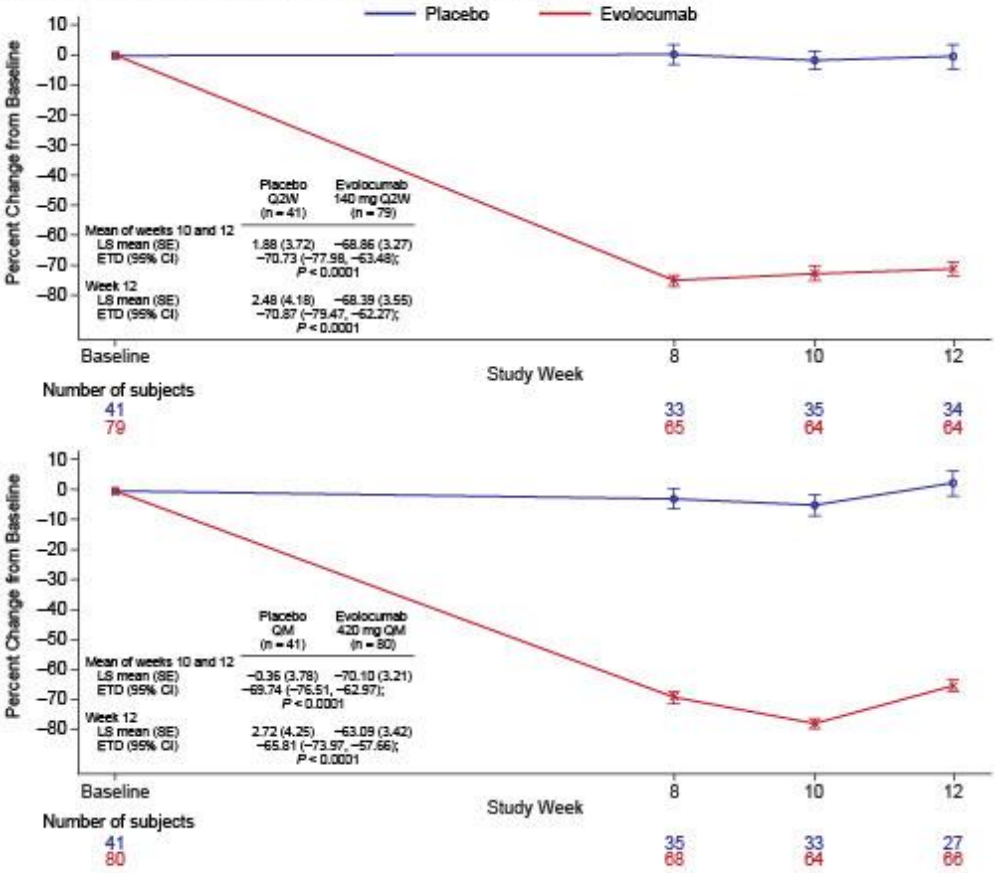
Background and Aims : The prevalence of dyslipidemia in China is approximately 40%, and many patients treated with lipid-lowering therapies fail to achieve LDL-C goals. This study evaluated the effect of evolocumab on LDL-C levels in Chinese patients with primary hypercholesterolemia and mixed dyslipidemia with baseline LDL-C levels of ≥80 mg/dL or ≥130 mg/dL despite optimal stable statin therapy.

Methods: This was a Phase 3, multicenter, double-blind, randomized, placebo-controlled study conducted in China. The full analysis set used for analyses included 241 patients. Patients received evolocumab 140 mg SC Q2W (N=79), evolocumab 420 mg SC QM (N=80), placebo SC Q2W (N=41), or placebo SC QM (N=41) for 12 weeks. Co-primary endpoints were mean percent change in LDL-C from baseline to weeks 10 and 12, and percent change from baseline to week 12. Subjects' treatment-emergent adverse events (TEAEs) were assessed.

Results: At baseline, mean (SD) age was 60.2 (10.3) years, mean (SD) LDL-C was 116.1 (34.6) mg/dL, and 86% of patients had coronary artery disease (Table 1). There were statistically significant reductions in LDL-C from baseline to the mean of weeks 10 and 12, and from baseline to week 12, with evolocumab 140 mg Q2W (−68.9%, −68.4%) and evolocumab 420 mg QM (−70.1%, −63.1%) versus placebo (Figure 1). The subject incidence of TEAEs and serious adverse events was similar between the evolocumab and

placebo groups (Table 2), and no new safety concerns were

Figure 1. Mean Percent Change in LDL-C from Baseline for Evolocumab 140 mg Q2W (A) and Evolocumab 420 mg QM (B) versus Placebo



LS mean was calculated from a repeated measures linear effects model which included treatment group, stratification factors, scheduled visit, and the interaction of treatment with scheduled visit as covariates. ETD was calculated with placebo as the reference within each dose frequency. Vertical lines represent standard error of the mean. CI, confidence interval; ETD, estimated treatment difference; SE, standard error; Q2W, every 2 weeks; QM, every month.

Table 1. Summary of Baseline Demographic and Clinical Characteristics

	Placebo		Evolocumab		Overall (N = 241)
	Q2W (N = 41)	QM (N = 41)	140 mg Q2W (N = 79)	420 mg QM (N = 80)	
Sex, n (%) Male	30 (73.2)	31 (75.6)	51 (64.6)	51 (63.8)	163 (67.6)
Age, years, mean (SD)	57.8 (9.8)	59.4 (10.9)	61.2 (10.6)	60.9 (9.8)	60.2 (10.3)
Weight, kg, mean (SD)	70.2 (10.1)	71.7 (13.6)	67.9 (13.2)	70.1 (12.8)	69.7 (12.7)
LDL-C, mg/dL, mean (SD)	120.9 (42.2)	117.1 (28.2)	113.7 (37.7)	115.5 (30.1)	116.1 (34.6)
Cardiovascular disease history, n (%)					
Coronary artery disease	36 (87.8)	34 (82.9)	69 (87.3)	68 (85.0)	207 (85.9)
Myocardial infarction	20 (48.8)	23 (56.1)	31 (39.2)	34 (42.5)	108 (44.8)
Coronary artery bypass graft	2 (4.9)	1 (2.4)	1 (1.3)	1 (1.3)	5 (2.1)
Percutaneous coronary intervention	29 (70.7)	26 (63.4)	53 (67.1)	57 (71.3)	165 (68.5)
Cerebrovascular or peripheral arterial disease	9 (22.0)	13 (31.7)	16 (20.3)	25 (31.3)	63 (26.1)

LDL-C, low-density lipoprotein cholesterol; Q2W, every 2 weeks; QM, every month; SD, standard deviation.

Table 2. Summary of Subject Incidence of TEAEs

	Placebo			Evolocumab		
	Q2W (N = 41)	QM (N = 41)	Overall (N = 82)	140 mg Q2W (N = 79)	420 mg QM (N = 80)	Overall (N = 159)
All TEAEs, n (%)	22 (53.7)	23 (56.1)	45 (54.9)	45 (57.0)	42 (52.5)	87 (54.7)
Grade ≥2	13 (31.7)	14 (34.1)	27 (32.9)	30 (38.0)	24 (30.0)	54 (34.0)
Grade ≥3	0 (0.0)	3 (7.3)	3 (3.7)	8 (10.1)	3 (3.8)	11 (6.9)
Grade ≥4	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)	1 (1.3)	2 (1.3)
Serious adverse events	2 (4.9)	4 (9.8)	6 (7.3)	6 (7.6)	1 (1.3)	7 (4.4)
Leading to discontinuation of IP	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fatal adverse events	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

IP, investigational product; Q2W, every 2 weeks; QM, every month; TEAEs, treatment-emergent adverse events.

noted.

Conclusions: Evolocumab 140 mg Q2W or 420 mg QM in combination with statins significantly lowered LDL-C levels in Chinese patients and was well-tolerated.

ID:111

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-09 Epidemiology of socioeconomic and psychosocial risk factors*

EVALUATION THE EFFECTIVENESS OF THE MEDICAL CARE QUALITY IN PATIENTS WITH DYSLIPIDEMIA

POSTER VIEWING SESSION

Oleksii Demikhov[1], Iya Dehtyarova[1], Nadiia Demikhova[2]
[1]Management, Sumy State University, Sumy, Ukraine, [2]Family Medicine, Sumy State University, Sumy, Ukraine

Background and Aims : The purpose of the study was to analyze the effectiveness of medical care quality for people with dyslipidemia at the primary level of medical care.

Methods: To determine the existing level of quality of medical care for patients with dyslipidemia, who are on dispensary registration with a general practitioner-family medicine, we investigated 769 patients from 18 to 69 years (men - 337 (43.82±3.58%), women - 432 (56.12±3.58%)) according to the performance of indicators of the quality of medical care for patients with dyslipidemia.

Results: For identify the current level of medical care quality for patients with the dyslipidemia who are under long-term observation of general practitioners we observed and analysed medical records. Study showed that application of the model of health care quality management based on internal audit has improved the quality of rendering medical services: the number of patients with normal cholesterol level increased from 14.04% to 38.55%, with non-control cholesterol level reduced from 28.97±2.02% to 11.15±1.40% (17.82%). Results of monitoring patients: - irregularly control the cholesterol level of 37.09±2.16% of the respondents; - did not measure cholesterol level 8.27±1.22%; - irregularly take medication 52.30±2.22%; - 32±2.08% of respondents did not attend a doctor with a preventive goal; - the main reason for the irregular intake of drugs and the control of cholesterol level is that patients "forget" - 48.34±2.22%.

Conclusions: The necessary conditions for improving the quality of medical care is the creation of a regulatory and methodological framework for managing the quality of medical services in a health care institution.

ID:110

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

MORPHOLOGICAL CHANGES OF RATS THYROID GLAND UNDER THE INFLUENCE OF MODERATE DEGREE OF CELLULAR DEHYDRATION

POSTER VIEWING SESSION

Andrii Demikhov[1], Valentyna Bumeister[2], Inna Khomenko[2], Kateryna Mykhailychenko[2], Olha Yarmolenko[2], Olha Prykhodko[2], Nadiia Demikhova[1]
[1]Family Medicine, Sumy State University, Sumy, Ukraine, [2]Morphology, Sumy State University, Sumy, Ukraine

Background and Aims : Nowadays the diseases of thyroid gland become a topical medical issue. The thyroid gland is highly sensitive to changes of water-electrolyte balance. **Aims**: Study of morphometric indices of thyroid tissue on an animal model of moderate degree of cellular dehydration.

Methods: 12 white laboratory rats of reproductive age were involved into the experiment. During 20 days 6 animals ate granulated compound feed and forcibly drank 1.5% sodium chloride solution 3 ml thrice daily. 6 rats remained intact for correct comparative analysis. The histological preparations of the thyroid gland were made by standard methods, stained with hematoxylin and eosin, and studied using light microscopy and software "SCPR-2017-Zen 2 lite".

Results: The analysis of morphometric data shows the increase in follicle area by 29.1%(p=0.000004) and colloid area by 51.61%(p=0.000001) compared to the control. The outer long diameter of the follicles increases by 14.37%(p=0.000346), and the outer short diameter – by 10.74%(p=0.001), which is a sign of geometric restructuring of the follicles that become elongated. The inner long and short diameters are greater than the control at 26.13%(p=0.000065) and 24.68%(p=0.000004) respectively. It confirms an increasing in colloid area mentioned above and a 9.87%(p=0.076612) increase in follicular epithelium area. The last index is connected with the decrease in the height of thyrocytes by 12.58%(p=0.01102). Moreover, an increase in the colloid accumulation index by 30.7%(p=0.000002) and a decrease in the follicular-colloidal index by 14.75% p=0.00001) is determined.

Conclusions: The results indicate a thyroid hypofunction and its inability to withstand adverse factors.

ID:107

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

FACTORS ASSOCIATED WITH REBLEEDING AFTER COIL EMBOLIZATION IN PATIENTS WITH ANEURYSMAL SUBARACHNOID HEMORRHAGE

POSTER VIEWING SESSION

Kum Whang, Jong W. Choi, Jy Kim
Neurosurgery, Wonju Severance Christian Hospital, Wonju, Gangwon-do, Korea, Republic of

Background and Aims : Aneurysmal subarachnoid hemorrhage (aSAH) has a high mortality rate, and hemorrhage amounts and perioperative rebleeding importantly determines prognosis. However, despite adequate treatment, prognosis is poor in many ruptured aneurysm cases. In this study, we identified and evaluated factors related to perioperative rebleeding in patients with aSAH.

Methods: The medical and surgical records of 179 patients that underwent endovascular embolization for a ruptured cerebral aneurysm at a single institution from 2014 to 2016 were retrospectively analyzed to identify risk factors of rebleeding. All patients were examined for risk factors and evaluated for increased hemorrhage by brain CT at 3 days after surgery.

Results: This series included 54 men (32.5%) and 112 women (67.5%) of mean age 58.3 ± 14.3 years. After procedures, 26 patients (15.7%) experienced rebleeding, and 1 of these (0.6%) experienced an intraoperative aneurysmal rupture. External ventricular drainage (EVD) (OR 5.389, [95% CI 1.171-24.801]) and modified Fisher grade (OR 2.037, [95% CI 1.077-3.853]) were found to be independent risk factors of rebleeding, and perioperative rebleeding was strongly associated with patient outcomes ($p<0.001$).

Conclusions: We concluded the rebleeding risk after aSAH is greater in patients with large hemorrhage amounts and a high pre-operative modified Fisher grade, and thus, we caution neurosurgeons should take care in such cases.

ID:100

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

ASSOCIATION POSTPRANDIAL HYPERTRIGLYCERIDEMIA, CAROTID INTIMA-MEDIA THICKNESS AND BODY MASS INDEX IN PATIENTS WITH CORONARY ARTERY DISEASE COMBINED WITH NONALCOHOLIC LIVER STEATOSIS.

POSTER VIEWING SESSION

Mariya Grechanyk
Internal Medicine, Dnipro State Medical University, Dnipro, Ukraine

Background and Aims : To estimate the frequency of postprandial hypertriglyceridemia (PPG), carotid intima-media thickness and body mass index (BMI) in patients with coronary artery disease (CHD) combined with nonalcoholic liver steatosis (NALS).

Methods: We studied 61 patients with CAD in combination with NALS mean age 57,8±2,04 (group A) and 20 patients with CAD without NALS mean age 56,6±4,6 (group B). Patients with diabetes were excluded. The study group was divided into 3 subgroups according to BMI (subgroup 1 (35%) - patients who are overweight, 2 (40%) - obesity 1 degree, 3 (25%) - obesity grade 2. Studied PPG, carotid intima-media thickness.

Results: Frequency of exposure of atherosclerotic carotid plaques in a group A – 82%, was higher than in a group B – 64% (p <0,05). In group A unstable plaques found significantly more often (31%, p = 0,01), than in the control group B (8%). Revealed an increase in the level of TG after fat load test in group A by 57% (from 2.27 [1.74; 2.77] mmol/l to 3.56 [2.60; 4.89] mmol/l), in the group B by 203% (s 1.24 [1.05; 1.86] mmol/l to 3.76 [1.64; 5.51] mmol/l). An increase in postprandial TG levels in subgroup 1 by 74%, in the subgroup 2 with obesity 1 degree by 51%, in the group 3 with obesity 2 degrees by 40%.

Conclusions: In patients with CAD in combination with NALS, PPG was associated with a decrease in the increasing of PPG levels depending on body weight. There was correlation between PPG and unstable plaques (r=0,75, p=0,03) in a subgroup 2.

ID:99

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-12 Adipose tissue biology and pathology*

THE ADIPOKINE PROGRANULIN PROTECTS AGAINST ISCHEMIA REPERFUSION-INDUCED ARRHYTHMIAS IN A RAT MODEL

POSTER VIEWING SESSION

Asma M. Alyahya
Cardiovascular Research Group, Department Of Physiology, king Saud University, Riyadh, Saudi Arabia

Background and Aims : Acute myocardial infarction is precipitated by occlusion of the coronary arteries resulting in sudden death. Restoration of coronary flow has damaging effects on cardiac myocytes causing an increase in infarct size and lethal arrhythmias due to ischemia-reperfusion injury. Progranulin, an adipokine, has shown cardioprotective properties and has been expressed in atherosclerotic tissue, however, its effect on ischemia reperfusion-induced arrhythmias has not been explored. The study at hand examines the effect of progranulin on ischemia reperfusion-induced arrhythmias in a rat model of acute myocardial ischemia-reperfusion injury.

Methods: Progranulin was administered to male Wistar rats prior to exposure to acute myocardial ischemia-reperfusion injury. Left ventricular function and electrocardiography was monitored during the total period of ischemia and reperfusion. Rats did not receive anti-arrhythmic agents. Ventricular tachycardia was identified as the presence of four or more successive ventricular premature beats. Ventricular fibrillation was distinguished by a change in rate and shape from beat to beat without a recognizable QRS complex.

Results: Progranulin significantly reduced cardiac ventricular tachycardia and ventricular fibrillation after acute myocardial ischemia-reperfusion injury as well as arrhythmia scores. Furthermore, progranulin administration reduced cardiac injury and mortality rate.

Conclusions: The study provides novel evidence of the protective effect of progranulin against acute myocardial ischemia reperfusion-induced arrhythmias in a rat model. The ability of progranulin to protect against lethal arrhythmias may be attributed to its cardioprotective activity against ischemic insult to cardiac myocytes. A deeper look into the molecular mechanisms and clinical implications of its anti-arrhythmic properties is required.

ID:85

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

ASSOCIATION BETWEEN OXIDIZED LP(A) AND HDL FUNCTIONS IN SLEEP APNEA SYNDROME

POSTER VIEWING SESSION

Yasuhiro Endo[1], Makoto Sasaki[1], Manami Teramoto[1], Yumiko Suenaga[1], Makoto Ayaori[2], Hideaki Nakayama[3], Yuichi Inoue[4], Katsunori Ikewaki[1]
[1]Department Of Internal Medicine, National Defense Medical College, Tokorrozawa, Japan, [2]Department Of Cardiology, Tokorozawa Heart Center, Tokorozawa, Japan, [3]Department Of Somnology, Tokyo Medical University, Tokyo, Japan, [4]Institute Of Neuropsychiatry, Japan Somnology Center, Tokyo, Japan

Background and Aims : Obstructive Sleep Apnea Syndrome (OSA) is associated with an increased risk for cardiovascular disease. Previously, we found that cholesterol efflux capacity (CEC), an anti-atherogenic function of HDL, was attenuated in OSA patients. OxLp(a), an oxidized form of Lp(a), was previously reported to be present in human atheroma and was associated with the cardio- ankle vascular index (CAVI) in hypertensive patients. This study investigated the association of OxLp(a) with HDL functions and clinical parameters in sleep apnea syndrome.

Methods: A total of 116 OSA patients who underwent polysomnography tests from April 2017 to April 2019 have participated in this study. Blood samples were obtained on the next day of the polysomnography test. We measured serum OxLp(a) levels by ELISA. After excluding 33 patients whose OxLp(a) levels were undetectable, 83 patients were enrolled in this cross-sectional study.

Results: Eligible patients were exclusively males (95%) with middle age. We performed a multivariable linear analysis that CEC was positively associated with Log OxLp(a) adjusted for age, hypertension, Diabetes Mellitus, Dyslipidemia, HDL-C, and Log hsCRP.(β=0.199 p=0.04). Arylesterase activity, an anti-oxidative function of HDL, was negatively associated with log oxLp(a) in the same model (β＝－0.24 p=0.04). Mutivariable logistic regression was performed to evaluate the association between elevated OxLp(a) （＞0.068nmol/l: Median） and high AHI (＞17.5 :Median) to find that high AHI was significantly correlated with elevated OxLp(a) (odds:0.33 (0.12-0.92)).

Conclusions: In summary, OxLp(a) was positively correlated with CEC and high AHI, but negatively with arylesterase in OSA, suggesting that OxLp(a) may be a biomarker for HDL dysfunctionality in OSA.

ID:84

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CLINICAL MANAGEMENT PROCESSES TO IMPROVE ADHERENCE OF PATIENTS TO OPTIMAL THERAPY OF CARDIOVASCULAR DISEASE

POSTER VIEWING SESSION

Roman Goloshchapov-Aksenov, Dmitry Kicha, Oleg Rukodaynyy, Pavel Volkov
Cardiology, Interventional And Hybrid Surgery Technology, Российский университет дружбы народов, Москва, Russian Federation

Background and Aims : An important principle of clinical management processes for improving cardiovascular care is to increase patient adherence to optimal therapy **Aim.**To revealthe adherence of patients with cardiovascular diseases to optimal medication.

Methods: Material and methods. A direct continuous questionnaire survey of patients with cardiovascular diseases (n = 1018) was carried out using a modified D. Morisky et al. questionnaire (1986). The degree of patientsadherence to the fulfillment of doctors recommendations at the stage of the initial interview and after 6 and 24 months was compared and the effectiveness of clinical management for improve of adherence was assessed ($p<0.05$).

Results: At the stage of the first consultation, low adherence of patients to complex therapy to antihypertensive therapy was established (23.8%); high adherence was reveal in the group of patients after angioplasty to dual antiplatelet therapy (99%), in patients with atrial fibrillation to anticoagulant therapy - 86%, and in patients with diabetes to glucose-lowering therapy - 98%. After 6 and 24 months of observation, including after the provision of endovascular and surgical care, adherence to optimal medication in patients of all groups increased to 99.9%и 96%($p <0.05$).

Conclusions: Clinical management in the healthcare process optimizes the control of the effectiveness of the fulfillment of medical prescriptions, including self-control by patients of hemodynamic and other indicators. The formation of trusting relationships in the doctor-patient system is the most important principle of the continuity in clinical management of the adherence of patients to optimal therapy of cardiovascular disease

ID:71

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

THE CHANGE OF LDL-C AND TREATMENT PATTERNS AMONG DOCUMENTED CAD/MI PATIENTS WHO UNDERWENT CAG IN TAIWAN: A RETROSPECTIVE COHORT STUDY

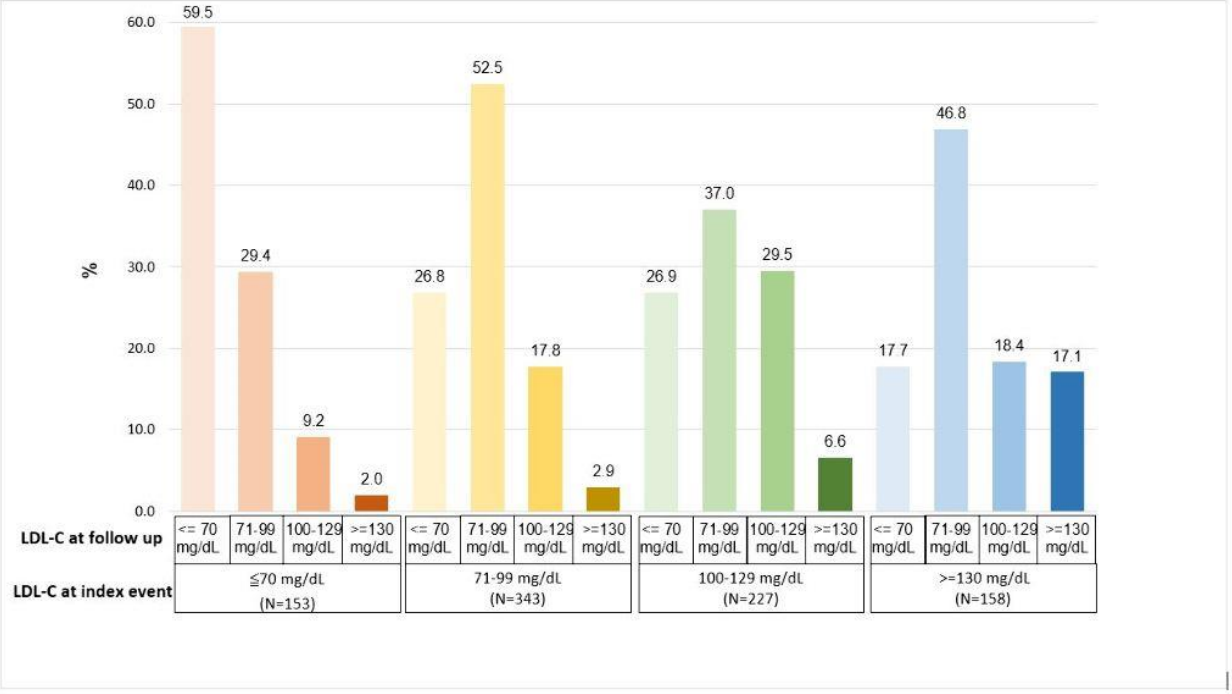
POSTER VIEWING SESSION

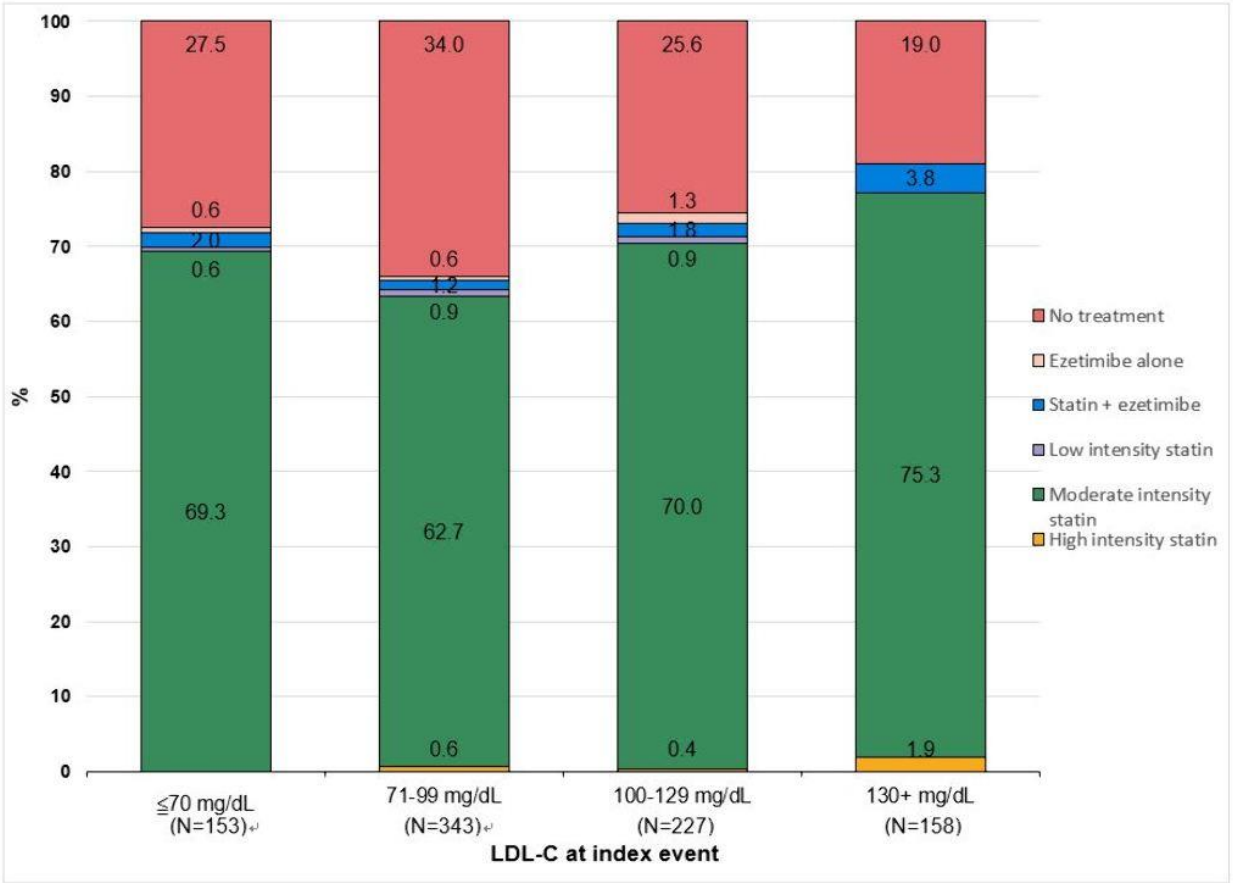
Chieh Min Chen[1], Chia-Yun Hsu[2], Hung-Ju Lin[3], Ho-Min Chen[2], Yea-Harn Yang[4], Wei-Ju Chen[4], Fei-Yuan Hsiao[1], Wen-Jone Chen[3]
[1]Graduate Institute Of Clinical Pharmacy, College Of Medicine, National Taiwan University, TAIPEI, Taiwan, [2]Health Data Research Center, National Taiwan University, TAIPEI, Taiwan, [3]Division Of Cardiology, Department Of Internal Medicine, National Taiwan University Hospital, TAIPEI, Taiwan, [4]Amgen Taiwan Limited, Amgen Taiwan Limited, TAIPEI, Taiwan

Background and Aims : Limited studies using electronic medical records describe LDL-C goal attainment after coronary artery disease/myocardial infarction (CAD/MI). We aimed to describe changes in LDL-C and treatment patterns after a documented CAD/MI by coronary angiography (CAG) in a medical center in Taiwan.

Methods: In this retrospective cohort study, we identified adult patients admitted between 2012/1/1 and 2016/6/30 for documented CAD/MI by CAG (admission date as the index event), using the integrated medical database of National Taiwan University Hospital (NTUH-iMD). Of those, patients receiving lipid testing at index event and 6 months after index event were included. The treatment pattern was evaluated within 1 month after index event. LDL-C goal attainment was defined as follow-up LDL-C ≦70 mg/dL as recommended by the 2013 ESC/EAS guideline.

Results: Among 881 patients enrolled, 717 (81.4%) were male with mean age of 63.1 years (SD:11.7y). At the index event, 153 patients (17.4%) had their LDL-C level at≦70 mg/dL; 343 (38.9%) were at 71-99 mg/dL; 227 (25.8%) at 100-129 mg/dL; and 158 (17.9%) at≧130 mg/dL. At a 6-month follow-up, a total of 272 (30.9%) attained LDL-C control goal: the proportion of goal attainment ranged from 17.7% to 59.5% by baseline LDL-C groups (**Figure1**). Within one month after the index event, 247 patients (28.0%) still received no lipid-lowering treatment, ranging from 19.0% to 34.0% by baseline LDL-C levels (**Figure2**).





Conclusions: Even though treatment guidelines have been established, this real-world study shows the lipid management of documented CAD/MI patients undergoing CAG remains suboptimal in Taiwan.

ID:51

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

NMDA-RECEPTORS ANTAGONIST INFLUENCE ON EATING BEHAVIOR IN SYRIAN GOLDEN HAMSTERS UNDER CARBOHYDRATE METABOLISM EXPERIMENTAL PATHOLOGIES

POSTER VIEWING SESSION

Tetiana Briukhanova[1], Dmytro Lytkin[2], Andriy Zagayko[3]
[1]Biological Chemistry, National University of Pharmacy, Kharkiv National Medical University, Kharkiv, Ukraine, [2]Biological Chemistry, National University of Pharmacy, Kharkiv, Ukraine, [3]Scientific Department, Medical center of physical rehabilitation and sport medicine, Kharkiv, Ukraine

Background and Aims : It is well-known, that under diabetes mellitus (DM) and related disorders pathological changes of eating behavior are observed. Aim of our work was to study the potential influence of NMDA-receptors antagonist memantine on feeding behavior under experimental DM in Syrian golden hamsters.

Methods: Experimental studies were carried out in Syrian golden hamsters (n=40). Animals were divided in 4 groups (intact control – IC; animals with DM – DM induced by high calorie diet and streptozotocin injections; animals with DM which memantine (DM+memantine) or metformine (DM+metformine) or combination of drugs (DM+memantine+metformine) were administrated during 2 weeks intragastrically. The number of food acceptance acts and mean time of eating (in seconds) were assessed for feeding behavior evaluation. Blood glucose level and insulin content were measured.

Results: It was found that DM modelling provoke a significant increasing in number of food acceptance acts (in 65.4%) and mean time of eating (in 41.7%) compare to IC group. Metformine and memantine administration correct these pathological changes, but combination of the medicines demonstrated the most effective influence on marker's normalization comparison with the DM and DM+metformine groups. All behavioral markers changes correlated with a proportional basal glycemia and insulin resistance levels decreasing. These findings indicate that memantine can regulate the feeding behavior in animals under the pathological changes of carbohydrate metabolism.

Conclusions: NMDA-antagonist memantine has a potential correct influence on feeding behavior pathological changes under the experimental diabetes mellitus in hamsters.

ID:175

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

DYSLIPIDEMIA AND THE CLINICAL MANIFESTATIONS OF ATHEROSCLEROSIS IN THE ELDERLY

POSTER VIEWING SESSION

Volha Sujayeva[1], Ganna Kravchenko[2]
[1]Laboratory Of Chronic Ischemic Heart Disease, Republican Scientific and Practical Centre "Cfrdiology", Минск, Belarus, [2]Laboratory Of Coronary Artery Disease, Republican Scientific and Practical Centre "Cardiology", Minsk, Belarus

Background and Aims : Aim: to identify the effect of dyslipidemia on the clinical manifestations of atherosclerosis in elderly.

Methods: We studied 96 patients aged 70.6 (66.0; 73.0) years, 33 (33.3%) - men, 63 (66.7%) - women. Hypertension grade I-III had 87 (91%), heart failure NYHA class I-II had 78 (81%) of 96. We performed: carotid ultrasound, endothelium-dependent relaxatione (D. Celeamajer et al., 1992), echocardiography using the Vivid-9 GE (USA) equipement; computed tomography angiography of the coronary arteries (CTA CA) and coronary calcium index (CCI) using dual-energy, 384-slice CT scanner of the premium class Siemens Somatom Force from General Electric Medical Systems (Germany); biochemical blood tests (lipids, glucose, uric acid, apolipoprotein A-1 (ApoA-1) and apolipoprotein B (ApoB).

Results: According to carotid ultrasound 96.9% of patients had carotid artery stenoses. We found high or very high cardiovascular risk according to CCI in 49.3% elderly patients. Aortic valve calcification had 67.9%, mitral valve - 75% of all includied according to heart CT data. We also revaelase vasomotor endothelial dysfunction in 64.6% of patients, while 1/3 of them had pathological vasoconstriction in response. We studied positive correlation ($p<0.05$) between degree of carotid stenosis and CCI. On the other hand CCI was significantly higher in smokers, patients with diabetes mellitus and in alcohol abusers. We revealed coronary arteries stenoses in 78.5% of patients according to CTA CA.

Conclusions: We found high prevalence of clinical/subclinical manifestations of atherosclerosis in elderly people, which were interrelated with indicators of the blood lipid spectrum, dictates the need for statin therapy for both primary and secondary prevention.

ID:187

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

RESPONSE OF LIPOPROTEINS TO A MEAL TOLERANCE TEST IN PATIENTS WITH TYPE 2 DIABETES AND HYPERTRIGLYCERIDEMIA

POSTER VIEWING SESSION

Shizuya Yamashita[1], Hidenori Arai[2], Koutaro Yokote[3], Eiichi Araki[4], Neil Hounslow[5], Kenichiro Ikeda[6], Toshiaki Nojima[7], Hideki Suganami[7], Shun Ishibashi[8]
[1]Department Of Cardiology, Rinku General Medical Center, Izumisano, Japan, [2]President, National Center for Geriatrics and Gerontology, Obu, Japan, [3]Department Of Endocrinology, Hematology And Gerontology, Chiba University Graduate School of Medicine, Chiba, Japan, [4]Department Of Metabolic Medicine, Faculty Of Life Sciences, Kumamoto University, Kumamoto, Japan, [5]Medical Affairs, Kowa Pharmaceutical Europe Co. Ltd., Wokingham, United Kingdom, [6]Medical Affairs Department, Kowa Company, Ltd., Tokyo, Japan, [7]Clinical Data Science Department, Kowa Company, Ltd., Tokyo, Japan, [8]Division Of Endocrinology And Metabolism, Department Of Internal Medicine, Jichi Medical University School of Medicine, Shimotsuke, Japan

Background and Aims : High fasting TG is a marker of increased postprandial TG-rich lipoproteins and their remnants. Non-fasting TG is said to be 20-25% higher than fasting TG. It remains unclear what determines the non-fasting lipid profile. The aim of this study was to examine lipid parameters in fasting and postprandial states and to explore their relationship in patients with type 2 diabetes (T2D) and hypertriglyceridemia.

Methods: This was a post-hoc analysis of a pemafibrate phase 3 clinical trial in Japanese patients with T2D and hypertriglyceridemia who underwent a meal tolerance test (N=68). Baseline data before starting the study drug were analyzed. The blood sampling was conducted at 0, 1, 2, 4.5 and 6.5 h after taking the test meal (592 kcal).

Results: After taking the test meal, TG increased from 256.8 mg/dL (0 h) to 274.8 mg/dL (1 h, +11.0%), 330.8 mg/dL (2 h, +36.3%), 341.8 mg/dL (4.5 h, +42.1%) and 285.8 mg/dL (6.5 h, +19.7%). The postprandial apoB48 time course was similar to that of TG, whereas the increase in RemL-C was slower. $AUC_{0\text{-}6.5h}$-TG and $AUC_{0\text{-}6.5h}$-RemL-C were significantly associated with baseline values for TG, RemL-C, apoB48, apoC2, apoC3 and apoE.

Conclusions: In patients with T2D and hypertriglyceridemia, plasma TG levels increased up to approximately 1.5-fold after taking the test meal. Postprandial TG and RemL-C increases can be predictable from the baseline values for TG, RemL-C, apoB48, apoC2, apoC3 and apoE.

ID:281

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

SUBCLINICAL ATHEROSCLEROSIS DEVELOPMENT DURING PHYTOESTROGEN THERAPY

POSTER VIEWING SESSION

Tatiana V. Kirichenko[1], Irina Y. Yudina[2], Alexander N. Orekhov[1]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [2]Institute Of Clinical Medicine Named After N.v. Sklifosovsky, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation

Background and Aims : The study was aimed to evaluate the effect of phytoestrogen therapy with natural preparation based on grape seeds, green tea leaves and hop cones on the progression of carotid atherosclerosis in peri- and postmenopausal women.

Methods: The progression of carotid intima-media thickness (cIMT) was evaluated in 315 perimenopausal women aged 40-55 years and in 231 postmenopausal women aged 60-69 years, all study participants were free of cardiovascular disease. The assessment was done by B-mode ultrasound at baseline and after 12 and 24 months of follow-up.

Results: The study revealed no statistically significant changes in the rate of cIMT progression in perimenopausal women treated with phytoestrogens or placebo. By contrast, a statistically significant difference in the rate of atherosclerosis development was observed in postmenopausal women treated with phytoestrogens as compared to placebo (p=0.008). The rate of cIMT progression in the placebo group of postmenopausal women was 0.019 mm/year that corresponded to a significant increase of cIMT during the observation period (p=0.012), while the rate of cIMT progression in phytoestrogen postmenopausal recipients was 0.011 mm/year, and the change of cIMT wasn't statistically significant within 2 years of follow-up (p=0.101).

Conclusions: The obtained results suggest that postmenopausal women can be a suitable cohort for trials assessing the anti-atherosclerosis effects of phytoestrogen preparations. In particular, the beneficial effect of phytoestrogens on cIMT progression was demonstrated in postmenopausal women. This work was supported by the Russian Science Foundation (Grant #22-25-00498).

ID:251

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 Cholesterol efflux and reverse cholesterol transport*

EICOSAPENTAENOIC ACID (EPA, C20:5 N-3) INCREASED ABCA1-MEDIATED CHOLESTEROL EFFLUX FROM J774 MOUSE MACROPHAGES OR THP-1 HUMAN MACROPHAGES BY MODULATING SECRETED EICOSANOIDS

POSTER VIEWING SESSION

Hani Dakroub[1], Maxime Nowak[1], Kodjo Nouwade[2], Sana Tfaili[2], Bastien Prost[3], Audrey Solgadi[3], Pierre Chaminade[2], Jean-Louis Paul[1], Natalie Fournier[1]
[1]Ea 7357-lip(sys)2, Atherosclerose Et Macrophages: Impact Des Phospholipides Et Des Fonctions Mitochondriales Sur Le Trafic Et L'efflux Du Cholesterol Cellulaire, University Paris Saclay, Faculty of Pharmacy, CHATENAY-MALABRY, France, [2]Ea7357-chimie Analytique Pharmaceutique, University Paris Saclay, Faculty of Pharmacy, CHATENAY-MALABRY, France, [3]Ipsit-samm, University Paris Saclay, Faculty of Pharmacy, CHATENAY-MALABRY, France

Background and Aims : A diet rich in eicosapentaenoic acid (EPA, C20:5 n-3) is cardioprotective. We studied *in vitro* the impact of EPA membrane incorporation on the anti-atherogenic ABCA1 efflux pathway in the absence or presence of LPS to create the inflammatory microenvironment observed within atherosclerotic plaques.

Methods: J774 mouse macrophages or human monocytic leukemia THP-1 cells differentiated into macrophages were supplemented (or not) for 34 h with 70 µM EPA. Macrophages were incubated with or without 100 ng/mL LPS for 16 h and isotopic cholesterol efflux to lipid-free apolipoprotein AI was measured after 4 h of incubation. Secreted eicosanoids were quantified by RP-UHPLC coupled to LTQ Orbitrap Velos Pro® HRMS.

Results: In both models, EPA-treated macrophages exhibited decreased level of arachidonic acid (AA, C20:4 n-6) associated with high level of EPA. EPA decreased ABCA1 functionality from J774 macrophages (-19%), whereas it increased ABCA1 functionality from THP-1 macrophages (+24%). In an inflammatory environment, EPA increased cholesterol efflux from both J774 macrophages (+53%) and THP-1 macrophages (+47%). Importantly, prostaglandin E3, leukotriene D4, lipoxin A4 and 14-15 hydroxyeicosatetraenoic acid are positively related to ABCA1 cholesterol efflux.

Conclusions: In conclusion, in inflammatory conditions, EPA increased ABCA1 functionality from both mouse and human macrophages likely by altering the balance of cellular eicosanoids produced from AA or EPA. This observation may partly explain the cardioprotective effect of EPA confirmed in recent clinical trials. In addition, our results illustrate that the *in vitro* impact of EPA on the ABCA1 cholesterol efflux pathway may vary according to the phenotype of macrophages.

ID:280

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

MONOCYTE ACTIVATION IN PATIENTS WITH CAROTID ATHEROSCLEROSIS AND OBESITY

POSTER VIEWING SESSION

Tatiana V. Kirichenko[1], Natalya N. Shaposhnikova[2], Yurgita R. Varaeva[2], Taisiya V. Tolstik[1], Yulia V. Markina[1], Alexander M. Markin[1], Alexander N. Orekhov[1], Antonina V. Starodubova[3]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [2]Department Of Cardiovascular Pathology And Diet Therapy, Federal Research Centre for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation, [3]Department Of Medical And Preventive Nutrition, Federal Research Centre for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation

Background and Aims : Currently, obesity is considered as a pro-inflammatory condition, which contributes to increased atherogenesis and the development of cardiovascular diseases. This pilot study was aimed to evaluate the role of pro-inflammatory monocyte activation in atherosclerosis development in obese patients.

Methods: Totally 20 patients with mean BMI 38.4(9.3) kg/m^2 and mean age 59.9(5.4) years old were divided into 2 groups: 11 participants with carotid atherosclerosis and 9 atherosclerosis-free participants. Leucocytes were extracted from whole blood by standard ficoll-gradient method followed magnetic separation of CD14+ cells. Monocyte activation was expressed as a ratio of non-stimulated and LPS-stimulated secretion of pro-inflammatory cytokines TNF-α and IL-1 measured by ELISA.

Results: Monocyte activation by TNF-α was significantly higher in obese patients with atherosclerosis than in atherosclerosis-free patients with obesity: 22.4(11.9) vs. 11.0(7.3), respectively, p=0.018. Monocyte activation by IL-1 was also significantly higher in patients with atherosclerosis than in atherosclerosis-free participants: 86.6(92.7) vs. 13.8(16.2) respectively, p=0.027.

Conclusions: This pilot study demonstrated significantly increased monocyte activation in patients with atherosclerosis and obesity compared with patients without atherosclerosis, however, it is necessary to expand the study groups and the panel of cytokines. This work was supported by the Russian Science Foundation (Grant № 22-15-00252).

ID:278

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

IDENTIFICATION OF A MIRNA BASED-SIGNATURE ASSOCIATED WITH ACUTE CORONARY SYNDROME: EVIDENCE FROM THE FLORINF STUDY

POSTER VIEWING SESSION

Meyer Elbaz[1], Julien Faccini[2], Elisa Grousset[2], Jean-Bernard Ruidavets[3], Cecile Vindis[2]
[1]Cardiology-cic Cardiomet, Rangueil Hospital, Toulouse, France, [2]Cic Cardiomet, INSERM, Toulouse, France, [3]Epidémiologie Et Analyses En Santé Publique, INSERM 1027, Toulouse, France

Background and Aims : The discovery of novel biomarkers that improve risk prediction models of acute coronary syndrome (ACS) is essential to better identify and stratify very high-risk patients. MicroRNAs (miRNAs) are essential non-coding modulators of gene expression. Circulating miRNAs have recently emerged as important regulators and fine-tuners of physiological and pathological cardiovascular processes; therefore, specific miRNAs expression profiles may represent new risk biomarkers. The aim of the present study was i) to assess changes in circulating miRNAs levels associated with recent acute coronary syndrome (ACS) and ii) to evaluate the incremental value of adding circulating miRNAs to a clinical predictive risk model.

Methods: The study population included ACS patients (n=99) and control subjects (n=103) with high cardiovascular risk but without any previous myocardial infarction or coronary event. Based on a miRNA profiling in a matched derivation case-control cohort, 21 miRNAs were selected for validation.

Results: Comparing ACS cases versus controls, 7 miRNAs were significantly differentially expressed. Multivariate logistic regression analyses demonstrated that among the 7 miRNAs tested, 5 were independently associated with the risk of ACS. A receiver operating characteristic (ROC) curve analysis revealed that the combination of miR-122+miR-150+miR-195+miR-16 to the clinical model provides the best performance with an increased AUC from 0.882 to 0.924 (95% CI 0.885-0.933, p = 0.003).

Conclusions: In conclusion, our study identified a powerful signature of circulating miRNAs providing additive value to traditional risk markers for ACS prediction.

ID:277

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

PRO-INFLAMMATORY CYTOKINES SECRETION BY CULTURED MONOCYTES OF OBESE PATIENTS WITH ATHEROSCLEROSIS

POSTER VIEWING SESSION

Tatiana V. Kirichenko[1], Yurgita R. Varaeva[2], Natalya N. Shaposhnikova[2], Taisiya V. Tolstik[1], Yulia V. Markina[1], Alexander M. Markin[1], Alexander N. Orekhov[1], Antonina V. Starodubova[3]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [2]Department Of Cardiovascular Pathology And Diet Therapy, Federal Research Centre for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation, [3]Department Of Medical And Preventive Nutrition, Federal Research Centre for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation

Background and Aims : Inflammation is one of the key factors in the development of cardiovascular complications of obesity, in particular, atherogenesis, currently the mechanisms of inflammation in obesity are widely studied. The aim of this study was the evaluation of pro-inflammatory cytokines secretion by cultured monocytes of obese patients with and without carotid atherosclerosis.

Methods: In total, 20 obese patients were included in the study, 11 participants had atherosclerosis lesions in carotid arteries and 9 were free of atherosclerosis. Basal and LPS-stimulated secretion of pro-inflammatory cytokines TNF-α and IL-1 was investigated by ELISA in primary culture of patients' monocytes derived from whole blood by ficoll-gradient extraction followed magnetic separation of CD14+ cells.

Results: Basal secretion of TNF-α didn't differ between groups with/without atherosclerosis and was 6.2(0.6)/6.6(0.3), respectively, p=0.072. Basal secretion of IL-1 was 5.1(7.2) in atherosclerosis group and 18.2(17.3) in non-atherosclerosis group, p=0.059. LPS-stimulated secretion of both cytokines was higher in atherosclerotic patients, but only for TNF-α the difference was significant: TNF-α was 136.6(74.2) vs. 72.0(46.2) in non-atherosclerosis group, p=0.029; IL-1 was 201.7(172.1) vs. 105.1(58.2) in non-atherosclerosis group, p=0.102.

Conclusions: A study on a larger sample of patients is needed to clarify the role of inflammatory status of monocytes in the development of atherosclerosis in obese patients. This work was supported by the Russian Science Foundation (Grant № 22-25-00414).

ID:274

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

RUTAECARPINE, A BIOACTIVE CONSTITUENT ISOLATED FROM TETRADIUM RUTICARPUM, PREVENTS ENDOTHELIAL INFLAMMATION

POSTER VIEWING SESSION

Xiumei Wu[1], Zhenghong Liu[2], Mengyun Xu[2], Suowen Xu[2], Jianping Weng[1]
[1]Department Of Endocrinology And Metabolism, Guangdong Provincial Key Laboratory Of Diabetology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, [2]Institute Of Endocrine And Metabolic Diseases, The First Affiliated Hospital Of Ustc, Division Of Life Sciences And Medicine, University Of Science And Technology Of China, Laboratory of Metabolics and Cardiovascular Diseases, hefei, China

Background and Aims : Endothelial inflammation and dysfunction contribute significantly to atherosclerosis. Rutaecarpine, isolated from Chinese medicinal herb-*Tetradium ruticarpum*, is a bioactive alkaloid with anti-atherosclerotic effects via suppressing macrophage-derived foam cell formation. However, the pharmacological effects and molechanism whereby rutaecarpine protects against endothelial dysfunction remain unknown. Given inflammation is a significant contributor to endothelial dysfunction and atherosclerosis, the present study was designed to examine the pharmacological effects of rutaecarpine in regulating endothelial inflammation and the mechanism of action involved.

Methods: HUVE cells were pre-incubated with rutaecarpine (5, 10μM) overnight and then treated with TNFα(10ng/ml) for 6hours. Cell viability, endothelial inflammation,monocyte adhesion and NF-κB pathway were investigated by CCK-8 assays, wb, qPCR and luciferase assays.

Results: We found rutaecarpine did not have endothelial toxicity ranging from 1 to 10μM. Rutaecarpine significantly alleviated endothelial inflammation induced by TNFα, with decreased ICAM1,VCAM1 and E-selectin expression. Of relevance, the anti-inflammatory effects of rutaecarpine lead to ameliorated monocyte adhesion to TNFα-activated endothelium. Mechanistically, rutaecarpine downregulated the transcriptional activity of NF-κB, without influencing the activation of the upstream MAPK (p38,JNK,ERK) signaling pathway and nuclear translocation of NF-κB. To gain a comprehensive understanding of endothelial protective effects of rutaecarpine, we performed a transcriptomic profing study in rutaecarpine-treated endothelial cells in the presence of TNFα. Our RNA-seq and integrated bioinformatic analysis revealed rutaecarpine suppressed inflammatory pathways as well as activated the Nrf2 pathway.

Conclusions: Rutaecarpine ameliorates endothelial inflammation by inhibition of NF-κB and activation of Nrf2. Our findings suggest the therapeutic potential of anti-inflammatory alkaloid compounds from herbal medicine against endothelial dysfunction and associated.

ID:270

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

PHARMACOLOGICAL INHIBITION OF IRAK1 AND IRAK4 PREVENTS ENDOTHELIAL INFLAMMATION AND ATHEROSCLEROSIS IN MICE

POSTER VIEWING SESSION

Xiumei Wu[1], Mengyun Xu[2], Zhenghong Liu[2], Zhidan Zhang[2], Yujie Liu[2], Sihui Luo[2], Xueying Zheng[2], Suowen Xu[2], Jianping Weng[1]
[1]Department Of Endocrinology And Metabolism, Guangdong Provincial Key Laboratory Of Diabetology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, [2]Institute Of Endocrine And Metabolic Diseases, The First Affiliated Hospital Of Ustc, Division Of Life Sciences And Medicine, University Of Science And Technology Of China, Laboratory of Metabolics and Cardiovascular Diseases, hefei, China

Background and Aims : Inflammation associated endothelial dysfunction represents a pivotal contributor to atherosclerosis. Increasingly evidence implicated IL1-R/TLR signaling as a nodal point in inflammation and development of atherosclerosis. Recent large-scale clinical trials suggested the therapeutic potential of anti-inflammatory therapy targeting IL-1β and IL-6 in anti-atherosclerosis. The present study examined the pharmacological effects of IRAK1/4i in regulating endothelial inflammation and atherosclerosis.

Methods: HUVE cells were pre-treated with IL-1R-associated kinase 1and4 inhibitors(IRAK1/4i,5 μM) overnight and then incubated with LPS(1μg/ml) for 6hours. Cell viability, endothelial inflammation, monocyte adhesion and NF-κB pathway were investigated by CCK-8 assays,wb,qPCR and luciferase assays. *In vivo*, ApoE$^{-/-}$mice(n=9-10/group) were fed with high cholesterol diet and orally administered with IRAK1/4i(20 mg/kg/d) for 8 weeks. After sacrifice, we collected serum and tissues to evaluate the atherosclerotic lesion,collagen content and lipid metabolism by biochemical detection,pathological examination,wb,qPCR.

Results: Dual pharmacological inhibition of IRAK1 and IRAK4 by an IRAK1/4i is more effective against LPS induced endothelial inflammation, than IRAK1 inhibitor or IRAK4 inhibitor monotherapy. IRAK1/4i showed little endothelial toxicity at concentrations from 1-10μM. Inhibition of IRAK1/4 alleviated endothelial activation induced by LPS *in vitro,* evidenced by attenuated monocyte adhesion to the endothelium. Mechanistically, blockade of IRAK1/4 ameliorated the transcriptional activity of NF-κB. *In vivo,* IRAK1/4i significantly reduced atherosclerotic lesion size in the aortic sinus, increased hepatic LDLR protein level, and lowered LDL-C level, without affecting other lipid parameters or glucose tolerance.

Conclusions: Dual pharmacological inhibition of IRAK1 and IRAK4 attenuates endothelial inflammation, lowering LDL-C levels and reduces atherosclerosis. Our study reinforces the central standing of anti-inflammatory therapy in cardiovascular therapeutics.

ID:265

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

GENETIC AND EPIGENETIC INTERACTION IN STABILIZATION MECHANISM OF HIGHLY CALCIFIED CAROTID PLAQUES

POSTER VIEWING SESSION

Hiroyuki Katano[1], Mitsuhito Mase[2]
[1]Neurosurgery And Medical Informatics, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, [2]Neurosurgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Background and Aims : To investigate the molecular regulation mechanism involved in stabilization of carotid calcified plaques.

Methods: The carotid plaques collected by endarterectomy are divided into high and low calcification plaque groups based on the Agatston calcium score (CS), and comprehensive gene expression analysis was performed.

Results: The mRNA microarray showed significant upregulation of angiopoietin-like protein 4 (ANGPTL4) mRNA and downregulation of fibroblast growth factor receptor 2 (FGFR2) mRNA in highly calcified plaques. The miRNA microarray with verifying by qRT-PCR was performed and the total gene signals of hsa-miR-4530 and -133b were significantly inversely correlated with CS. DNA methylation comprehensive analysis and data mining revealed that hypomethylation of receptor activity modifying protein 1 (RAMP1) was commonly extracted in the promoter and tissue-specific CpG island shore regions. Whole exome analysis disclosed, in highly calcified plaques, significantly more ATP binding cassette subfamily C member 6 (ABCC6) mutations that cause generalized arterial calcification of infancy (GACI) by SNV.

Conclusions: ANGPTL4 enhancement and FGFR2 inhibition were observed at the mRNA and protein levels, and angiogenesis inhibition induced anti-arteriosclerosis. By suppressing hsa-miR-4530 and -133b targeting ANGPTL4, the gene expression was enhanced. In addition, the enhancement of RAMP1 by DNA hypomethylation brought about anti-arteriosclerosis effect from CGRP action. Hsa-miR-133b was also involved in the promotion of calcification via RUNX2, and RAMP1 by itself. DNA mutation of ABCC6, which is strongly involved in vascular calcification, was also observed. While calcification is promoted, anti-arteriosclerosis by interaction of various factors may contribute to stability in highly calcified carotid plaques.

ID:261

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

RELATIONSHIP BETWEEN THE CHOLESTEROL AND TRIGLYCERIDE CONTENT OF LIPOPROTEIN SUBCLASSES AND CAROTID INTIMA-MEDIA THICKNESS: RESULTS FROM THE KYUSHU AND OKINAWA POPULATION STUDY (KOPS)

POSTER VIEWING SESSION

Hiroaki Ikezaki[1], Masumi Ai[2], Mitsuyo Okazaki[3], Jun Hayashi[1], Nobuyuki Shimono[1], Ernst J. Schaefer[4]
[1]Department Of General Internal Medicine, Kyushu University Hospital, Fukuoka, Japan, [2]Department Of Insured Medical Care Management, Tokyo Medical and Dental University, Tokyo, Japan, [3]Professor Emeritus, Tokyo Medical and Dental University, Tokyo, Japan, [4]Cardiovascular Nutrition Laboratory, Tufts University, Boston, United States of America

Background and Aims : The association between 20 lipoprotein cholesterol and triglycerides subclasses and carotid intimal medial thickness (cIMT) progression has not been evaluated fully. Our goal was to assess which lipoprotein subclasses were associated with max cIMT levels.

Methods: Levels of cIMT and 20 lipoprotein cholesterol and triglycerides subclasses using gel permeation high-performance liquid chromatography (GP-HPLC) were analyzed in 864 men and women (mean age 57 years, free of chronic liver or kidney diseases and off cholesterol-lowering, hormone replacement, or adrenocorticosteroid medications). Univariate and multivariate regression analyses were performed to examine the relationships between lipoprotein subclasses and max cIMT levels.

Results: Max cIMT levels were 0.90 mm in women and 0.97 mm in men. After adjustment for age, gender, systolic blood pressure, smoking habits, diabetes, and hypertension treatment, elevated low-density lipoprotein cholesterol-2 and -3 were associated with higher max cIMT levels in both women and men. Decreased high-density lipoprotein cholesterol-7 was associated with higher max cIMT levels only in women (all *P* for trend < 0.05). However, no associations were found between any triglyceride subclasses and max cIMT levels.

Conclusions: Our data indicate that elevated smaller LDL cholesterol levels separated by GP-HPLC were significantly associated with max cIMT in both men and women. Our results support the concept that small dense LDL cholesterol is the most atherogenic lipoprotein parameter.

ID:253

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

ANGPTL3 INDUCES A PROINFLAMMATORY RESPONSE IN THP-1 DERIVED MACROPHAGES

POSTER VIEWING SESSION

Ilaria Rossi[1], Ilenia Milani[1], Maria Giovanna Lupo[2], Nicola Ferri[2]
[1]Dipartimento Di Scienze Del Farmaco, Universitá degli Studi di Padova, Padova, Italy, [2]Dipartimento Di Medicina, Universitá degli Studi di Padova, Padova, Italy

Background and Aims : ANGPTL3 is a hepatokine known for its activity as negative regulator of lipoprotein lipase with its N-terminal domain. Besides the direct lipid activity, its C-terminal domain interacts with integrin αVβ3. Our aim was to evaluate the potential direct pro-atherogenic action of ANGPTL3 to predict a possible protective role of mAb anti-ANGPTL3 evinacumab on atherosclerotic plaque development.

Methods: We utilized cultured THP-1 derived macrophages polarized towards a pro-inflammatory phenotype and evaluated their inflammatory phenotype in response to the treatment with human recombinant ANGPTL3 (hrecANGPTL3). By western-blot, RT-qPCR and ELISA assays, we analysed the expression of genes and proteins involved in lipid metabolism and inflammatory response and modulate the interaction of ANGPTL3 with αVβ3 integrin with RGD peptide.

Results: Our results demonstrated that administering 100ng/mL hrecANGPTL3 increases the expression of proinflammatory cytokines IL-1B, IL-6 and TNFα (respectively 1.87±0.08, 1.35±0.11, 1.57±0.49 fold vs.control) in THP-1 derived macrophages, thus demonstrating the positive involvement of ANGPTL3 on inflammation. The secretion of TNFα increased by 1.98±0.4 fold vs control. RGD peptide, on the other side, decreased the production of IL-1B by 98% (0.02 ± 0.02 fold vs.control) on THP-1 cells. Moreover, triglyceride and total cholesterol concentration increases respectively by 30% and 18% comparing with control when hrecANGPTL3 is added.

Conclusions: These results lead us to state a possible direct involvement of ANGPTL3 on the inflammatory process that leads to plaque formation through the integrin αVβ3. Our results, although obtained in in vitro model, predict a possible vascular directed effect of evinacumab that needs to be further investigated in vivo.

ID:252

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

ASSOCIATION OF SUBCLINICAL ATHEROSCLEROSIS AND IL-1 SECRETION BY MONOCYTES IN PATIENTS WITH RHEUMATOID ARTHRITIS

POSTER VIEWING SESSION

Tatiana V. Kirichenko[1], Elena V. Gerasimova[2], Alexander M. Markin[1], Yulia V. Markina[1], Anastasia I. Bogatyreva[1], Daria A. Gerasimova[3], Alexander N. Orekhov[1], Tatiana V. Popkova[2]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [2]Laboratory Of Systemic Rheumatic Diseases, V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation, [3]Institute Of Pharmacy Named After A.p. Nelyubin, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation

Background and Aims : Patients with rheumatoid arthritis (RA) are at high risk of atherosclerosis development, due to their inflammatory status. This study was aimed to assess the association of carotid atherosclerosis with IL-1 secretion by cultured monocytes from patients with RA.

Methods: 15 patients with RA aged 53.8(14.4) were included. 7 participants were atherosclerosis-free and 8 had atherosclerotic lesions in carotids. B-mode ultrasound was conducted to identify atherosclerotic status. Primary culture of monocytes was obtained from blood leucocytes by magnetic separation of CD14+ cells. Basal and LPS-stimulated IL-1 concentration was estimated by ELISA after 24 hours of incubation, after 5 days of rest, and in 24 hours after re-stimulation with LPS.

Results: In atherosclerosis-free group unstimulated IL-1 secretion was 150.6(106.9) pg/ml; LPS-stimulated - 1287.9(908.0) pg/ml, (p=0.023). After rest period, IL-1 concentration decreased to 240.3(187.9) pg/ml, (p=0.035). After re-stimulation with LPS, IL-1 secretion was 100.3(55.7) pg/ml. In carotid atherosclerosis group unstimulated secretion of IL-1 was 246.7(84.8) pg/ml; LPS-stimulated - 1582.6(1391.4) pg/ml, (p=0.073). After rest period, IL-1 concentration decreased to 505.8(381.3) pg/ml, (p=0.063). After re-stimulation with LPS, the secretion of IL-1 was 130.0(66.5) pg/ml and did not differ significantly from the secretion of cells incubated without LPS - 141.3(51.2) pg/ml, (p=0.725). The difference between groups wasn't significant in all points.

Conclusions: IL-1 secretion by cultivated monocytes of patients with RA was higher in patients with carotid atherosclerosis, but the results didn't reach statistical significance. A study on a larger cohort is necessary. This work was supported by the Russian Science Foundation (Grant № 22-15-00199).

ID:249

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

REAL WORLD EFFICACY OF BEMPEDOIC ACID IN STATIN-INTOLERANT PATIENTS WITH HIGH CARDIOVASCULAR RISK

POSTER VIEWING SESSION

Eamon P. Mccarron, Paul Hamilton, Brona V. Roberts
Belfast, Royal Victoria Hospital, Belfast, United Kingdom

Background and Aims : Background Bempedoic acid (an ATP citrate lyase inhibitor) has recently been licensed for the treatment of dyslipidaemia in patients who are intolerant of statins. We aimed to assess if the tolerability and efficacy seen in clinical trials could be replicated in statin-intolerant patients in routine clinical practice.

Methods: Methods Fifteen patients with high cardiovascular risk and statin intolerance were offered bempedoic acid 180mg once daily as monotherapy (N=3) or in combination with ezetimibe 10mg once daily (N=12). Fourteen were being treated as primary prevention and one as secondary prevention. They were reviewed after approximately three months of treatment to assess tolerability and lipid-lowering effect.

Results: Results At review, five patients has stopped taking bempedoic acid reporting side-effects similar to those experienced with statins. Ten patients reported that they were continuing with treatment (67 % tolerance rate). Lipid profiles demonstrated no LDL reduction in two patients, raising questions of treatment adherence. However in the eight patients who did experience a fall in LDL-cholesterol, mean reduction was 1.5 mmol/L (32.3%). Both the rate of tolerability and the average fall in LDL seen in our patients are comparable to what has been seen in clinical trials.

Conclusions: Conclusions Clinical trial data cannot always be replicated in real-world practice, particularly when it concerns issues such as adverse effects and treatment adherence. However our data on our early experience with this agent confirm it as a useful additional option for clinicians managing hyperlipidaemia.

ID:188

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

INTENSITY OF LIPID-LOWERING THERAPY, ADHERENCE AND LDL-CHOLESTEROL GOAL ATTAINMENT IN PATIENTS WITH CORONARY HEART DISEASE

POSTER VIEWING SESSION

Faizan Mazhar[1], Paul Hjemdahl[2], Catherine M. Clase[3], Kristina Johnel[1], Tomas Jernberg[4], Juan J. Carrero[2]
[1]Department Of Medical Epidemiology And Biostatistics, Karolinska Institutet, Stockholm, Sweden, [2]Clinical Pharmacology Unit, Clinical Epidemiology Division, Department Of Medicine, Karolinska Institutet, Solna, Sweden, [3]Department Of Medicine And Health Research Methods, Evidence And Impact, McMaster University, Ontario, Canada, [4]Department Of Clinical Sciences, Danderyd University Hospital, Karolinska Institutet, Stockholm, Sweden

Background and Aims : To examine patterns of lipid-lowering therapy (LLT) use, and persistence and adherence among coronary heart disease (CHD) patients and their association with lipoprotein cholesterol (LDL-C) goal attainment.

Methods: Observational study among 26,768 adult patients who had suffered a myocardial infarction or had been revascularized in Stockholm, during 2012–18. Study outcomes included initiation of LLT, discontinuation, re-initiation, adherence to treatment and LDL-C goal attainment according to the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) dyslipidaemia guidelines from 2011 (LDL-C < 1.8 mmol/L or ≥50% LDL-C reduction) and 2016 (LDL-C < 1.8 mmol/L and ≥50% LDL-C reduction).

Results: 71% of patients claimed an LLT prescription within 30-days post-discharge, 62% of which were for high-intensity LLT. Rates of high-intensity LLT prescribing increased over time, from 12% in 2012 to 78% in 2018. During median follow-up of 3 (IQR 2-5) years, most patients (73.2%) persisted with statin treatment, 26.3% temporarily/permanently discontinued, and 0.5% changed to non-statin LLT. Only 1.3% discontinued statin treatment permanently. Throughout observation, about 80% of patients showed good statin adherence (proportion of days covered ≥80%), but overall LDL-C target attainment was only 52% at 1-year of follow-up and <50% during subsequent years. LDL-C goal attainment was highest among patients receiving high-intensity statin treatment and showing good treatment adherence.

Conclusions: In a secondary prevention population with coronary heart disease, the rates of LDL-C target attainment remained low throughout the course of therapy despite an increasing use of high-intensity LLT and good treatment adherence/persistence.

ID:247

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

CORRELATIONS BETWEEN HDL CHOLESTEROL RATIO AND SLEEP DISORDERED BREATHING IN PATIENTS WITH HYPERTENSION AND DIABETES MELLITUS

POSTER VIEWING SESSION

Olena Buriakovska[1], Anna Isayeva[2]
[1]Complex Risk Reduction Of Chronic Non-communicable Diseases, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Ukraine, Ukraine, [2]Complex Risk Reduction Of Chronic Non-communicable Diseases, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine

Background and Aims : The aim of research was to assess correlations between sleep disordered breathing and levels of lipids in patients with hypertension and diabetes mellitus.

Methods: 118 patients with hypertension with middle age 57,93±10,66 y.o. were enrolled to this study. Exclusion criteria included the history of myocardial infarction or stroke, heart failure with ejection fraction below 45%, resistant arterial hypertension, treatment with glucocorticosteroids, moxonidine, reserpine, β-blockers, hypnotic drugs. Total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol were determined. To detect sleep disordered breathing (obstructive sleep apnea, central sleep apnea, SpO2) a portable monitoring device SOMNOcheck micro was used (2013, Germany). Statistical analysis was performed using SPSS 17.0 software.

Results: The level of HDL was correlated positively with SpO2 level (r=0,76; p<0,01). However there was not found significant correlations between HDL level and central events at the night (r=0,32; p=0,27). Although, the negative correlation between body mass index (BMI) and SpO2 (r=-0,57; p=0,01) was found. No correlations were detected for glucose and creatinine levels. At the same time, no relationships between episodes of central apnea and blood lipids and anthropometric parameters were found.

Conclusions: The concentration of HDL is associated with SpO2 level according to night monitoring.

ID:240

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

MONOCYTE ACTIVATION IN CORONARY HEART DISEASE AND TYPE 2 DIABETES

POSTER VIEWING SESSION

Tatiana V. Kirichenko[1], Ludmila V. Nedosugova[2], Leila A. Bochkareva[2], Karine O. Galstyan[2], Alexander N. Orekhov[3], Igor A. Sobenin[1]
[1]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [2]Department Of Endocrinology, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation, [3]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation

Background and Aims : Diabetes mellitus (DM) is characterized by accelerated atherosclerosis development, which leads to significant increase of cardiovascular mortality in diabetic patients. Chronic systemic inflammation plays an important role in the pathogenesis of DM, and probably increase the risk of atherosclerosis and atherosclerotic cardiovascular diseases. The aim of this study was to assess the pro-inflammatory activation of blood monocytes in coronary heart disease (CHD) patients with/without DM.

Methods: Totally, 55 CHD patients were included (28 were first time diagnosed with DM and 27 with no glucose metabolism disorders). Proinflammatory monocyte activation was evaluated as a ratio of spontaneous and induced secretion of proinflammatory cytokine TNF-α measured in primary culture of blood-derived monocytes of study participants after 24h-incubation with and without IFN-ɣ by enzyme-linked immuno-sorbent assay.

Results: In CHD without DM group spontaneous TNF-α secretion was 151(70) pg/ml, IFN-ɣ-induced secretion was 139(51) pg/ml, while in diabetic group spontaneous and IFN-ɣ-induced secretion of TNF-α was significantly higher - 750(92) pg/ml, $p<0.05$ and 1571(111) pg/ml, $p<0.05$, respectively.

Conclusions: Increased pro-inflammatory activation of monocytes in diabetes mellitus may be the cause of accelerated atherogenesis, since monocytes are key cells in the development of atherosclerotic lesions. Further research is needed to identify the mechanisms of monocyte activation and their role in atherogenesis. This work was supported by the Russian Science Foundation (Grant #22-25-00149).

ID:237

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

MONOCYTE ACTIVATION IN ATHEROSCLEROSIS ASSOCIATED WITH AUTOIMMUNE RHEUMATIC DISEASES

POSTER VIEWING SESSION

Tatiana V. Kirichenko[1], Elena V. Gerasimova[2], Tatiana V. Popkova[2], Alexander M. Markin[1], Yulia V. Markina[1], Anastasia I. Bogatyreva[1], Daria A. Gerasimova[3], Alexander N. Orekhov[1]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [2]Laboratory Of Systemic Rheumatic Diseases, V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation, [3]Institute Of Pharmacy Named After A.p. Nelyubin, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation

Background and Aims : The pro-inflammatory activation of monocytes may responsible for the the tendency to chronic inflammation, which underlies autoimmune rheumatic diseases (ARDs) and atherosclerosis. It is known that atherosclerosis progression is accelerated in patients with ARDs. The aim of this study is to investigate the association of monocyte activation and carotid atherosclerosis in ARDs patients.

Methods: Isolation of monocytes was carried out according to the standard procedure for obtaining a leukocyte fraction in a Ficoll gradient and subsequent selection of CD14 + cells using magnetic separation. After isolation, the cells were cultured in X-Vivo medium. To assess the degree of monocyte activation, cells were stimulated by the addition of LPS. Monocyte activation was expressed as a ratio of LPS-stimulated/basal secretion of TNF-α. Secretion of TNF-α was determined by ELISA.

Results: Totally 24 participants with ARDs (15 rheumatoid arthritis (RA), 9 systemic lupus erythematosus (SLE)) mean aged 50.4(13.3) years were included in the study. Monocyte activation was significantly lower in atherosclerosis group 8.1(8.1) vs. 21.0(15.2), p=0.015, that is, in atherosclerosis-free group basal TNF-α secretion was 196.7(233.7), LPS-stimulated secretion – 2122.3 (839.9) pg/ml; in atherosclerosis group, the basal secretion was 330.4(272.9), LPS-stimulated secretion – 1528.7(759.7) pg/ml. At the same time, in atherosclerosis group, monocyte activation was the same in patients with RA and SLE; in atherosclerosis-free group, activation was significantly higher in patients with RA (p=0.029).

Conclusions: A study on a larger number of patients will clarify the link between monocyte activation and ARDs-associated atherosclerosis. This work was supported by the Russian Science Foundation (Grant № 22-25-00358).

ID:223

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

ASSOCIATION OF D-DIMER WITH LONG-TERM PROGNOSIS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH ACUTE CORONARY SYNDROME

POSTER VIEWING SESSION

Bing-Yang Zhou, Qi Zhang, Hong-Liang Cong, Le Wang
Department Of Cardiology, Tianjin Chest Hospital, Tianjin, China

Background and Aims : Type 2 diabetes mellitus (DM) accounts for more and more individuals worldwide. D-dimer has been demonstrated to be associated with cardiovascular diseases. However, the potential impact of D-dimer on the long-term prognosis of acute coronary syndrome (ACS) in the special population with type 2 DM is not available. We aim to explore the association of D-dimer with outcomes in DM patients with ACS.

Methods: A total of 2265 consecutive patients with DM and ACS were eligible in the study. Patients were divided into four groups according to quartiles of D-dimer concentration. Univariate and multivariate Cox regression analysis were conducted to explore the prognostic value of D-dimer for future outcomes.

Results: Patients with higher level of D-dimer presented with higher percentage of major adverse cardiovascular events (MACEs) (23.7%), all-cause death (18.3%) and cardiovascular (CV) death (9.4%) in Quartile 4. In multivariate Cox regression analysis, D-dimer was demonstrated to be independently associated with MACEs, all-cause death and CV death. The prognostic value of D-dimer is still significant in subgroups of HbA1C <7% and ≥7%. In Kaplan–Meier analysis, higher D-dimer showed poorer prognosis in MACEs, all-cause death and CV death (all log rank p <0.001). The area under the curve (AUC) by receiver operating characteristic (ROC) curve analysis is 0.609 for MACEs, 0.708 for all-cause death, 0.747 for CV death (p <0.001)

Conclusions: The present study demonstrated the independent predictive value of D-dimer for outcomes in DM patients with ACS. In addition, for the first time, we explored the prognostic value in different glucose control status.

ID:221

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

AUTONOMIC FUNCTION EVALUATION WITH SDANN IN ELDERLY PATIENTS WITH ACUTE ISCHEMIC STROKE

POSTER VIEWING SESSION

Mayumi Masumura, Atsuyuki Ohno
Cardiology, Shizuoka City Shimizu Hospital, Shizuoka, Japan

Background and Aims : The autonomic function is associated with age and the prognosis of cardiovascular diseases. However, it is unclear how severely autonomic function is damaged in elderly patients after acute ischemic stroke.

Methods: Hospitalized patients of 70 years old and over with acute ischemic stroke who performed 24-hour Holter electrocardiography (ECG) from January to October 2021 in a single hospital were studied. To assess autonomic function based on the heart rate variability, we used SDANN (the standard deviation of the averaged normal-to-normal RR interval) during sinus rhythm measured by Holter ECG. As an indicator of atherosclerosis, maximum IMT (intima-media thickness) was measured by a carotid echogram.

Results: There were 62 patients (79.1+/-6.4 years, male 65%, BMI 22.5+/-3.5 kg/m2). Of those, 73% (n=45) had a history of hypertension, 32% (n=20) had diabetes, and 34% (n=21) had smoking history. SDANN was 41.9+/-30.5msec. Subgroup analysis revealed that the lower SDANN group (SDANN 40msec and under, n=27) had a higher prevalence of diabetes compared to the higher SDANN group (p=0.02). Age, sex, max IMT, hypertension, smoking history, and statin use are not statistically significant between the groups. The average SDANN in patients with diabetes was significantly lower compared to those without diabetes (34.2+/-4.4 vs. 48.1+/-3.0, p=0.012).

Conclusions: The average value of SDANN was extremely low compared to the reports in the past literature. It is considered that parasympathetic activity is severely damaged in elderly patients with acute ischemic stroke. When limited to the elderly, there is no difference in SDANN depending on age but is affected by diabetes.

ID:220

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

MANAGEMENT OF SIGNIFICANTLY ELEVATED LIPOPROTEIN(A) IN PATIENTS WITHOUT ESTABLISHED ASCVD

POSTER VIEWING SESSION

Christian Schrock
Lipidology Research, Lp(a) CARE Foundation, Minneapolis, United States of America

Background and Aims : EAS/ESC and Canadian Cardiovascular Society (CCS) Guidelines recommend that everyone should have a determination of Lp(a) level once in a lifetime. 20% of the population will be found to have elevated Lp(a) above 50mg/dL (125nmoles/L) {high Lp(a)}. High Lp(a) produces significant risk of ASCVD particularly CAD. The majority of high Lp(a) patients will not have established ASCVD but need recommendations.

Methods: The EAS/EAS, CCS and other guidelines and literature addressing management of patients with highLp(a) without ASCVD were studied to determine consistency and strength of recommendations.

Results:

Recommendations	Basis	Outcome
PEDIGREE EVALUATIION		
Accurate family history of ASVD	Higher incidence of ASCVD in high Lp(a) pedigrees	Improved management of pedigree
Lp(a) testing of pedigree	Inherited disease with most members of pedigree affected	Patients with highLp(a) identified
LABORATORY EVALUATIONS		
Routine Lipid Panel	Often "LDL-C" is elevated with highLp(a) 50% of heterozygous FH have highLp(a)	Appropropriate treament of elevated "LDL-C" Recognition and treatment of FH patients
hs-CRP testing	Increased hs-CRP increases risk with high Lp(a)	Recognition of patients at higher risk
EVALUATIONS		
Careful ausculation for aortic murmur, if found, consider echocardiogram	High association of Calcified Aortic Valve Stenosis (CAVS) with high Lp(a)	Proper managment of CAVS
Coronary artery calcium (CAC)	Higher Ca++ Scores associated with high Lp(a)	Identfication of patients with high probability of CAD

Conclusions: If recommendations for universal testing for Lp(a) are followed, 20% of the population will be found to have highLp(a)>50mg/dL. We have found evidence of the value of certain testing and evaluation of this group of patients despite no previously established ASCVD.

ID:208

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

CORRELATION OF MONOMERIC C-REACTIVE PROTEIN LEVEL WITH SUBCLINICAL CAROTID ATHEROSCLEROSIS PROGRESSION IN PATIENTS WITH LOW-GRADE CAROTID STENOSES AND MODERATE SCORE RISK

POSTER VIEWING SESSION

Ivan Melnikov[1], Sergey Kozlov[2], Olga Pogorelova[3], Maria Tripoten[3], Leyla Khamchieva[3], Tatiana Balakhonova[3], Olga Saburova[4], Yuliya Avtaeva[4], Maria Zvereva[4], Tatiana Kuznetsova[5], Lyudmila Prokofieva[1], Zufar Gabbasov[4]
[1]Laboratory Of Stem Cells, National Medical Research Center of Cardiology, Moscow, Russian Federation, [2]Laboratory Of Problems Of Atherosclerosis, National Medical Research Center of Cardiology, Moscow, Russian Federation, [3]Department Of Ultrasonography Diagnostic Methods, National Medical Research Center of Cardiology, Moscow, Russian Federation, [4]Laboratory Of Cell Hemostasis, National Medical Research Center of Cardiology, Moscow, Russian Federation, [5]Department Of Neurohumoral And Immunologic Diagnostics, National Medical Research Center of Cardiology, Moscow, Russian Federation

Background and Aims : Residual inflammatory risk is identified by hsCRP level ≥2.0 mg/l. Monomeric CRP (mCRP) is an emerging inflammatory biomarker. We studied whether mCRP level is a better predictor of carotid atherosclerosis (CA) progression than hsCRP in patients with low-grade CA and moderate SCORE risk which achieved target LDL cholesterol (LDL-C) level.

Methods: The study comprised 80 patients of both genders 53.1±5.8 years old with moderate SCORE risk, LDL-C 2.7-4.8 mmol/l and hemodynamically insignificant (<50% stenosis) subclinical CA. All patients were prescribed statin to achieve LDL-C level <2.6 mmol/l and followed up for 7 years. At the completion of follow up subclinical CA progression, which was defined by the increase in the plaque number, was assessed by ultrasonography by the same operator, hsCRP and mCRP level was measured. Mann-Whitney U Test was used for intergroup comparison.

Results: Patients were divided by mCRP level 7.2 μg/l and hsCRP level 2.0 mg/l. The increase in the plaque number was 0.58±0.64 vs. 1.44±1.15 in patients with mCRP <7.2 μg/l and ≥7.2 μg/l, respectively. Thus, mCRP level ≥7.2 μg/l was associated with the 2.5 times higher increase in the plaque number ($p=0.006$, statistical power =0.88). The increase in the plaque number was 0.67±1.01 vs. 1.06±0.99 in patients with hsCRP <2.0 mg/l and ≥2.0 mg/l, respectively. However, the difference was statistically insignificant ($p=0.14$, statistical power = 0.27).

Conclusions: mCRP level independently of hsCRP correlates with subclinical CA progression in patients with moderate SCORE risk and achieved target LDL-C. This work was supported by the Russian Science Foundation grant # 22-25-00054.

ID:206

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

ASSOCIATIONS OF THE FATTY ACIDS WITH THE CONCENTRATION OF ANTIOXIDANT ENZYMES IN THE BLOOD IN MEN WITH CORONARY HEART DISEASE

POSTER VIEWING SESSION

Viktoriya S. Shramko[1], Eugeniia V. Striukova[1], Yana V. Polonskaya[1], Ekaterina M. Stakhneva[1], Alexey V. Kurguzov[2], Elena V. Kashtanova[1], Yuliya I. Ragino[1]
[1]Branch Of Ic&g Sb Ras, Research Institute of Internal and Preventive Medicine – Branch of IC&G SB RAS, Novosibirsk, Russian Federation, [2]Ministry Of Health Of The Russian Federation, The Federal State Budgetary Institution "National Medical Research Center named academician E.N. Meshalkin", Novosibirsk, Russian Federation

Background and Aims : Objective: to identify associations of fatty acids (FAs) with the antioxidant enzymes in the blood of men with coronary heart disease (CHD).

Methods: The study included: control group – 20 men without CHD, core group – 60 men with CHD. The core group was divided into subgroups: subgroup I – with the presence of vulnerable atherosclerotic plaques, subgroup II – with the absence of vulnerable atherosclerotic plaques. The levels of FAs, free radicals, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) were analyzed in the blood.

Results: In patients with CHD, compared with the control group: 1) were higher in the levels of SOD, CAT, myristic, palmitic, palmitoleic and octadecenoic FAs; 2) were lower in the levels of GPx, α-linolenic, docosapentaenoic, docosahexaenoic and arachidonic FAs. In subgroup I were found: 1) negative associations of SOD – with linoleic, eicosatrienoic, arachidonic, eicosapentaenoic, docosapentaenoic and docosahexaenoic FAs, positive associations – with palmitic acid; 2) positive correlations of CAT level with palmitoleic and stearic acids; 3) negative associations between of GPx and palmitic, palmitoleic, stearic and octadecenoic FAs. In subgroup II, the results of the correlation analysis were markedly different.

Conclusions: Changes in the levels of antioxidant enzymes, and a disbalance of the FAs profile, probably indicate active oxidative processes in the body and may indicate the presence of atherosclerotic changes in the vessels. The study was conducted within the framework of: budget topic under State Task No. AAAA–A17-117112850280-2, with the support of bioresource collections; financial support from the Government of the Novosibirsk Region.

ID:200

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

INSULINRESISTANCE, LEVEL OF LEPTIN AND BODY MASS INDEX IN PATIENTS WITH CORONARY ARTERY DISEASE COMBINED WITH NONALCOHOLIC LIVER STEATOSIS.

POSTER VIEWING SESSION

Mariya Grechanyk[1], Olexandr Kuryata[2]
[1]Internal Medicine, Dnipro State Medical University, Dnipro, Ukraine, [2]Internal Medecine, Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine, Dnipro, Ukraine

Background and Aims : To estimate the frequency of insulinresistance (IR), level of leptin and body mass index (BMI) in patients with coronary artery disease (CHD) combined with nonalcoholic liver steatosis (NALS).

Methods: We studied 61 patients with CHD in combination with NALS mean age 57,8±2,04 (group A) and 20 patients with CHD without NALS mean age 56,6±4,6 (group B). Patients with diabetes were excluded. The study group was divided into 3 subgroups according to BMI (subgroup 1 (35%) - patients who are overweight, 2 (40%) - obesity 1 degree, 3 (25%) - obesity grade 2. Studied IR, level of leptin, BMI.

Results: Higher levels of leptin(by 87%) was detected in patients with CAD in combination with NALS, compared to a group of patients without NALS. The increase in leptin levels depended on body weight – from the overweight group to the group with 2 class obesity($p<0.05$). 82% of patients with CAD and NALS had IR. HOMA1-IR index in patients with 2 class obesity was 3.4 compared to the group of patients with 1 class obesity - 2.35 and overweight patients - 2.26($p<0.05$). According to HOMA1-IR index IR was detected in 7% of the overweight patients, in 22% patients with 1 class obesity and in 62% with 2 class; and 86%, 72% and 84% according to the HOMA2-IR index($p<0.05$).

Conclusions: According to the results of ROC analysis of significant predictors of liver steatosis in the group of patients with CAD were levels of leptin and BMI (AUC for leptin – 0.69 (0.56-0.82), AUC for BMI 0.86 (0.76-0.97)).

ID:191

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

CLINICAL CASE: EVALUATION OF THE EFFECT OF LIRAGLUTIDE THERAPY ON MYOCARDIAL PERFUSION ACCORDING TO SPECT DATA IN AN OBESE PATIENT

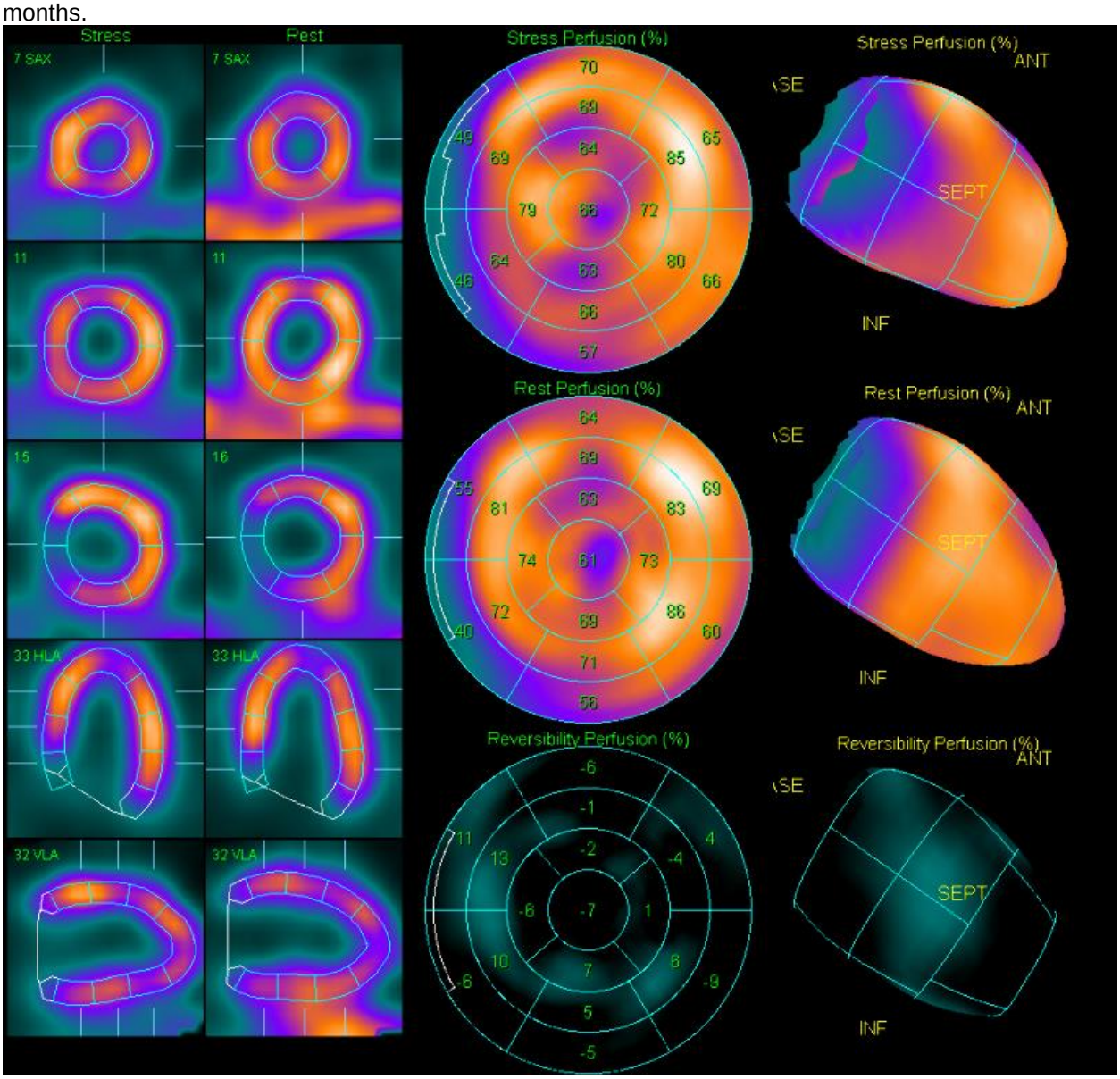
POSTER VIEWING SESSION

Polina Rezinkina[1], Igor V. Sergienko[2], Aleksey Ansheles[3]
[1]Atherosclerosis Phenotypes Laboratory, National Medical Research Center of Cardiology, Moscow, Russian Federation, [2]Atherosclerosis Phenotypes Laboratory, National Medical Research Center of Cardiology, Moscow, Russian Federation, [3]Department Of Radionuclide Diagnostics And Positron Emission Tomography, National Medical Research Center of Cardiology, Moscow, Russian Federation

Background and Aims : evaluation of the effect of Liraglutide therapy on myocardial perfusion in obese patient with high CVR in the preclinical stage of atherosclerosis

Methods: Patient K., female, 27 years old with Metabolic syndrome, smoker. Anamnesis: Arterial hypertension stage I, grade II. Impaired glucose tolerance. Dyslipidemia. NAFLD, steatohepatitis. Initial therapy: Bisoprolol 2,5 mg/day. Obesity 3 (BMI=40, waist circumference=123 cm). Ultrasound examination revealed no atherosclerotic lesions of brachiocephalic arteries. Considering the risk factors, the patient is in the High CVR category. According to results of myocardial SPECT: radiopharmaceutical (RFP) distribution in LV is diffusely uneven, with no large focal perfusion defects or myocardial damage. Pronounced myocardium LV perfusion disorders at the microcirculation level are determined (Picture1). The patient has been initiated with Liraglutide therapy at a dose of 3 mg/day within 7

months.

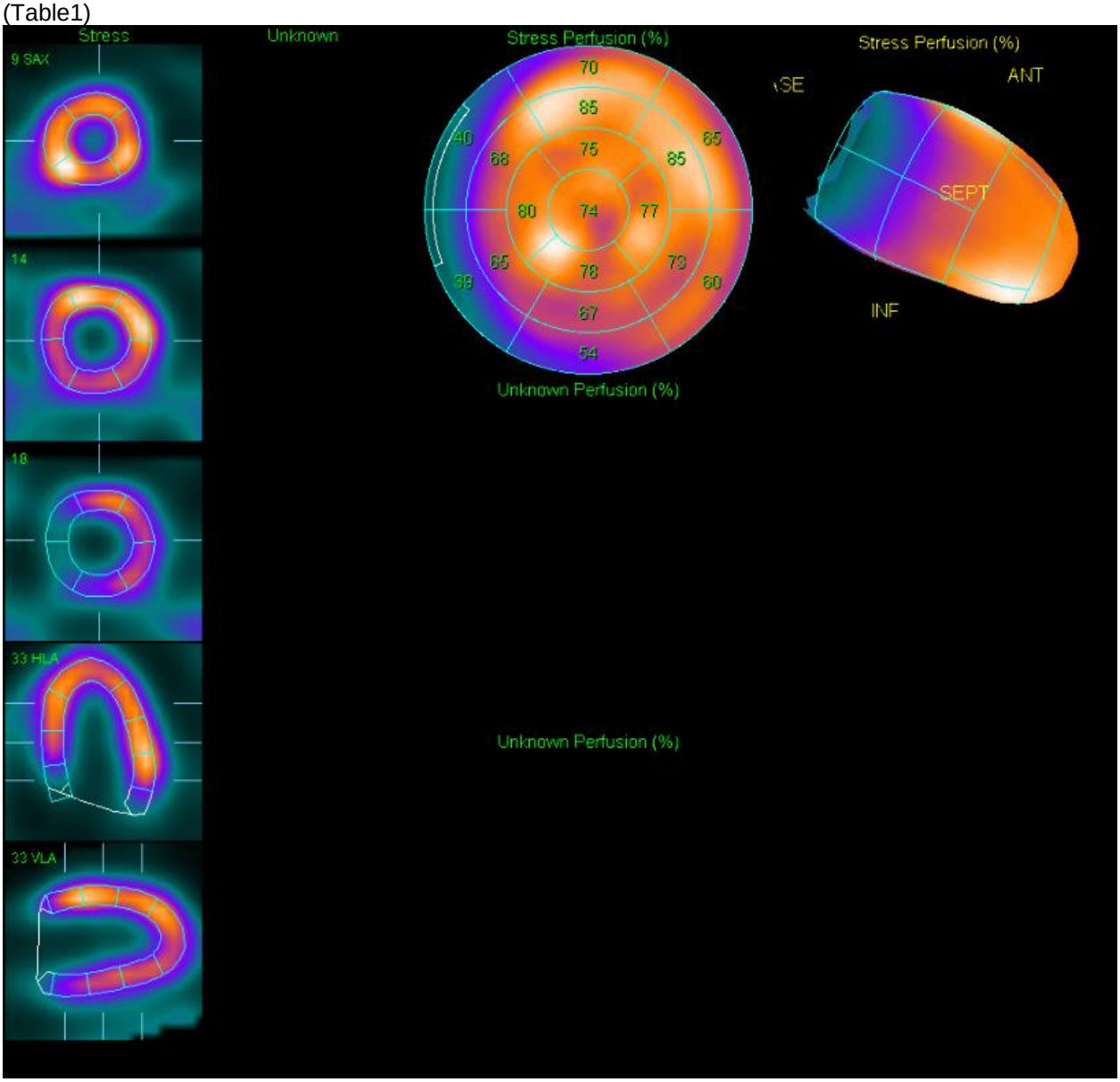


Results: After 7 months on physical examination there is obesity regress down to 2 degree: BMI=35,9; -11 cm in waist circumference. According to the blood test, a significant decrease in LDL-cholesterol, Total cholesterol, Glucose, HbA1c levels is determined. However, there is also an increase of Triglycerides level.
(Table1)

	Visit 1 24 December 2020	Visit 2 15 July 2021
Anthropometric data		
Height (cm)	166	166
Weight (kg)	110	99 (-10%)
Body mass index (BMI)	40	35,9 (-10,3%)
Obesity degree	3	2
Waist circumference (cm)	123	112 (-8,9%)
Blood test indicators		
Total cholesterol (mmol/l)	5,92	4,94 (-13,5%)
LDL-cholesterol (mmol/l)	4,03	2,77 (-31,3%)
HDL-cholesterol (mmol/l)	0,85	1,6 (+46,9%)
Triglycerides (mmol/l)	2,29	3,66 (+59,8%)
Glucose (mmol/l)	6,71	5,25 (-21,8%)
HbA1c (%)	6,00	5,10 (-15%)
Adiponectin (µg/mL)	1,56	4,18 (+167,9%)
Leptin (ng/mL)	33,32	39,90 (+19,5%)
Resistin (ng/mL)	3,73	4,96 (+32,9%)
Myocardial SPECT parameters		
Peak Ejection Rate (PER, EDV/s,)	2,86	3,47
Peak Filling Rate (PFR, EDV/s)	3,77	4,45
SSS (Summed Rest Score)	7	5
Str Extent	5	3
Ejection fraction (EF, %)	58	60
End diastolic volume (EDV, ml)	93	70

Myocardial SPECT results in dynamic: RFP distribution in LV is practically even. LV perfusion disorders at the microcirculation level are determined to a much lesser extent. (Picture2). According to contractility parameters, there is an improvement of systolic and diastolic LV function.

(Table1)



Conclusions: Liraglutide may affect myocardial perfusion at the microcircular level. Further research is likely to expand the indications for the prescription of GLP-1 receptor agonists in overweight/obese patients in the preclinical stage of atherosclerosis.

ID:504

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-10 Modified lipoproteins*

STUDY OF IMMOBILIZED NEURAMINIDASE EFFECT ON THE LDL SIALYLATION STATUS IN MICE

POSTER VIEWING SESSION

Dmitry A. Kashirskikh[1,2,3], Alexander M. Markin[2], Evgeny Bezsonov[2], Natalia O. Zheleznyak[1,4], Anastasia S. Vlasova[5], Nelya R. Yakhina[1,6], Igor A. Sobenin[3,7], Alexander N. Orekhov[1,3,8]
[1]Institute For Atherosclerosis Research, Institute for Atherosclerosis research, Moscow, Russian Federation, [2]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [3]Laboratory Of Angiopathology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation, [4]Faculty Of Bioingeneering And Bioinformatics, Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [5]Faculty Of Pediatrics, Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [6]Faculty Of Medical Biology, Pirogov Russian National Research Medical University, Moscow, Russian Federation, [7]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [8]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation

Background and Aims : Modified low density lipoprotein (LDL) is the cause of the initial atherosclerotic lesions. One of the most significant modifications of LDL in humans is desialylation. A murine model of stable reduced sialylation of LDL cholesterol should complement information on the role of the desialylation process in atherogenesis.

Methods: Male C57BL/6 mice, 8–12 weeks old, were randomly assigned to treatment and control groups for a one-week experiment (n=80 per group) and a four-week experiment (n=50 per group). The experimental groups were injected with 0.02 units of neuraminidase immobilized on mouse IgG and the control groups were treated with saline. For the four-week experiment, the experimental group was administered once a week. Blood samples were collected and LDL were isolated by ultracentrifugation. The content ratio of LDL sialic acid to protein was used for comparing the sialylation status between groups.

Results: A single administration of the drug decreased LDL sialic acid level by an average of 30% in the experimental group compared with the control values. It was observed from 1 hour to 4 days after an injection. On days 5-7 sialic acid level was recovered. The decrease in LDL sialic acid level was revealed only after 14 and 28 days with the drug administration every 7 days.

Conclusions: Administration of immobilized neuraminidase every 4 days lowers the level of sialic acid LDL by about 30% compared to the control. This will allow to model the process observed in patients with atherosclerosis. This work was supported by the Russian Science Foundation (Grant **#22-25-00391**).

ID:386

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

CHILD-PARENT CASCADE SCREENING FOR FAMILIAL HYPERCHOLESTEROLAEMIA IN SLOVENIA

POSTER VIEWING SESSION

Jaka Šikonja[1], Matej Mlinarič[2], Urša Šuštar[2,3], Barbara Jenko Bizjan[3], Jernej Kovač[3], Katarina Trebušak Podkrajšek[3,4], Tadej Battelino[1,2], Urh Groselj[1,2]
[1]Faculty Of Medicine, University of Ljubljana, Ljubljana, Slovenia, [2]Department Of Endocrinology, Diabetes, And Metabolic Diseases, University Children's Hospital, UMC Ljubljana, Ljubljana, Slovenia, [3]Clinical Institute For Special Laboratory Diagnostics, University Children's Hospital, UMC Ljubljana, Ljubljana, Slovenia, [4]Institute Of Biochemistry, Faculty Of Medicine, University of Ljubljana, Ljubljana, Slovenia

Background and Aims : Familial hypercholesterolaemia (FH) leads to a lifelong increased level of low-density lipoprotein (LDL) and childhood-onset atherosclerosis. Untreated patients have a high risk for cardiovascular events however, the majority remains underdiagnosed. Child-parent cascade screening program was recently started in Slovenia and our objective was to evaluate its effectiveness.

Methods: We conducted a prospective cascade screening of 156 parents from 132 families, 50% female, average age 46 years, all Caucasians. Parents of paediatric index cases with genetically confirmed FH were invited to the lipid out-patient clinic, preferably the parent with higher cholesterol levels. We searched electronic medical records of parents for a previous diagnosis of FH. The results were statistically analysed with an independent samples t-test.

Results: Disease-causing variants were found in 92% of families, in the remaining 7% we included only one parent and there was only one family where both parents were tested negative. Variants for FH were 72% in *LDLR*, 28% in *APOB,* and none in *PCSK9*. Less than 10% had a personal history of a cardiovascular event. We diagnosed FH for the first time in 86% of all patients, the remaining 14% already had a clinical diagnosis.

Conclusions: Most included participants had genetically confirmed FH and the diagnosis was made for the first time in more than 85% of patients. The presented cascade screening programme identifies affected parents before the clinical manifestation of atherosclerosis.

ID:544

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

INDICATORS OF CENTRAL PRESSURE AND ARTERIAL STIFFNESS IN PATIENTS WITH MYOCARDIAL INFARCTION DEPENDING ON THE CONTRACTILE FUNCTION OF THE LEFT VENTRICLE

POSTER VIEWING SESSION

Valentin Oleynikov, Luidmila Salyamova, Angelina Khromova, Olga Kvasova, Irina Matrosova, Marina Lukyanova
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : To conduct a comparative analysis of central pressure and arterial stiffness parameters in patients with STEMI, depending on the initial level of the left ventricular ejection fraction (LV EF).

Methods: The study included 148 patients with STEMI, mean age 51.5 (CI% 50.1; 52.9) years. On the 7-9th day from STEMI echocardiography using the MyLab (Esaote, Italy) with the determination of LVEF was performed; examination of the common carotid arteries (CCA): local systolic pressure loc Psys, stiffness indices α and β. Applanation tonometry was performed using a Sphygmocor device (AtCor Medical, Australia). The parameters were analyzed: systolic (SBPao), pulse (PPao) pressure in the aorta and carotid-femoral pulse wave velocity (cfPWV). The patients were divided into 3 groups. Group 1 included 79 people with preserved EF (≥50%), group 2 - 53 patients with mid-range EF (40-49%); Group 3 - 16 patients with reduced EF (<40%).

Results: In group 1 SBPao was 102.2(CI%100.0;104.5)mmHg, in the 2nd group - 100.5(CI%97.8;103.3)mmHg, in the 3rd group - 94.3(CI%89.3;99.3)mmHg (p1-3=0.005;p2-3=0.014). The cfPWV in the 1st group was 8.1(CI%7.7;8.5) m/s, in the 2nd group - 8.2(CI%7.7;8.7)m/s, in group 3 - 7.4(CI%6.4;8.4)m/s (p1-2-3>0.05). The α and β indices in group 1 - 4.9(CI%4.3;5.4) and 9.8(CI%8.8;10.9), in group 2 - 4.9(CI%4.3;5.5) and 10.0(CI%8.7;11.2); group 3 - 6.2(CI%5.1;7.3) (p1-3=0.049;p2-3=0.023) and 12.6(10.3;14.8) (p1-3=0.044;p2-3=0.022). In the 1st group locPsys was 107.7(CI%105.0;110.4) (p1-3=0.003); in group 2 - 104.3(CI%101.0;107.6) (p2-3=0.029); group 3 - 97.7(CI%91.7;103.7)mmHg.

Conclusions: The EF<40% in STEMI patients was associated with decreased central and local SBP, and deterioration of local stiffness indices of the carotid arteries.

ID:542

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-07 Nutrition, nutraceuticals*

SCREENING AND VALIDATION STRATEGIES FOR NATURAL EXTRACTS AGAINST CARDIOVASCULAR DISEASES: LINGONBERRY AND BLACKBERRY EXTRACTS BENEFICIALLY ACT ON CHOLESTEROL METABOLISM IN-VITRO AND IN-VIVO.

POSTER VIEWING SESSION

Clemens Röhrl
Center Of Excellence Food Technology And Nutrition, University of Applied Sciences Upper Austria, Wels, Austria

Background and Aims : Decreasing circulating LDL-cholesterol levels leads to decreased risk for cardiovascular diseases. Natural compounds are capable of lowering LDL-cholesterol even on top of lifestyle modification or medication.

Methods: To identify novel plant-derived compounds to lower plasma LDL-cholesterol levels, we performed a high-content screen based on the transcriptional activation of the promoter of the LDL receptor (LDLR). Identified hits were thoroughly validated in human hepatic cell lines in terms of increasing LDLR mRNA and protein levels, lowering cellular cholesterol levels and increasing cellular LDL uptake. Furthermore, selected extracts were applied to mice. In addition, we present an independent screening approach to identify natural extracts that increase cholesterol efflux from macrophages.

Results: By means of screening and incremental validation *in-vitro*, aqueous extracts prepared from leaves of lingonberries (*Vaccinium vitis-idea*) as well as blackberries (*Rubus fructicosius)* were found to have effects comparable to lovastatin, a prototypic cholesterol-lowering drug. When applied *in-vivo* in mice, both extracts induced subtle increases in hepatic LDLR expression. Additionally, a significant increase in HDL-cholesterol was observed. Moreover, we present screening results including preliminary validation for natural extracts, that increase cholesterol efflux from macrophages with the aim to identify novel natural inhibitors of foam cell formation.

Conclusions: Taken together, aqueous extracts from lingonberry or blackberry leaves were identified and characterized as strong candidates to provide cardiovascular protection.

ID:569

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

NATURAL IGM RECOGNIZING OXIDATION-SPECIFIC EPITOPES BLOCK NETOSIS INDUCED BY EXTRACELLULAR VESICLES

POSTER VIEWING SESSION

Anna S. Ondracek[1], Taras Afonyushkin[2], Soreen Taqi[2], Thomas M. Hofbauer[1], Maria Ozsvar Kozma[2], Smriti Sharma[1], Thomas Scherz[1], Dietrich Beitzke[3], Christoph Testori[4], Irene M. Lang[1], Christoph J. Binder[2]
[1]Internal Medicine Ii, Cardiology, Medical University of Vienna, Wien, Austria, [2]Department Of Laboratory Medicine, Medical University of Vienna, Vienna, Austria, [3]Department Of Biomedical Imaging And Image-guided Therapy, Medical University of Vienna, Vienna, Austria, [4]Department Of Emergency Medicine, Medical University of Vienna, Vienna, Austria

Background and Aims : Neutrophil extracellular traps (NETs) have emerged as important contributors to thrombus formation in acute myocardial infarction (AMI) fueling the pro-thrombotic milieu. Obtaining insights on inducers and inhibitors of NETosis is of high importance. We have previously demonstrated that a subset of extracellular vesicles (EV) carrying oxidation specific epitopes (OSE), products of lipid peroxidation, is elevated in AMI. Importantly, natural IgM antibodies targeting OSE are considered for their protective role in cardiovascular disease. We hypothesized that EVs could promote NET formation and investigated a potential protective function of OSE-IgM to counteract this effect.

Methods: AMI patients were recruited at first medical contact. NET markers, EV, and IgM were assessed in consecutive blood samples. Myocardial function was documented by cardiac magnetic resonance. EV were isolated by differential centrifugation from patient plasma and activated THP-1 cells. NETs were measured by ELISA for DNA-myeloperoxidase complexes and immunofluorescence microscopy.

Results: EV from patient plasma and in vitro generated EV induced NETosis in primary human neutrophils and HL-60 neutrophilic cells. The malondialdehyde (MDA)-specific LRO4 antibody, but not a control IgM, reduced the NETogenic effect of EV. Consistent with these findings, the ratio between the circulating MDA+ fraction of CD45+ EV and MDA-specific IgM at the culprit site correlated with the NET surrogate marker dsDNA and predicted heart function at six months.

Conclusions: Both in vitro generated and in vivo released patient EV induced NET formation, and natural antibodies recognizing MDA inhbited this effect. The balance between MDA-MVs and MDA-IgM during AMI may represent a potential prognostic and therapeutic target.

ID:531

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

MUSCLEBLIND-LIKE (MBNL) PROTEIN FAMILY OVEREXPRESSION LEAD TO PRO-SYNTHETIC PHENOTYPE MODULATION OF ARTERIAL HUMAN VASCULAR SMOOTH MUSCLE CELLS IN DIABETES MELLITUS

POSTER VIEWING SESSION

Mario O. Ihsan[1], Damian M. Tan[2], Umamaheswari Muniasamy[1], Mei Shan Ong[1], Xiao Yun Lin[3], Chuen Neng Lee[1,3], Rajkumar Dorajoo[4], Vitaly Sorokin[1,3]
[1]Department Of Surgery, Yong Loo Lin School Of Medicine, National University of Singapore, Singapore, Singapore, [2]School Of Applied Science, Temasek Polytechnic, Singapore, Singapore, [3]Department Of Cardiac, Thoracic And Vascular Surgery, National University Hospital, National University Health System, Singapore, Singapore, [4]Genome Institute Of Singapore, Agency for Science, Technology and Research (A*STAR), Singapore, Singapore

Background and Aims : Diabetes Mellitus (DM) is a metabolic disorder affecting ten percent of the worldwide population. The morbidity of DM patients is strongly correlated to cardiovascular diseases (CVD), including cerebrovascular disease, peripheral vascular conditions, and ischemic heart disease. Previous studies have shown that vascular smooth muscle cells (VSMC) from DM patients are often functionally impaired with increased expressions of inflammatory and pro-fibrotic genes. Given its importance in arteriopathy, we aim to understand better the molecular pathway leading to VSMC phenotype modulation in DM.

Methods: Primary VSMC were obtained from patients undergoing coronary artery bypass graft surgery. Cells were cultured and harvested for subsequent RNA-Seq analysis, immunoblotting, and phenotypic characterizations.

Results: Based on RNA-Seq analysis, we found that DM VSMC transcript highlights pathways associated with vascular remodeling, such as cell adhesion, cell proliferation, and extracellular matrix reorganization. We also found increased expressions of the Muscleblind-like protein family (MBNL1, MBNL2, and MBNL3) in DM VSMC at both mRNA and protein levels. Using network analysis, we established the importance of the MBNL protein family in VSMC phenotype modulation. Further assessment of VSMC phenotypic characteristics revealed that DM VSMC had a pro-synthetic phenotype, marked by increased cell proliferation, downregulation of contractile VSMC-associated genes (*ACTA2*, *ACTG2*, and *TAGLN*), and upregulation of fibroblast-related genes (*LUM*, *DCN*, and *S100A4*) as opposed to non-DM VSMC.

Conclusions: Our study highlights the shift in DM human primary VSMC towards pro-synthetic phenotype. The upregulation of the MBNL protein family is likely involved in the VSMC phenotype modulation and could be a potential therapeutic target for DM-associated arteriopathy.

ID:570

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

FACTORS, ASSOCIATED WITH MAJOR ADVERSE EVENTS IN RURAL MALES WITH ARTERIAL HYPERTENSION AT LONG-TERM FOLLOW-UP

POSTER VIEWING SESSION

Kyrylo Mikhaliev[1], Tetiana Nimtsovych[2], Anatolii Kravchenko[1], Vitalii Gurianov[3], Tamara Chursina[4], Svitlana Stanislavska[1]
[1]Internal Medicine, SIS "RPC PCM" SAD, Kyiv, Ukraine, [2]Cardiology, PNPE «Khmelnytskyi Regional Cardiovascular Center» Khmelnytskyi Regional Council, Khmelnytskyi, Ukraine, [3]Medical And Biological Physics And Informatics, Bogomolets National Medical University, Kyiv, Ukraine, [4]Internal Medicine, Clinical Pharmacology And Occupational Diseases, Bukovinian State Medical University, Chernivtsi, Ukraine

Background and Aims : To study the factors, associated with major adverse events (MAEs) in rural males with uncomplicated arterial hypertension (HTN) at long-term follow-up.

Methods: The prospective study enrolled 160 rural males with uncomplicated primary HTN (mean age 50 ± 6 years). We analyzed clinical and instrumental data. High-to-very high SCORE cardiovascular risk was identified in 102 (63,7%) patients. Blood pressure visit-to-visit variability (VVV) was assessed by standard deviation and coefficient of variation (CV) (derived from the four consecutive visits). Left ventricular (LV) hypertrophy (by echo) was detected in 129 (80,6%) patients. The median of follow-up was 27 months (interquartile range 24-30 months). During the follow-up period, 14 (8,8%) patients presented with MAEs (totally, 17 events): acute cerebrovascular event (n=9); myocardial infarction (n=2); first-onset atrial fibrillation (AF) (n=2); AF transition in permanent pattern (n=2); and relative LV ejection fraction decline >10% (n=2).

Results: At multivariable analysis, the factors, associated with MAEs at long-term follow-up, were as follows: SCORE cardiovascular risk (per 1 % increase: HR 1,09 (95% CI 1,01-1,17); p=0,034); mean arterial pressure (MAP) (per 1 mm Hg increase: HR 1,23 (95% CI 1,07-1,41); p=0,003); CV (MAP) (per 1% increase: HR 1,41 (95% CI 1,08-1,83); p=0,012); and LV myocardial mass, indexed by height^{2,7} (per 1 g/m^{2,7} increase: HR 1,07 (95% CI 1,03-1,11); p=0,001).

Conclusions: Long-term MAEs in rural HTN males were associated with SCORE cardiovascular risk, MAP, MAP VVV (by CV) and LV myocardial mass index (by height^{2,7}). These factors should be taken into account while MAEs risk stratification in rural males with uncomplicated HTN.

ID:572

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE INFLUENCE OF VISCERAL OBESITY ON THE VALUE OF VASCULAR AGE IN PATIENTS WITH ARTERIAL HYPERTENSION, OBESITY AND TYPE 2 DIABETES MELLITUS.

POSTER VIEWING SESSION

Irina Starodubtseva[1], Maria Derevyanchenko[2], Mikhail Statsenko[2]
[1]Internal Diseases, NN Burdenko Voronezh State Medical University, Voronezh, Russian Federation, [2]Internal Diseases, Volgograd State Medical University, Volgograd, Russian Federation

Background and Aims : Aim: to evaluate the effect of visceral obesity on the value of vascular age in patients with arterial hypertension (AH), obesity, type 2 diabetes mellitus (DM).

Methods: Material and Methods: 320 patients with stages II-III of AH 45-70 years old were divided into 4 groups: "isolated" AH (group 1), AH and obesity (group 2), AH, obesity and type DM (group 3), AH and DM without obesity (group 4). The clinical status, parameters of visceral obesity, and vascular age were assessed. Nonparametric statistical methods were used.

Results: Results: At least 50% of all patients had visceral obesity, despite the absence of obesity by body mass index in groups 1 and 4: 57.5 vs 100.0 vs 100.0 vs 50.0% in groups 1, 2, 3 and 4 groups, respectively ($p < 0.0001$). The visceral obesity index VAI was significantly higher among 3 group in comparison with 1 and 4 groups (2.96 [2.36; 3.98] vs 1.87 [1.40; 2.67] vs 2.22 [1.61; 3.26] respectively). Vascular age was statistically significantly lower in group 1 in comparison with groups 3, 4 (64.0 [57.8; 71.0] vs 69.0 [62.0; 73.0] and 69.5 [66.0 ; 74.3] years, respectively), as well as in group 2 in comparison with 4 (64.0 [56.5; 70.5] vs 69.5 [66.0; 74.3] years).

Conclusions: Conclusion. The features of the influence of visceral obesity on the value of vascular age in patients with hypertension were revealed as obesity and type 2 diabetes join it.

ID:530

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ACUTE CORONARY SYNDROME OUTSIDE AND DURING THE COVID-19 PANDEMIC

POSTER VIEWING SESSION

Natalia A. Koriagina, Vladimir S. Koriagin, Alexey I. Maltcev, Sofia G. Shulkina
Polyclinic Department, Perm state medical university, Perm, Russian Federation

Background and Aims : To analyze the register of patients with acute coronary syndrome (ACS) from September to November 2018-2019 and 2020 in the midst of the Covid-19 pandemic.

Methods: The retrospective study was carried out at the vascular center. The register includes 952 patients with ACS in 2018 and 1,033 patients in 2019, as 964 patients in 2020 during the Covid-19 pandemic.

Results: In 2018, the age 67 years, the mortality rate was 3.94%.Myocardial infarction with ST-segment elevation (STEMI) - 47%, myocardial infarction without ST-segment elevation (NSTEMI) - 23%. 43.6% were registered with coronary heart disease (CHD). 12.5% had a history of diabetes mellitus (DM), 31.2% a arterial hypertension (AH). This cardiovascular event recurred in 4% of patients. Average bed-days 9.73. In 2019, the age of 68 years, the mortality- 4.35%. STEMI 47.5%, STEMI 28%. 52.1% of patients were registered CHD. DM 13.0%, AH - 39.6%. For 3.8%, MI in 2019 was repeated. Average bed-days 9.92. In 2020, the patients were 66 years old, with a mortality rate of 6.25%. STEMI - 50.5%, STEMI - in 17.5%. 28.5% DM, 40.8% - AH. This cardiovascular event was repeated for 4.7% of patients. Bed-days indicator is 8.85.

Conclusions: Initial analysis reveals that the group of patients with ACS in 2020 was younger. ACS in combination with DM was almost 2 times more common during the pandemic. The proportion of patients registered with the dispensary increased over the period 2018-2019-2020, the mortality rate in the 2020 group had a clear upward trend.

ID:526

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

BENEFICIAL PLEIOTROPIC EFFECTS OF ATORVASTATIN IN PERITONEAL DIALYSIS PATIENTS WITHDRAWN BY AUTHOR

POSTER VIEWING SESSION

Natalia Stepanova, Olena Burdeyna, Victoria Driianska
Nephrology And Dialysis, State Institution “Institute of Nephrology National Academy of Medical Science of Ukraine", Kyiv, Ukraine

Background and Aims : Recent studies demonstrate a large number of non-lipid modifiable effects of statins in various diseases. However, although atherogenic dyslipidemia is a common feature in peritoneal dialysis (PD) patients, statins use is supported by limited data and there is a general lack of research on their pleiotropic effects in this patients’ cohort.

Methods: A total of 114 PD patients with an average age of 55 (48-65) years and a dialysis vintage of 41 (24-60) months were included in this prospective cohort study. PD patients (n = 54) who had started receiving atorvastatin before or after dialysis initiation and been treated with atorvastatin no less than 3 months were included in the Atorvastatin Group. PD patients (n = 60) who have never taken statins consisted of Atorvastatin-free Group. PD adequacy tests and concentrations of interleukins (IL) -6, -10, tumor necrosis factor-alpha (TNF-a), and monocyte chemoattractant protein-1 (MCP-1) in PD effluent (PDE) were evaluated in all study participants. The PDE cytokines concentrations were measured using ELISA test kits. The data presented as median (Me) and the interquartile ranges (Q25-Q75) and compared using the Mann-Whitney test.

Results: PDE cytokines assessment at a median follow-up period of 12.6 (7.3-17.6) months demonstrated significantly lower concentrations of all studied cytokines in the Atorvastatin Group compared with the Atorvastatin-free Group (Table 1). Moreover, the atorvastatin users had higher weekly creatinine clearance, peritoneal weekly Kt/V, and, accordingly, total weekly Kt/V compared to the Atorvastatin-free
Group.

Table 1. The PDE cytokine concentrations and the dialysis adequacy parameters according to atorvastatin treatment in PD patients.

Parameters	Atorvastatin Group (n = 54)	Atorvastatin-free Group (n = 60)	*p*-value
PDE IL-10, pg/mL	3.2 (3.0-5.2)	8.9 (5.9-15)	< 0.001
PDE IL-6, pg/mL	28.7 (18.2-60.7)	53.9 (26.3-128.5)	< 0.001
PDE TNF-α, pg/mL	2.5 (0.7-5.0)	5.2 (2.1-8.8)	< 0.001
PDE MCP-1, pg/mL	13.0 (9.0-17.0)	17.1 (10.2-22.7)	0.038
CrCL, L/week	48.5 (41.8-55.5)	43.4 (36.6-50.7)	0.03
Total weekly Kt/V urea	2.4 (1.8-3.2)	1.9 (1.5-2.5)	< 0.001
Peritoneal weekly Kt/V urea	2.2 (1.9-3.1)	2.08 (1.4-2.5)	0.05
Kidney weekly Kt/V urea	0.08 (0.05-0.67)	0.04 (0.02-0.79)	0.96

Conclusions: Atorvastatin treatment was associated with low intraperitoneal inflammation and better dialysis adequacy in our cohort of PD patients.

ID:604

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

TRIGLYCERIDE–GLUCOSE (TYG) INDEX FOR ACUTE MYOCARDIAL INFARCTION PATIENTS WITH OR WITHOUT METABOLIC FATTY LIVER (MAFLD): A RETROSPECTIVE STUDY

POSTER VIEWING SESSION

Mingwei Wang, Chunyi Wang
Hangzhou Institute Of Cardiovascular Diseases, Affiliated Hospital of Hangzhou Normal University, Hangzhou, China

Background and Aims : There are no clear predictors for acute myocardial infarction (AMI) with metabolic-associated fatty liver disease (MAFLD). Triglyceride–glucose (TyG) index has a predictive effect on the prognosis of cardiovascular diseases. The purpose of this retrospective study was to evaluate the correlation of TyG index in AMI patients with or without MAFLD.

Methods: A total of 107 AMI patients diagnosed with MAFLD based on B-ultrasound and medical history were retrospectively included as the MAFLD group. Then, 87 AMI patients diagnosed without MAFLD were selected as the non-MAFLD group. The clinical data were the indicators within 24 h after admission. TyG index was calculated as Ln (fasting triglycerides (TG) (mg/dl) × blood glucose (mg/dl)/2).

Results: The TG, blood glucose, and TyG index of the MAFLD group were higher than those of the non-MAFLD group. The TG, blood glucose, and prevalence of MAFLD of the higher index group were higher than those of the lower index group.

Conclusions: The TyG index can be used as an indicator to evaluate the prognosis and related risks of AMI patients with MAFLD.

ID:594

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EFFECT OF EFFECTIVE LIPID-LOWERING THERAPY ON POSTINFARCTION CARDIAC REMODELING

POSTER VIEWING SESSION

Alena Golubeva, Vera Galimskaya, Anastasia Babina, Natalia Donetskaya, Nadezhda Burko, Valentin Oleynikov
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : to evaluate the effect of effective therapy with atorvastatin on hemodynamic parameters and global deformation in patients with pathological postinfarction remodeling.

Methods: the study included 114 STEMI patients aged 52(44;58) years. Patients have been taking atorvastatin 40-80 mg/day within 12 months after STEMI. Initially and 12 months after, echocardiography was performed using a MyLab ultrasound scanner (Esaote, Italy). EDVi (ml/m2), ESVi ml/m2, global longitudinal (GLS,%), circumferential (GCS,%), radial strain (GRS,%), and twist (Twist,º) were measured. The criterion for pathological LV remodeling was considered as an increase in EDVi ≥20%. Evaluation of the lipid-lowering therapy was based on a decrease of LDL by 12 months to 1.4 mmo/L and by 50% from initial.

Results: Among patients (n=39) with pathological postinfarction LV remodeling, the following groups were retrospectively identified: 1 - 17 people who achieved the target LDL values; 2 - 22 patients with LDL-C below target level. In group 1 initial GCS - 17.2(95%CI, 14.5-19.8)%, repeated - 15.5(95% CI, 12.1-16.4)% ($p<0.05$); initial GRS - 28.4(95%CI, 24.3-32.6)%, after 12 months - 23.5(95%CI, 20.5-26.6)% ($p<0.05$); Twist initially - 8.8(95%CI, 7.6-10.0)%, repeated - 8.2(95%CI, 6.9-9.3)% ($p>0.05$). In group 2, GLS decreased from 15.4(95%CI, 13.8-17.1)% to 13.3(95%CI, 11.7-15.2)% ($p<0.01$); GCS initially - 17.2(95%CI, 15.3-19.2)%, after 12 months - 14.1(95%CI, 11.9-16.4)% ($p<0.01$); GRS initially - 28.6(95%CI, 24.9-32.4)%, after 12 months - 22.9(95%CI, 20.0-25.9)% ($p<0.01$); Twist initially - 9.7(95%CI, 8.6-10.7)%, repeated - 8.8(95%CI, 7.6-9.9)% ($p<0.05$).

Conclusions: failure to achieve the target lipid level in patients with pathological postinfarction remodeling is accompanied by a more pronounced negative dynamics of the heart biomechanical parameters.

ID:518

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EVALUATION OF THE EFFECT OF LONG-TERM LIPID-LOWERING THERAPY ON THE DYNAMICS OF REGIONAL ARTERIAL STIFFNESS IN PATIENTS WITH PRIMARY ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Valentin Oleynikov, Irina Matrosova, Natalia Borisova, Nadezhda Burko, Marina Lukyanova
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : to assess the dynamics of regional arterial stiffness by volume sphygmography in patients with STEMI on the background of long-term effective lipid-lowering therapy.

Methods: The study included 43 patients with primary STEMI: 37 men (86.1%) and 6 women (13.9%) mean age 43 (95%CI 48; 59) years; weight 80.5 (CI95% 75; 90) kg; BMI - 26.9 (95%CI 24.9; 29.7)kg/m2. On the 7th-9th day from STEMI and 24 weeks after the assessment of regional vascular stiffness using a VaSera-1000 device (Fukuda Denshi, Japan), was performed by volume sphygmography. The cardio-ankle vascular index (CAVI) was determined: CAVI-1, L-CAVI-1 and CAVI-1/L-CAVI-1; the augmentation index (AI) was automatically calculated. All patients were prescribed atorvastatin 80 mg/day during the first 24-96 hours of STEMI. In case of non-reaching the target level of LDL-C ≤1.4 mmol/L and a decrease by ≥50% after 5-6 weeks, ezetimibe 10 mg daily was added

Results: Against the background of lipid-lowering therapy, a significant improvement in the indicators of true arterial stiffness was observed: a decrease in CAVI-1 from 8.2+0.9 to 7.1 (CI 95% 6.7; 7.8) (p=0.04), decrease in CAVI-1/L-CAVI-1 from 8.1 (CI 95% 8.0; 8.5) to 7.2 (CI 95% 6.7; 7.8) (p=0.02). The augmentation index significantly decreased from 1.07 (95% CI 0.9; 1.2) to 0.95+0.1 (p=0.03)

Conclusions: 24-week therapy with atorvastatin 80 mg in patients with primary STEMI, according to the volume sphygmography, is accompanied by a decrease in the true stiffness of the arterial wall and a decrease in the augmentation index.

ID:582

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

RELATIONSHIP BETWEEN BIOMARKERS AND GLOBAL MYOCARDIAL STRAIN PARAMETERS IN PATIENTS WITH CARDIOVASCULAR PATHOLOGY AND METABOLIC DISORDERS AFTER COVID-19-ASSOCIATED PNEUMONIA

POSTER VIEWING SESSION

Tatiana Petelina[1], Natalia Musikhina[2], Elena Yaroslavskaya[3], Elena Gorbatenko[3], Natalia Galeeva[4], Ksenia Avdeeva[1], Anastasia Shcherbinina[1], Luidmila Gapon[1]
[1]Arterial Hypertension Department, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tyumen, Russian Federation, [2]Urgent Cardiology Department, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tyumen, Russian Federation, [3]Department Of Ultrasound Diagnostics, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tyumen, Russian Federation, [4]Physiotherapeutic Treatment Department, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tyumen, Russian Federation

Background and Aims : To study dynamics of biomarkers of inflammatory response and to estimate their association with parameters of ventricular systolic function in arterial hypertension (AH) and coronary artery disease (CAD) patients with and without metabolic disorders (MD) such as obesity and impaired carbohydrate metabolism of those who underwent COVID-19-associated pneumonia.

Methods: The study included 264 patients (56.97±8.48 years). Gr.1 (n=116) involved AH and CAD patients without MD, gr.2 (n=148) AH and CAD patients with MD. Age, volume of lung damage were comparable. Baseline parameters of complete blood count, biochemistry were assessed on the day of hospitalization. In-depth analysis of biomarkers and echocardiography with speckle tracking were performed 3 months after.

Results: Initially in both groups, statistically significant exaggeration of the normal range of maximum CRP; NLR; PLR; ESR were registered. Dynamics of CRP, NLR, PLR, ESR reached normative values in both groups after 3 months, however, hs-CRP was 4.75±2.09 and 7.06±3.13 mg/l with exaggeration of value in gr.2 ($p<0.001$). Global myocardial strain parameters were significantly more apparent in gr.2. In both groups, parameters of the strain were positively correlated with parameters of RBC, HGB, HCT, creatinine, APTT. Additionally, relationship with LYM was revealed in gr.1, positive relationship with CRP, TG, GFR, and negative with HDL-C was found in gr.1.

Conclusions: In group of patient with AH, CAD and MD after COVID-19, more significant alteration was detected in global myocardial strain associated with changed parameters of hematological and inflammatory biomarkers, correction of which can lead to optimization of contractile ventricular function.

ID:590

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH PRIMARY MYOCARDIAL INFARCTION IN COMBINATION WITH COVID-19

POSTER VIEWING SESSION

Valentin Oleynikov, Luidmila Salyamova, Karina Korenkova, Kristina Polezhaeva, Natalia Donetskaya, Anastasia Babina
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : To conduct a comparative analysis of traditional cardiovascular risk factors in patients with primary myocardial infarction (MI) with and without COVID-19

Methods: The study included 66 patients aged 35 to 70 years, hospitalized for MI (STEMI, NSTEMI). All patients were divided into two groups. Group 1 included 23 people with MI within two weeks after a confirmed COVID-19 or during hospitalization for MI with revealed signs of COVID-19 (positive PCR test). Group 2 included 43 patients without SARS-Cov-2. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), glucose were determined

Results: In group 1 TC was 4.9(CI% 4.3;5.5)mmol/L, LDL-C - 3.3(CI% 2.8;3.8) mmol/L, HDL-C - 0.97(CI% 0.84;1.10) mmol/L, TG - 1.7(CI% 1.3;2.1) mmol/L, glucose - 7.1(CI% 6.6;7.7) mmol/L. In group 2 TC was 5.8(CI% 5.3;6.2)mmol/L (p=0.024), LDL-C was 4.0(CI% 3.6;4.3)mmol/L (p=0.027), HDL-C - 1.22(CI%1.13;1.31)mmol/L (p=0.003), TG - 1.5(CI% 1.2;1.8)mmol/L (p=0.437), glucose - 5.9(CI% 5.5;6.3)mmol/L (p=0.0008). In group 1, 4 or more risk factors were identified in 96% of patients (n=22), in group 2 - in 79% (n=34) patients (p=0.066).

Conclusions: With a comparable frequency of traditional cardiovascular risk factors, patients with MI and COVID-19 were older in age and more often had abdominal obesity, had a low prevalence of burdened heredity and tobacco dependence. With a comparable frequency of dyslipidemia, patients with AMI showed a predominance of lipid profile indicators, while in the first group, low HDL values were found. The higher glucose levels in COVID-19 patients are likely due in part to their immunosuppressive therapy.

ID:591

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

STRUCTURAL STUDIES ON LDL FROM PATIENTS WITH HIGH AND LOW LIPOPROTEIN (A)

POSTER VIEWING SESSION

Yubexi Correa[1], Martin Jansen[2], Clement Blanchet[3], Felix Roosen-Runge[1], Jan S. Pedersen[4], Marité Cárdenas[1]
[1]Biomedical Science, Malmö University, Malmö, Sweden, [2]Institute Of Clinical Chemistry And Laboratory Medicine, University Medical Center Freiburg, Freiburg, Germany, [3]Embl, The Deutsches Elektronen-Synchrotron, Hamburg, Germany, [4]Interdisciplinary Nanoscience Centre Inano, Aarhus University, aarhus, Denmark

Background and Aims : To map LDL total fraction ultrastructure as a function of composition, in terms of lipid serum profiles and presence of lipoprotein (a).

Methods: LDL ultrastructure is secured via Small Angles X-Ray Scattering (SAXS) and the use of the semianalytical super ellipsoid of the revolution model. Blood samples were obtained from four male, adult individuals with different combinations of total cholesterol (TC)-triglyceride (TGA) serum levels, respectively: low/low, high/low, low/high, and high/high. Two of them have high Lp(a) levels and the other two have low. LDL total, large buoyant, and small dense subfractions were isolated by ultracentrifugation. SAXS data were collected on these samples in TBS buffer at 8, 25, and 37 °C in the P12 beamline at EMBL, Hamburg. This enables to characterize of LDL structure below, at, and above the melting temperature of its cholesteryl ester-rich core. T-tests are performed to compare the data.

Results: We observed that there seems to be no trend between the radius or ellipticity when comparing patients with high Lp(a) (A and B) and low Lp(a) (D and C). However, the radius of LDL particles increases when TC and TGA decreases and when TC and TGA increase the particles are more spherical (figure1).

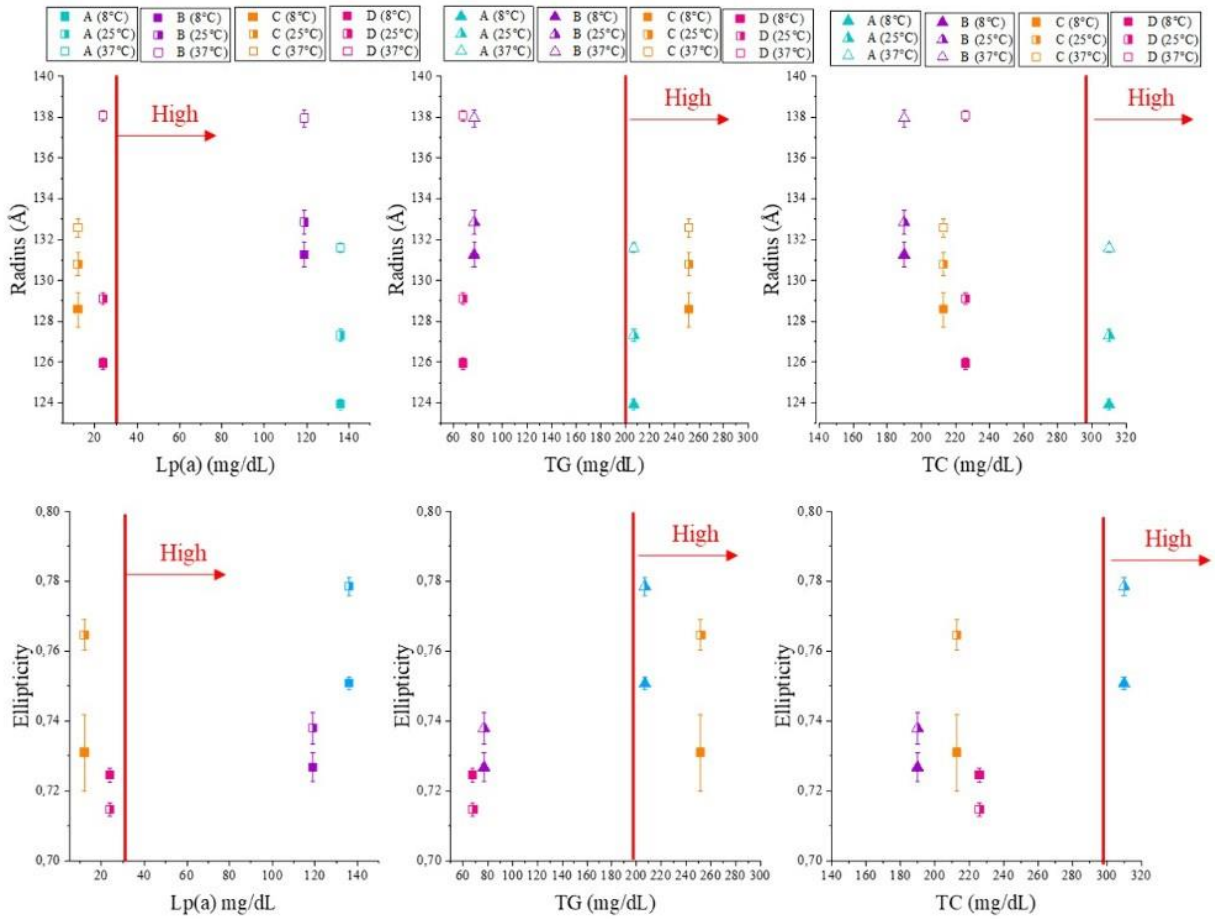


Figure1. Parameters. Triangles (▲) on TG and TC plots means patients with high Lp(a)

Conclusions: The analysis by SAXS allowed us to determine the different parameters that describe the internal structure of the LDL particles (Radius, Ellipticity, etc). Finally, It was possible to establish the structural difference of LDL according to its Lp(a), TGA, and TC content.

ID:523

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-09 Epidemiology of socioeconomic and psychosocial risk factors*

IRRATIONAL BELIEFS AND HEALTH ANXIETY IN RELATION TO HYPERTENSION, HYPERCHOLESTEROLEMIA AND LIFESTYLE BEHAVIORS; THE ATTICA EPIDEMIOLOGICAL STUDY.

POSTER VIEWING SESSION

Christina Vassou[1], Thomas Tsiampalis[1], Ekavi N. Georgousopoulou[2], Christina Chrysohoou[3], Mary Yannakoulia[1], Christos Pitsavos[3], Mark Cropley[4], Demosthenes B. Panagiotakos[1]
[1]Department Of Nutrition And Dietetics, Harokopio University, Athens, Greece, Kallithea, Greece, [2]School Of Medicine Sydney, University of Notre Dame, Sydney, Australia, [3]First Cardiology Clinic, School Of Medicine, University of Athens, Greece, Athens, Greece, [4]School Of Psychology, University of Surrey, Guildford, United Kingdom

Background and Aims : To evaluate the association between psychological characteristics (irrational beliefs and health anxiety), medical conditions and lifestyle behaviors, among apparently healthy adults.

Methods: During the ATTICA prospective cohort study (2002-2012) that was carried out in Greece, 845 participants (18-89 years) free of cardiovascular disease and type 2 diabetes underwent psychological evaluations through the Irrational Beliefs Inventory (IBI, range 0-88) and the Whitley Index scale (WI, range 0-14).

Results: Mean IBI score was 53±10/88 in men and 51±11/88 in women (p=0.68).Mean WI score 3.7±3/14 in men and 3.6±3/14 in women. It was revealed that participants who had high irrational beliefs and high health anxiety were mostly women, older, less educated, and less physically active as compared to the other three groups of participants (low irrational beliefs – low health anxiety, high irrational beliefs– low health anxiety and low irrational beliefs– high health anxiety) (all p-values <0.05).They also had a higher BMI (obesity) and higher hypertension levels (all p-values<0.05), compared to the other three aforementioned groups. On the other hand, it was observed that participants with high irrational beliefs and low health anxiety were younger and men as compared to the other three groups (all p-values <0.001).No association of irrational beliefs and health anxiety with family history of diabetes and baseline hypercholesterolemia was revealed (all p-values>0.05).

Conclusions: People with specific psychological characteristics present differences in their medical status and lifestyle behaviors.Especially, those with high irrational beliefs and health anxiety seem to be more burdened.This finding may initiate a discussion for future research in mental and physical health.

ID:593

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

DYNAMICS OF THE LIPID PROFILE IN POSTINFARCTION PATIENTS DURING HIGH-DOSE THERAPY WITH ATORVASTATIN

POSTER VIEWING SESSION

Valentin Oleynikov, Elena Averyanova, Yulia Barmenkova, Alena Golubeva, Anastasia Oreshkina
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : To assess the dynamics of the lipid profile in patients within 24 months after myocardial infarction with ST segment elevation (STEMI) during high-dose therapy with atorvastatin

Methods: The study included 104 STEMI patients, mean age 52 (95% CI40.5-64) years. All patients have been receiving treatment for STEMI, including high-dose therapy with atorvastatin 40-80 mg/day. Initially, at 12, 24, 48 and 96 weeks of treatment, the lipid profile was analyzed: total cholesterol (TC), triglycerides, low-density lipoprotein cholesterol (LDL-C). Compliance assessment was carried out according to the Morisky-Green questionnaires. The target level of LDL-C was considered as achievement of <1.4 mmol/l and its decrease by more than 50% from the initial values.

Results: A decrease in TC has been observed at 12 weeks of therapy - from 6.02(95%CI 5.72-6.33) to 3.65(95%CI 3.47-3.83) (p=0.00002), at week 48 the TC level was 3.73(95%CI 3.42-3.97)mmol/l (p=0.0001), by 96 weeks - 3.78 (95%CI 3.56-4.05) (p=0.0001). LDL-C decreased by week 12 from 3.7(95%CI 2.12-4.38) to 2.12(95%CI 1.97-2.27) (p=0.00008), by the 24th week up to 2.12 (95%CI 1.97;2.27) (p=0.00002), 48th week - 2.11(95%CI 1.93;2.29) (p=0.000010); 96th - 2.59(95%CI 2.36;2.81) (p=0.001). According to the Morisky-Green scale 2-8% of patients had low adherence to treatment by 48th week, by 96 weeks - 12% (p=0.013).

Conclusions: Monotherapy with high doses of atorvastatin contributes to the achievement of the target level of atherogenic lipids in 45-51% of patients in the first year after STEMI, a decrease in adherence to treatment observed by the 2nd year is accompanied with the decrease of the lipid-lowering effect.

ID:609

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

INFLUENCE OF MINERAL BONE DISEASE BIOMARKERS IN CAROTID MODELING AS A MARKER OF EARLY ATHEROSCLEROSIS IN DIALYSIS PATIENTS

POSTER VIEWING SESSION

Eqrem Hasani[1], Merita Rroji[2], Nereida Spahia[3]
[1]Emergency Medicine, University Hospital Center " Mother Tereza", Tirana, Albania, [2]Nephrology, University Hospital Center, Tirana, Albania, [3]Nephrology, University Hospital Center " Mother Tereza", Tirana, Albania

Background and Aims : Atherosclerosis contributes to cardiovascular morbidity in dialysis patients. We evaluated the relationship between CKD-Mineral Bone Disease (MBD) biomarkers, residual renal function (RRF), inflammation, and other risk factors in carotid modeling as a marker of early atherosclerosis in peritoneal dialysis (PD) compared with hemodialysis (HD) patients.

Methods: We studied 35 stable PD and 49 HD patients on renal replacement therapy (RRT) for 3 to 24 months. We classified patients with atherosclerosis if they have CIMT >10 mm and or presence of plaque evaluated by B- mode ultrasonography.

Results: Out of our total dialysis population study of 84 patients, 15.9% were diabetics. Atherosclerosis was found in 66.3% of patients and 93.4% of the diabetic population. There was no significant difference in the presence of atherosclerosis between PD and HD patients [51.7 vs. 63.6% HD, respectively]. Expectedly, PD patients had a higher RRF ($P < 0.001$), 24 h urine volume ($P < 0.01$); C-reactive protein ($P = 0.03$), and a lower serum phosphate ($P = 0.027$), PTH ($P < 0.042$), alkaline phosphatase ($P < 0.032$), and albumin levels $P < 0.003$) compared to hemodialysis patients. Multiple regression analysis showed that apart from traditional risk factors for atherosclerosis, such as age and diabetes, RRF, phosphate, alkaline phosphatase, and pulse pressure (PP) were independent risk factors

Conclusions: Our study showed a link of atherosclerosis with CKD-MBD metabolic abnormalities secondary to renal failure. We demonstrated a novel, independent association between RRF and atherosclerosis, underlining the positive role of the RRF in the outcome of dialysis patients.

ID:567

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

ASSOCIATION OF VITAMIN D SUPPLEMENTATION WITH STATIN-ASSOCIATED MUSCLE SYMPTOMS: A SYSTEMATIC REVIEW

POSTER VIEWING SESSION

Chong Boon Teo[1], Pek Yan Tan[1], Ryan Yong Kiat Tay[1], Joan Khoo[2], Wann Jia Loh[2]
[1]Yong Loo Lin School Of Medicine, National University of Singapore, Singapore, Singapore, [2]Department Of Endocrinology, Changi General Hospital, Singapore, Singapore

Background and Aims : Although low vitamin D levels is associated with statin-associated muscle symptoms (SAMS), it remains unclear if vitamin D supplementation leads to symptom improvement. We performed a systematic review to evaluate the association of vitamin D supplementation on the resolution or reduction of SAMS.

Methods: We searched Medline (PubMed), Embase and Cochrane Library from inception till 5 May 2021. Full length articles that reported on the association between vitamin D supplementation in adult patients with SAMS were included.

Results: Main Outcome and Measure: Resolution or reduction of SAMS post vitamin D supplementation. We identified 8 interventional studies comprising 669 participants. Vitamin D supplementation was associated with improved statin tolerance in 509 out of 606 (83.9%) patients across the remaining 7 studies that reported patient numbers after supplementation (95%CI=0.81-0.87, I2=72% n=7). None of the studies were randomized controlled trials and hence placebo effect of vitamin D could not be ruled out. Nocebo effect of statin was also not assessed by any of the studies hence it is unclear if the symptoms perceived by patients to be SAMS were truly caused by statin.

Conclusions: Vitamin D supplementation in patients with mild-moderate vitamin D insufficiency was associated with improvement of SAMS. However, the relationship between vitamin D supplementation and SAMS was possibly confounded by the nocebo and placebo effects. Randomized controlled trials addressing both placebo effect of vitamin D and nocebo effect of statins are required to conclusively assess the utility of vitamin D supplementation in improving SAMS.

ID:566

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

UTILIZATION OF BOTH IRISIN AND APELIN IN PREDICTION OF HEART FAILURE WITH PRESERVED EJECTION FRACTION IN TYPE 2 DIABETES MELLITUS PATIENTS

POSTER VIEWING SESSION

Alexander A. Berezin[1,2], Ivan M. Fushtey[2]
[1]Internal Medicine, Zaporozhye State Medical University, Zaporozhye, Ukraine, [2]Internal Medicine, Zaporozhye Medical Academy of Postgraduating Education, Zaporozhye, Ukraine

Background and Aims : Background: Irisin and apelin are a powerful regulatory peptide having an autocrine regulator of cardiac and vascular reparation. The aim of the study was to investigate whether serum levels of both irisin and apelin predict HF with preserved ejection fraction (HFpEF) in patients with T2DM.

Methods: One hundred and eight HF patients with T2DM having HFpEF (n=58), HF with mildly reduced ejection fraction (HFmrEF, n=22), HF with reduced ejection fraction (HFrEF, n=28) aged from 41 to 62 years and 20 non-HF patients with T2DM. Healthy control group was consisted of 25 individuals matched with age and sex. We polled at baseline demographic and anthropometric information, data for hemodynamic performances by B-mode echocardiography, Doppler and TDI, and the levels of biomarkers including irisin, apelin, N-terminal pro-brain natriuretic peptide (NT-proBNP) by ELISA.

Results: The levels of irisin were significantly higher in HFpEF patients than in HFrEF individuals, whereas healthy volunteers and T2DM non-HF patients demonstrated lower concentrations of these peptides. On contrary, apelin levels were significantly increased in HF patients mainly with HFrEF. There were not significant differences between the levels of these biomarkers in HFrEF and HFmrEF. Multivariate logistic regression analysis revealed that adding irisin and apelin to NT-proBNP as independent variables to the predictive model sufficiently improved discriminative ability of whole model for HFpEF.

Conclusions: Multidirectional changes in the levels of irisin and apelin in T2DM patients had better predictive value for HFpEF that simultaneous increase and decrease in the circulating levels of these peptides.

ID:537

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY-DERIVED ENDOTHELIAL SHEAR STRESS IN MYOCARDIAL BRIDGING

POSTER VIEWING SESSION

Andreas Giannopoulos[1], Basil Bolt[2], Dominik Benz[1], Michael Messerli[1], Moritz Schwyzer[1], Elia Von Felten[1], Christel Kamani[3], Dimitri Patriki[2], Cathrine Gebhard[1], Aju Pazhenkottil[1], Christoph Graeni[4], Philipp Kaufmann[1], Ronny R. Buechel[1], Oliver Gaemperli[5]
[1]Cardiac Imaging, Nuclear Medicine Department, University Hospital Zurich, Zurich, Switzerland, [2]Cardiac Imaging, Nuclear Medicine Department,, University Hospital Zurich, Zurich, Switzerland, [3]Nuclear Medicin, CHUV, Lausanne, Switzerland, [4]Cardiology, Universitätsspital Bern, Bern, Switzerland, [5]Cardiology, Hirslanden Clinic, Zurich, Switzerland

Background and Aims : In Myocardial Bridging (MB), a segment of coronary arteries with an intramural course, the proximal to the MB arterial segment frequently shows plaque formation, while the MB itself is typically spared. We aimed to describe the endothelial shear stress (ESS) mileu in arteries with MBs and to investigate the association of atherosclerosis presence with hemorheological characteristics.

Methods: Consecutive patients with MBs at CCTA were retrospectively (3/2016-5/2017) identified. Coronary lumen was segmented, 3D reconstructed and ESS was calculated using a standard CFD approach. ESS was analyzed for the segments: i) within the MB, ii) 5mm proximal to MB, iii) first 5mm within the MB. ESS in segments ii) vs. iii) was compared in arteries with plaques proximal to the MB vs. without plaques.

Results: In 36 patients/arteries analyzed, there was no difference when comparing ESS in the proximal vs. mid vs. distal MB segments (1.5 Pa vs. 1.4 Pa vs 1.9 Pa, p=ns). ESS did not fluctuate proximally to MBs vs. 5 mm within MBs (1.4 Pa vs 1.4 Pa, p=0.56). Around the MBs' entrance, ESS did not differ, in arteries with plaques (N: 12, 1.4 Pa vs 1.2 Pa, p=0.81) and without plaques (N: 24, 1.5 Pa vs 1.6 Pa, p=0.29).

Conclusions: MBs are characterized by ESS homogeneity and normal ESS values without significant ESS variations around their inlet, potentially explaining the lack of atherosclerosis within MBs. ESS might not play a role in atherogenesis proximally to the MBs, by similar ESS patterns in arteries with plaque and without plaques proximal to MBs.

ID:545

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

LATE ADVERSE EVENTS AFTER SURGICAL REVASCULARIZATION IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE: ASSOCIATION WITH COMPLIANCE TO STATIN THERAPY

POSTER VIEWING SESSION

Olga Yepanchintseva[1], Inga Shklianka[1], Kyrylo Mikhaliev[2], Oleg Zharinov[3], Borys Todurov[4]
[1]Department Of Diagnostics Of Pathology Of The Heart And Great Vessels, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine, [2]Internal Medicine, SIS "RPC PCM" SAD, Kyiv, Ukraine, [3]Department Of Functional Diagnostics, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine, [4]Ceo, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine

Background and Aims : To study the association of late adverse events (LAEs) after isolated coronary artery bypass grafting (CABG) in patients with stable coronary artery disease (SCAD) with compliance to statin therapy (ST).

Methods: 155 SCAD patients (mean age 61±8 years; 139 (89,7%) males) after isolated CABG were followed over a period of 12 months after surgery. Twenty-four (15,8%) of 152 patients presented with LAEs (totally, 29 cases; no data in 3 patients). The LAEs profile was predominantly presented by the cases of heart failure progression and left ventricular (LV) ejection fraction (EF) decline >10% (14 cases [48%]). At one year follow-up, 4 patients died. Data on long-term compliance with discharge ST were available in 151 patients: pattern 1 (P1) – withdrawal of previously prescribed ST (n=22), P2 – continuation of low- or moderate-intensity ST, irrespective to its discharge intensity (n=105), and P3 – continuation of previously prescribed high intensity ST (n=24).

Results: Patients with LAEs (vs. no-LAEs, respectively) were characterized by more prevalent P1 cases (43,5% vs. 9,4%; p<0,001). The continuation of low-to-moderate-intensity ST (P2) tended to be more frequent among patients without LAEs (vs. LAEs, respectively): 72,6% vs. 52,2% (p=0,082). The P3 frequency did not differ significantly between both groups of comparison.

Conclusions: The LAEs after CABG in patients with SCAD were associated with more frequent withdrawal of previously prescribed ST. Preserving compliance to statin therapy is an important priority at long-term observation after CABG.

ID:512

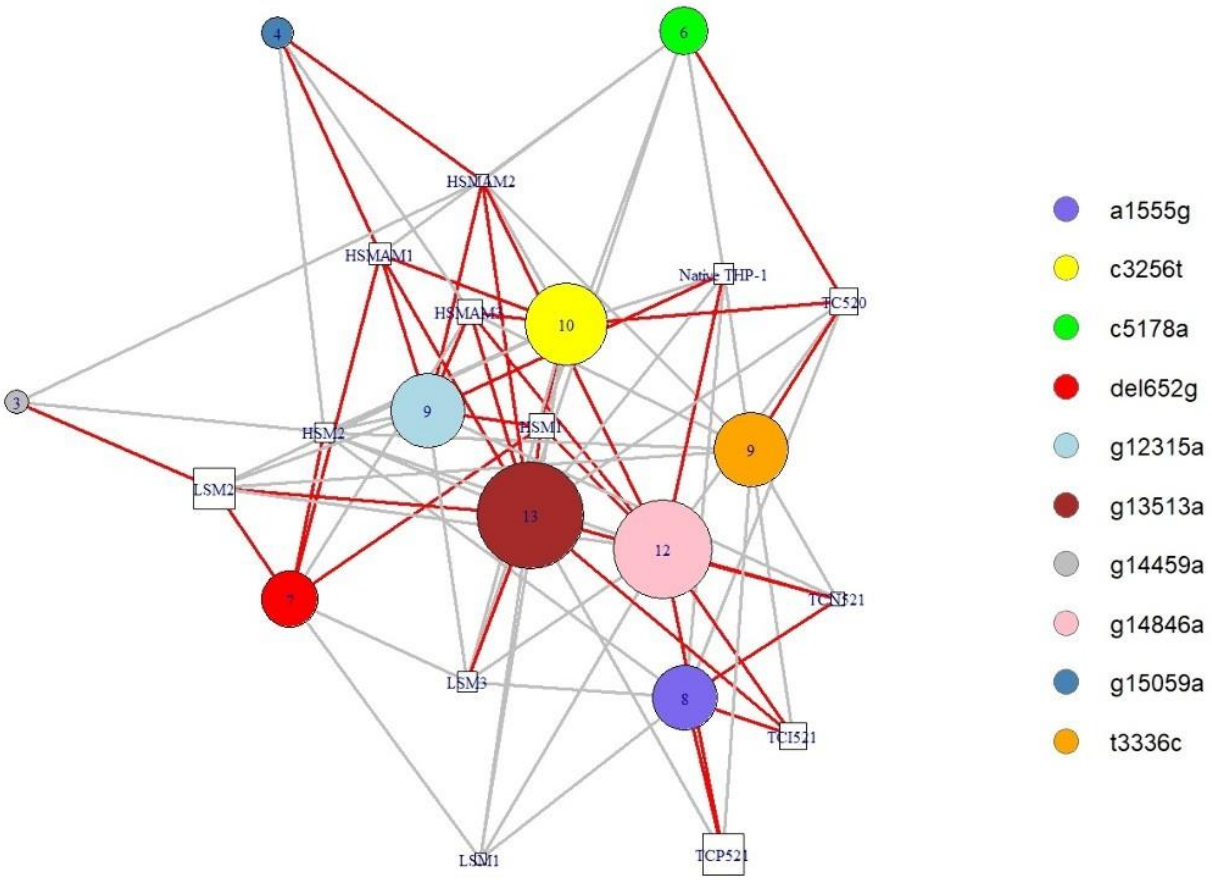
Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

CONTRIBUTION OF ATHEROSCLEROSIS-RELATED MITOCHONDRIAL MUTATIONS TO THE CELLULAR OXYGEN ABSORPTION IN THE HUMAN MACROPHAGES

POSTER VIEWING SESSION

Andrey V. Omelchenko[1], Victoria A. Khotina[2], Vasily N. Sukhorukov[3]
[1]Department Of Scientific Research, Institute for Atherosclerosis Research, Moscow, Russian Federation, [2]Laboratory Of Angiopathology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation, [3]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation

Background and Aims : Mitochondrial dysfunction (include via mutation burden) is likely involved in atherogenesis. Thus, it is nearly impossible to find out the meaning and individual role of each mutation for the disturbance of biological function using laboratory approaches (see Fig.1). Aim of this research to assess individual impact of mutations in cell oxygen consumption. Figure 1. The network of macrophages-derived cell lines (rectangles) and their mutations (circles), which was studied in this research.



Methods: The initial data were the results of biological experiments with 14 hybrid monocyte-derived macrophages obtained from patients with varying stages of atherosclerosis. Models based on network

analysis, linear and nonlinear models, models based on frequency analysis, regression models based on machine learning and combinatorial models of the regression of the oxygen absorption rate from the level of heteroplasmy and the type of mutation were developed in the R programming language.

Results: It was found that mutations in the genes tRNA (g12315a, c3256t) and rRNA (a1555g) decrease the rate of oxygen absorption by 47%, 58%, and 18%, respectively. The mutation in the Coenzyme Q - cytochrome c reductase (g15059a) gene is neutral. And mutations in the NADH dehydrogenase (g14459a, c5178a, t3336c, g13513a), tRNA (del652g) and Coenzyme Q - cytochrome c reductase (g14846a) genes increase the rate of absorption by 68%, 114%, 21%, 10%, 88% and 48%, respectively (all p-values are less than 0.001).

Conclusions: Computational biology can be used for the role establishment of mtDNA mutations in atherosclerosis. This work was supported by the Russian Science Foundation (Grant # 22-15-00233).

ID:550

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

GENDER CHARACTERISTICS OF THE COURSE AND TREATMENT OF ACUTE MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Natalia A. Koriagina[1], Vladimir S. Koriagin[1], Sofia G. Shulkina[1], Iliya V. Krakhotin[1], Inna L. Gulyaeva[2]
[1]Polyclinic Department, Perm state medical university, Perm, Russian Federation, [2]Department Of Pathological Physiology, PSMU, Perm, Russian Federation

Background and Aims : The aim of the study was to study the gender characteristics of the course of acute myocardial infarction (MI).

Methods: The study included 372 patients aged 31 to 93 yrs (64.5 ± 12.3 years) with a diagnosis of MI, who were divided into 2 groups (gr.) by gender: Gr.1 - 140 (37.6%) , women, gr. 2 - 232 (62.4%) men.

Results: The average age of women is 70.77 ± 11.7 yrs, of men - 60.52 ± 11.5. In women, MI was significantly more likely to develop against the background of arterial hypertension ($p < 0.044$), diabetes mellitus ($p < 0.002$) and obesity ($p < 0.043$), and the prevalence of smoking was higher in the male ($p < 0.001$). The GRACE in women is higher than in men ($p < 0.007$). The most common complication of MI in both groups was acute heart failure (HF), which was recorded in 53.7% of women and 55.5% of men (RR 0.96; 95% CI 0.75– 1.23; $p > 0.05$). The frequency of deaths was statistically significantly higher in women; they were more often registered as hospitalized (11.4% versus 6.4%; RR 1.79; 95% CI 0.94–3.43; $p < 0.05$), so and post-hospital mortality (9.2% versus 6.4%; RR 1.44; 95% CI 0.68–3.02; $p > 0.05$).

Conclusions: The most significant risk factors for the development of MI in women are diabetes mellitus, arterial hypertension and obesity. The course of myocardial infarction in women is associated with the development of severe heart failure, and the immediate prognosis and outcome of myocardial infarction in women is more unfavorable than in men.

ID:554

Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

THE ASSOCIATION OF VISIT-TO-VISIT BLOOD PRESSURE VARIABILITY WITH SCORE2 CARDIOVASCULAR RISK IN UKRAINIAN RURAL MALES WITH ARTERIAL HYPERTENSION

POSTER VIEWING SESSION

Kyrylo Mikhaliev[1], Tetiana Nimtsovych[2], Anatolii Kravchenko[1], Vitalii Gurianov[3], Tamara Chursina[4], Svitlana Stanislavska[1]
[1]Internal Medicine, SIS "RPC PCM" SAD, Kyiv, Ukraine, [2]Cardiology, PNPE «Khmelnytskyi Regional Cardiovascular Center» Khmelnytskyi Regional Council, Khmelnytskyi, Ukraine, [3]Medical And Biological Physics And Informatics, Bogomolets National Medical University, Kyiv, Ukraine, [4]Internal Medicine, Clinical Pharmacology And Occupational Diseases, Bukovinian State Medical University, Chernivtsi, Ukraine

Background and Aims : To study the association of blood pressure (BP) visit-to-visit variability (VVV) with cardiovascular risk, assessed by SCORE2 model, in Ukrainian rural males with arterial hypertension (HTN).

Methods: The cross-sectional study enrolled 160 Ukrainian rural males with uncomplicated primary HTN (mean age 50 ± 6 years). Seventy three (45,6 %) patients were overweight; 85 (53,1 %) patients were active smokers. The vast majority of patients (97,5%) presented with dyslipidemia of different magnitude. The SCORE2 model was used to assess cardiovascular risk (considering Ukraine as very high risk region). BP VVV (of systolic BP (SBP) and diastolic BP [DBP]) was assessed by means of standard deviation (SD) and coefficient of variation (CV) (derived from the four consecutive visits). The enrolled sample was subdivided into the groups with high (n=82; 51,3%) and low (n=78; 48,7%) blood pressure variability (HBPV, LBPV).

Results: The HBPV group (vs. LBPV, respectively) was characterized by the higher average SCORE2 risk (median, quartiles: 12% (8-16%) vs. 33% (26-41%); $p<0,001$), thus being entirely represented by patients with very high SCORE2 cardiovascular risk pattern. The SCORE2 risk correlated significantly with SD (SBP) ($\rho = 0,766$; $p<0,001$), CV (SBP) ($\rho = 0,743$; $p<0,001$) SD (DBP) ($\rho = 0,635$; $p<0,001$) and CV (DBP) ($\rho = 0,613$; $p<0,001$).

Conclusions: BP VVV in Ukrainian rural hypertensive males was associated with SCORE2 risk, with the entirely very high cardiovascular risk profile in case of HBPV.

ID:533

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

HEME OXYGENASE-1 INDUCTION PROMOTES HUMAN PLURIPOTENT STEM CELL DIFFERENTIATION INTO ENDOTHELIAL CELLS AND VASCULAR REPAIR

POSTER VIEWING SESSION

Wei-Cheng Jiang, Shaw-Fang Yet
Institute Of Cellular And System Medicine, National Health Research Institutes, Zhunan, Taiwan

Background and Aims : Endothelial cells (ECs) have a crucial role in reendothelialization for repairing denuded arteries. Heme oxygenase-1 (HO-1) is a stress response protein that degrades prooxidant heme and generates molecules with antioxidative and anti-inflammatory properties. Given that redox status is critical in stem cell differentiation, our aims are to investigate the effects of HO-1 induction on human pluripotent stem cells (hPSCs) differentiation toward ECs and reendothelialization after arterial injury.

Methods: We utilized a three-step protocol to differentiate hPSCs (hESCs and hiPSCs) into ECs. Cells were treated with or without hemin at different stages to induce HO-1 expression; EC characteristics and proliferative capacity were then evaluated. To examine the effect of HO-1 induction on arterial repair, we employed a mouse guide wire injury model to denude arterial endothelium. Following injury, biocompatible thermoresponsive gel embedded with vehicle or hemin was then applied around the injured artery. The arteries were harvested at different time points.

Results: Compared with vehicle, hemin increased cell number of hPSCs-differentiated ECs, concomitant with enhanced HO-1 level, expression of EC-related genes, and tube formation capacity. *In vivo*, hemin application increased HO-1-positive cells on the luminal surface one week after arterial denudation. Two weeks after injury, hemin-treated arteries had more CD31-positive area on the luminal surface and decreased neointima size in comparison with vehicle-treated arteries.

Conclusions: Collectively, our results indicate that HO-1 induction by hemin promotes EC differentiation from hPSCs and reduces intimal hyperplasia after vascular injury, likely through enhanced reendothelization. HO-1 induction might be a therapeutic strategy following vascular injury.

ID:538

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CORONARY ARTERY BYPASS GRAFTING IN PATIENTS WITH CONCOMITANT DIABETES MELLITUS: PERIOPERATIVE PROFILE AND EARLY POSTOPERATIVE COMPLICATIONS

POSTER VIEWING SESSION

Olga Yepanchintseva[1], Kyrylo Mikhaliev[2], Oleg Zharinov[3], Borys Todurov[4]
[1]Department Of Diagnostics Of Pathology Of The Heart And Great Vessels, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine, [2]Internal Medicine, SIS "RPC PCM" SAD, Kyiv, Ukraine, [3]Department Of Functional Diagnostics, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine, [4]Ceo, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine

Background and Aims : To evaluate perioperative profile and early postoperative complications (EPOCs) in patients with stable coronary artery disease (SCAD) and diabetes mellitus (DM), undergoing isolated coronary artery bypass grafting (CABG).

Methods: We enrolled 600 consecutive SCAD patients (mean age 61±9 years, 511 (85,2%) males), undergoing isolated CABG. DM type 2 was diagnosed in 212 (35,3%) patients. We analyzed perioperative clinical and instrumental data, and EPOCs cases. Totally, EPOCs were registered in 112 (18,7%) patients.

Results: The DM group, as compared to SCAD patients without DM, was characterized by the higher prevalence of females (21,7% vs. 11,1%, respectively; p<0,001) and moderate-to-severe obesity cases (15,6% vs. 4,9%, respectively; p<0,001), as well as the higher frequency of patients with 3-vessel disease (87,7% vs. 73,7%, respectively; p<0,001). EPOCs were more prevalent in DM group (vs. no-DM: 32,1% and 11,3%, respectively; p<0,001), namely due to the higher frequency of acute kidney injury, acute heart failure and acute cerebrovascular events cases. Consequently, the perioperative profile of DM patients, as opposed to no-DM patients, included longer inotropic support and intensive care.

Conclusions: The concomitant DM worsens coronary atherosclerosis burden and perioperative profile in patients undergoing isolated CABG, namely by the higher frequency of EPOCs, requiring longer intensive care. Further investigations aimed at the EPOCs risk reduction are needed for SCAD patients with concomitant DM, undergoing surgical revascularization.

ID:536

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PATIENT ADHERENCE TO LIPID-LOWERING AND OTHER THERAPY WITHIN 24 MONTHS AFTER MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Yulia Barmenkova, Elena Averyanova, Karina Korenkova, Nadezhda Burko, Anastasia Oreshkina, Valentin Oleynikov
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : To assess the patient adherence to treatment within 96 weeks after STEMI.

Methods: The study included 98 STEMI patients, mean age 52 (46; 58) years. Percutaneous coronary intervention with stenting of the infarct-related artery was performed 6.3 (3.3; 10.2) hours after the pain onset. The assessment of the received medication and compliance was carried out at discharge from the hospital, 12 and 24 months after STEMI based on the survey and the results of the Morisky-Green scale.

Results: All patients have been taking statins up to a year after STEMI, 97% of patients continued taking statins by month 24 (p=0.245). All patients received double antiplatelet therapy (acetylsalicylic acid+clopodogrel/ticagrelor) after discharge, 99% (p=1.0) - by month 12, 42% - by month 24 (p<0.001). Adherence to ACE inhibitors/ARB - 77%, 73% (p=0.742) and 69% (p=0.335) at the corresponding periods, and the number of patients continuing to take β-blockers decreased from 85% to 75% (p=0.174). The number of patients taking diuretics - 17%, 16% (p=0.849), 18% (p=0.853). By the 24th month, the number of patients taking calcium antagonists decreased - 3% vs 10% (p=0.045). The number of patients who scored >3 points decreased from 8% to 2% (p=0.105). By 24 months the number of patients who missed taking medications increased to 12% (p=0.013).

Conclusions: In the first year after STEMI, patients were found to be highly compliant, especially to statins. By the end of the second year, a decrease in adherence to therapy is recorded, which is obviously associated with an uncomplicated late post-infarction period.

ID:611

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

THE ABILITY TO DONATE LIPID-FREE APOA-I AS A PRIMARY CHOLESTEROL ACCEPTOR AT CHOLESTEROL EFFLUX IS A NEW FUNCTIONAL PROPERTY OF HDL

POSTER VIEWING SESSION

Alexander D. Dergunov, Veronika B. Baserova, Dmitry Y. Litvinov
Structural Fundamentals Of Lipoprotein Metabolism, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation

Background and Aims : The relation between apoA-I dissociation and HDL concentration that may determine the atheroprotective properties of HDL remains unknown.

Methods: HDL was prepared from plasma samples of 48 middle-aged male patients without coronary atherosclerosis by precipitation of apoB-containing lipoproteins by polyethylene glycol. Urea-induced HDL denaturation and concomitant apoA-I dissociation were followed by the increase of apoA-I-containing prebeta-fraction in immunoreplica after HDL electrophoresis in agarose gel and by the increase of ABCA1-mediated efflux of fluorescent analogue BODIPY-Cholesterol from RAW 264.7 macrophages.

Results: Urea-induced apoA-I dissociation from HDL surface occurs as a cooperative transition from lipid-bound to fully dissociated apolipoprotein. The resistance of HDL structure to denaturation was compared by the *D* parameter that corresponds to the degree of apoA-I dissociation after the incubation of HDL preparations at the same dilution for 6 hrs at 25°C at pH 7.4 in 4.25 M urea as a half-transition region. The *D* parameter negatively correlated with choline-containing phospholipid level in HDL preparations (r = -0.603, $p = 5.8 \cdot 10^{-6}$). Dissociated apoA-I determines the increase of ABCA1-mediated efflux of BODIPY-Cholesterol from RAW 264.7 macrophages to patient HDL.

Conclusions: The stability of apolipoprotein-lipid interactions depends on the level of HDL phospholipids at apoA-I distribution between lipid and water phases. The fraction of extracellular lipid-free apoA-I may increase in atheroma with local acidosis and low HDL level as a compensatory trigger of ABCA1-dependent cholesterol efflux from macrophage. The ability of HDL to donate lipid-free apoA-I as a primary cholesterol acceptor may represent a new functional property of HDL.

ID:514

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

DEVELOPMENT OF APPROACHES TO SUBCELLULAR ANTIATHEROSCLEROTIC THERAPY

POSTER VIEWING SESSION

Yulia V. Markina[1], Alexander M. Markin[1,2], Taisiya V. Tolstik[1], Ulyana S. Zotova[1], Anton Y. Postnov[1], Igor A. Sobenin[3,4], Alexander N. Orekhov[1,4,5]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Department Of Histology, Cytology And Embryology, Peoples' Friendship University of Russia (RUDN University), Moscow, Russian Federation, [3]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [4]Laboratory Of Angiopathology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation, [5]Institute For Atherosclerosis Research, Institute for Atherosclerosis research, Moscow, Russian Federation

Background and Aims : We have studied changes in the accumulation of protoporphyrin IX (PpIX) induced by exposure to 5-aminolevulinic acid (5-ALA). Cytoplasmic hybrids were the object. PpIX, a widely used photosensitizer in clinical practice, is produced by 5-ALA in mitochondria in the heme synthesis reaction cascade. With an increased intake of 5-ALA from the outside, excess PpIX accumulates in cells at an increased concentration. The accumulation of PpIX depends on the metabolic activity of the mitochondria in cells.

Methods: We examined nine cybrid lines and a control (THP-1). Using a mitochondrial dye, MitoTracker™ Orange (Thermo Fisher Scientific), we assessed the functional state of mitochondria in individual cells. Laser scanning confocal microscopy (561 nm) with spectral resolution was used to record the fluorescence signal in the cells.

Results: PpIX accumulation depends on the functional state of the mitochondria. These cell activity can vary under the influence of a different set of mutations in the mitochondrial genome. In the described series of experiments, six of the nine cybrid lines showed an increase in PpIX accumulation compared with control. There was a positive correlation between the concentration of PpIX in the cell and mitochondrial potential.

Conclusions: Thus, we confirmed the possibility of selective elimination of dysfunctional mitochondria with the selection of a laser dose sufficient for the death of pathological mitochondria as a result of the photodynamic effect. Moreover, as a result of such exposure, normally functioning mitochondria and the cell will not be destroyed. This work was supported by the Russian Science Foundation («Research Institute of Human Morphology» Grant#22-25-00190).

ID:564

Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

APELIN13 LEVEL IN PATIENTS WITH ESSENTIAL HYPERTENSION AND PREMATURE BEATS

POSTER VIEWING SESSION

Anastasia Ivankova[1], Nataliia Kuzminova[1], Yevgenia Ivanova[2]
[1]Internal Medicine 1, National Pirogov Memorial Medical University, Vinnytsya, Vinnytsya, Ukraine, [2]Physical Training And Mps, National Pirogov Memorial Medical University, Vinnytsya, Vinnytsya, Ukraine

Background and Aims : Background. Today the world is actively studying various metabolic markers of cardiovascular risk and apelin13 is one of them. It has a positive effect on the cardiovascular system because it counteracts the renin-angiotensin system, has an antihypertensive and positive inotropic effect. Aim. To assess apelin13 level in patients with essential hypertension and premature beats.

Methods: Materials and Methods. The study involved 156 patients with stage II essential hypertension (EH), including 124 with frequent premature beats. They formed the main clinical group of the study. Another 32 patients with EH II had no cardiac arrhythmias and formed the comparison group. We also examined 30 healthy normotensive individuals. They were referred to the control group. General clinical examination, office blood pressure measurement, 12-lead ECG, ECG monitoring, and apelin13 serum level were performed in all patients who agreed to participate in the study.

Results: . In patients with EH, the level of apelin13 was significantly lower ($p < 0.0001$) compared with healthy individuals, both in patients with EH II and arrhythmias, and EH II without arrhythmias. The mean value of apelin13 in all patients with hypertension was 919 (755; 1177) pg/ml. It was 29.9% ($p < 0.0001$) lower than the corresponding concentration in healthy individuals and 12.1% 0.002 lower than the level of apelin13 in patients with EH II without arrhythmias.

Conclusions: Conclusion. In patients with essential hypertension, the level of apelin13 was significantly lower compared to control. Moreover, the mean level of apelin13 in patients with essential hypertension and premature beats was significantly lower than in patients with hypertension but without arrhythmia.

ID:515

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

APOLIPOPROTEINS A1 LEVEL IN THE PLASMA OF PATIENTS WITH COVID-19

POSTER VIEWING SESSION

Liubov K. Sokolova, Julia B. Belchina, Volodymir M. Pushkarev, Olena I. Kovzun, Victor V. Pushkarev, Mykola D. Tronko
Diabetology, Institute of Endocrinology, Kyiv, Ukraine

Background and Aims : The COVID-19 infection is associated with dyslipidemia and cardiovascular complications. The aim of the study was to determine the content of ApoA1, ApoB, and oxLDL in the plasma of patients with COVID-19, diabetes mellitus (DM), and cardiovascular disease (CVD).

Methods: The research protocol was approved by the Ethics Committee of the Institute. All patients signed an informed consent for further diagnostic and scientific research. Blood plasma from 60 patients with DM (25 men, 35 women) and 21 patients with DM, CVD and COVID-19 (10 men, 11 women) was used. The blood from healthy people was used as the control ApoA1/ApoB, and oxLDL were determined using ELISA kits (Elabscience, US).

Results: It was shown that the level of ApoA1 in the blood of patients with type 2 diabetes and especially with COVID-19 was significantly lower than in the blood of healthy people. The level of ApoB and oxLDL in the blood of patients with COVID-19 was significantly higher (2.3 and 3.8 times, respectively) than in the blood of healthy people. There were differences between patients with COVID-19 without concomitant diseases and COVID-19 with diabetes or CVD.

Conclusions: Thus, levels of ApoA1, ApoB, and oxLDL may be promising markers of COVID-19.

ID:520

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

RELATIONSHIP BETWEEN THE AREA OF AMPLIFICATION OF THE MAGNETIC RESONANCE SIGNAL AND THE DEFORMATION CHARACTERISTICS OF THE LV IN PATIENTS WITH STEMI

POSTER VIEWING SESSION

Valentin Oleynikov, Elena Averyanova, Natalia Donetskaya, Vera Galimskaya, Anastasia Babina, Alena Golubeva
Therapy, Penza State University, Penza, Russian Federation

Background and Aims : to assess the relationship between the area of signal amplification according to cardiac MRI and deformation characteristics obtained by speckle echocardiography in patients with STEMI.

Methods: the study included 18 patients aged 54.8±6.8 years with STEMI. All included persons underwent echocardiography on the 7–9th day on a Vivid GE E95 Healthcare device. Longitudinal Strain/LS, Circumferential Strain/CS, and Radial Strain/RS were determined for 16 left ventricular segments using EchoPAC software version 202 (GE Healthcare). All subjects underwent cardiac MRI (Philips Ingenia, 1.5T) with intravenous administration of a Gd-containing contrast agent 0.2 ml/kg. The signal amplification area index (%) was calculated segment by segment. One-way regression analysis was used to assess the patterns between the indicators.

Results: A total of 288 LV segments were analyzed. It was found that all deformation characteristics are interrelated with the area of myocardial damage. A strong association was demonstrated by LS and CS: the weight factors of one-factor models were 0.3 ($F = 21.78$; $p = 0.000001$; $R2 = 0.071$), for CS 0.27 ($F = 10.26$; $p = 0.00007$; $R2 = 0.047$), respectively. An inverse relationship was found between the signal amplification area and RS, the weight factor was -0.17 ($F = 7.92$; $p = 0.0052$; $R2 = 0.03$).

Conclusions: the zone of necrosis extending from the endocardium to the epicardium leads to the greatest reduction in longitudinal and circumferential strain. The inverse dependence of the area of signal amplification on radial strain indicates the role of this strain in maintaining of LV systolic function.

001

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

NORMOXIC HIF-1A STABILIZATION AT THE VASCULAR BARRIER IN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Mohsen Abdi Sarabi, Sönke Weinert, Rüdiger Braun-Dullaeus
Division Of Cardiology And Angiology, University Hospital Magdeburg, Department of Internal Medicine, Magdeburg, Germany

Background and Aims : Not much is known about hypoxia-inducible factor (HIF)-1α stabilization under normoxic conditions. We hypothesize that micromilieu factors (MF) induce normoxic HIF-1α stabilization, which could represent a first trigger for the development of atherosclerosis through a loss of the endothelial barrier function (EBF).

Methods: To detect HIF1α-stabilizing MF using *live cell imaging* experiments, we generated HIF-1α-mKate2-expressing HEK293 cells as a deep red biosensor. Human coronary artery endothelial cells (HCAECs) were then treated with preselected MF. Normoxic HIF-1α stabilization was confirmed by *live cell imaging* and microscopy-independent methods such as Western blot.

Results: We demonstrated that MF, particularly pro-inflammatory cytokines and growth factors such as TNF-α and IGF-I, cause significant normoxic HIF-1α stabilization in HCAECs. However, the level of prolyl 4-hydroxylase-2 (PHD2) protein and hydroxylated HIF-1α protein does not change after normoxic HIF-1α stabilization. Therefore, normoxic HIF-1α stabilization by MF is independent of steps leading to degradation of this transcription factor such as hydroxylation. Instead, we could demonstrate that MF activate the Akt/mTOR pathway as well as the MEK/ERK pathway. Subsequently, P70S6 kinase and eukaryotic translation initiation factor 4E (eIF4E) are phosphorylated and activated resulting in upregulation of HIF-1α protein. The activation of NF-κB pathway is also observed, which may indirectly contribute to the normoxic upregulation of HIF-1α protein by MF.

Conclusions: Our data show that MF stabilize HIF-1α under normoxic conditions. Next, the functional consequences, such as barrier function and the secretome derived from HCAECs, will be investigated.

002

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

ENDOTHELIUM FUNCTION IN CHILDREN WITH HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Eugenia S. Slastnikova[1], Dinara I. Sadykova[1], Liliia F. Galimova[2], Chulpan D. Khaliullina[1]
[1]Hospital Pediatrics, Kazan State Medical University, Kazan, Russian Federation, [2]Pediatric Cardiology, Republican Children's Hospital, Kazan, Russian Federation

Background and Aims : The aim of this study was to establish the features of endothelial function in children with heterozygous familial hypercholesterolemia in order to optimize the early diagnosis of the disease.

Methods: We analyzed the case histories of 61 patients over 18 years old with an established diagnosis of a heterozygous form of familial hypercholesterolemia (FH)on the basis of "City Clinical Hospital No. 7" in Kazan (Russian federation). The next step was cascade screening - step-by-step identification of patients with FH among members of the proband's family. 87 relatives of the first were identified - children (son, daughter) and the second line of kinship (grandchildren, nephews) under 18 years old. The main study group consisted of 44 children (41 people - first-line relatives, 3 children - second-line relatives) who were diagnosed with a heterozygous form of FH according to Simon Broome's criteria, which amounted to 50.6% of the total sample. The comparison group consisted of 43 healthy children aged 5 to 17 years, without changes in lipids.

Results: Median endothelin-1 level was 0.048 (0.028–0.0734) fmol/mlin the control group. Analysis showed a statistically significant increase in the studied indicator by 6.8 times in FH children (0.3075 fmol/ml, $p < 0.001$) relative to the control group. Comparing the nitric oxide in the blood serum of patients, it was revealed that its indicators in the group with FH were statistically significantly higher by 3 times compared with the control group.

Conclusions: FH was accompanied by a statistically significant increase in the level of endothelin-1 and nitric oxide in the blood serum.

003

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

INCREASED RAAS ACTIVATION IS ASSOCIATED WITH CALCIFIED PLAQUE BURDEN, ADVERSE PLAQUE CHARACTERISTICS AND FFR SIGNIFICANT CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Ruurt A. Jukema[1], Ruben Winter De[1], Pepijn Diemen Van[1], Roel Driessen[1], A.H. J. Danser[2], Ingrid Van Den Berg-Garrelds[2], Pieter Raijmakers[3], Peter Ven Van De[4], Paul Knaapen[1], Ibrahim Danad[1], Guus Waard De[1]
[1]Cardiology, Amsterdamumc, location VUmc, Amsterdam, Netherlands, [2]Pharmacology And Vascular Medicine, Department Of Internal Medicine, Erasmus MC, Rotterdam, Netherlands, [3]Radiology, Nucleur Medicine & Pet Research, Amsterdamumc, location VUmc, Amsterdam, Netherlands, [4]Epidemiology & Data Science, Amsterdamumc, location VUmc, Amsterdam, Netherlands

Background and Aims : Renin-angiotensin-aldosterone-system (RAAS) activity has been linked to coronary artery disease (CAD) and coronary microvascular dysfunction (CMD). In this study we investigated if increased RAAS activation is related to CAD, high risk plaque (HRP), myocardial perfusion and CMD in chest pain patients.

Methods: Venous renin as a measure for RAAS activation was quantified by immunoradiometric assay in 205 patients (64% men; age 58 ± 9 years) with suspected CAD. Patients underwent 256-slice coronary CT angiography for (quantitative) plaque analysis and coronary artery calcium (CAC) scoring, [^{15}O]H2O PET perfusion imaging and invasive FFR measurements in all coronary arteries. Patients were categorized into three groups based on FFR (≤0.80) and hyperemic MBF <2.3 ml/min/g: (1)obstructive CAD (n=92), (2)CMD (n=26) or (3)no or nonobstructive CAD (n=85).

Results: Significant associations were found between renin and CAC score, TPV and MBF (r=0.22; r=0.23; r=-0.19 respectively, p<0.001 for all). After correction for baseline characteristics including RAAS inhibiting therapy renin associated positively with CAC score and TPV, but not with hyperemic MBF (p<0.01; p=0.02 and p=0.23). Patients with high risk plaque displayed higher levels of renin (mean logarithmic renin 1.25±0.43 vs. 1.12±0.35 pg/ml; p=0.04). Compared to no or nonobstructive CAD patients, renin was significantly elevated in obstructive CAD patients but not in CMD patients (mean logarithmic renin 1.06±0.34 vs. 1.23±0.36; p<0.01 and 1.06±0.34 vs. 1.16±0.41 pg/ml; p=0.65).

Conclusions: RAAS activity measured by renin concentration is elevated in patients with coronary atherosclerosis and high risk plaque but not in patients with CMD.

004

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

PROTEOMIC PROFILING OF ENDOTHELIAL CELLS TREATED WITH CALCIPROTEIN PARTICLES

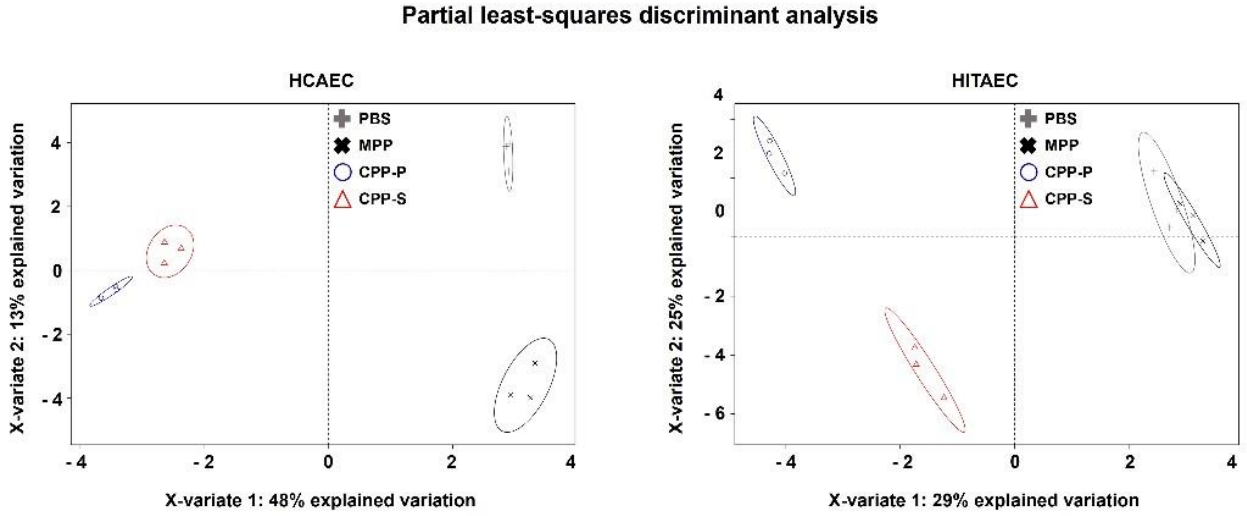
POSTER VIEWING SESSION

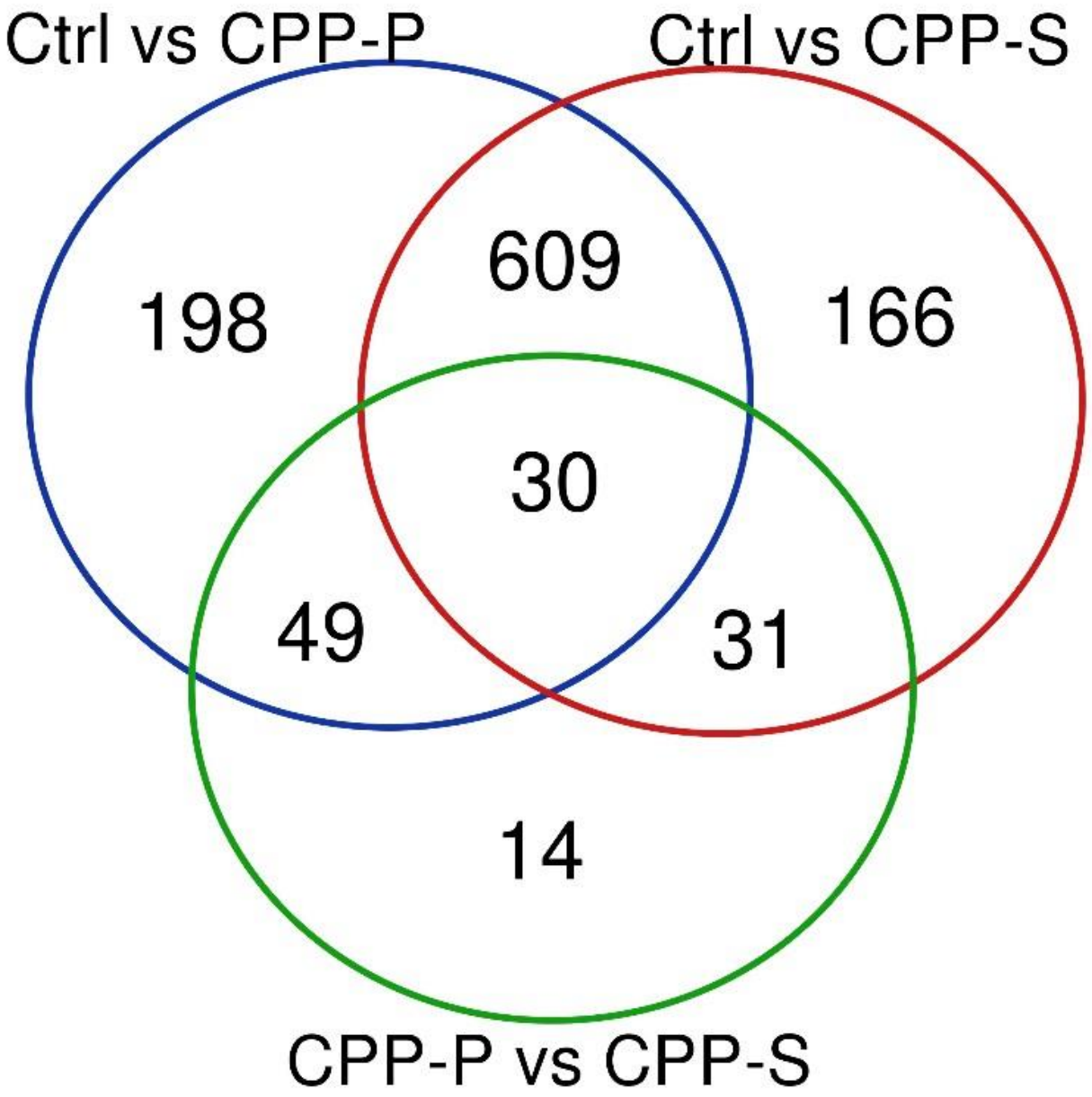
Arseniy Lobov[1], Daria K. Shishkova[2], Bozhana R. Zainullina[3], Victoria E. Markova[2], Anton G. Kutikhin[2]
[1]Department Of Regenerative Biomedicine, Research Institute of Cytology, St. Petersburg, Russian Federation, [2]Laboratory Of Molecular, Translational, And Clinical Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [3]Centre For Molecular And Cell Technologies, St. Petersburg State University, St. Petersburg, Russian Federation

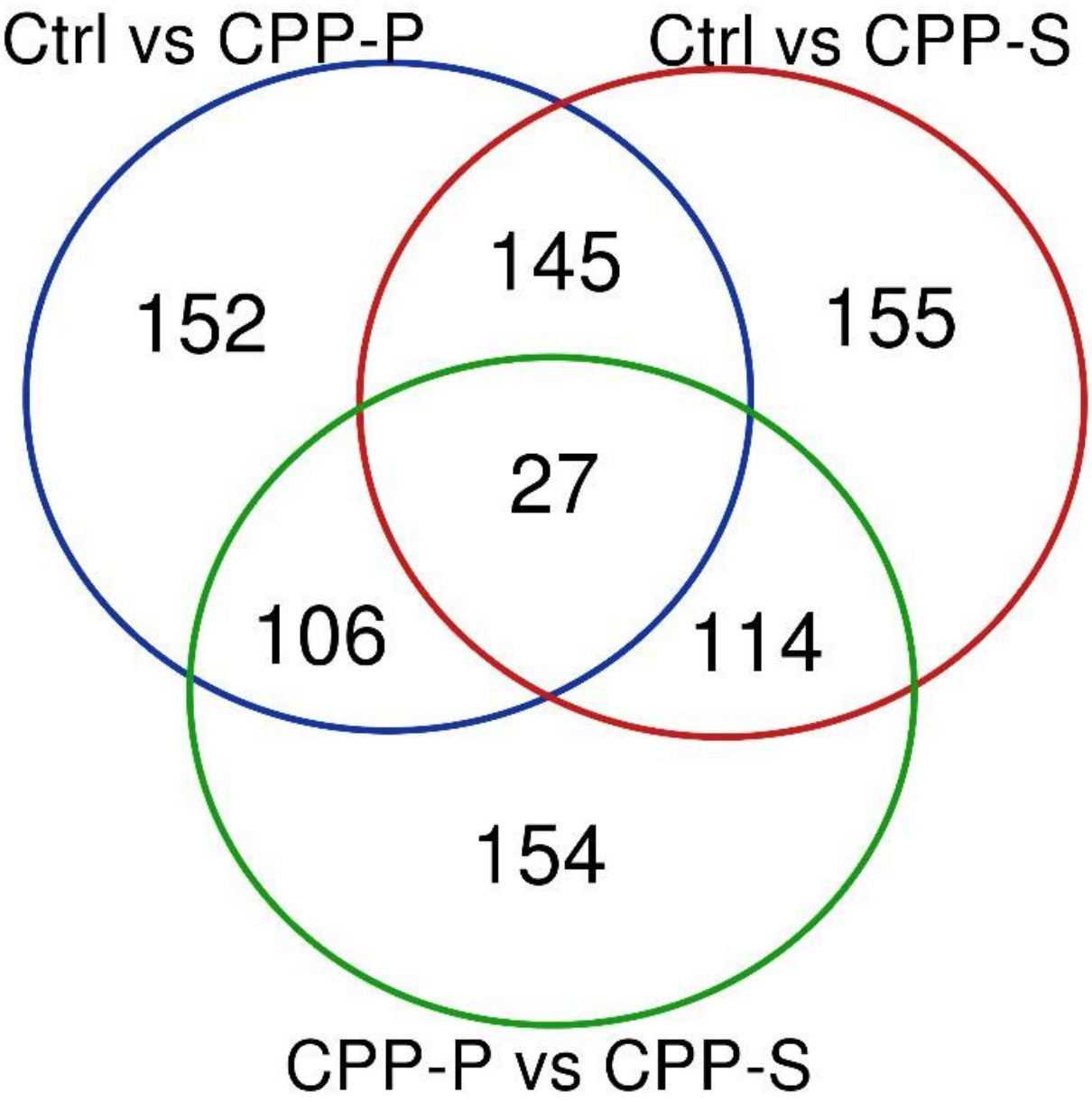
Background and Aims : Calciprotein particles (CPPs), generated in human blood to cope with mineral stress, represent both a physiological tool for aggregating excessive calcium and phosphate and a trigger of pathological events upon the internalisation by endothelial cells (ECs). However, unbiased proteomic profiling of CPP-treated ECs have not been performed.

Methods: Primary human coronary artery (HCAEC) and internal thoracic artery ECs (HITAEC) were exposed to primary (CPP-P) or secondary (CPP-S) CPPs for 24 hours. Label-free proteomic profiling was performed by liquid chromatography-tandem mass spectrometry with ion mobility (TimsToF Pro). Bioinformatic analysis was conducted using PEAKS Studio Xpro and R software environment. Proteins identified with false discovery rate <1% and having ≥2 unique peptides were included into further analysis.

Results: We found significant differences in global expression profile of HCAEC exposed to either CPP-P (420/466 up/downregulated proteins) or CPP-S (389/447 up/downregulated proteins). HITAEC showed less pronounced response to both CPP-P (209/221 up/downregulated proteins) and CPP-S (234/207 up/downregulated proteins). Analysis of GO terms identified certain categories upregulated upon the exposure to CPP-P or CPP-S (cellular respiration, regulation of cytochrome c release from mitochondria, response to oxidative stress, cellular response to reactive oxygen species, response to hydrogen peroxide, response to organonitrogen compound, response to endoplasmic reticulum stress, regulation of macroautophagy, vacuolar acidification, response to wounding).




Ctrl vs CPP-P
Ctrl vs CPP-S
198
609
166
30
49
31
14
CPP-P vs CPP-S



Conclusions: CPP-P and CPP-S promote considerable changes in the proteomic (in particular mitochondrial- and lysosomal-related) profile of ECs. Funding: This study was funded by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities, Research Topic No. 0419-2021-001).

005

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

CONDITIONED MEDIUM FROM CALCIPROTEIN PARTICLE-TREATED ENDOTHELIAL CELLS PROVOKES ENDOTHELIAL DYSFUNCTION IN HEALTHY ENDOTHELIUM

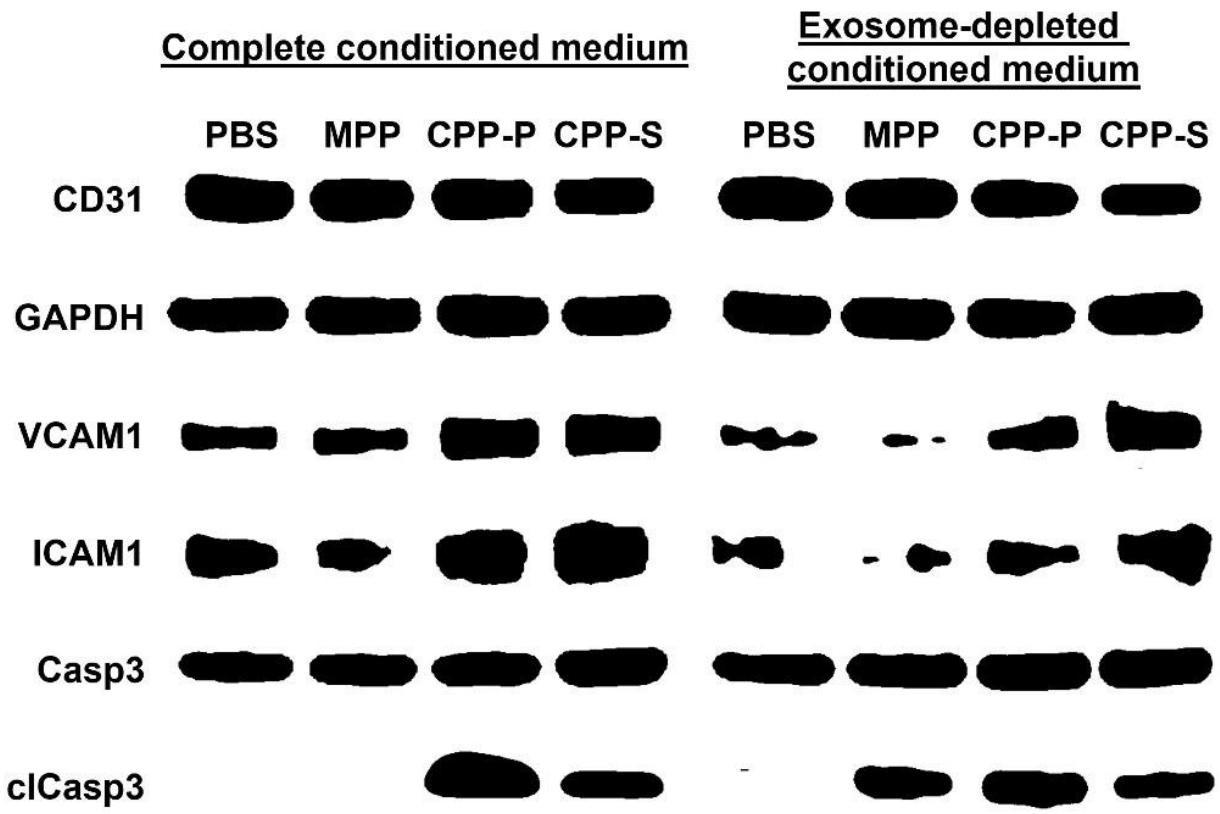
POSTER VIEWING SESSION

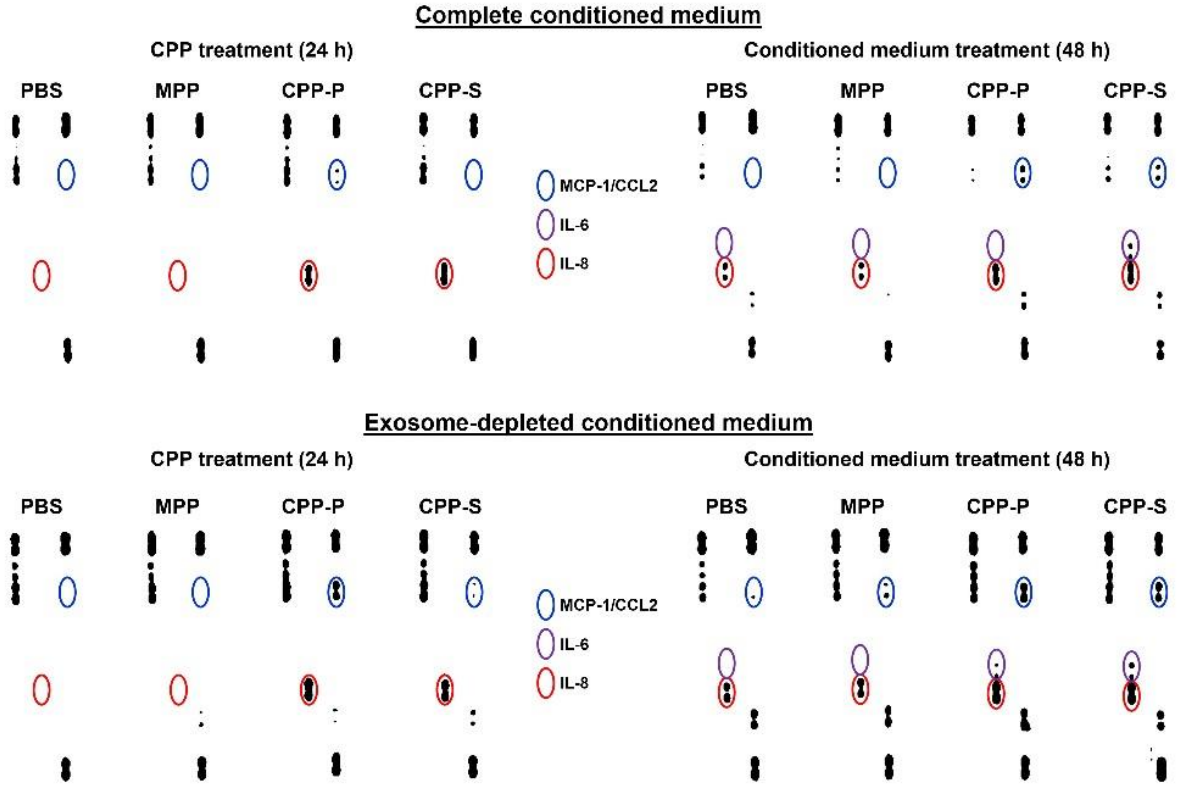
Daria K. Shishkova, Victoria E. Markova, Maxim Y. Sinitsky, Anna V. Sinitskaya, Anastasia Y. Kanonykina, Anton G. Kutikhin
Laboratory Of Molecular, Translational, And Clinical Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

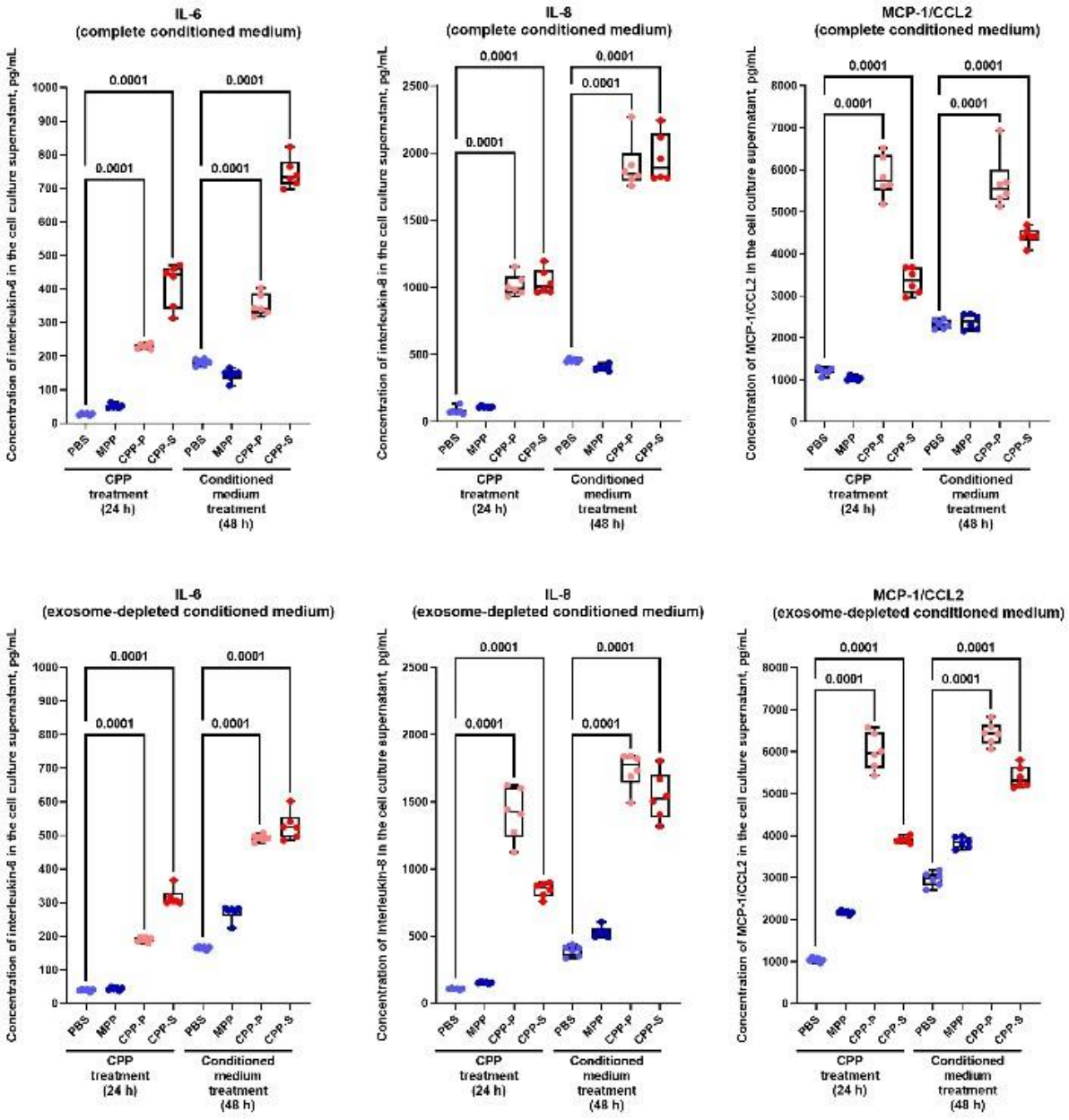
Background and Aims : Calciprotein particles (CPPs), generated in human blood to cope with mineral stress, represent both a physiological tool for aggregating excessive calcium and phosphate and a trigger of pathological events upon the internalisation by endothelial cells. However, it is unclear whether pro-inflammatory activation of CPP-treated endothelial cells initiates hazardous paracrine effects deleterious to healthy endothelium.

Methods: Conditioned medium from primary human coronary artery endothelial cells (HCAEC) treated with either innocuous magnesiprotein particles (MPP) or primary (CPP-P) or secondary (CPP-S) calciprotein particles for 24 hours has been added to healthy HCAEC for another 24 hours upon the optional exosome depletion. Endothelial response was then evaluated by qPCR, Western blotting, and dot blot/ELISA measurements of pro-inflammatory cytokines in the cell culture supernatant.

Results: Both complete and exosome-depleted conditioned medium from CPP-P and CPP-S-treated HCAEC induced regulated cell death of healthy HCAEC via caspase-3 cleavage and caused their pro-inflammatory activation by means of increased expression of cell adhesion molecules (VCAM1 and ICAM1) and pro-inflammatory cytokine genes (*IL6*, *CXCL8*, *CCL2*, *CXCL1*, and *MIF*). Further, addition of conditioned medium to healthy HCAEC provoked the production of IL-6 and MCP-1/CCL2 into the culture medium in addition to IL-8 which elevation has been primarily triggered by CPP treatment.


Complete conditioned medium
Exosome-depleted conditioned medium
PBS
MPP
CPP-P
CPP-S
PBS
MPP
CPP-P
CPP-S
CD31
GAPDH
VCAM1
ICAM1
Casp3
clCasp3


Complete conditioned medium
CPP treatment (24 h)
Conditioned medium treatment (48 h)
PBS
MPP
CPP-P
CPP-S
PBS
MPP
CPP-P
CPP-S
MCP-1/CCL2
IL-6
IL-8
Exosome-depleted conditioned medium
CPP treatment (24 h)
Conditioned medium treatment (48 h)
PBS
MPP
CPP-P
CPP-S
PBS
MPP
CPP-P
CPP-S
MCP-1/CCL2
IL-6
IL-8



Conclusions: Treatment of HCAEC with CPPs induces physiologically significant paracrine effects which can result in endothelial dysfunction in healthy endothelium, underscoring the importance of anti-CPP therapy implementation. Funding: This study was funded by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities, Research Topic No. 0419-2021-001).

006

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

THE ASSOCIATION OF SOLUBLE ENDOGLIN AND ENDOTHELIAL DYSFUNCTION IN TYPE 2 DIABETES MELLITUS AND FAMILIAL HYPERCHOLESTEROLEMIA: IMPACT OF STATIN THERAPY

POSTER VIEWING SESSION

Martina Lasticova[1], Jakub Visek[1], Vladimír Blaha[1], Milan Bláha[2], V. Liptak[1], Petr Nachtigal[3]
[1]3rd Department Of Internal Medicine - Gerontology And Metabolism, University Hospital Hradec Králové and Charles University, Hradec Kralove, Czech Republic, [2]The 4th Department Of Internal Medicine - Hematology, University Hospital Hradec Králové, Hradec Králové, Czech Republic, [3]Biological And Medical Sciences, Faculty of Pharmacy in Hradec Kralove, Charles University, Hradec Kralove, Czech Republic

Background and Aims : Background: Soluble endoglin (sEng) was demonstrated to be increased in type 2 diabetic patients (T2DM) correlating with chronic diabetic vascular complications. In addition, it promotes development of endothelial dysfunction (ED). **Aim:** To evaluate the impact of sEng level changes with respect to its downstream pathways, endothelial dysfunction and vascular inflammation biomarkers beyond glycemic control.

Methods: Methods: We studied patients with T2DM (n=29, 54.9±5.0 years, BMI 26.2±1.5kg/m2), and patients with familial hypercholesterolemia (FH) (n=29, 58.2±12.5 years). Patients with T2DM and FH were treated with atorvastatin/rosuvastatin 20–40mg daily. Analysis was performed at baseline, after 1 month and 1 year of treatment (lipids, sEng, CD40 Ligand, sP-selectin and MCP-1).

Results: Results Patients with T2DM and FH had pathological serum lipids. Total cholesterol (TC) in T2DM was 5.5±1.0 mmol, LDL-c 3.8±1.0 mmol/l, and after treatment with statin decreased - TC to 3.8±0,7mmol/l, LDL-c to 2.2±0.7 mmol/l. TC in FH was 7.5±1.4mmol/l, LDL-c 5.6±1.2mmol/l, and decreased after therapy - TC to 4.2±0,6mmol and LDL-c to 2.4±0.6mmol/l (P<0.01). Patients with T2DM had lower HDL-c (1.2±0.3mmol/l) than FH patients (1.5+0.4mmol/l, P<0.01). Diabetic patients had higher sEng than FH (P=0.06), lower PCSK9 (P<0.001), higher CD40 Ligand (P<0.02) and sP-selectin (P<0.01). One year therapy with statin did not influence sEng levels in T2DM and FH.

Conclusions: Conclusions Besides dyslipidemia T2DM is associated with biochemical parameters of ED. Therapy of dyslipidemia with statin improves lipid profile, plasma level of soluble endoglin is not affected. Supported by AZV CZ NV17-31754A.

007

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

EICOSAPENTAENOIC ACID (EPA) INCREASED ENDOTHELIAL NITRIC OXIDE SYNTHASE (ENOS) LEVELS AND PROTEINS ASSOCIATED WITH CELLULAR RESPONSES TO OXIDATIVE STRESS DURING INFLAMMATION

POSTER VIEWING SESSION

Samuel C.R. Sherratt[1,2], Peter Libby[3], Deepak L. Bhatt[3], Hazem Dawoud[4], Tadeusz Malinski[4], Preston Mason[2,3]
[1]Department Of Molecular, Cellular, And Biomedical Sciences, University of New Hampshire, Durham, United States of America, [2]Lab, Elucida Research, Beverly, United States of America, [3]Department Of Medicine, Cardiovascular Division, Brigham & Women's Hospital, Boston, United States of America, [4]Nanomedical Research Laboratory, Ohio University, Athens, United States of America

Background and Aims : Eicosapentaenoic acid (EPA) administered as icosapent ethyl (IPE) reduced cardiovascular (CV) ischemic events (REDUCE-IT) in contrast to trials using docosahexaenoic acid (DHA)-containing formulations in statin-treated patients. EPA improves endothelial cell (EC) function and nitric oxide (NO) bioavailability, features that may reduce atherothrombotic events. We measured the effects of EPA versus DHA on eNOS expression and coupling efficiency.

Methods: Human umbilical vein ECs (HUVECs) were pretreated with the cytokine IL-6 at 12 ng/ml for 2 h and then EPA or DHA (40 µM) for 24 h. Proteomic analysis was performed on cell lysates from each treatment group by LC/MS. Only significant (p<0.05) changes in expression between treatment groups >1-fold were analyzed by differential enrichment analysis of proteomics data (DEP) bioinformatic package in R.

Results: EPA and DHA significantly stimulated or repressed the expression of 544/472 and 864/767 proteins, respectively, compared with IL-6 alone. Specifically, EPA increased expression of eNOS by 1.1-fold (p=0.014) as compared to DHA. EPA, but not DHA, increased dimethylarginine dimethylaminohydrolase (DDAH-1) and DDAH-2 levels, enzymes that hydrolyze endogenous eNOS inhibitors. Additionally, EPA increased proteins that limit oxidative stress, including glutathione reductase (1.1-fold) thioredoxin (1.2-fold), and peroxiredoxin species (PRDX1, 2, 5).

Conclusions: Under inflammatory conditions, EPA significantly increased expression of eNOS and proteins that enhance activity and reduce oxidative stress as compared to DHA. These changes in protein expression during inflammation may contribute to preserved vascular EC function and reduced CV risk.

008

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

EICOSAPENTAENOIC ACID DECREASES APOC-III EXPRESSION IN RESPONSE TO AIR POLLUTION PARTICLES IN PULMONARY ENDOTHELIAL CELLS

POSTER VIEWING SESSION

Samuel C.R. Sherratt[1,2], Peter Libby[3], Deepak L. Bhatt[3], Hazem Dawoud[4], Tadeusz Malinski[4], Preston Mason[1,3]
[1]Lab, Elucida Research, Beverly, United States of America, [2]Department Of Molecular, Cellular, And Biomedical Sciences, University of New Hampshire, Durham, United States of America, [3]Department Of Medicine, Cardiovascular Division, Brigham & Women's Hospital, Boston, United States of America, [4]Nanomedical Research Laboratory, Ohio University, Athens, United States of America

Background and Aims : Air pollution is the fourth leading contributor to global mortality. Small particulate matter (PM) specifically increases circulating triglyceride (TG) levels, a cardiovascular (CV) risk factor. Apolipoprotein C-III (ApoC-III) is associated with TG-rich lipoproteins and inhibits lipase activity, thus increasing TG levels. The omega-3 fatty acid, eicosapentaenoic acid (EPA), reduces TGs and events in patients with high CV risk (REDUCE-IT). We measured the effects of EPA on expression of ApoC-III in pulmonary endothelial cells (PECs) during exposure to finely-sized and urban-sourced PMs.

Methods: PECs were pretreated with EPA (40 μM) for 2 h before addition of fine PMs (mean diameter 2.8 μm) or urban PMs (mean diameter 5.85 μm) at 50 μg/mL for 8 h. Proteomic analysis was performed on lysates from each treatment group by LC/MS. Only significant (p<0.05) changes in expression between treatment groups >1-fold were analyzed and included in gene set enrichment analyses of biological pathways.

Results: ECs challenged with fine PMs and urban PMs significantly increased/decreased expression of 160/170 and 95/86 proteins, respectively, relative to control, including increased expression of ApoC-III by 2.0-fold (p=4.36×10^{-11}) and 1.4-fold (p=2.0×10^{-7}). EPA pre-treatment significantly increased/decreased expression 108/97 and 187/160 proteins related to fine and urban PMs, respectively, and reduced ApoC-III expression 1.1-fold relative to both PMs (p=0.033, p=0.021).

Conclusions: Multiple PM fractions significantly modulated protein expression, including ApoC-III in pulmonary ECs that was reduced with EPA. This finding reveals a potential novel mechanism of TG-lowering for EPA and lower CV risk that is deserving of further study in patients exposed to air pollution.

009

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

EICOSAPENTAENOIC ACID (EPA) INCREASES DETOXIFICATION PROTEINS AND REDUCES REACTIVE OXYGEN SPECIES IN PULMONARY ENDOTHELIAL CELLS DURING EXPOSURE TO URBAN AIR POLLUTION

POSTER VIEWING SESSION

Samuel C.R. Sherratt[1,2], Peter Libby[3], Deepak L. Bhatt[3], Hazem Dawoud[4], Tadeusz Malinski[4], Preston Mason[2,3]
[1]Department Of Molecular, Cellular, And Biomedical Sciences, University of New Hampshire, Durham, United States of America, [2]Lab, Elucida Research, Beverly, United States of America, [3]Department Of Medicine, Cardiovascular Division, Brigham & Women's Hospital, Boston, United States of America, [4]Nanomedical Research Laboratory, Ohio University, Athens, United States of America

Background and Aims : Particulate matter (PM) in air pollution contributes to cardiovascular (CV) disease due to increased production of reactive oxygen species (ROS), such as peroxynitrite ($ONOO^-$), in the pulmonary vasculature. Eicosapentaenoic acid (EPA) treatment reduced ischemic events in statin-treated patients with high CV risk (REDUCE-IT). We measured the effects of EPA on pulmonary endothelial cell (PEC) protein expression during exposure to urban pollutant PMs.

Methods: PECs were pretreated with EPA (40 μM) for 2 h before addition of PMs (50 μg/mL) collected from urban air for 8 h. Cells were stimulated with calcium to measure the time-dependent production of nitric oxide (NO) and $ONOO^-$ using porphyrinic nanosensors. Proteomic analysis was performed on cells from each treatment group by LC/MS. Significant ($p<0.05$) changes in expression between treatment groups >1-fold were included in gene set enrichment analyses (GSEA).

Results: ECs challenged with PMs showed a significant, 35% increase in $ONOO^-$ release compared with control (188±12 to 254±11 nM), while pre-treatment with EPA reduced $ONOO^-$ release 20% (202±9 nM, $p<0.01$). The urban PMs also reduced expression of PRDX-1, a detoxifying enzyme, by 1.1-fold ($p=0.016$), and EPA increased PRDX-1 expression 1.1-fold ($p=0.030$) relative to the PMs. EPA also significantly modulated 14 proteins in the “cellular response to oxidative stress” pathway, including SOD1 (1.2-fold), PRDX-2 (1.2-fold), and thioredoxin (1.2-fold).

Conclusions: EPA significantly reduced $ONOO^-$ release and increased expression of proteins that detoxify ROS from urban air PMs in pulmonary ECs. These effects of EPA indicate a potentially beneficial and novel anti-inflammatory and mechanism pertinent to people exposed to air pollution.

010

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

SGLT2 INHIBITORS MAY REVERSE THE DAMAGING EFFECT OF OXIDIZED CHOLESTEROL ON THE INTEGRITY OF HUVECS AND ALLEVIATE ASSOCIATED INFLAMMATORY RESPONSE.

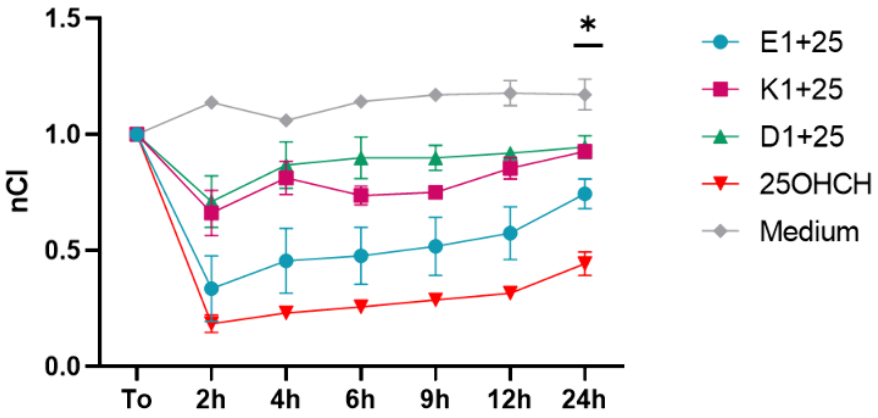
POSTER VIEWING SESSION

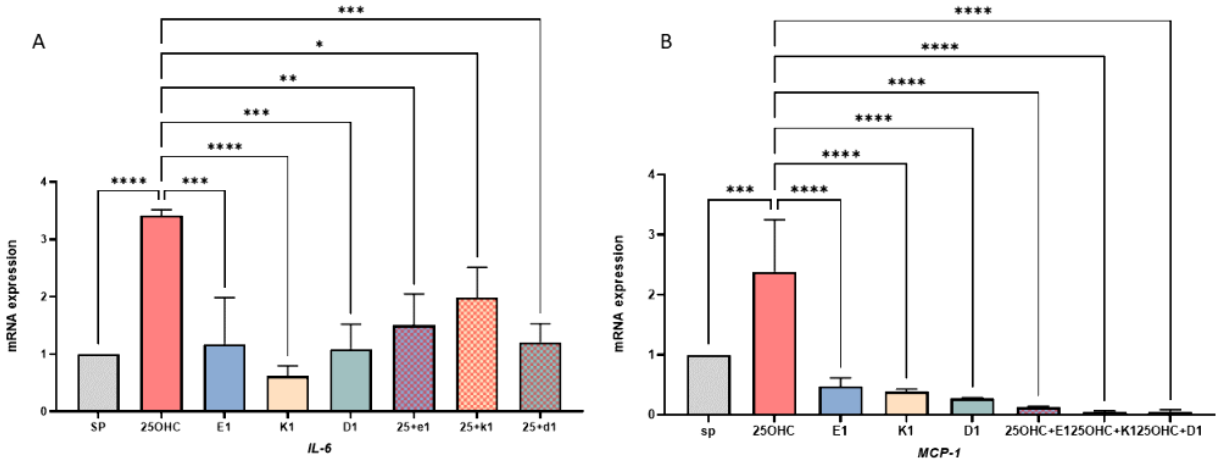
Agnieszka Pawlos[1], Marlena Broncel[2], Ewelina Woźniak[2], Paulina Gorzelak-Pabiś[2]
[1]Department Of Internal Diseases And Clinical Pharmacology, Laboratory Of Tissue Immunopharmacology, Medical University in Lodz, Lodz, Poland, Łódź, Poland, [2]Department Of Internal Diseases And Clinical Pharmacology, Laboratory Of Tissue Immunopharmacology, Medical University in Lodz, Lodz, Poland

Background and Aims : SGLT2 inhibitors bring many benefits to patients with increased cardiovascular risk. The aim of the study was to assess and compare the effect of SGLT 2 inhibitors; empagliflozin, canagliflozin and dapagliflozin on the loss of integrity and inflammatory activation of endothelial cells caused by 25-hydroxycholesterol (25-OHC) *in vitro*.

Methods: HUVECs were incubated with: (1) 25-hydroxycholesterol 10 µg/ml, (2) empa 1µM, (3) cana 1µM, (4) dapa 1µM and (5) 25-OHC+ empa 1µM, (6) 25-OHC+ cana 1µM, (7) 25-OHC+ dapa 1µM and medium as control (8). The integrity of endothelial cells was analyzed with the use of xCELLigence system. The mRNA expression of IL-6 and MCP-1 was measured in the real-time PCR.

Results: 25-hydroxycholesterol significantly lowered the integrity of endothelial cells (fig.1) and elevated the mRNA expression of IL-6 (fig.2A) and MCP-1 (fig.2B) in comparison to medium control. Following HUVECs stimulation with empa, cana and dapa significantly reverted the damaging effect of 25-OHC on the endothelial barrier integrity after 24 hours ($p < .05$) (Fig.1) in the xCELLigence system and decreased the mRNA expression of IL-6($p < .05$) (fig.2A) and MCP-1 ($p < .05$) (fig.2B) in the real-time PCR as compared to 25-
hydroxycholesterol.





Conclusions: SGLT2 inhibitors including empagliflozin, canagliflozin and dapagliflozin were able to alleviate the damaging effect of oxysterol on the integrity of endothelial cells *in vitro*. This effect was associated with significant reduction of inflammation. The protective effect of empa, cana and dapa on endothelial cells was similar for all members of SGLT2 inhibitors.

011

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

DETECTION AND ANALYSIS OF MITOCHONDRIAL LESIONS IN ATHEROSCLEROSIS USING THE ELECTRONIC MICROSCOPE

POSTER VIEWING SESSION

Margarita A. Sazonova[1], Vasily V. Sinyov[2], Anastasia I. Ryzhkova[1], Marina D. Sazonova[1], Natalya A. Doroshchuk[1], Alexander N. Orekhov[3], Igor A. Sobenin[4]
[1]Laboratory Of Angiopathology, FSBSI “Institute of General Pathology and Pathophysiology”, Moscow, Russian Federation, [2]Laboratory Of Medical Genetics, FSBI «National Medical Research Center of Cardiology» Ministry Of Health products RF, Moscow, Russian Federation, [3]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [4]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation

Background and Aims : The aim of this study was a comparative electron microscopic analysis of mitochondria from lipofibrous plaques and normal aortic intima.

Methods: Electron microscopic analysis of normal segments of intima and atherosclerotic plaques of aortas tissue samples was conducted using microscope Hitachi H7000. We investigated 315 mitochondria from cells of 38 aortas, 156 mitochondria of them were from atherosclerotic plaques and 159 mitochondria were from normal intima.

Results: According to the obtained results, only 2% of mitochondria from normal intima (3 from 159) had changes in mitochondrial structure. At the same time, such changes were present in 15% of mitochondria from lipofibrous plaques of aortas (23 from 156). In mitochondria from atherosclerotic plaques, changes in the structure of cristae, edema of matrix, vacuole-like and myelin-like structures formation were observed.

Conclusions: In mitochondria from atherosclerotic plaques, destructive changes of cristae, matrix edema, vacuole-like and myelin-like structures were found. The presence of structural changes in mitochondria of calls from atherosclerotic lesions allows us to suppose that there can be disorders on biochemical and genetic level in mitochondria. This study was supported by Russian Science Foundation (Grant # 20-15-00364).

012

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

ROLE OF TYROSINE PHOSPHATASE PTP PEST IN SHEAR STRESS INDUCED ENDOTHELIAL FUNCTION

POSTER VIEWING SESSION

Rakesh K. Tiwari, Shivam Chandel, Madhulika Dixit
Department Of Biotechnology, INDIAN INSTITUTE OF TECHNOLOGY MADRAS, CHENNAI, India

Background and Aims : Shear stress has a powerful influence on endothelial phenotype and function particularly in determining the expression of pro- and anti-atherosclerotic genes. Laminar blood flow is protective against atherosclerotic plaque formation whereas turbulent or disturbed blood flow facilitates atherosclerosis. Inhibition or gene deletion of protein tyrosine phosphatases (PTPs) improves endothelial health. PTP inhibitors may be potent treatment options for endothelial dysfunction. Deletion of a protein tyrosine phosphatase PTP PEST impaired vascular development and reduced endothelial cell number causing embryonic lethality. Despite being imperative for vascular development, the explicit role of PTP PEST in endothelium is unknown. Both shear stress and PTP PEST are crucial for embryonic development. Furthermore, promoter region of PTP PEST contains shear stress responsive elements. Hence, the aim of this study is to assess the role of PTP PEST in shear induced endothelial function.

Methods: We designed a shear instrument that can be used to impart laminar shear stress (LSS) simulating the flow conditions '*in-vitro*' on endothelial cells. Expression level of PTP PEST was checked after LSS of 12 dyne/cm^2, in EA.hy926 by western blot. Intracellular localization of PTP PEST upon LSS was examined in EA.hy926 cells by confocal microscopy.

Results: Expression level of PTP PEST increased significantly at 30 minutes and 60 minutes after exposure to LSS. LSS for 6 hrs induced nuclear import of PTP-PEST.

Conclusions: LSS induces differential protein expression as well as subcellular localization of PTP PEST. Exploring the molecular mechanism in this phenomenon may reveal PTP PEST as a potential target in shear induced endothelial function.

013

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

CRITICAL IMPACT OF ENDOGLIN BLOCKAGE IN ENDOTHELIAL DYSFUNCTION INDUCED BY HYPERCHOLESTEROLEMIA AND HYPERGLYCEMIA IN HUMAN AORTIC ENDOTHELIAL CELLS

POSTER VIEWING SESSION

Katarína Tripská[1], Ivone Cristina Igreja Sá[1], Matej Vicen[1], Samira Eissazadeh[1], Zuzana Svobodová[1], Barbora Vitverová[1], Radim Havelek[2], Charles Theuer[3], Carmelo Bernabeu[4], Petr Nachtigal[1]
[1]Faculty Of Pharmacy In Hradec Králové, Charels University, Department of Biological and Medical Sciences, Hradec Králové, Czech Republic, [2]Faculty Of Medicine In Hradec Králové, Charles University, Department of Medical Biochemistry, Hradec Králové, Czech Republic, [3]President And Ceo, Tracon Pharmaceuticals, Inc., San Diego, United States of America, [4]Consejo Superior De Investigaciones Científicas (csic), Centro de Investigaciones Biológicas Margarita Salas, Madrid, Spain

Background and Aims : Endoglin (Eng), the TGF-β co-receptor, plays an important role in endothelial dysfunction and TRC105 is an antibody that blocks Eng and its signaling. Here we have investigated for the first time, the TRC105 effects on the Eng expression, signaling, and function in endothelial dysfunction induced by hypercholesterolemia (simulated by 7-ketocholesterol [7K], the most common oxysterol in plasma) and hyperglycemia (simulated by high glucose [HG]).

Methods: In the hypercholesterolemia study, human aortic endothelial cells (HAECs), passage 5, were treated with TRC105 (300 µg/mL) for 1 hour, followed by the addition of 7K (10 µg/mL) for 12 hours. In the hyperglycemia study, HAECs were exposed to HG (45 mM) for 60 hours, followed by the addition of TRC105 (300 µg/mL) for 12 hours, and cells treated with 5mM glucose and 40 mM mannitol served as osmotic control. Protein levels, adhesion, and transmigration of monocytes were assessed by flow cytometry, mRNA expression was measured by qRT-PCR.

Results: 7K and HG treatment increased protein levels of Eng and NF-κB, as well as adhesion and transmigration of monocytes through HAECs monolayer. TRC105 pretreatment reduced the 7K and HG induced Eng protein levels and Smad signaling. Despite increased protein levels of cell adhesion molecules (P-selectin and VCAM-1), TRC105 also prevented 7K and HG induced adhesion and transmigration of monocytes through endothelial monolayers.

Conclusions: These results suggest that TRC105-mediated Eng blockage can counteract the 7K and HG induced endothelial dysfunction in HAECs, suggesting that Eng might be a potential therapeutic target in disorders associated with elevated cholesterol and glucose levels.

014

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

THE ACUTE EFFECTS OF MEALS RICH IN SATURATED OR UNSATURATED FATTY ACIDS ON CELL ADHESION MOLECULES AND EX-VIVO CYTOKINE PRODUCTION IN HEALTHY MEN (COCOHEART STUDY)

POSTER VIEWING SESSION

Gloria Wong, Miriam Clegg, Kim G. Jackson, Julie A. Lovegrove
Department Of Nutritional Sciences, University of Reading, Reading, United Kingdom

Background and Aims : Saturated fatty acids (SFA) may contribute to the development of atherosclerosis via activation of inflammatory responses and endothelial expression of cell adhesion molecules. Although coconut oil is gaining popularity in the UK diet, little is known about the effects of this plant-derived SFA-rich oil on markers of inflammation and endothelial function. The aim of this study was to compare the effects of SFA-rich oils (coconut oil with butter) and vegetable oils on postprandial plasma cell adhesion molecules (intercellular adhesion molecule-1, vascular adhesion molecule-1(VCAM-1), E-selectin and P-selectin) and cytokine production (interleukin (IL)6, IL-10, IL-1b, tumour necrosis factor a, C-X-C motif chemokine ligand 5 (CXCL5) and C-C motif chemokine ligand 5) in men.

Methods: A single-blind, randomised cross-over postprandial study was conducted in 13 men. Participants consumed sequential high-fat meals rich in butter, coconut or vegetable oils on three occasions. Ex-vivo cytokine production was measured using whole blood culture after stimulation (24h) with bacterial lipopolysaccharides. Cytokines and plasma cell adhesion molecules were analysed by Luminex.

Results: A significant mealxtime interaction was evident for postprandial plasma VCAM-1, with a different pattern of response after the vegetable than butter and coconut oil containing meals (p=0.040). Although not significant, there was a tendency for the incremental area under the curve for the postprandial VCAM-1 response to be lower, and CXCL5 response to be higher, after the SFA-rich than vegetable oil meals.

Conclusions: Our findings reveal a difference in postprandial VCAM-1 response between the test fats and a tendency to promote proinflammatory cytokines after SFA-rich oils than vegetable oil.

015

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-01 Endothelial cell function and biology*

THE PROTECTIVE EFFECT OF EMPAGLIFLOZIN ON DNA OXIDATIVE CHANGES IN A MODEL OF VASCULAR ENDOTHELIAL DAMAGE WITH OXIDIZED CHOLESTEROL

POSTER VIEWING SESSION

Ewelina Woźniak[1], Marlena Broncel[1], Bożena Bukowska[2], Paulina Gorzelak-Pabiś[1]
[1]Department Of Internal Diseases And Clinical Pharmacology, Medical University in Lodz, Lodz, Poland, [2]Department Of Biophysics Of Environmental Pollution, University in Lodz, Lodz, Poland

Background and Aims : Empagliflozin is an inhibitor of the sodium glucose co-transporter-2 (SGLT-2i). SGLTs-2i exert potential a pleiotropic anti-atherosclerotic effect by reducing vascular inflammation and improving endothelial dysfunction. **The aim of this study** was to assess the effect of oxidized cholesterol on human umbilical vascular endothelial cells (HUVECs). The study also examines the protective and repairing effect of empagliflozin in a model of vascular endothelial damage with 25-hydroxycholesterol (25-OHC).

Methods: HUVECs were treated with compounds induce DNA single-strand breaks (SSBs) using the comet assay. Oxidative DNA damage was detected using endonuclease III (Nth) or human 8 oxoguanine DNA glycosylase (hOOG1). Intracellular ROS was measured using the molecular probe H2-DCFDA. The concentrations of the empagliflozin are comparable to therapeutic variable 1-10 µM. Statistical analysis was conducted using one-way analysis of variance (ANOVA) followed by Tukey's post hoc multiple comparison procedure. The difference was considered significant for $p < 0.05$.

Results: 25-hydroxycholesterol caused DNA SSBs, induced oxidative damage and increased ROS in the HUVECs; ROS level was lowered by empagliflozin. This effect was not dose-dependent: both tested concentrations of empagliflozin reduced ROS production. Empagliflozin was able to reduce the level of oxidative damage of pyrimidines and purines induced by oxysterol to the level of control cells.

Conclusions: 25-hydroxycholesterol induced DNA SSBs, as well as oxidative damage to purines and pyrimidines and increased ROS in human HUVECs. All damage was ameliorated by empagliflozin. The observed changes strongly suggest that empagliflozin indirectly support DNA repair by inhibiting ROS production.

016

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

DIMETHYLARGININE DIMETHYLAMINOHYDROLASE (DDAH-2) REGULATES THE MACROPHAGE INNATE RESPONSE AND COULD BE A TARGET FOR ATHEROSCLEROTIC THERAPY: HIGH-THROUGHPUT RNA-SEQ APPROACH

POSTER VIEWING SESSION

Sarah Alanazi, Fiona Leiper, James Leiper
Institute Of Cardiovascular And Medical Sciences, University of Glasgow, Glasgow, United Kingdom

Background and Aims : Background: Atherosclerosis is a chronic inflammatory disease characterised by the build-up of arterial lipid plaques. M1 macrophages have a crucial role in progression and pathogenesis of atherosclerosis. Dimethylarginine dimethylaminohydrolase (DDAH) enzymes metabolise the endogenous nitric oxide synthase (NOS) inhibitor, asymmetric dimethylarginine (ADMA), an independent risk factor for atherosclerosis. Two isoforms are known for DDAH, each with distinct tissue specificity. In mice atherosclerotic models, DDAH-1 overexpression reduced plaque formation through ADMA. Macrophages express DDAH-2, however DDAH/ADMA signalling and its role in atherosclerosis is not well studied in this cell. **Aim:** To delineate the role of macrophage DDAH-2/ADMA signalling in the regulation of atherosclerosis-related genes.

Methods: RNA-sequencing of lipopolysaccharide-treated peritoneal macrophages from LysMcre-DDAH2$^{-/-}$ mice and their littermate controls was conducted (*n=3*). Differential gene expression analysis was carried out with DESeq using Wald test, and significantly enriched processes and pathways (p-adj <0.01) were examined using GO and KEGG.

Results: Compared with wildtype, 625 genes were altered with DDAH-2 knockout: 452 were up-regulated and 173 were down-regulated (p-adj<0.01; FC >2). 70 genes were associated with lipid binding, 143 with cell adhesion, 197 with apoptosis and 8 with monocyte differentiation (p-adj<0.01), all processes which are implicated in atherosclerosis. Significantly enriched KEGG pathways were identified, involving complement and coagulant cascades, endocytosis and G-protein coupled receptor signalling.

Conclusions: This study identified DDAH-2-regulated processes in M1 macrophages that are closely associated with atherosclerosis. This study gave an insight into macrophage pathways regulated by DDAH-2 which can be targeted to further understand the role of DDAH/ADMA and potentially manage inflammation in atherosclerosis.

017

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

THE ROLE OF ACTIVATOR PROTEIN-1 (AP-1) TRANSCRIPTION FACTORS IN DIABETES ASSOCIATED ATHEROSCLEROSIS

POSTER VIEWING SESSION

Waheed Khan[1], Man K.S. Lee[2], Anna M. Watson[1], Scott Maxwell[1], Mark E. Cooper[1], Andrew Murphy[2], Sara Baratchi[3], Karin A. Jandeleit-Dahm[1]
[1]Diabetes, Monash University, Melbourne, Australia, [2]Haematopoiesis And Leukocyte Biology Laboratory, Baker Heart and Diabetes Institute, Melbourne, Australia, [3]Health And Biomedical Sciences, RMIT University, Melbourne, Australia

Background and Aims : Atherosclerotic cardiovascular disease is the leading cause of death in individuals with diabetes. Endothelial activation and foam cell formation are crucial steps in the plaque development. Diabetes and blood flow-mediated shear stress are independent risk factors. Regions of turbulent blood flow where the blood flow represents low shear stress such as arterial bends are known to develop atherosclerosis. However, the mechanisms linking diabetes and shear stress to the atherosclerosis are not known.

Methods: To address this, we applied single cell RNA sequencing (scRNA-seq) to identify cell specific transcriptional changes of the diabetic aorta. Further mechanistic experiments were performed in human aortic endothelial cells (HAECs) and THP-1-derived macrophages. For scRNA-seq, viable cells from diabetic murine aorta (10 weeks post streptozotocin induced diabetes in *Apoe*$^{-/-}$ mice) were subjected to scRNA-seq library preparation (10X Genomics) and Illumina Nova-seq 6000.

Results: Graph-based clustering identified several cellular clusters including endothelial cells, macrophages, and foam cells. Pathway analysis identified cell specific pathways such as cholesterol metabolism and oxidative phosphorylation in foam cells and “flow shear stress and atherosclerosis” in endothelial cells. AP-1 transcription factors were most significantly dysregulated genes in these pathways. In vitro experiments demonstrated that Oil-red-O staining of THP-1-derived macrophages stimulated with high glucose and ox-LDL showed increased foam cell formation which was blunted by an AP-1-specific inhibitor, T5224. In addition, in HAECs grown in presence of high glucose (HG) and low shear stress, T-5224 stimulation blunted the transcriptional changes caused by HG.

Conclusions: These findings identified AP-1 as a novel therapeutic target in diabetes associated atherosclerosis.

018

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

A MATHEMATICAL MODELING APPROACH FOR ELUCIDATING THE SIGNALING PATHWAYS INVOLVED IN MACROPHAGE CHOLESTEROL HOMEOSTASIS AND VALIDATION OF AEBP1 ROLE IN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Amin Majdalawieh[1], Abdul Jarrah[2], Israa Alhamarna[2], Fatima Al Zoubi[2]
[1]Biology, Chemistry And Environmental Sciences, American University of Sharjah, Sharjah, United Arab Emirates, [2]Mathematics And Statistics, American University of Sharjah, Sharjah, United Arab Emirates

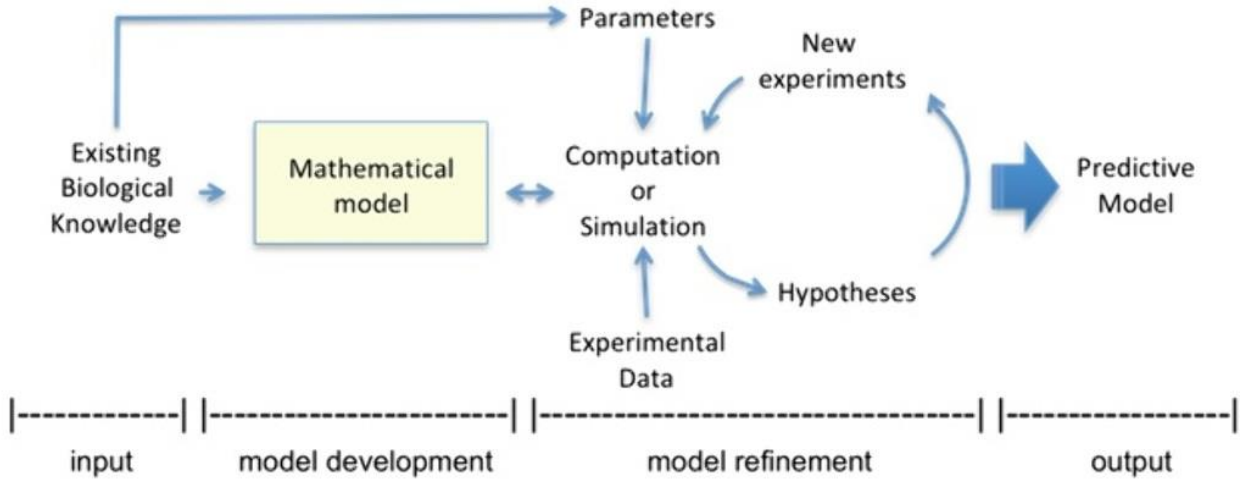
Background and Aims : Atherosclerosis is an immunoinflammatory disease, characterized by the development of cholesterol-rich arterial plaques, leading to several CVDs and is the major cause of death worldwide. Our goal is to construct a predictive, dynamic mathematical network model of atherosclerosis that integrates *in vitro* and *in vivo* results to uncover the role of macrophages in atherosclerosis.

Methods: We conducted a comprehensive literature search to identify relevant molecules involved in macrophage cholesterol homeostasis, inflammation, and atherosclerosis. We than constructed a dynamic logical model of the core components of the assembled network (Boolean network) and analyzed the network using GINsim and CellDesigner. The different steps of mathematical modeling are summarized in the figure.

Results: Using mathematical modeling, we developed a network of all known players implicated in macrophage cholesterol homeostasis. The logical modeling approach was used to obtain a dynamic multistate logical model of the molecular network of pathways involved in macrophage cholesterol homeostasis. Special attention was given to validating the role of AEBP1 as a novel diagnostic and therapeutic biomarker of atherosclerosis. The developed model identified essential interactions and key elements to predict the outcome of some perturbations.

Conclusions: Modeling and simulation approaches will allow us to assemble the known relevant molecules and their interactions into a network of pathways. Our model can be used to predict missing interactions, and hence, suggest new laboratory experiments to further understand macrophage cholesterol homeostasis and atherosclerosis. Our study will hopefully contribute to the development of new therapeutic approaches toward the prevention/treatment of

atherosclerosis.



019

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

DISTINCT FUNCTIONAL PHENOTYPES BETWEEN MAJOR MODELS OF FOAMY MACROPHAGES: CONSEQUENCES AND IMPACT IN THE FIELD OF THERAPEUTIC RESEARCH

POSTER VIEWING SESSION

Julien Brevier[1], Edouard Gerbaud[2], Coraline Borowczyk[3], Janaina Grevelinger[3], Jeanny Laroche-Traineau[3], Sébastien Marais[4], Marie-Josée Jacobin-Valat[3], Gisèle Clofent-Sanchez[3], Florence Ottones[3]
[1]Umr 7252 Xlim, Université de Limoges, limoges, France, [2]Centre De Recherche Cardio Thoracique, Inserm U 1045, Hôpital Haut Lévêque, Pessac, France, [3]Cnrs Umr 5536, university of bordeaux, bordeaux, France, [4]Ums 3420 Cnrs-us4 Inserm, Bordeaux Imaging Center, Bordeaux, France

Background and Aims : Beside pro-atherogenic inflammatory macrophages (MP), the role of foamy MP (FM) in atherogenesis may depend on their ability to sustain cholesterol efflux. Targeting FM was already envisioned as a therapeutic approach of atherosclerosis but requires further characterization of FM models. Two models are currently used: the Mox and the Mac, using oxidized LDL (oxLDL) and acetylated LDL respectively. To set up and characterize a physiopathological model of FM, we stimulated MP with oxLDL and a carotid extract (CE) from patient biopsies and compared its functional phenotype to that of Mox and Mac.

Methods: The different models were either labelled with different fluorescent antibodies and analyzed by Flow cytometry or analysed by TPEF imaging of NADH and FAD (previously used to distinguish M1, M2 and FM/Mox; Borowczyk *et al.*, 2020).

Results: Both flow cytometry analysis and Principal Componant Analysis (combining flow cytometry data and TPEF data) showed that Mac are closer to the M2 phenotype, than the Mox. Interestingly adding CE may immunomodulate both models, in accordance with its high IL10 content (no shown).

Conclusions: These phenotypic and optical differences between FM models may explain functional differences previously described. Moreover, our preliminary study reveals that these models present differential energy metabolism. It is therefore essential to use relevant pathophysiological models of FM to study their implication in atherogenesis and to develop new FM-targeting diagnostic and/or therapeutic approaches. We will further use the Mox+CE models to isolate and characterize specific human antibodies for plaque imaging and therapy.

020

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-03 Macrophages in lipid metabolism and atherosclerosis*

IL-7 KNOCKDOWN AGGRAVATED CHOLESTEROL ACCUMULATION IN MACROPHAGES THROUGH THE ACTIVATION OF THE ATF6 BRANCH OF THE ENDOPLASMIC RETICULUM STRESS.

POSTER VIEWING SESSION

Vasily N. Sukhorukov[1,2], Victoria A. Khotina[1,2], Vladislav A. Kalmykov[1], Maryam Bagheri Ekta[1], Alexander N. Orekhov[1]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Angiology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation

Background and Aims : The endoplasmic reticulum (ER) stress is closely associated with atherosclerosis. ER stress can lead to foam cell formation and inflammatory pathways activation. On the other side, modified LDL and pro-inflammatory cytokines may provoke ER stress via diverse mechanisms. The aim of our study was to assess the impact of IL-7 in ER-stress activation under lipid accumulation.

Methods: THP-1 monocytes were cultured in RPMI 1640 medium (10% fetal bovine serum, 1% penicillin-streptomycin, 2 mM L-glutamine). Monocytes were differentiated in macrophage-like cells using 100 nM phorbol 12-myristate 13-acetate treatment for 48 h. Foam cells were generated by incubation with atherogenic LDL for 24 h. The siRNA knockdown of the IL-7 gene was performed in THP-1 cells for 24 h before total RNA extraction. Gene expression was measured by qPCR analysis.

Results: The knock-down of the IL7 gene aggravated cholesterol accumulation in THP-1 cells incubated with atherogenic LDL. We estimated the expression of ER stress transducer, PERK, ATF6, IRE 1α, and NF-kB to determine the possible mechanism of increased cholesterol accumulation. The knock-down of IL-7 has up-regulated ATF6 and NF-kB expression in THP-1 cells treated with atherogenic LDL. ATF6 gene expression was found to be increased by 6.6-fold, and NF-kB expression was enhanced by 14.7 times. Atherogenic LDL didn't affect ATF6 and NF-kB expression in the cells without the IL-7 knockdown.

Conclusions: The IL-7 knockdown may be involved in the cholesterol accumulation via the ATF6 pathway and NF-kB activation in macrophages. This work was supported by Russian Science Foundation (Grant #22-25-00393).

021

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

MONOCYTES OF PATIENTS WITH ASYMPTOMATIC ATHEROSCLEROSIS ARE CHARACTERIZED BY A REDUCED ABILITY TO FORM IMMUNE TOLERANCE TOWARDS LIPOPOLYSACCHARIDE

POSTER VIEWING SESSION

Egor Chegodaev[1], Alexander N. Orekhov[1], A Zhuravlev[1], Marina V. Kubekina[2], Nikita Nikiforov[2], Marina A. Nikolaeva[3], Alla A. Shabalina[3]
[1]Research Institute Of Human Morphology, AP Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Center For Precision Genome Editing And Genetic Technologies For Biomedicine, Institute of Gene Biology, Russian Academy of Sciences, Moscow, Russian Federation, [3]Gynecology And Perinatology Of Ministry Of Healthcare Of Russian Federation, Laboratory of Clinical Immunology, National Medical Research Center for Obstetrics, Moscow, Russian Federation

Background and Aims : Tolerance of the immune response is a phenomenon in which cells, under the influence of various microbial components, lose their susceptibility to subsequent similar influences; it is one of the most important mechanisms for the completion of the inflammatory phase of the innate immune response. We hypothesized that the ability of blood monocytes from patients with atherosclerosis to form innate immune tolerance may be altered.

Methods: The study included 46 healthy patients with normal intima-media thickness (IMT) of the carotid arteries and 26 patients with atherosclerosis with thickened IMT. CD14+ monocytes were isolated from blood and stimulated with 1μg/ml LPS (1st stimulation) for 1 day. Then the cells were washed with PBS and cultured in fresh medium for 6 days. Then, LPS was added again (2nd stimulation) for 1 day. Secretion of IL-1β, IFN-α2,IFN-γ,TNF-α,CCL2,IL-6,IL-8,IL-10,IL-12p70,IL-17A,IL-18,IL-23, and IL-33 were measured in supernatants at each stage by ELISA.

Results: Macrophages of patients with atherosclerosis more actively secreted CCL2, IL6 and IL10 after two stimulations with LPS. Moreover, the degree of secretion of these cytokines significantly ($p<0.01$) correlated directly with IMT.

Conclusions: Circulating monocytes from patients with atherosclerosis have a reduced ability to form immune tolerance during differentiation into macrophages, which is manifested in increased secretion of the powerful monocyte chemotaxis factor CCL2 and other inflammatory mediators IL6 and IL10. This finding may mean that the causes of chronification of inflammation in the vascular wall may lie at the level of circulating monocytes or even their precursors in the bone marrow. Supported by RSF (Grant No.20-15-00337).

022

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

SEA BUCKTHORN FRUITS – POTENTIAL LIPID-LOWERING ACTIVITY AND PREVENTIVE ROLE IN ATHEROSCLEROSIS-LINKED LOW-GRADE INFLAMMATION FROM EPITHELIAL CELLS TO LEUKOCYTES RESPONSE

POSTER VIEWING SESSION

Monika E. Czerwińska[1], Aleksandra Wilczak[2], Piotr Michel[3], Matthias F. Melzig[4]
[1]Department Of Biochemistry And Pharmacogenomics, Medical University of Warsaw, Warsaw, Poland, [2]Students' Scientific Association At The Department Of Pharmacognosy And Molecular Basis Of Phytotherapy, Medical University of Warsaw, Warsaw, Poland, [3]Department Of Pharmacognosy, Medical University of Lodz, Lodz, Poland, [4]Institute Of Pharmacy, Freie Universitaet of Berlin, Berlin, Germany

Background and Aims : The extracts from fruits of sea buckthorn (*Hippophaë rhamnoides*, HR) have been considered in the protection against hipoxia-induced transvascular fluid leakage in rats [1] and oxidized low-density lipoprotein induced injuries of endothelial cells [2]. The first aim of the study was an assessment of anti-inflammatory activity of an aqueous extract of HR fruit (5-100 µg/mL) expressed as inhibition of cytokines (IL-8, IL-6, IL-10, TNF-α, IL-1β) secretion in LPS/IL1β-stimulated human neutrophils, monocytes/macrophages, and differentiated human adenocarcinoma Caco-2 cell line. Secondly, the inhibitory effect of HR extract on the activity of pancreatic lipase (PL) was purposed.

Methods: The HR extract composition was determined with HPLC-DAD-MS^n. Cytokines secretion was monitored with immunosorbent assay. The effect on PL activity was tested using fluorescence assay *in vitro*.

Results: The extract modulated the secretion of cytokines by human leukocytes. Additionally, it decreased the secretion of IL-8 in Caco-2 cells from 5.22 in stimulated cells to 3.02 pg/mg protein in cells treated with HR at the concentration of 100 µg/mL. The IC_{50} value for PL activity was 59.8 ± 4.6 µg/mL.

Conclusions: In conclusion, the HR extract might prevent the low-grade chronic inflammation through the decrease of chemotactic factors release by immune and epithelial cells. In addition, it is likely to prevent atherosclerosis development decreasing the absorption of fats. Acknowledgements: This project was financially supported by the National Science Centre, Poland (grant no. 2016/23/D/NZ7/00958).
References: [1] Puroshothaman, J. et al. Brain Research Bulletin 2008, 77, 246–252. [2] Bao, M. et al. Journal of Cardiovascular Pharmacology 2006, 48, 834–841

023

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

EARLY CAROTID ATHEROSCLEROSIS AND MIRNA EXPRESSION. A PRELIMINARY REPORT

POSTER VIEWING SESSION

Flavia Del Porto[1], Noemi Cifani[2], Pasqualino Sirignano[3], Maurizio Taurino[3], Maria Proietta[4]
[1]Medicina Clinica E Molecolare, Aousa, Uoc Medicina Interna, Sapienza Università di Roma, Roma, Italy, [2]Medicina Clinica E Molecolare, Sapienza Università di Roma, Roma, Italy, [3]Medicina Clinica E Molecolare, Aousa, Uoc Chirurgia Vascolare, Sapienza Università di Roma, Roma, Italy, [4]Uoc Medicina Interna, AOU Sant'Andrea, Roma, Italy

Background and Aims : MicroRNAs (miRNAs) are small non-coding RNAs that control gene expression post transcriptionally and regulate several biological processes. Considering their effects on cholesterol and glucose metabolism, blood pressure, inflammation and immune cell activation, it is conceivable that their dysregulation can play a role in atherosclerosis. Based on such premises, the aim of this study was to evaluate the expression of miRNA-33 and 155 in early carotid artery atherosclerosis.

Methods: Among patients attending to the Outpatients Clinic of Department of Atherosclerosis and Dyslipidaemia, Sant'Andrea Hospital, Rome, we selected 5 patients with intima media thickness (IMT) values>1.1 mm (group A) and 5 patients with IMT<1.1 mm (Group B). All patients underwent to physical evaluation, routine tests, and carotid artery ultrasound. Moreover, miRNA 155 and miRNA 33 expression in PBMC was evaluated using the two-step protocol of TaqMan MicroRNA Assays.

Results: No significant differences regarding age, sex, diabetes, dyslipidaemia, blood pressure, BMI and smoke were observed between the groups. In group A we found a significant increase of miRNA 33 expression (p0.0097), whereas no significant differences were observed regarding miRNA155..

Conclusions: Results of this study demonstrated a higher expression of miRNA-33 in peripheral blood of patients with early carotid atherosclerosis compared to patients sharing the same risk factors but not displaying increased values of IMT. Considering the role of this miRNA in lipid metabolism and in inflammation, it is likely that its dysregulation can represent an early event in plaque development.

024

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

SERUM IL-6 CONCENTRATION CORRELATES WITH PLAQUE VULNERABILITY AND RUPTURE IN PATIENTS WITH SEVERE CAROTID STENOSIS

POSTER VIEWING SESSION

Barbara Dietel, Katharina Urschel, Miyuki Tauchi, Stephan Achenbach
Department Of Cardiology And Angiology, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany

Background and Aims : Myocardial or cerebral infarction is frequently caused by rupture of a vulnerable plaque. While imaging modalities can measure the degree of vessel stenosis, evaluation of plaque vulnerability remains challenging. We investigated whether plaque vulnerability is associated with distinct blood parameters, which could identify patients at high risk for rupture.

Methods: Carotid plaque specimens and corresponding blood samples were collected from 89 patients undergoing endarterectomy. Three age- and sex-matched patient cohorts were identified, based on classification into stable (n=25), vulnerable (n=40) and ruptured (n=22, ruptured fibrous cap (FC)) plaques. Neovascularization was evaluated by assessing CD31-stained plaque neovessels. Serum concentration of defined cytokines, chemokines and growth factors was measured by magnetic bead-based multiplex technology.

Results: Clinical correlation showed an increased incidence of ischemic stroke in patients with ruptured plaque compared to patients with an intact FC. Vulnerable plaques had a thinner FC, a larger lipid core and increased neovascularization compared to stable lesions. Serum analysis showed most pronounced differences for circulating IL-6 levels. Compared to patients with intact FC, patients with ruptured plaque had significantly higher serum IL-6 concentration (9.3 vs. 7.1 pg/ml, $p<0.001$). Raised IL-6 levels were also observed for patients with vulnerable compared to stable plaques (7.8 vs. 5.8 pg/ml, $p<0.05$). To a lesser extent, this was also observed for IL-8 (7.8 vs. 6.0 pg/ml, $p<0.05$). MCP-1 levels were slightly higher in patients with ruptured plaque (222 vs. 158 pg/ml, $p<0.05$).

Conclusions: The observed results show a significant association of IL-6 serum levels with carotid plaque vulnerability.

025

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

THE ROLE OF IRG1 IN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Lara Haase[1,2], Laura Neises[2], Nicole Kiweler[2], Iris Adrian[3], Johannes Meiser[2], Jochen Schneider[1,4,5]
[1]Medical Translational Research, Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Belvaux, Luxembourg, [2]Cancer Metabolism Group, Department Of Oncology, Luxembourg Institute of Health, Luxembourg, Luxembourg, [3]Medical Center, Department Of Psychiatry And Psychotherapy, Saarland University, Homburg, Saar, Germany, [4]Medical Center, Department Of Internal Medicine Ii, Saarland University, Homburg, Saar, Germany, [5]Department Of Internal Medicine, Centre Hospitalier Emile Mayrisch, Esch sur Alzette, Luxembourg

Background and Aims : The immune responsive gene 1 (*IRG1*) is expressed in macrophages after a pro-inflammatory stimulus. The gene induces the production of itaconate in the cell, which reportedly promotes anti-inflammatory mechanism through inhibition of succinate dehydrogenase (SDH) and activation of NRF2. This study aims to understand the role of itaconate in macrophages in inflammatory vascular diseases.

Methods: *Apoe-/-Irg1-/-* and *Apoe-/-Irg1+/+* mice are fed during 12 weeks with a high fat diet. Blood and spleen are further processed to characterize the immune cells. The aorta as well as the aortic valve are stained with oil-red-o to quantify the plaques. Bone marrow derived macrophages (BMDMs) are differentiated from the bone marrow of IRG1 deficient mice and are metabolically profiled to further understand the mechanism induced by itaconate in macrophages.

Results: The amount of plaques in the aorta was reduced in female IRG1 deficient mice compared to their IRG1 wild-type (WT) littermates. However, the plaque size in the aortic valve was similar. The immune cell characterization did not show any significant difference between IRG1 deficient and WT animals. The *ex vivo* study shows a change of the proline metabolism in IRG1 deficient BMDMs after a pro-inflammatory stimulus.

Conclusions: Our data demonstrate that the absence of itaconate decreases the plaque amount in the aorta in ApoE deficient female mice. We are now investigating the metabolic shifts induced by itaconate in macrophages to understand its role in atherosclerosis.

026

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

BRUTON'S TYROSINE KINASE INHIBITION TO SUPPRESS MAST CELL ACTIVATION IN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Esmeralda Hemme, Lucie Delfos, Marie A.C. Depuydt, Mireia N A Bernabé Kleijn, Frank H Schaftenaar, Amanda C. Foks, Johan Kuiper, Ilze Bot
Biotherapeutics, LACDR, Leiden University, Leiden, Netherlands

Background and Aims : Upon atherosclerosis progression, mast cells accumulate within atherosclerotic plaques and activation of mast cells contributes to the progression and destabilization of plaques. Mast cells can be activated by crosslinking of the Fcε-receptor-I (FcεRI) with IgE-antigen complexes. Bruton's tyrosine kinase (BTK) is involved in the downstream signaling of FcεRI-mediated mast cell activation and degranulation. In this study, we assessed the effects of the BTK inhibitor Acalabrutinib on FcεRI-mediated mast cell activation, plaque progression and destabilization in an atherosclerotic mouse model.

Methods: Male LDLr$^{-/-}$ mice, 7-11 weeks old, were treated with Acalabrutinib (25mg/kg p.o., n=15) or control solvent (n=14) three times per week for eight weeks. During treatment, mice were fed a Western-type diet (WTD) to induce atherosclerotic plaque formation. After eight weeks, mice were sacrificed and hearts were isolated to determine atherosclerotic plaque size and stability by histology. Aortas were harvested to examine mast cell activation in the plaque by flow cytometry.

Results: After eight weeks of Acalabrutinib treatment in LDLr$^{-/-}$ mice, a significant 59% reduction in the frequency of mast cells was observed in aortic plaques (0.24±0.06%) compared to control mice (0.57±0.08%,$p<0.05$), while relative mast cell activation status was not affected. However, Acalabrutinib treatment (size:12.3±2%;collagen:14.5±1.9%) did not significantly affect atherosclerotic plaque size and collagen content when compared to control mice (size:11.5±1.4%;collagen: 13.6±1.5%).

Conclusions: Conclusively, these findings suggest that Acalabrutinib treatment leads to reduced migration of mast cells to the atherosclerotic plaques of LDLr$^{-/-}$ mice, but does not directly affect mast cell activation and initial atherosclerotic lesion development.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

HEALTHFUL NUTRITION DECREASES VULNERABILITY TO ENVIRONMENTAL POLLUTANT-INDUCED INFLAMMATORY DISEASES: IMPLICATIONS IN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Bernhard Hennig[1], Pan Deng[2]
[1]College Of Medicine, University of kentucky, Lexington, United States of America, [2]Pharmacology, University of Kentucky, Lexington, United States of America

Background and Aims : Multifactorial interactions linked to exacerbated disease pathologies of atherosclerosis and other CVDs include pro-inflammatory chemical and non-chemical stressor. Many environmental pollutants or chemical stressors with pro-oxidant and pro-inflammatory properties include persistent organic pollutants, such as polychlorinated biphenyls (PCBs). Dioxin-like PCBs can increase endothelial cell dysfunction and activation, leading to induction of inflammatory genes. Recent data suggest that genetic and lifestyle factors are independently associated with susceptibility to CVD. Thus, potential biological interactions between chemical and non-chemical stressors and buffers will determine disease outcome.

Methods: The mechanism of inulin intervention was explored using system biology approaches.

Results: Using lipidomics, we found that inulin-fed mice displayed decreased plasma ceramides, which are pro-inflammatory lipid species and biomarkers of cardiometabolic disease. Liver transcriptomic analysis revealed that Smpd3, a gene that encodes neutral SMase (NSMase), was downregulated in inulin-fed mice. Additionally, hepatic NSMase activity was lower in inulin-fed mice than in controls. Taken together, these results showed that the dietary fiber inulin can decrease plasma ceramide levels through reduction in NSMase expression and activity, suggesting a new mechanism by which dietary fiber could reduce cardiometabolic disease risk.

Conclusions: Our data support the hypothesis that dietary intervention that targets the gut microbiota may be an effective means of attenuating dioxin-like pollutant-mediated diseases.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

VIRIDANS STREPTOCOCCAL IMMUNOPOSITIVITY ASSOCIATES WITH CALCIFIED CORONARY PLAQUE AREA AND CORONARY STENOSIS SEVERITY. THE TAMPERE SUDDEN DEATH STUDY (TSDS)

POSTER VIEWING SESSION

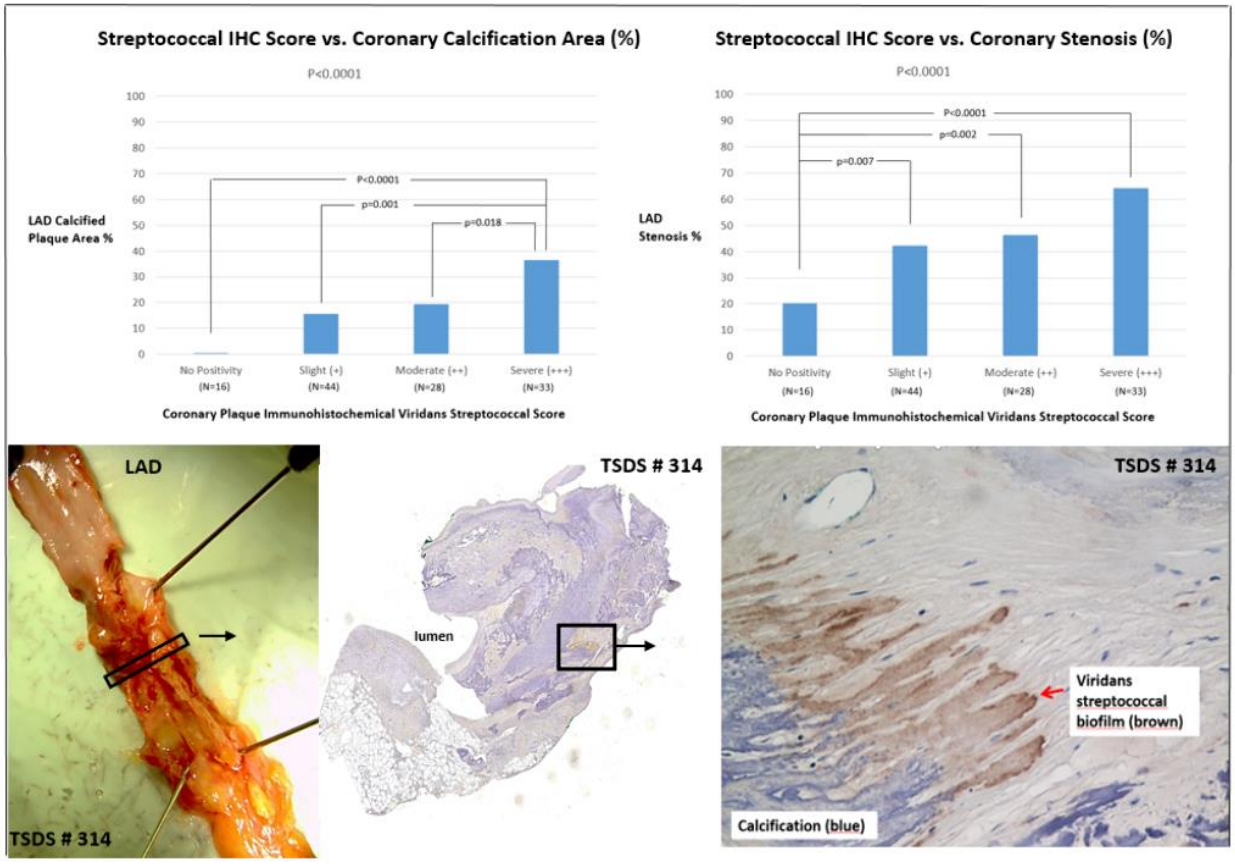
Pekka Karhunen[1], Sohvi Hörkkö[2], Emma Hakamaa[3], Sari Tuomisto[1], Kati Sundström[1], Tanja Pessi[1], Vesa Karhunen[1], Tuomo Iivonen[4], Anni Oksala[4], Anne-Mari Louhelainen[4], Sirkka Goebeler[4], Mika Martiskainen[4], Terho Lehtimäki[1]
[1]Faculty Of Medicine And Health Technology, Tampere University, Tampere, Finland, [2]Clinical Microbiology, Synlab Finland Ltd, Helsinki, Finland, [3]Department Of Medicine, Semmelweiss University, Budapest, Hungary, [4]Forensic Medicine, Finnish Institute for Health and Wellfare, Helsinki, Finland

Background and Aims : Development of atherosclerosis shares features of chronic inflammation. Most chronic infections are considered to be due to biofilms. We have shown that coronary atheromas and thrombosis aspirates harbor DNA from several oral bacteria among which DNA from viridans group streptococci was the most common. In the oral cavity viridans streptococci act as early colonizers in the formation of dental biofilm which calcifies into dental plaque. Here we studied whether viridans streptococcal immunopositivity correlates with coronary calcification and stenosis percentage.

Methods: The surface areas of atherosclerosis lesion types (fatty, fibrous, calcified, complicated) and stenosis percentage were measured in the left anterior descending (LAD) coronary artery of 121 victims of sudden out-of-hospital death in the Tampere Sudden Death Study (TSDS). Coronary sections were stained immunohistochemically with a pool of antibodies raised against 3 most common viridans streptococcal strains. The strength of the immunopositivity was scored into no positivity (-), slight (+), moderate (++) or severe (+++).

Results: In age-adjusted analysis viridans streptococcal immunohistochemistry score associated highly significantly ($p<0.0001$) with larger calcified plaque area and more severe coronary stenosis ($p<0.0001$) but not with fibrous plaque area ($p=0.68$) or fatty streak area ($p=0.052$). The calcification process of

immunopositive biofilm-like structures was seen inside coronary atheroma sections.



Conclusions: Viridans streptococcal immunopositivity of coronary atheromas was linked with coronary atheroma calcification and stenosis but not with other atherosclerosis lesion types. This suggests a new mechanism involved in the calcification of coronary atheroma.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

HIGHER ORAL PORPHYROMONAS GINGIVALIS ABUNDANCE IS ASSOCIATED WITH THE PRESENCE OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN HIGH-RISK PATIENTS AND IN PATIENTS WITH HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Paolo Magni[1,2], Pamela Pignatelli[3], Damiano D'Ardes[4,5], Elena Olmastroni[1], Luca Scorpiglione[4], Francesco Cipollone[4], Adriano Piattelli[3], Alberico L. Catapano[1,2], Maria Cristina Curia[6], Marco Bucci[4,7]
[1]Dept. Of Pharmacological And Biomolecular Sciences, Universita' degli Studi di Milano, Milan, Italy, [2]Polo Scientifico E Tecnologico, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Multimedica Hospital, Milan, Italy, [3]Department Of Medical, Oral And Biotechnological Sciences, Università degli Studi "Gabriele d'Annunzio" di Chieti-Pescara, Chieti, Italy, [4]Regional Center For The Study Of Atherosclerosis, Hypertension And Dyslipidemia, "SS Annunziata" Hospital - ASL Chieti, Chieti, Italy, [5]Internal Medicine, G. D'Annunzio University of Chieti, Chieti, Italy, [6]Department Of Pharmacy, Università degli Studi "Gabriele d'Annunzio" di Chieti-Pescara, Chieti, Italy, [7]Medicine And Aging Sciences, G. D'Annunzio University of Chieti, Chieti, Italy

Background and Aims : Low-grade chronic inflammation, promoted by dysbiosis of gut and oral microbiota, may contribute to individual susceptibility to ASCVD. High oral *Porphyromonas gingivalis* (PG) and lower *Fusobacterium nucleatum (FN)* concentrations have been associated with clinical and experimental atherosclerosis. We assessed oral PG and FN abundance in very high-risk patients with previous ASCVD and with or without heterozygous FH and in healthy control subjects.

Methods: In this cross-sectional study, 36 patients with previous ASCVD (9 with genetically proven heterozygous FH and 27 without FH) and 31 healthy unmatched controls were selected to quantify oral PG and FN abundance by qPCR and assess oral health status.

Results: Compared to controls, patients with previous ASCVD (including 9 FH subjects) were older (67 *vs* 57 years; p=0.001), and had higher BMI (27 vs 23.5 kg/m^2; p=0.002) and TC (232 vs 162 mg/dL; p=0.04). Very few subjects were smokers and no significant differences were observed in oral health parameters. ASCVD patients showed higher PG abundance than controls (1101.3 *vs* 192.4, p=0.03). A trend to higher PG abundance was specifically found in FH/ASCVD patients, compared to non-FH/ASCVD patients and controls (1462.9 vs 813.8 vs 192.4, respectively; p=0.06). FN abundance was comparable in ASCVD patients and controls (209.9 *vs* 202.4; p=0.65).

Conclusions: Higher oral PG abundance is present in very high-risk patients with previous ASCVD, with or without FH, suggesting a potential relationship with CV events. Future studies will assess the predictive value of PG abundance measurement in ASCVD risk stratification.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

MATURE NATURAL KILLER TYPE 2 CELLS AND EXPERIMENTAL ATHEROSCLEROSIS

POSTER VIEWING SESSION

Jasmine Nour[1], Fabrizia Bonacina[1], Annalisa Moregola[1], Rossella Bellini[1], Cecilia Garlanda[2], Alberico L. Catapano[1,3], Giuseppe Danilo Norata[1,4]
[1]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Department Of Immunology And Inflammation, Istituto Clinico Humanitas, IRCSS, Rozzano (Milan), Italy, [3]Irccs, Multimedica Hospital, Sesto San Giovanni, Italy, [4]Sisa Center, Bassini Hospital, Cinisello Balsamo (Milan), Italy

Background and Aims : Natural killer cells are bone marrow-derived innate lymphoid cells, playing a key role in the antiviral and antitumoral response. Among different developmental stages, mature Natural Killer 2 (mNK2,CD27^{-}CD11b^{+}) show the highest cytotoxic activity and increase in number and responsiveness following Il-1r8 deficiency. Our aim was to study the role of mNK2 in experimental atherosclerosis.

Methods: 8 weeks old-*Ldlr*-/- and *Il-1r8*-/-*Ldlr*-/- (double KO,DKO) male mice were fed with standard diet (STD) or western-type diet (WTD) for 12 weeks. Plasma lipid profiling, extensive immunophenotyping by flow cytometry and histological analysis of atherosclerotic plaques were performed to evaluate changes in lipid metabolism and atherosclerosis progression.

Results: Circulating mature Natural Killer 2 cells significantly increased in *Ldlr*-/- mice when fed with WTD when compared to STD fed mice ($p<0,01$). To next test whether mNK2 could play a pathogenic role during atherogenesis, we generated an experimental model presenting higher levels of mNK2 on an atheroprone background, by crossing *Il-1r8*-/- mice with *Ldlr*-/- mice. Neither plasma lipid profile nor immune cell distribution – circulating and tissue-resident – was affected in DKO mice compared to *Ldlr*-/- mice. When fed WTD, DKO mice presented a significant increase in circulating mNK2 ($p<0,0001$) and monocytes ($p<0,05$), as compared to *Ldlr*-/- animals. These differences, however, were not associated with increased plaque burden, collagen deposition or macrophage infiltration. In parallel, plasma cholesterol (1218,8±251,8 vs 1129,2±445,3 mg/dl) and triglyceride levels (519,1±125,3 vs 447,8±189,2 mg/dl) were similar.

Conclusions: Our data suggest that mature Natural Killer cells 2 do not impact atherosclerosis development in an atheroprone experimental model.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

REDUCED CIRCULATING ANGIOGENIC T-CELL FREQUENCY CAN PREDICT SUBCLINICAL VASCULAR STIFFNESS DURING THE EARLIEST STAGE OF RHEUMATOID ARTHRITIS

POSTER VIEWING SESSION

Javier Rodríguez-Carrio[1,2], Mercedes Alperi-López[1,3], Patricia López[1,2], Ángel I. Pérez-Álvarez[4], Ana Suárez[1,2]
[1]Area Of Metabolism, Instituto de Investigación Sanitaria del Principado de Asturias, Oviedo, Spain, [2]Area Of Immunology, University of Oviedo, Oviedo, Spain, [3]Department Of Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain, [4]Department Of Neurology, Hospital Universitario Central de Asturias, Oviedo, Spain

Background and Aims : chronic inflammation, such as in rheumatoid arthritis (RA), impairs vascular homeostasis, although exact mechanisms are unknown. Angiogenic T-cells (Tang) are known to participate in vascular repair, but their connection with cardiovascular (CV) endpoints has not been studied. Our aim was to evaluate circulating Tang levels in RA and their associations with subclinical CV endpoints (subclinical atherosclerosis and vascular stiffness).

Methods: 84 untreated RA patients, 14 individuals with clinical arthralgia and 28 matched healthy controls (HC) were recruited. Tang (CD3+CD31+CXCR4+) frequency was assessed by flow cytometry in peripheral blood. Carotid plaque occurrence, cIMT and stiffness parameters were analyzed by Doppler-US.

Results: Tang were decreased in RA and arthralgia compared to HC (both p<0.010). Tang levels were not related to traditional CV risk factors, body mass index, waist circumference (all p>0.050) nor with the modified SCORE (r=-0.070, p=0.542) or Framingham Risk Score (r=-0.013, p=0.907). Conversely, disease activity accounted for the Tang depletion observed in RA (DAS28: b=-0.436 [95%CI: -0.306, -0.109], p=<0.001). In RA, Tang frequency was unrelated to atherosclerosis occurrence (p=0.556) or cIMT (r=0.136, p=0.245). However, Tang paralleled stiffness parameters: vascular strain (VS:r=0.373, p=0.013), vascular distensibility (VD:r=0.479, p=0.004), vascular stiffness (VSf:r=-0.400, p=0.007) and pressure-strain elastic modulus (PSEM:r=-0.373, p=0.013). Tang frequency was an independent predictor of stiffness parameters in multivariate models: VS (p=0.035), VD (p=0.028), VSf (p=0.033) and PSEM (p=0.016).

Conclusions: this is the first study supporting an association between Tang levels and subclinical CV endpoints. Altered Tang levels may be a biomarker of premature vascular stiffness during the earliest RA stages.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

GLYCA BUT NOT CRP IS AN INFLAMMATORY BIOMARKER OF LONGITUDINAL CHANGES IN BMI AND ADIPOSITY IN ADOLESCENTS WITH OBESITY

POSTER VIEWING SESSION

Toby Mansell[1], Siroon Bekkering[2], Costan G. Magnussen[3], Amy Vlahos[1], Brooke Harcourt[1], Zoe Mccallum[4], Kung-Ting Kao[5], Matthew A. Sabin[5], Markus Juonala[6], Richard Saffery[1], David Burgner[1], Christoph Saner[1]
[1]Infection And Immunity, Murdoch Children`s Research Institute, Parkville, Australia, [2]Dept Of Internal Medicine And Radboud Institute For Molecular Life Sciences, Radboud University Medical Centre, Nijmegen, Netherlands, [3]Menzies Institute For Medical Research, University of Tasmania, Hobart, Australia, [4]Department Of Pediatrics, The Royal Children`s Hospital, Parkville, Australia, [5]Department Of Pediatric Endocrinology, The Royal Children`s Hospital, Parkville, Australia, [6]Department Of Medicine, University of Turku and Division of Medicine, Turku, Finland

Background and Aims : We aimed to investigate relationships between adiposity measures and inflammatory markers in children and adolescents with obesity, and whether changes in adiposity measures were associated with change in inflammation over time.

Methods: In the Childhood Overweight Biorepository of Australia (COBRA) cohort study, measures of adiposity (body mass index, BMI; percentage above the 95th BMI-centile; waist circumference, WC; waist/height ratio, WtH; total body fat percentage, %BF; truncal body fat percentage, %TF) and inflammation markers (glycoprotein acetyls, GlycA; high-sensitivity C-Reactive Protein, hsCRP; total white blood cell count, WBC; and neutrophil/lymphocyte ratio) were collected at two time points (n=262 at baseline, n=98 at follow-up, mean interval 5.8 years). Cross-sectional and longitudinal associations were investigated using linear regression models adjusted for age and sex.

Results: All adiposity measures were cross-sectionally associated with GlycA, hsCRP and WBC at both time points. Change in each adiposity measure (except for %BF) was positively associated with change in GlycA and WBC, but not hsCRP.

Conclusions: In children and adolescents with obesity, adiposity measures are cross-sectionally associated with a range of inflammatory markers. Change in adiposity in either direction during adolescence is reflected in concomitant change in GlycA and WBC, but is not related to change in hsCRP.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

PCSK9 IMPERCEPTIBLY AFFECTS CHEMOKINE RECEPTOR EXPRESSION IN VITRO AND IN VIVO

POSTER VIEWING SESSION

Sai Sahana Sundararaman[1], Linsey Peters[2], Sumra Nazir[2], Andrea Bonnin-Marquez[2], Janneke E. Bouma[2], Soyolmaa Bayasgalan[3], Yvonne Doering[3], Emiel Van Der Vorst[4]
[1]Institute For Molecular Cardiovasculaar Research (imcar), Uniklinik RWTH Aachen, Aachen, Germany, [2]Institute For Molecular Cardiovasculaar Research (imcar), Uniklinik RWTH Aachen, Aachen, Germany, [3]Institute For Cardiovascular Prevention (ipek), Ludwig-Maximilians-Universität, München, Germany, [4]Institute For Molecular Cardiovascular Research (imcar), RWTH Aachen University, Aachen, Germany

Background and Aims : Proprotein convertase subtilin/kexin type 9 (PCSK9) is a protease that gained importance in cardiovascular biology due to its regulatory action on the low-density-lipoprotein receptor (LDLR). However, PCSK9 can also act independent of LDLR to cause vascular pathologies. We hypothesized that PCSK9 affects the expression of the chemokine-receptors CXCR4, CCR8, CCR5 and CCR2 and inflammatory cytokines, all major mediators of inflammation, to influence cardiovascular health.

Methods: We overexpressed PCSK9 in mice and evaluated the effects on chemokine-receptor expression levels in different immune cells using flow-cytometry and effects on plasma cytokines using multiplex analysis. Furthermore, mouse and human macrophages, human smooth muscle cells (SMCs) and human endothelial cells (ECs) were stimulated with PCSK9 *in-vitro* in the presence/absence of an inflammatory environment, to investigate effects on chemokine-receptor expression levels using flow-cytometry and inflammatory cytokine release using ELISA.

Results: It could be observed that *in-vivo* overexpression of PCSK9 did not have major influences on plasma cytokine levels nor on chemokine-receptor expression, although CCR8 was increased in blood neutrophils, while CCR2 was decreased in splenic T-cells. *In-vitro* PCSK9 treatment of macrophages and human SMCs did not results in any effect on these chemokine-receptors or cytokines. Interestingly, PCSK9 increased CXCR4 expression in ECs which coincided with increased IL-6 release.

Conclusions: Hence, we conclude that the inflammatory effects of PCSK9 are largely independent of the here investigated chemokine receptors and further research is required to pinpoint the interactions of PCSK9 with other inflammatory mediators, which would be of high importance to fully understand the mechanism by which PCSK9 affects CVDs.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

CORRELATION OF SALUSIN BETA WITH HS-CRP AND ADMA IN HYPERTENSIVE CHILDREN AND ADOLESCENTS

POSTER VIEWING SESSION

Anna Wasilewska, Elżbieta Kuroczycka-Saniutycz, Witold Olański, Urszula Kołakowska
Pediatric Nephrology Department, Medical University of Bialystok, Białystok, Poland

Background and Aims : The emerging evidence has recently shown an evident dependence between recently identified
salusin peptides and atherosclerosis, and their important roles as endogenous modulators of atherogenesis. It
was reported that the development of atherosclerosis could also be affected by endogenous salusin-β overproduction in vascular lesions.

Methods: This prospective cohort study was conducted in two groups of children: HT – 58 patients with essential hypertension (HT); R - 30 participants with white-coat HT (R). We analysed the relationship between
serum salusin- α and salusin- β levels and ADMA, SDMA and hs- CRP in children and adolescents with essential hypertension.

Results: Serum level of salusin- α in each sample was under the sensitivity of method. Serum level of salusin-β
was statistically significantly higher in hypertension group when compared to the reference group ($p<0.05$) and
correlated positively with serum hs-CRP [rho=0.47; $p<0.01$] and asymmetric dimethylarginine (ADMA) [rho=0.32; $p<0.05$]. There was no significant association between salusin-β and symmetric dimethylarginine
(SDMA) [rho=0.27; $p>0.05$].

Conclusions: This preliminary study showed that the concentration of salusin-β is associated with circulating level
of hs-CRP and ADMA in teenagers with hypertension. Further studies are needed to find out if salusin-β levels
may indicate for endothelial dysfunction and form the basis for the development of new therapeutic agent.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-04 Inflammation, immunity and infection in atherosclerosis*

HIGH-THROUGHPUT SCREENING ASSAY IDENTIFIES DRUGS THAT MODULATE THE RELEASE OF VASCULO-INFLAMMATORY EXTRACELLULAR VESICLES ENRICHED IN MITOCHONDRIAL CONTENT

POSTER VIEWING SESSION

Lucia Zisser[1], Taras Afonyushkin[1], Florian Puhm[2], Anna Ringler[3], Stefan Kubicek[3], Marcus Hacker[4], Christoph J. Binder[1]
[1]Department Of Laboratory Medicine, Medical University of Vienna, Vienna, Austria, [2]Département De Microbiologie-infectiologie Et D'immunologie, Centre Hospitalier de l'Université Laval, Quebec, Canada, [3]Molecular Discovery Platform, Research Center for Molecular Medicine (CeMM) of the Austrian Academy of Sciences, Vienna, Austria, [4]Department Of Biomedical Imaging And Image-guided Therapy, Medical University of Vienna, Vienna, Austria

Background and Aims : Extracellular vesicles (EVs) are recognized for their role in different pathological settings, including cardiovascular disease. Previously, we had shown that mitochondria contribute to the content and pro-inflammatory capacity of EVs released by activated monocytic cells. We therefore aimed to identify the mechanisms mediating the release of EVs enriched in mitochondrial content (mito+ EVs).

Methods: We used the CEMM Library of Unique Drugs to conduct a flow-cytometry based, unbiased high-throughput screen to identify compounds modulating the release of mito+ EVs by LPS-activated monocytic THP-1 cells. In parallel, we assessed whether the drugs intervened with the general pro-inflammatory response of the cells by measuring the level of IL-8 and IL-1β in conditioned media.

Results: Seven of 265 drugs significantly reduced the number of mito+ EVs by more than 20%. Of these, paromomycin, an antibacterial and antiparasitic aminoglycoside, did not affect IL-8 and IL-1β production, suggesting that its effect is specific for EV release. We validated these findings by demonstrating that paromomycin reduces mitochondrial 16S/18S ribosomal RNA content ratio of EVs (t-test: p=0.02, 95%CI: 0.40-0.86 fold of control), which was also reflected by a diminished capability of EVs to induce pro-inflammatory TNFα and Type I INF pathway related gene expression in vascular cells.

Conclusions: Paromomycin specifically reduces the release of the highly pro-inflammatory subset of EVs enriched in mitochondrial content. Therefore, we aim to identify and assess the pathways affected by paromomycin as targets for modulation of pro-inflammatory EV release.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-05 Extracellular matrix and calcification*

SEX-SPECIFIC FEATURES OF HUMAN FIBRO-CALCIFIC AORTIC VALVE DISEASE

POSTER VIEWING SESSION

Julia Böttner[1], Petra Büttner[1], Sarah Werner[1], Michael Borger[2], Holger Thiele[1], Florian Schlotter[1]
[1]Cardiology, Heart Center Leipzig, Leipzig, Germany, [2]Cardiac Surgery, Heart Center Leipzig, Leipzig, Germany

Background and Aims : Fibro-calcific aortic valve disease (FCAVD) is a highly prevalent valvular disorder, associated with high morbidity and mortality. Fibrotic extracellular matrix (ECM) remodeling and calcific mineral deposition disturb valvular microarchitecture and function. Recent data suggest phenotypic differences in female and male FCAVD patients. Females have a higher contribution of fibrosis. Males have a more calcific phenotype. Here we investigated the role of donor sex in a FCAVD *in vitro* model.

Methods: VICs derived from aortic valve replacements of male and female patients were isolated. All patients gave their written informed consent. We evaluated proliferation and differentiation. Real-time impedance spectroscopic monitoring was used to characterize *in vitro* calcification of male versus female VIC in normal or procalcifying medium for 21 days. We monitored collagen secretion and mineralized matrix deposition.

Results: Male and female VICs have comparable proliferation. Impedimetric real-time monitoring revealed major impedance reduction of a prior confluent cell layer following PM treatment, indicating initial cell loss and cell selection. Female VICs showed significantly less reduction of cellular impedance than male VICs ($p<0.001$), suggesting male VICs being more sensitive to PM treatment. In male VICs maximal loss of cellular impedance was significantly faster (186 ± 1 h) than in female VICs (321 ± 25 h; $p<0.001$). After 21 days the maximal increase of impedance due to ECM deposition and mineralization was significantly higher in male than female VICs ($p<0.001$).

Conclusions: Donor sex plays a role in FCAVD *in vitro* as assessed by impedimetric spectroscopy. Our findings may contribute to the understanding of sex-specific disease progression.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-05 Extracellular matrix and calcification*

SERUM OSTEOCALCIN FORMS AND OSTEOCALCIN-EXPRESSING ENDOTHELIAL PROGENITOR CELLS ARE INDEPENDENT BIOMARKERS OF CORONARY ATHEROSCLEROTIC DISEASE SEVERITY

POSTER VIEWING SESSION

Hosam E. Shahrour[1], Sahar Al Fahom[2], Ghassan Al-Massarani[2], Ahmad R. Alsaadi[3], Paolo Magni[4,5]
[1]Department Of Biochemistry And Microbiology, Damascus University, Damascus, Syria, [2]Department Radiation Medicine, Atomic Energy Commission of Syria, Damascus, Syria, [3]Department Of Internal Medicine, Damascus University, Damascus, Syria, [4]Polo Scientifico E Tecnologico, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Multimedica Hospital, Milan, Italy, [5]Dept. Of Pharmacological And Biomolecular Sciences, Universita' degli Studi di Milano, Milan, Italy

Background and Aims : Osteocalcin (OC), an osteoblast-derived regulator of metabolic processes, and circulating early endothelial progenitor cells (EPC, CD34−/CD133+/KDR+) expressing OC (OC+) may represent a pathophysiological link between bone metabolism and the vasculature and be involved in the pathophysiology of vascular atherosclerotic calcification. This study assessed the association of plasma levels of different OC forms and of EPC-OC+ count with the severity of disease in patients with documented coronary atherosclerosis (CAD).

Methods: Patients (n=59) undergoing coronary angiography were divided according to stenosis severity into 2 groups: 1. early coronary atherosclerosis (ECA) (n=22), and 2. late coronary atherosclerosis (LCA) (n=37). Total OC (TOC), carboxylated OC (cOC), undercarboxylated OC (unOC) were quantified by ELISA. EPC-OC+ count was assessed by flow cytometry.

Results: Circulating EPC OC+ count was significantly different between ECA and LCA groups. unOC and unOC/TOC ratio were inversely correlated with EPC OC+ count. A significant decrease in TOC and unOC plasma levels was associated with greater cardiovascular risk factors (CVRFs) number. EPC-OC+ count positively correlated with LDL-C, total cholesterol, and triglycerides, with a greater significance in the LCA group. No association between TOC, ucOC and cOC levels and severity of CAD was found.

Conclusions: In this study, a significant association between EPC-OC+ count, CAD severity and CVRFs was observed, suggesting an active role for EPC-OC+ in the pathogenesis of CAD. An inverse correlation between TOC, ucOC, and number of CVRFs was also observed, suggesting that OC, regardless of its carboxylation status, may be relevant to improve metabolic profile and lower CV risk.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-05 Extracellular matrix and calcification*

PROTEIN CARBAMYLATION ASSOCIATES WITH COLLAGEN IN ATHEROSCLEROTIC PLAQUE AND IMPACTS MACROPHAGE FUNCTIONS

POSTER VIEWING SESSION

Valeria Saar-Kovrov[1], Aleksandra Pawlowska[2], Juliane Hermann[3], Marion J. Gijbels[1], Judith Sluimer[1], Vera Jankowski[3], Marjo M.P.C. Donners[1], Joachim Jankowski[1,3], Erik A.L. Biessen[1,3]
[1]Pathology Department, Cardiovascular Research Institute Maastricht (carim), Maastricht UMC+, Maastricht, Netherlands, [2]Bèta, Sciences And Technology, Zuyd University of Applied Sciences, Heerlen, Netherlands, [3]Institute For Molecular And Cardiovascular Research (imcar), Uniklinik Aachen, Aachen, Germany

Background and Aims : Carbamylation is a post-translational protein modification increased in CKD patients as well as in late-stage atherosclerotic plaques in patients without CKD. Carbamylation was shown to cause pro-atherogenic alteration in plasma proteins and was significantly associated with increased mortality in CKD patients. However, the exact mechanisms and role of protein carbamylation in atherogenesis are not known.

Methods: Human atherosclerotic plaque samples (n=27, ranging from early to advanced stages) were analyzed by immunohistochemistry for extent of carbamylated lysine (carb-lys). Parallel advanced plaque sections were analyzed by mass spectrometry imaging for carbamylated collagen peptides. Functional effects of carbamylated collagen on primary human peripheral-blood derived macrophages (PBMCs) were studied *in vitro* by analyzing the cell's functional profile on a microscale multiassay platform. Results were analyzed using Mann-Whitney U non-parametric t-test and expressed in mean±SD.

Results: Carb-lys signal was found in plaque smooth muscle cells, macrophages, and extracellular matrix and showed significantly higher positive relative area in advanced compared to early-stage plaques (160.39% increase, p=0.008). Mass spectrometry imaging showed increased relative intensity of carbamylated collagen type I and IV peptides compared to non-modified in advanced plaque samples. PBMCs seeded on carbamylated collagen compared to non-modified showed reduced ROS production (39.85% reduction, p=0.029) and a trend towards decreased phagocytosis (9.48% reduction, p=0.097).

Conclusions: Carbamylation is an abundant protein modification in late-stage atherosclerotic plaque associated with smooth muscle cells, macrophages, and collagens. *In vitro*, carbamylated collagen impaired ROS production and phagocytosis of human macrophages. The exact molecular mechanism of plaque protein carbamylation and its functional repercussions require further investigation.

039

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-05 Extracellular matrix and calcification*

CHANGES IN INTRA- AND EXTRACRANIAL CAROTID PLAQUE CALCIFICATION: A TWO-YEAR FOLLOW-UP STUDY.

POSTER VIEWING SESSION

Taihra Zadi[1], Dianne H.K. Van Dam-Nolen[2], Mueez Aizaz[3], Anja Van Der Kolk[4,5], Paul Nederkoorn[6], Jeroen Hendrikse[4], M. Eline Kooi[3], Aad Van Der Lugt[2], Daniel Bos[2,7]
[1]Radiology And Nuclear Medicine, Erasmus Medical Center, Rotterdam, Netherlands, [2]Radiology And Nuclear Medicine, Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands, [3]Radiology And Nuclear Medicine, Carim School For Cardiovascular Diseases, Maastricht University Medical Center, Maastricht, Netherlands, [4]Radiology And Nuclear Medicine, University Medical Center Utrecht, Utrecht, Netherlands, [5]Radiology, Radboud University Medical Center, Nijmegen, Netherlands, [6]Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands, [7]Epidemiology, Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands

Background and Aims : Extra- and intracranial carotid plaque calcification has gained rapid interest given its potential plaque-stabilizing effects, yet information on temporal changes in plaque calcification remains scarce. Hence, we evaluated changes in carotid plaque calcification over two years follow-up in patients with symptomatic carotid artery disease.

Methods: This study is based on the PARISK-study, with TIA/minor stroke patients with ipsilateral mild-to-moderate carotid artery stenosis (<70%). We included 79 patients (25% female, mean age 66 years) who underwent serial CTA imaging with a two year interval. We assessed the volume of extra- and intracranial carotid artery calcification (ECAC and ICAC) and calculated the difference between baseline and follow-up ECAC and ICAC volume. We performed multivariable regression analyses to investigate the association between change of ECAC or ICAC with cardiovascular determinants.

Results: ECAC. We found both increase(46.2%) and decrease(34%) in ECAC volume during two year follow-up, with both a statistically significant correlation with baseline ECAC volume (OR0.72[95%CI=0.58;0.90] respectively OR2.24[95%CI=1.60;3.13]).We found a significant correlation for the change in ECAC volume with diabetes (β0.46[95%CI=0.03-0.89]) and baseline ECAC volume (β0.81[95%CI=0.73;0.88]). ICAC. We found both increase(45.0%) and decrease(25.0%) in ICAC volume. The ICAC decrease was significantly correlated with baseline ICAC volume (OR2.17[95%CI=1.48;3.16]), age (OR2.00[95%CI=1.19;3.38]) and use of antihypertensive drugs (OR3.79[95%CI=1.20;11.96]).The overall change of ICAC volume was also statistically significant correlated with diabetes (β0.92[95%CI=1.59;7.02]), use of oral hypoglemic drugs (β0.86[95%CI=0.12;1.59]) and baseline ICAC volume (β0.71[95%CI=0.55;0.87]).

Conclusions: Progression was seen in a narrow majority, associated with baseline lower calcification volume. We also found regression in calcification volume, associated with higher baseline calcification volume.

040

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

EFFECTS OF ASPERGLAUCIDE ON ENDOTHELIUM FUNCTION IN 2K1C HYPERTENSIVE RATS

POSTER VIEWING SESSION

Mutay Aslan[1], Filiz Basralı[2], Pınar Ülker[2], Tuğçe Çeker[1], Nur Özen[2], Çağatay Yılmaz[1], Özlem Elpek[3]
[1]Medical Biochemistry, Akdeniz University, Antalya, Turkey, [2]Physiology, Akdeniz University, Antalya, Turkey, [3]Pathology, Akdeniz University, Antalya, Turkey

Background and Aims : This study aimed to investigate the effects of Asperglaucide (ASP) on endothelial nitric oxide synthase (eNOS) expression, vascular fluidity and vascular endothelial function in the two-kidney one-clip (2K-1C) model of renovascular arterial hypertension.

Methods: Forty male wistar rats, were randomized to one of the following groups: control (C), sham-operated (SO), ASP treated, hypertensive (H) and H + ASP treated. Hypertension was induced by surgery and mean arterial pressure (MAP) was monitored by tail-cuff method during 4 weeks of ASP treatment. At the end of experimental period, blood samples and thoracic aorta were obtained. Vascular dilator and constrictor responses were measured in organ baths while red blood cell deformability was determined by rotational ektacytometry. Protein and gene expression of eNOS were evaluated in thoracic aorta by immunocytochemical and quantitative PCR analysis, respectively.

Results: Asperglaucide treatment significantly decreased MAP in hypertensive rats and caused significant improvement in endothelium dependent vascular dilator and constrictor responses. Red blood cell deformability was significantly increased in hypertensive rats treated with ASP as compared to hypertensive rats alone. Administration of ASP lead to a significant increase in both eNOS protein and gene expression in both normotensive and hypertensive rats.

Conclusions: Asperglaucide was found to significantly lower blood pressure in hypertensive rats 1 week after treatment by increasing endothelium-mediated relaxation response. Asperglaucide treatment resulted in improvement in phenylephrine -mediated contractile responses, which were impaired in the hypertension group. Asperglaucide also increased blood flow and eNOS gene expression in hypertensive rats. **Acknowledgements:** This study was supported by a grant from TUBİTAK #219S713.

041

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

THE GREEN TEA POLYPHENOL, (−)-EPIGALLOCATECHIN (EGC), IMPROVES INFLAMMATORY PHENOTYPE OF PERIVASCULAR ADIPOSE TISSUE BY OXIDIZING HYDROGEN SULFIDE (H2S) TO POLYSULFIDES (H2SN)

POSTER VIEWING SESSION

Jerzy Beltowski
Department Of Pathophysiology, Medical University of Lublin, Lublin, Poland

Background and Aims : Perivascular adipose tissue (PVAT) produces vasodilating and anti-inflammatory factors. However, in obesity/metabolic syndrome PVAT phenotype changes to pro-inflammatory one. Recently, it has been demonstrated that green tea polyphenols such as EGC oxidize the gasotransmitter hydrogen sulfide (H_2S) to polysulfides (H_2S_n); the important signaling molecules (Redox Biol 2020; 37:101731). We examined the effect of EGC on periaortic adipose tissue (PAT) phenotype in rats fed high fat diet (HFD).

Methods: Rats were fed regular diet or HFD for 1 month as well as were treated or not with EGC (10 mg/kg/day). The expression of pro- and antinflammatory factors was measured in PAT by qRT-PCR. H_2S and H_2S_n levels in PAT were measured by electrochemical sensor.

Results: Expression/secretion of leptin, resisting, TNF-alpha, IL-6 and MCP-1 was higher and adiponectin was lower in PAT of obese rats which was accompanied by increased H_2S production. The H_2S and H_2S_n donors, Na_2S and Na_2S_4, had pro- and anti-inflammatory effects on PAT, respectively. Administration of EGC in HFD rats reduced the expression of leptin, resistin, TNF-alpha, IL-6 and MCP-1 and increased the expression of adiponectin. In addition, EGC reduced M1 macrophage marker, inducible NO synthase (iNOS), and increased the expression of M2 markers, IL-10 and arginase-1. The effects of EGC were mimicked by Na_2S_4. EGC decreased H_2S and increased H_2S_n in PAT of obese rats.

Conclusions: . EGC has the anti-inflammatory effect on perivascular adipose tissue mediated by oxidation of H_2S to H_2S_n. This effect may contribute to anti-atherosclerotic properties of green tea polyphenols.

042

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

VASCULAR WALL DAMAGE IN ATHEROSCLEROTIC CARDIOVASCULAR DISEASE; POSITIVE EFFECT OF EXTRACELLULAR VESICLE-BASED NANOTHERAPEUTICS ON ENDOTHELIAL DYSFUNCTION AND ITS KEY MOLECULAR PLAYERS

POSTER VIEWING SESSION

Karla I. Comarita[1], Alina Constantin[1], Alexandra Vîlcu[1], Anastasia Procopciuc[1], Florentina Safciuc[2], Nicoleta Alexandru[1], Emanuel Dragan[3], Miruna Nemecz[1], Alexandru Filippi[4], Adriana Georgescu[1]
[1]Pathophysiology And Pharmacology, Institute Of Cellular Biology And Pathology Nicolae Simionescu, Bucharest, Romania, [2]Biopathology And Therapy Of Inflammation, Institute Of Cellular Biology And Pathology Nicolae Simionescu, Bucharest, Romania, [3]Core Laboratory Units, Institute Of Cellular Biology And Pathology Nicolae Simionescu, Bucharest, Romania, [4]Biophysics, Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania

Background and Aims : Aim: Herein, we explored the potential beneficial effects of extracellular vesicles (EVs) from subcutaneous adipose tissue stem cells (EVs-ADSCs) or bone marrow mesenchymal stem cells (EVs-MSCs) transfected or not with Smad2/3siRNA on endothelial dysfunction and its key molecular players.

Methods: Methods: Golden Syrian hypertensive-hyperlipidemic (HH) hamsters, which mimic human atherosclerosis, were transplanted with EVs-ADSCs or EVs-MSCs transfected or not with Smad2/3siRNA. Healthy or HH animals were used as controls.

Results: Results: By comparison with the HH group, the EV-based treatment of HH animals induced a significant decrease in the plasma parameter levels and a noticeable improvement in the structure and function of the investigated blood vessels (thoracic aorta and carotid artery) along with a decrease in the key molecules that modulate the inflammatory response: **(1)** a decrease of inflammatory marker expression (COL1A, α-SMA, Cx43, VCAM-1, MMP-2); **(2)** a slight infiltration of total/M1 macrophages and T-cells; **(3)** a reduced level of cytosolic ROS production; **(4)** a significant diminution in TGF-β1 and AngII plasma concentrations; **(5)** significant structural and functional improvements; **(6)** an reduced protein expression profile (Smad2/3, ATF-2, NF-kBp50/p65) and a significant decrease in the expression level of the miRNA panel (miR21,-29a,-192,-200b,-210,-146a).

Conclusions: Conclusions: The EV-based treatment, especially the EVs-ADSCs-based one, led to regression of arterial dysfunction and its key molecular players, while the EV transfection with Smad2/3siRNA had a better effect, amplifying the ability of EVs-ADSCs or EVs-MSCs to regress endothelial dysfunction. **Acknowledgement:** CNCS-UEFISCDI, project no. PN-III-P1-1.2-PCCDI-2017–0527 (Contract no. 83PCCDI/2018), project no. PN-III-P1-1.1-TE-2019–0811, within PNCDI III" (Contract no. TE 97/2020), and Romanian Academy.

043

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

SEX HORMONE RECEPTOR PATHWAY IS ASSOCIATED WITH CAROTID PLAQUE INSTABILITY IN MEN

POSTER VIEWING SESSION

Diana Di Iorio, Karina Gasbarrino, Huaien Zheng, Stella S. Daskalopoulou
Division Of Experimental Medicine, Department Of Medicine, Faculty Of Medicine, Research Institute of the McGill University Health Centre, McGill University, Montreal, Canada

Background and Aims : Plaque composition differs between sexes, where men develop more unstable plaques than women. Given that sex hormones influence the vasculature differently between sexes, we hypothesize that sex hormones and their receptors may affect plaque instability. Herein, we investigated the role of the sex hormone receptor pathway in plaque instability in men and women with carotid atherosclerosis.

Methods: Blood samples and carotid plaque specimes were collected from men and postmenopausal women who underwent a carotid endarterectomy (n=160). Peripheral blood monocytes were isolated and analyzed by qRT-PCR for gene expression of estrogen receptor α and β (ER-α, ER-β), G protein-coupled estrogen receptor (GPER), and androgen receptor (AR). Plaques were histologically classified into 4 groups (n=40/group): women-stable/women-unstable and men-stable/men-unstable. Protein expression of ER-α, ER-β, GPER, and AR was quantified using immunohistochemistry and western blot (analysis underway). Plaque gene expression was assessed using qRT-PCR.

Results: No differences in clinical charactertistics (i.e., BMI, comorbidity status, medications) were observed across patient groups. Blood monocytes from both sexes showed gene expression of ER-α and GPER but not ER-β and AR; however expression was not associated with plaque instability in either sex. Men had significantly greater ER-α, ER-β, GPER, and AR protein expression in unstable vs stable plaques ($p<0.05$) and compared to women ($p<0.05$). In men, unstable plaques demonstrated a ~50% decrease in AR gene expression compared to stable plaques ($P<0.001$), and had signficantly less AR gene expression compared to women ($p<0.05$).

Conclusions: Our preliminary findings indicate a possible association between sex hormone receptor expression and plaque instability in men.

044

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-06 Vascular biology of the arterial wall: Miscellaneous*

SINGLE-CELL AND SPATIALLY RESOLVED TRANSCRIPTOME ANALYSIS REVEALS CELLULAR HETEROGENEITIES AND NOVEL REGULATORS OF ATHEROSCLEROTIC PLAQUE DESTABILIZATION

POSTER VIEWING SESSION

Jessica Pauli[1], Zhiyuan Wu[1], Chika Yokota[2], Greg Winski[3], Valentina Paloschi[1], Anne Dueck[4], Stefan Engelhardt[4], Hans-Henning Eckstein[5], Muredach P. Reilly[6], Lars Maegdefessel[1]
[1]Gefäßchirurgie, Vaskuläre Biologie, Klinikum rechts der Isar der Technischen Universität München, München, Germany, [2]Scilifelab, Stockholm University, Stockholm, Sweden, [3]Cardiovascular Medicine, Karolinska Institute, Stockholm, Sweden, [4]Institut Für Pharmakologie Und Toxikologie, Klinikum rechts der Isar der Technischen Universität München, München, Germany, [5]Gefäßchirurgie, Klinikum rechts der Isar der Technischen Universität München, München, Germany, [6]College Of Physicians & Surgeons, Columbia Universtiy Irving Medical Center, New York, United States of America

Background and Aims : Background: Cardiovascular diseases, including atherosclerosis, are the major cause of death in western societies, still molecular mechanisms of plaque destabilization remain unclear. Long non-coding RNAs (lncRNAs) are one example of novel molecular modulators, as their expression is highly cell-type specific.

Methods: Methods: We utilized combined total (bulk) RNA and single cell (sc) RNA to study the transcriptome of advanced carotid artery lesions from patients undergoing carotid endarterectomy in our vascular surgery clinic. Additionally, we performed hybridization-based RNA *in situ* sequencing (HybRISS) to indicate where cluster-defining genes are located within the plaques.

Results: Results: In this current study, four sequencing datasets were investigated (total RNA from early vs. late lesions from the same individual patient and unstable vs. stable lesions from individual patients; two separate scRNA-seq datasets).16 lncRNAs were cross-referenced between all four datasets. All of these lncRNAs presented a cell-type specific expression pattern, with 11 lncRNAs being significantly enriched in different smooth muscle cell (SMC) clusters. We found all newly identified lncRNAs conserved in our scRNA-seq datasets of genetically mutated (*LDLR-/-*) Yucatan mini-pigs and the inducible carotid artery plaque rupture mice (*ApoE-/-*). The cluster-defining genes from the human scRNA-seq data were then located in human carotid artery tissue sections using the HybRISS method to unravel their distinct location within these plaques.

Conclusions: Discussion: Taken together, our datasets, methods and different animal-models demonstrate that combining bulk with scRNA-seq data and spatially resolved sequencing methods are powerful tools to identify and characterize novel lncRNAs being expressed by a certain cell-type in the disease progression.

045

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

FEATURES OF GLOBAL LONGITUDINAL DEFORMATION OF THE LEFT VENTRICLE IN RELATION TO CORONARY AND CAROTID ATHEROSCLEROSIS IN PATIENTS WITH CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Rano Alieva[1], Shukhratjon N. Doniyorov[2], Feruza M. Bekmetova[1]
[1]Cihd,atherosclerosis, RSSMC, Tachkent, Uzbekistan, [2]Cardiovascular Imaging, Republican Specialized Scientific Practical Medical Center of Cardiology, Tashkent, Uzbekistan

Background and Aims : Identify the relationship of the LV deformation properties with the presence of coronary and carotid atherosclerosis in patients with CAD.

Methods: 94 patients with CAD of class II-IV aged 40 to 70 years were studied by the general clinical and laboratory blood tests, Holter -ECG monitoring, TTE, 2D-Echo with speckle tracking (STE), ultrasound of carotid artery lesions and coronary angiography (CAG). The SYNTAX score was calculated retrospectively in accordance with the SYNTAX evaluation algorithm. All patients were divided into 2 groups: group 1 included patients with a low syntax index (0-22); group 2 included patients with an average syntax index (23-32). A more objective quantitative assessment of the contractile function of the LV myocardium was obtained by assessing the global longitudinal deformation (GLS) and the strain rate (SR).

Results: A comparative analysis showed that in group 2, GLS and SR indicators were significantly lower than in group 1 ($P=0.0001$ and $P=0.0133$, respectively). GLS was significantly correlated with LVL ($r=-0.309$; $P<0.005$), with the degree of atherosclerotic damage to the coronary arteries ($r=0.925$; $P<0.005$) and the number of atherosclerotic plaques in the carotid arteries ($r=0.245$; $P<0.05$). SR was also correlated with LVL ($r=-0.281$; $P<0.005$), coronary artery disease ($r=0.767$; $P<0.0005$) and the number of atherosclerotic plaques of the carotid arteries ($r=0.233$; $P<0.05$).

Conclusions: The results obtained indicate the diagnostic value of STE with the determination of GLS and SR in a comprehensive assessment of severity of coronary and carotid atherosclerosis within group of patients with CAD.

046

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

EMBEDDING AND BACKSCATTERED SCANNING ELECTRON MICROSCOPY (EM-BSEM): A NOVEL APPROACH FOR THE WHOLE-SPECIMEN, ULTRASTRUCTURAL ANALYSIS OF CARDIOVASCULAR TISSUES

POSTER VIEWING SESSION

Rinat A. Mukhamadiyarov, Leo A. Bogdanov, Tatiana V. Glushkova, Daria K. Shishkova, Vladislav A. Koshelev, Alexey V. Frolov, Alexander N. Stasev, Anton A. Lyapin, Alexey V. Evtushenko, Anton G. Kutikhin
Laboratory Of Molecular, Translational, And Clinical Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Background and Aims : Currently, an ultrastructural analysis of cardiovascular tissues is significantly complicated. Sectioning of calcified or stent-expanded blood vessels or mineralised heart valves often leads to a critical loss of their integrity, demanding other methods to be developed.

Methods: Here, we designed EM-BSEM approach combining: 1) Routine tissue fixation in neutral phosphate buffered formalin; 2) Post-fixation and long-term staining with ascending concentrations of osmium tetroxide; 3) Counterstaining in alcoholic uranyl acetate or lanthanides; 4) Impregnation and embedding into epoxy resin; 5) Grinding and polishing to retrieve the sample and flatten its surface for electron microscopy; 6) Counterstaining with lead citrate followed by carbon sputtering; 7) Visualisation employing backscattered scanning electron microscopy.

Results: EM-BSEM provides an opportunity to investigate entire and intact tissue samples and acquire high-quality images at from 40- to 5,000-fold magnification. The benefits of EM-BSEM include: 1) an image resolution sufficient for both gross and detailed examination of elastic lamina degradation, (neo)intimal hyperplasia, (neo)vascularisation, intraplaque or intravalvular haemorrhages, foam cell formation, and extracellular matrix degradation; 2) a reliable identification of vascular cell populations and recognition of immune cell lineages; 3) a compatibility with the modern machine learning algorithms for the automated annotation of histological and cellular patterns.

Conclusions: As EM-BSEM fully retains integrity of calcified or stent-expanded tissues and combines high-magnification visualisation and rapid image acquisition, we suggest it as a suitable imaging modality for cardiovascular research. Funding: This study was funded by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities, Research Topic No. 0419-2021-001).

047

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

ACHILLES TENDON ULTRASOUND IN THE DIAGNOSIS OF HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (HEFH).

POSTER VIEWING SESSION

Laura Marquez Lopez[1], Irene Marquez Lopez[1], Aurora Gonzalez Estrada[1], David Leon Jimenez[1], Antonio Espino Montoro[2], Ovidio Muñiz Grijalvo[1], Luis Matias Beltran Romero[1]
[1]Internal Medicine, Hospital Universitario Virgen del Rocio, Seville, Spain, [2]Internal Medicine, Hospital Universitario Reina Sofia, Cordoba, Spain

Background and Aims : Evaluate the presence of xanthomas and the thickness of the Achilles tendon in patients under study for severe hypercholesterolemia (LDLc> 190 mg/dL) and compare if there are differences between patients with a diagnosis of HeFH with genetic confirmation (HeFH +) and those with an alternative diagnosis or with a negative genetic study (non HeFH +).

Methods: Observational study carried out on patients referred to Vascular Risk Unit of the Universitary Hospital Virgen del Rocio, Sevilla. Besides standard clinical and laboratory studies, an ultrasound of the Achilles tendon was performed to assess thickness and describe echo-structure abnormalities suggestive of xanthoma. We use R program for the stattiscal analysis.

Results: 38 patients were included, 23 women, median age 55 (IQR 43-62), 18 HeFH + (*image 1*). Absolute mean and maximum thickness of Achilles and adjusted by body surface area were associated with HFHe + (*image 2*). Achilles maximum thickness isolated and adjusting by body surface area showed similar performance, with AUC 0,73. 5,1mm of Achilles maximum thickness had a sensitivity of 0,67 and specifity of 0,8 for the diagnosis of HeFH + (*image*

Image 1: *General characteristics.*

N: 38 patients	
Women: Men	23:15
Age (years)	55 [43-62]
BMI (kg/m^2)	26,53 [24,4-29,3]
Tobacco:	
Smokers	5
Ex-smokers (>1 year)	10
Non smokers	22
Alcohol	3
Cardiovascular risk factors:	
Hypertension	9
DM	3
Dyslipidaemia	38
Cardiovascular event:	
Acute coronary syndrome	4
Ischemic heart disease without event	1
Family history of early cardiovascular event	8
Type of DLP:	
Heterozygous Familiar Hypercholesterolemia	17
HeFH + HiperLpa	1
Polygenic Hypercholesterolemia	10
Polygenic Hypercholesterolemia + HiperLpa	6
HiperLpa	2
Combined Familial Hypercholesterolemia	2
Total cholesterol	246 [209-290]
LDLc	162 [118-199]
maximum LDLc	244 [207-274]
Genetic test:	
Positive	18
Negative	8
Absent	12
Corneal arch	21
Murmurs:	
Cardiac	3
Carotid	4
Abdominal	1
Carotid plaques:	18
Score	3 [2-4]
Maximum thickness	2,2 [1,9-2,5]
High risk	4
Femoral plaques:	9
Score	3 [2-4]
Maximum thickness	2,4 [1,9-3,3]
High risk	2
Treatments:	
Statins:	35
• High power	25
• Moderate-low power	10
Ezetimibe	21
Resins	1
Fibrates	2
AntiPSCK9	1
ASA	8
Second antiplatelet	1

BMI: Body Mass Index. DM: Diabetes Mellitus. DLP: Dyslipidaemia. LDLc: cholesterol LDL. AAS: Acetylsalicylic Acid.

Quantitative variables are expressed as median and interquartile range, and qualitative variables as absolute values.

3).

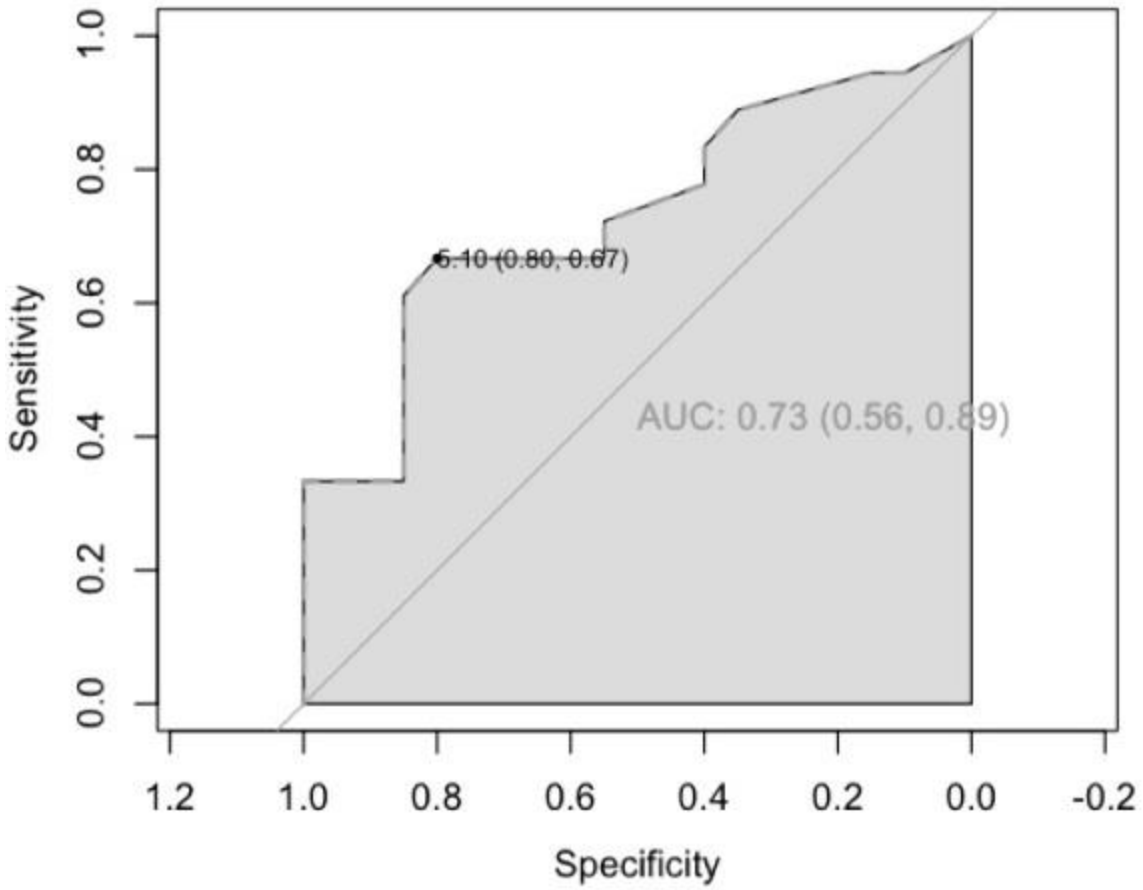
Image 2: *Xanthomas and thickness of the Achilles tendon according to the diagnosis of HeFH.*

	Total	HFHe +	No HFHe +	p
Achilles tendon				
Medium thickness	5,4 [4,33-5,61]	6,19 [4,54-7,53]	4,69 [4,3-4,91]	**0,015**
Maximum thickness	5,54 [4,4-5,9]	6,36 [4,73-7,65]	4,81 [4,3-5]	**0,013**
Xanthomas:	8	5	3	0,334
Medium thickness/body surface	3 [2,43-3,13]	3,56 [2,55-4,22]	2,64 [2,37-2,88]	**0,036**
Medium thickness/height	3,16 [2,66-3,29]	3,62 [2,57-4,45]	2,84 [2,68-2,99]	0,167
Maximum thickness/body surface	3,09 [2,49-3,16]	3,70 [2,6-4,39]	2,70 [2,4-2,87]	**0,029**
Maximum thickness/height	3,26 [2,7-3,42]	3,77 [2,63-4,66]	2,91 [2,72-3,02]	0,144

Quantitative variables are expressed as median and interquartile range, and qualitative variables as absolute values.

Image 3: *ROC curves.*

	AUC	IC95%
Medium thickness	0,71	0,53-0,87
Maximum thickness	**0,73**	0,56-0,89
Medium thickness/body surface	0,69	0,46-0,89
Medium thickness /height	0,63	0,38-0,85
Maximum thickness/body surface	**0,73**	0,50-0,91
Maximum thickness /height	0,66	0,42-0,87



Conclusions: Our patients with HFHe + presented greater tendon thicknesses compared to patients with another hyperlipidemias. Achilles maximum thickness (adjusted or not by body surface area) showed the best performance. In our patients with severe hypercholesterolemia, a maximun thickness higher than 5,1mm showed a good specifity but low sensitivity for the diagnosis of HeFH +.

048

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

RELATIONSHIP BETWEEN MAGNETIC RESONANCE IMAGING OF INTRAMUSCULAR ADIPOSE TISSUE (IMAT) VALUES AND SERUM ADIPOKINES LEVEL AMONG OBESE POPULATION

POSTER VIEWING SESSION

Khariah Mat Nor[1], Mazapuspavina Md-Yasin[2], Mazlifah Omar[3], Harbinder Jeet Singh Gurcharan Singh[4], Leny Suzana Suddin[5]
[1]Faculty Of Medicine Universiti Teknologi Mara (Uitm), Department of Radiology, Selangor, Malaysia, [2]Faculty Of Medicine Universiti Teknologi Mara (Uitm), Department of Primary Care Medicine, Selangor, Malaysia, [3]Faculty Of Medicine Universiti Teknologi Mara (Uitm), Department of Rehabilitation Medicine, Selangor, Malaysia, [4]Faculty Of Medicine Universiti Teknologi Mara (Uitm), Department of Physiology, Selangor, Malaysia, [5]Faculty Of Medicine Universiti Teknologi Mara (Uitm), Department of Public Health Medicine, Selangor, Malaysia

Background and Aims : Intramuscular adipose tissue (IMAT) is fat infiltrates between and/or within muscle fibres. To assess IMAT tissue surface area and examine the relationship between IMAT value with serum adipokines (leptin and adiponectin) among obese population.

Methods: This was a cross-sectional study. Obesity definition, Stage I: BMI ≥ 27.5 to < 35.0; Stage II: BMI ≥ 35.0 to < 40.0 and Stage III: BMI ≥ 40.0. Fasting blood was collected for serum adipokines. MRI hip joint (level of greater trochanter) to 10 cm above knee joint line were performed for IMAT values. MR images were post-processed using a semiautomatic segmentation program MATLAB R2016a; MathWorks. Continuous data presented as mean ± SD. Bivariate analysis using T-test, One-Way ANOVA for normally distributed, while Mann-Whitney U and Kruskal Wallis tests for skewed variables.

Results: Total 28 participants with 64.3% were female and 67.9% has Stage I obesity. The mean IMAT value was 11.71cm^2±4.01(SD) [95%CI:10.16,13.27]. The mean serum adiponectin was 5.28±2.06 µg/ml and leptin was 289.65±533.22 pg/ml. No difference in IMAT values between obesity stages and gender. IMAT values were higher among males (12.11±4.53), smokers (13.08±11.07), Stage II obesity (15.42±3.08), type 2 diabetes (15.64±11.57), and hypertension (11.68±11.72). No relationship between IMAT value with serum adiponectin ($r=0.10$, $p=0.627$) or serum leptin ($r=0.3$, $p=0.134$). However, a significant relationship was observed between serum leptin with obesity stage ($F_{2,25}=7.017$, $p=0.004$) and with gender category ($U=12.0$, $p<0.05$).

Conclusions: IMAT value distribution might not correlate with adipokines level or incrementally across obesity stages. A larger-scale study in the future is needed to verify this relationship.

049

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

COMBINATION OF OPTICAL COHERENCE TOMOGRAPHY AND MALDI MASS SPECTROMETRY IMAGING TO CHARACTERIZE CORONARY ARTERY LIPIDS IN AN ATHEROSCLEROTIC SWINE MODEL

POSTER VIEWING SESSION

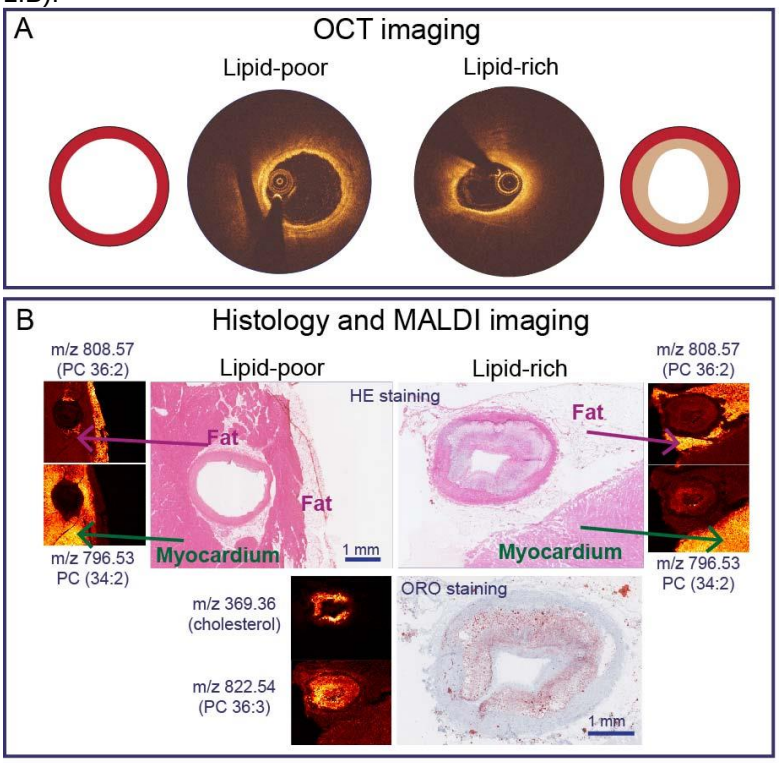
Francesca Razzi[1], Nuria Slijkhuis[2], Dirk-Jan Duncker[1], Jolanda Wentzel[2], Volkert Van Steijn[3], Gijs Van Soest[2], Heleen Van Beusekom[1]
[1]Experimental Cardiology, Erasmus MC, Rotterdam, Netherlands, [2]Cardiology, Erasmus Medical Center, Rotterdam, Netherlands, [3]Applied Sciences, TU Delft, Delft, Netherlands

Background and Aims : In-vivo imaging techniques like optical coherence tomography (OCT) can be used in patients to characterize lipid presence in atherosclerotic plaques (i.e. lipid-rich arteries). However, they do not provide detailed information on plaque lipid composition and distribution. The aim of this study was to identify, characterize and visualize distribution of lipids using MALDI-MSI in the regions that OCT detected as lipid-rich in swine atherosclerotic plaques.

Methods: LDL-receptor mutant swine (N=6) on high-fat diet developed coronary atherosclerosis with both lipid-rich and -poor plaques. In-vivo OCT was used to determine these two plaque types. Ex-vivo tissue sections were measured with a Waters Synapt G2Si with MALDI source and histology performed on consecutive sections. A Non-negativity Matrix Factorization (NMF) clustering algorithm was performed per animal to extract the main spectral features from the data and compare lipid distribution in lipid-rich and –poor arteries.

Results: OCT imaging identified lipid-rich and –poor arteries (Figure 1.A). NMF clustering of MALDI-MSI data showed components for different tissue types: myocardium, periadventitial fat and atherosclerotic plaque itself. Lipids in the myocardium and in the periadventitial fat consisted mainly of phosphatidylcholines (PCs) and were similar for healthy and lipid-rich arteries. Similarly, some lipids were present in both atherosclerotic and healthy arteries, such as PC(34:1) and sphingomyelin SM(34:1). The component for lipid-rich arteries consisted of lipid species not detected in healthy arteries, such as cholesterol and some PCs (Figure

1.B).



Conclusions: We showed that lipid-rich atherosclerotic plaque signals as detected by OCT corresponds to distribution of lipid species that are specific for lipid-rich atherosclerotic plaques.

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Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

OCULAR MICROCIRCULATION BLOOD FLOW ACUTELY INCREASES UPON CHOLESTEROL REMOVAL. THE EYES MIRROR OF THE HEART?

POSTER VIEWING SESSION

Tiziana Sampietro[1], Beatrice Dal Pino[1], Federico Bigazzi[2], Francesco Sbrana[1], Andrea Ripoli[1], Enrica Fontanelli[3], Mascia Pianelli[1], Roberta Luciani[1], Antonio Lepri[3], Giacomo Calzetti[4]
[1]Lipoapheresis Unit, Fondazione Toscana "Gabriele Monasterio", Pisa, Italy, [2]Lipoapheresis Unit, Fondazione Toscana "Gabriele Monastario", Pisa, Italy, [3]Institute Of Ophtalmology, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy, [4]Institute Of Ophtalmology, Università di Parma, Parma, Italy

Background and Aims : Lipoprotein apheresis (LA) acutely increases coronary microcirculation blood flow (BF) measured with different techniques, which are time-consuming, costly, and invasive. The ocular vasculature may be assumed as an easily accessible window to systemic microcirculation. Recent advances in imaging techniques enable to quantify ocular microcirculation blood flow (BF) in a quick and non-invasive manner, which represents a wonderful opportunity to study the short-term changes in optic nerve head (ONH) BF upon LA in inherited hypercholesterolemia (IH).

Methods: The study was performed at a reference centre for inherited dyslipidemias and involved 44 eyes of 22 patients with IH, including the same cohort previously studied for coronary microcirculation. Laser Speckle Flowgraphy (LSFG) was used to measure rest ONH BF before and few hours after LA. Main outcomes were 1) tissue average BF (referred to as ‘Mean Tissue’, MT) and arteriolar/venular average BF (referred to as ‘Mean Vessel’, MV). Eyes were statistically clustered in two groups based on pre-treatment ONH blood flow values.

Results: After a single LA session, plasma lipids decreased in both groups and ocular microcirculatory parameters increased in the group with lower pre-apheresis BF values. The mean increase from baseline was 7.0% for MT (*P*= 0.009) and 7.2% (*P*= 0.042) for MV,

respectively.

	Group 1 (n = 28)			Group 2 (n = 16)		
	Pre-apheresis low microcirculatory parameters			Pre-apheresis high microcirculatory parameters		
	Pre-LA	Post-LA	P	Pre-LA	Post-LA	P
Total cholesterol (mg/dl)	196 [180 - 260]	87 [76-113]	<0.001	182 [172 – 198]	88 [74 – 100]	<0.001
HDL cholesterol (mg/dl)	49 [45 – 54]	42 [37 - 46]	<0.001	49 [42 - 53]	41 [37 – 51]	<0.001
Triglycerides (mg/dl)	152 [111- 244]	59 [21 – 78]	<0.001	136 [110 – 205]	47 [32 – 73]	<0.001
LDL cholesterol (mg/dl)	119 [88 – 170]	40 [22 - 61]	<0.001	96 [85 – 122]	30 [18 – 44]	<0.001
MA	24.00 ± 3.86	25.82 ± 4.57	0.015	32.12 ± 4.15	31.52 ± 3.98	0.537
MT	13.83 ± 1.89	14.87 ± 2.59	0.009	16.92 ± 2.78	16.86 ± 2.48	0.946
MV	41.54 ± 7.00	44.77 ± 8.71	0.042	55.82 ± 8.17	52.65 ± 10.62	0.189

Table. Lipoprotein apheresis effects among the 2 groups (pre-apheresis low and high microcirculatory parameters) identified by machine learning analysis.

Legend. LA – Lipoprotein apheresis; MA - Mean All; MT - Mean Tissue; MV - Mean Vessel.

Conclusions: These findings, considered together with data already shown on coronary microcirculation, suggest a similarity between ocular and coronary BF response to LA. Ocular microcirculation BF might represent a versatile biomarker to evaluate microcirculatory system health, including coronary microcirculation. Plasma lipoproteins levels may influence rest ONH BF.

051

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-07 Imaging technology*

CORONARY MICROCIRCULATORY BLOOD FLOW SIGNIFICANTLY INCREASES UPON ACUTE AND CHRONIC CHOLESTEROL LOWERING. EVALUATION BY CADMIUM-ZINC-TELLURIDE CARDIAC IMAGING STRESS TEST

POSTER VIEWING SESSION

Tiziana Sampietro[1], Francesco Sbrana[1], Beatrice Dal Pino[1], Federico Bigazzi[1], Andrea Ripoli[1], Paolo Marzullo[2], Alessia Gimelli[2]
[1]Lipoapheresis Unit, Fondazione Toscana "Gabriele Monasterio", Pisa, Italy, [2]Department Of Nuclear Medicine, Fondazione Toscana "Gabriele Monastario", Pisa, Italy

Background and Aims : Aim of this pilot study was to evaluate, in patients with Familial Hypercholesterolemia disease, the impact of the lipid lowering approach on coronary endothelium, by the quantification of the absolute myocardial blood flow (MBF) and the coronary flow reserve (CFR), before and after treatment.

Methods: We selected 12 patients (mean age 59±6 years; male 75%) submitted to stress/rest dynamic myocardial perfusion scintigraphy (MPS) using the Cadmium-Zinc-Telluride camera; 6 patients were addressed to Lipoprotein Apheresis (LA), while the other 6 patients received PCSK9i therapy (evolocumab 140 mg every 2 weeks on 4/6 subjects – alirocumab 150 mg every 2 weeks on 2/6 subjects), according to clinical indications. All patients were submitted to the first MPS evaluation before starting LA or PCSK9i therapy; MPS was repeated after one day of first LA treatment, or after six months after PCSK9i treatment.

Results: Both lipid lowering treatment had a significant impact on patients' lipid profile. The acute effect of LA, resulted in a significant CFR increase and in a parallel decrease of summed defect score, indicating *a trend* an MBF improvement. The chronic treatment with PCSK9i shows a positive effect on MBF, at rest and after stress, compatible with a coronary microcirculation improvement (**Table**

1).

	CZT Scan Pre-LA (n = 6)	CZT Scan Post-LA (n = 6)	p	CZT Scan Pre PCSK9i (n = 6)	CZT Scan Post PCSK9i (n = 6)	p
Total cholesterol (mg/dl)	176 ± 43	94 ± 47	0.016	245 ± 37	158 ± 47	0.001
HDL cholesterol (mg/dl)	53 ± 20	45 ± 21	0.003	49 ± 4	52 ± 9	0.405
LDL cholesterol (mg/dl)	100 ± 37	25 ± 10	0.002	169 ± 36	82 ± 44	>0.001
Tryglicerides (mg/dl)	114 ± 60	45 ± 20	0.091	134 ± 60	121 ± 13	0.388
Overall - Basal MBF	0.54 ± 0.17	0.63 ± 0.12	0.079	0.57 ± 0.19	0.77 ± 0.09	0.017
Overall - Stress MBF	1.10 ± 0.43	1.48 ± 0.28	0.057	1.36 ± 0.29	1.85 ± 0.30	0.008
Overall - CFR	2.04 ± 0.80	2.32 ± 0.68	0.039	2.56 ± 1.00	2.62 ± 0.62	0.819
SDS	5.83 ± 2.32	3.83 ± 2.48	0.041	3.67 ± 0.82	3.00 ± 1.41	0.286

Legend: CFR – coronary flow reserve; CZT - Cadmium-Zinc-Telluride; LA – lipoprotein apheresis; MBF – myocardial blood flow; SDS - summed difference score.

Conclusions: Our preliminary data indicate a positive lipid lowering treatment effect on microcirculation and endothelial function, both in acute and chronic treatment. This study could confirm previous published results where lipid lowering therapy add beneficial effects to arterial homeostasis and, ultimately, improve organ perfusion.

052

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-08 Platelets, thrombosis and atherosclerosis*

THE APPLICATION OF QUARTZ CRYSTAL MICROBALANCE WITH DISSIPATION MONITORING (QCM-D) TO STUDY ADHESION OF PLATELETS UNDER FLOW CONDITIONS

POSTER VIEWING SESSION

Katarzyna Derszniak[1,2], Szczepan Zapotoczny[2], Maria Nowakowska[2], Stefan Chlopicki[1,3]
[1]Jagiellonian Centre For Experimental Therapeutics (jcet), Jagiellonian University, Kraków, Poland, [2]Faculty Of Chemistry, Jagiellonian University, Kraków, Poland, [3]Department Of Pharmacology, Jagiellonian University, Kraków, Poland

Background and Aims : The QCM-D system was applied to study the effects of prostacyclin (PGI_2)-, nitric oxide (NO)-, and carbon monoxide (CO) on $\alpha_{IIb}\beta_3$-mediated platelet adhesion in washed human platelets.

Methods: For QCM-D analysis, fibrinogen-modified gold-polystyrene sensors were used. For comparison convulxin-stimulated platelets were analyzed by Light Transmission Aggregometry (LTA).

Results: The paradoxical positive frequency shifts were registered collaterally to the positive dissipation shifts during the early phase of the interactions of non-stimulated platelets with fibrinogen-covered sensors. Carbon monoxide-releasing molecule (CORM-A1, 300 µM) suppressed these interactions, while nitric oxide donor (PAPA NO, 10 µM) or carbaprostacyclin ($cPGI_2$, 1000 ng/ml) did not, even though these two interventions inhibited the late phase of platelet adhesion. The negative frequency and positive dissipation shifts were both strongly reduced by high concentration of eptifibatide (5 µg/ml) as compared with IC_{50}=0.05 µg/ml for inhibition of platelet aggregation by eptifibatide established in LTA. However, the QCM-D recorded platelet response even with platelet suspensions < 200 000 plt/µl and low concentration of convulxin (< 30 ng/ml) in contrast to LTA assay.

Conclusions: Altogether, the QCM-D system gave a unique insight into the early-phase of platelets adhesion to fibrinogen reflected by the paradoxical positive frequency shifts followed by the progressive negative frequency shifts related to the full platelet activation and firm adhesion. The suppression of the frequency and dissipation shifts by CORM-A1, and the late-phase interactions by PAPA-NO and $cPGI_2$, suggested that the early response triggered by the fibrinogen-contact was independent on cGMP- or cAMP-mediated pathways but rather mediated by activation of platelet energy metabolism.

053

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-08 Platelets, thrombosis and atherosclerosis*

EXPOSURE TO PERFLUOROALKYL SUBSTANCES AND CARDIOVASCULAR DISEASE: EXPERIMENTAL AND EPIDEMIOLOGICAL EVIDENCE IN INDIA

POSTER VIEWING SESSION

Nitin Verma
Chitkara University School Of Pharmacy, Chitkara University, Baddi, India

Background and Aims : Polyfluoro- and perfluoroalkyl substances (PFAS) are organic chemicals extensively used worldwide for industrial and consumer products. Due to their chemical stability, PFAS represent a major cause of environmental pollution. PFAS accumulate in animal and human blood and tissues exerting their toxicity. Our aim is to establish the relationship between PFAS levels in the blood and its association with cardiovascular disorders.

Methods: We performed a review of the epidemiological studies exploring the relationship between exposure to PFAS and thromboembolic cardiovascular disease.

Results: An increase in cardiovascular disease or death related to PFAS exposure has been reported from cross-sectional and longitudinal observational studies with evidence concerning the relation with early vascular lesions and atherosclerosis. Several studies indicate an alteration in lipid and glucose metabolism disorders and increased blood pressure as a possible link with cardiovascular thromboembolic events. We also examined the recent evidence indicating that legacy and new PFAS can be incorporated in platelet cell membranes giving a solid rationale to the observed increase risk of cardiovascular events in the populations exposed to PFAS by directly promoting thrombus formation. Exposure to PFAS has been related to altered plasma membrane fluidity and associated with altered calcium signal and increased platelet response to agonists, both in vitro and ex vivo in subjects exposed to PFAS.

Conclusions: These findings offer mechanistic support to the hypothesis that platelet-centered mechanisms may be implicated in the increase in cardiovascular events observed in populations chronically exposed to PFAS.

054

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-09 Aortic valve stenosis*

PROTEOMIC PROFILING REVEALS UNIQUE SIGNATURES OF STRUCTURAL BIOPROSTHETIC VALVE DETERIORATION

POSTER VIEWING SESSION

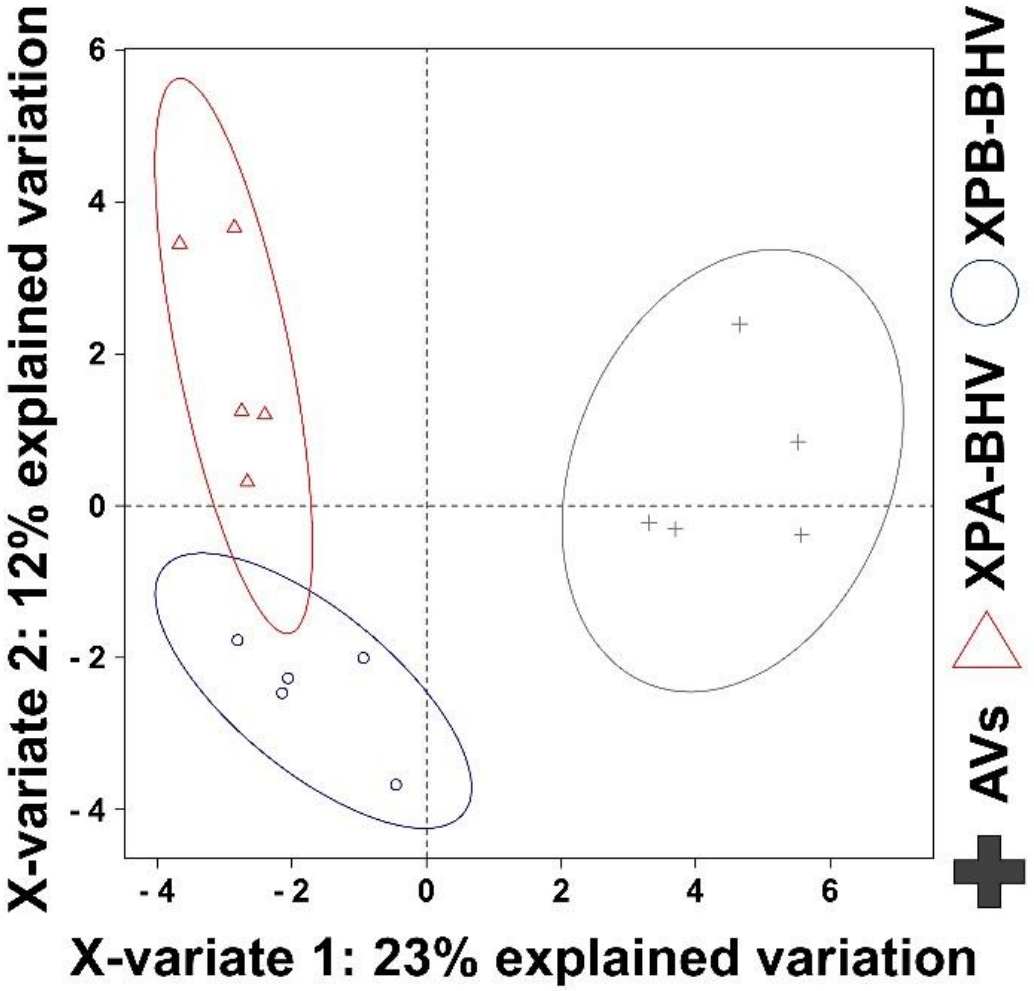
Arseniy Lobov[1], Alexander N. Kostyunin[2], Tatiana V. Glushkova[2], Daria K. Shishkova[2], Bozhana R. Zainullina[3], Evgeny A. Ovcharenko[2], Alexander N. Stasev[2], Alexey V. Evtushenko[2], Anton G. Kutikhin[2]
[1]Department Of Regenerative Biomedicine, Research Institute of Cytology, St. Petersburg, Russian Federation, [2]Laboratory Of Molecular, Translational, And Clinical Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation, [3]Centre For Molecular And Cell Technologies, St. Petersburg State University, St. Petersburg, Russian Federation

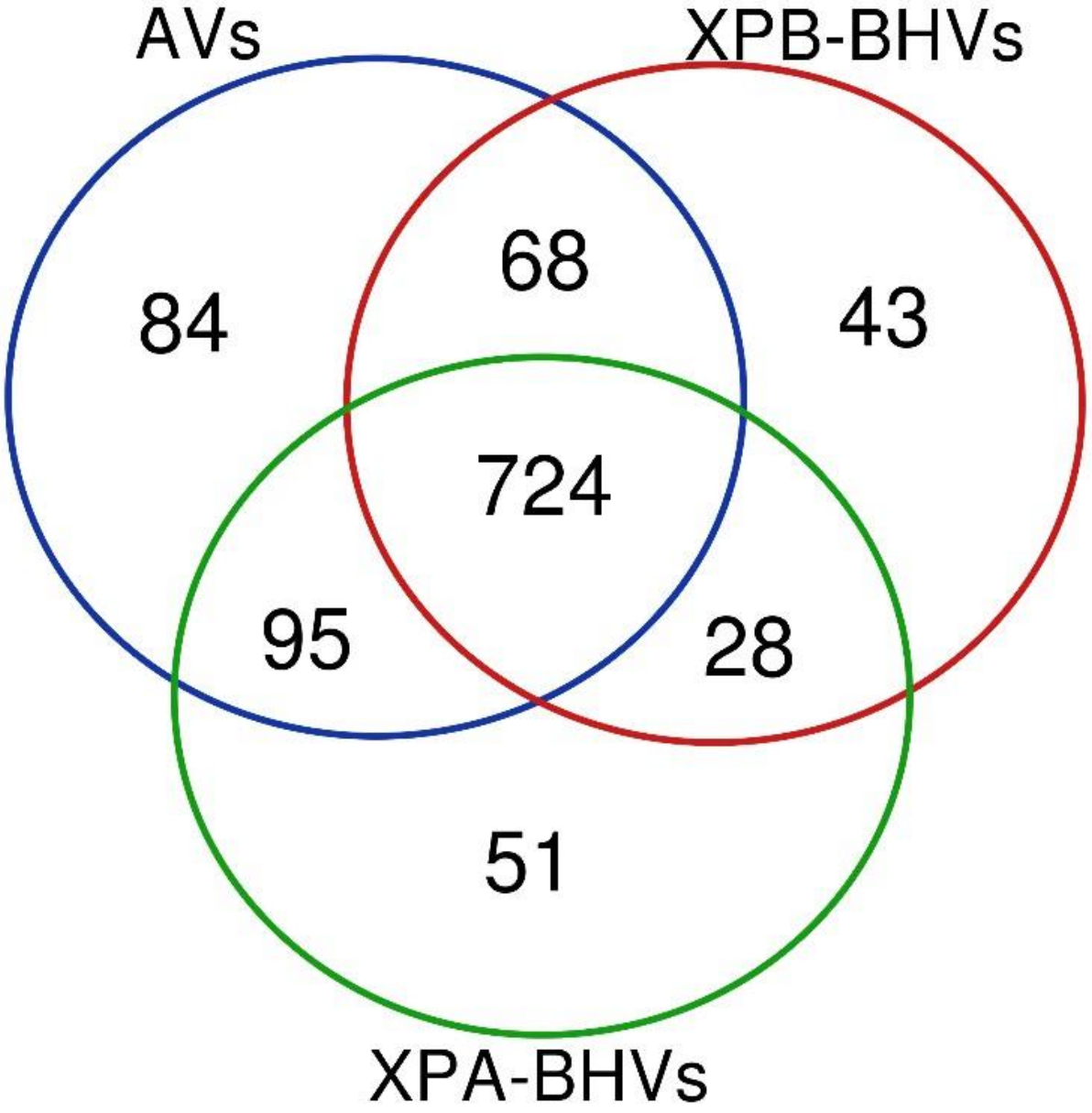
Background and Aims : Half of the bioprosthetic heart valves (BHVs) demand a repeated replacement within 15 years postimplantation because of structural valve deterioration (SVD). The pathogenesis of SVD is far from being fully understood, largely due to the lack of high-throughput investigation of failed BHVs.

Methods: Failed bovine xenopericardial (XPB-BHVs, n = 5)) and porcine xenoaortic (XPA-BHVs, n = 5) BHVs and dysfunctional AVs (n = 5) were excised during the heart valve replacement. Label-free proteomic profiling was performed by means of liquid chromatography-tandem mass spectrometry with ion mobility (TimsToF Pro). Bioinformatic analysis was conducted using PEAKS Studio Xpro and R software environment. Proteins identified with false discovery rate < 1% and having ≥ 2 unique peptides were included into further analysis.

Results: Out of 1,614 protein groups identified, 73 were unique for BHVs and 70 proteins were overexpressed in BHVs. Of these 143 protein groups, 73 belonged to five major categories: complement components (17), neutrophil markers (19), proteases (7), platelet markers and coagulation factors (18), and lipid metabolism-related proteins (12). Matrix metalloproteinases (MMP-8 and MMP-9) were documented in BHVs but not in AVs, whereas their tissue inhibitors (TIMP-1 and TIMP-2) were upregulated in AVs, together indicative of unbalanced proteolysis in the failing BHVs. Presumably, loosening and disintegration of prosthetic matrix upon the constant haemodynamic stress provoke excessive lipid deposition, coagulation, microthrombosis, and inflammation.

PLS-DA ordination of different valve types




AVs
XPB-BHVs
84
68
43
724
95
28
51
XPA-BHVs

Complement components

Category	Protein	Description	UniProt	Unique peptides	Native aortic valves		Bioprosthetic heart valves		Fold change
					Count	n	Count	n	
Unique proteins									
C	MASP2	Mannan-binding lectin serine protease 2	Q00987	2	0.0	0	5.2	6	Unique
Overexpressed proteins									
C	CO3	Complement C3	P01024	188	2988.4	5	5207.3	10	1.25
C	CO4A	Complement C4-A	P0C0L4	10	1307.6	5	1382.0	10	2.70
C	CO4B	Complement C4-B	P0C0L5	11	1317.8	5	1374.1	10	1.59
C	CO5	Complement component C5	P01031	57	91.2	5	730.3	10	5.84
C	CO7	Complement component C7	P10643	55	152.9	5	773.1	10	4.30
C	CO8A	Complement component C8 alpha chain	P07357	34	66.6	5	366.4	10	4.66
C	CO8B	Complement component C8 beta chain	P07358	44	144.8	5	510.6	10	4.04
C	CO8G	Complement component C8 gamma chain	P07360	16	78.8	5	375.9	10	4.56
C	CO9	Complement component C9	P02748	52	212.2	5	849.5	10	3.83
C	C1S	Complement C1s subcomponent	P09871	25	70.8	5	134.8	10	1.88
C	C4BPA	C4b-binding protein alpha chain	P04003	33	94.0	5	204.6	10	2.16
C	FHR5	Complement factor H-related protein 5	Q9BXR6	40	36.6	5	446.9	10	6.94
C	FHR2	Complement factor H-related protein 2	P36980	7	56.4	5	262.3	10	4.24
C	FHR1	Complement factor H-related protein 1	Q03591	3	108.0	5	452.4	10	3.87
C	PROP	Properdin	P27918	12	33.2	5	88.0	10	2.46
C	MASP1	Mannan-binding lectin serine protease 1	P48740	9	2.0	3	16.3	10	2.35

Neutrophils

Category	Protein	Description	UniProt	Unique peptides	Native aortic valves		Bioprosthetic heart valves		Fold change (log2)
					Count	n	Count	n	
Unique proteins									
N	PERM	Myeloperoxidase	P05164	30	4.8	1	78.4	10	Unique
N	ELNE	Neutrophil elastase	P08246	8	0.8	1	66.6	10	Unique
N	STOM	Stomatin	P27105	11	0.6	1	51.3	10	Unique
N	ITAX	Integrin alpha-X (CD11c)	P20702	13	0.0	0	13.9	8	Unique
N	CY24B	Cytochrome b-245 heavy chain (NADPH oxidase 2, NOX2)	P04839	10	0.0	0	13.3	9	Unique
N	PRTN3	Myeloblastin	P24158	4	1.6	1	45.2	10	Unique
N	PRG2	Bone marrow proteoglycan, eosinophil major basic protein	P13727	7	0.0	0	11.0	8	Unique
N	NCF1	Neutrophil cytosol factor 1	P14598	6	0.0	0	6.3	8	Unique
N	CATG	Cathepsin G	P08311	6	0.0	0	15.9	10	Unique
N	RAC2	Ras-related C3 botulinum toxin substrate 2	P15153	4	3.6	1	14.8	10	Unique
N	CAMP	Cathelicidin	P49913	5	0.0	0	15.1	10	Unique
N	MNDA	Myeloid cell nuclear differentiation antigen	P41218	9	0.0	0	13.0	9	Unique
N	ECP	Eosinophil cationic protein	P12724	4	0.0	0	10.9	6	Unique
Overexpressed proteins									
N	S10A9	Protein S100-A9	P06702	11	44.8	5	152.1	10	4.41
N	S10A8	Protein S100-A8	P05109	9	20.4	5	80.1	10	4.05
N	S10A7	Protein S100-A7	P31151	5	5.8	4	10.3	10	2.32
N	DEF1	Neutrophil defensin 1	P59665	6	17.6	5	37.7	10	3.38
N	TRFL	Lactotransferrin	P02788	43	13.2	5	133.4	10	3.49
N	QSOX1	Sulfhydryl oxidase 1	O00391	27	53.6	5	120.8	10	2.50

Proteases and their inhibitors

Category	Protein	Description	UniProt	Unique peptides	Native aortic valves		Bioprosthetic heart valves		Fold change
					Count	n	Count	n	
Unique proteins									
P	MMP9	Matrix metalloproteinase-9 (92 kDa type IV collagenase)	P14780	11	0.8	1	25.7	9	Unique
P	HYAL1	Hyaluronidase-1	Q12794	5	0.0	0	16.3	8	Unique
P	ADEC1	ADAM DEC1	O15204	4	0.0	0	6.8	8	Unique
P	MMP8	Matrix metalloproteinase-8 (neutrophil collagenase)	P22894	8	0.0	0	16.0	6	Unique
P	MMP19	Matrix metalloproteinase-19	O95542	5	0.0	0	2.2	7	Unique
PI	TIMP2	Metalloproteinase inhibitor 2	P16035	2	2.8	3	0.0	0	Unique
Underexpressed proteins									
Pi	TIMP1	Metalloproteinase inhibitor 1	P01033	8	76.2	6	10.3	6	TBD

Blood coagulation

Category	Protein	Description	UniProt	Unique peptides	Native aortic valves		Bioprosthetic heart valves		Fold change
					Count	n	Count	n	
Unique proteins									
BC	ITA2B	Integrin alpha-IIb (CD41)	P08514	31	1.6	1	98.9	10	Unique
BC	ITB3	Integrin beta-3	P05106	29	0.2	1	70.9	10	Unique
BC	URP2	Fermitin family homolog 3 (kindlin-3)	Q86UX7	20	0.2	1	61.6	10	Unique
BC	CD36	Platelet glycoprotein 4	P16671	9	0.2	1	28.6	9	Unique
BC	ITA6	Integrin alpha-6	P23229	9	1.0	1	12.8	8	Unique
BC	CXCL7	Platelet basic protein (CXCL7)	P02775	6	0.0	0	15.7	9	Unique
BC	GP1BA	Platelet glycoprotein Ib alpha chain (CD42b)	P07359	8	0.0	0	8.2	8	Unique
BC	GP1BB	Platelet glycoprotein Ib beta chain (CD42c)	P13224	5	0.0	0	10.5	9	Unique
BC	MMRN1	Multimerin-1	Q13201	17	0.0	0	21.7	7	Unique
BC	PLEK	Pleckstrin	P08567	10	0.0	0	10.1	7	Unique
BC	GP9	Platelet glycoprotein IX (CD42a)	P14770	4	0.0	0	6.8	6	Unique
BC	FA5	Coagulation factor V	P12259	22	0.0	0	26.5	10	Unique
BC	TFPI1	Tissue factor pathway inhibitor	P10646	3	2.2	1	6.2	9	Unique
Overexpressed proteins									
BC	FA7	Coagulation factor VII	P08709	4	3.8	4	16.1	10	2.44
BC	FA9	Coagulation factor IX	P00740	15	22.0	5	57.9	10	1.98
BC	FA10	Coagulation factor X	P00742	15	12.8	5	57.1	10	2.97
BC	CBPB2	Carboxypeptidase B2	Q96IY4	14	48.4	5	84.0	10	2.00
BC	ZPI	Protein Z-dependent protease inhibitor	Q9UK55	20	20.2	6	73.4	10	3.29

Lipid metabolism

Category	Protein	Description	UniProt	Unique peptides	Native aortic valves		Bioprosthetic heart valves		Fold change
					Count	n	Count	n	
Unique proteins									
L	APOA5	Apolipoprotein A-V	Q6Q788	23	0.0	0	55.8	10	Unique
L	APOC4	Apolipoprotein C-IV	P55056	6	2.4	1	19.4	9	Unique
L	LIPL	Lipoprotein lipase	P06858	8	0.0	0	31.1	10	Unique
L	LIPE	Endothelial lipase	Q9Y5X9	7	0.0	0	16.3	9	Unique
L	ANGL3	Angiopoietin-related protein 3	Q9Y5C1	4	0.2	1	5.7	10	Unique
L	ISK	Tsukushin	QN0UA8	7	0.0	0	27.2	9	Unique
L	PCSK9	Proprotein convertase subtilisin/kexin type 9	Q8NBP7	14	0.0	0	40.2	9	Unique
Overexpressed proteins									
L	APOE	Apolipoprotein E	P02649	35	232.6	5	930.0	10	4.01
L	APOF	Apolipoprotein F	Q13790	5	4.2	4	27.5	10	3.86
L	APOC2	Apolipoprotein C-II	P02655	7	32.6	5	73.6	10	2.21
L	APOC3	Apolipoprotein C-III	P02656	8	122.0	5	214.7	10	1.33
L	CD5L	CD5 antigen-like	O43866	11	11.6	5	29.2	10	3.39

Conclusions: In contrast to dysfunctional native AVs, failing BHVs suffer from complement-driven neutrophil invasion, excessive proteolysis, and unwanted coagulation. Funding: This research was funded by the Russian Science Foundation, grant number 21-75-10107.

055

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-10 Clonal Haematopoiesis*

NO EFFECT OF RADIATION-RELATED CLONAL HEMATOPOIESIS DRIVEN BY PPM1D MUTATIONS ON EXPERIMENTAL ATHEROSCLEROSIS DEVELOPMENT

POSTER VIEWING SESSION

Marta Amorós-Pérez, Virginia Zorita, Rosa Moro-Moro, Nuria Matesanz, Vanesa Viana-Huete, Alba Ferrer-Pérez, Jose J. Fuster
Hematovascular Pathophysiology Laboratory, Spanish National Center for Cardiovascular Research (CNIC), Madrid, Spain

Background and Aims : Clonal hematopoiesis (CH) is emerging as a new risk factor for atherosclerotic cardiovascular disease (CVD) and *PPM1D* is among the most commonly mutated genes in CH. Mutations in *PPM1D* are overrepresented in cancer survivors, and human and mouse studies support that the clonal expansion of *PPM1D* mutant hematopoietic cells is facilitated by cytotoxic cancer therapies. The aim of this study was to assess the role of *PPM1D* mutations on atherosclerosis development in a mouse model of radiation-related CH.

Methods: A non-conditioned bone marrow (BM) transplant was used to generate chimeric *Ldlr-/-* mice with a small fraction (~2%) of hematopoietic cells carrying the truncating *PPM1D(R451X)* mutation (*Ppm1d*$^{R451X/+}$*)*. Chimeric mice and wild-type controls were exposed intermittently to a small dose of radiation during 2 weeks (totaling 7x20 rad) and subsequently fed a high cholesterol diet for 12 weeks. White blood cells (WBC) and BM progenitors were analyzed by flow cytometry. Plaque size and composition were quantified by Oil-red-O staining and immunohistopathological assessment. The effects of the *PPM1D(R451X)* mutation on cell cycle progression, apoptosis and cytokine expression were evaluated in cultured murine BM-derived macrophages.

Results: *Ppm1d*$^{R451X/+}$ cells expanded in BM progenitors and WBCs in mice subjected to low-dose radiation, but not in non-irradiated controls. This expansion did not affect hematological parameters or the size and composition of atherosclerotic plaques. Apoptosis was decreased by ~20% in *Ppm1d*$^{R451X/+}$BMDM (p=0.01). The expression of PPM1D(R451X) did not affect cell cycle kinetics or cytokine expression.

Conclusions: Radiation-related clonal hematopoiesis driven by monoallelic *Ppm1d* mutations does not affect atherosclerosis development in mice.

056

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

UNCOVERING THE LINK BETWEEN ATHEROSCLEROSIS, WALL STRAIN AND VASA VASORA

POSTER VIEWING SESSION

Hanane Belhoul-Fakir[1,2,3], Susan Wu[2], Yen Yeow[2], Gabrielle Musk[4], Helen Kershaw[4], Christopher Lagat[5], Brian Evans[5], Michael L. Brown[6], Juliana Hamzah[1,2], Shirley Jansen[1,3,7,8]
[1]Curtin Medical School, Curtin University, Perth, Australia, [2]Targeted Drug Delivery, Imaging & Therapy, Harry Perkins Medical Research Institute, Nedlands, Australia, [3]Heart And Vascular Research Institute, Harry Perkins Medical Research Institute, Nedlands, Australia, [4]Large Animal Facility, University of Western Australia, Perth, Australia, [5]Wa School Of Mines: Mece, Faculty Of Science & Engineering, Curtin university, Perth, Australia, [6]School Of Public Health, Faculty Of Health Sciences, Curtin University, Perth, Australia, [7]Department Of Vascular And Endovascular Surgery, Sir Charles Gairdner Hospital, Perth, Australia, [8]Faculty Of Health Sciences, University of Western Australia, Perth, Australia

Background and Aims : Background: It is unclear why sudden haemorrhage occurs in early atherosclerotic plaques, and whether an injury to the medial layer of the artery through wall movement and strain can initiate atherosclerosis. **Hypothesis:** Atheroma initiation (atherogenesis) may be triggered by a fatiguing motion from pulse pressure injury to the medial layer of the arterial wall leading to lipid deposition from vasa vasora. **Aim:** To initiate atherogenesis by establishing injury to the medial layer of the abdominal aorta.

Methods: Method: Three healthy landrace, female pigs (aged 9-10 weeks) underwent laparotomy to inject autologous blood or saline at 11-15 sites along the lower abdominal aortic wall. Pigs received either high fat diet (HFD) for 12 weeks (throughout the whole experiment) or four weeks only. Aortas from laparotomised and control healthy pigs were serially-stained for multiple markers and analysed using 3DHistech SlideViewer and HistoQuant software.

Results: Results: Injection of blood or saline induced injury within the medial layer of the arterial wall, leading to lipid cluster formation, not observed in non-injected sites. The sites of trauma also showed high density of vasa vasora and inflammatory cells, and rearrangement of vascular smooth muscle cells. The intimal layer of the artery remained unaffected by the injury. These outcomes were most prominent in the hyperlipidaemic pig fed with HFD for 12 weeks.

Conclusions: Conclusion: We demonstrate that vascular trauma within the medial layer of the artery can trigger atherogenesis. The presence of vasa vasora in the injury sites suggests haemorrhagic sites can potentially occur at an early stage of atherosclerosis.

057

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

DIETARY CHOLINE SUPPLEMENTATION INCREASES THE PLASMA CONCENTRATION OF SEVERAL AMINO ACIDS DURING ATHEROSCLEROSIS DEVELOPMENT

POSTER VIEWING SESSION

Giulia Chiesa[1], Alice Colombo[1], Elsa Franchi[1], Stefano Manzini[1], Mariel A. García-Rivera[2], Jennifer Kirwan[2], Marco Busnelli[1]
[1]Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milano, Italy, [2]Core Facility Metabolomics, Berlin Institute of Health, Berlin, Germany

Background and Aims : Increased dietary intake of choline worsens the development of atherosclerosis in ApoE-KO mice. Gut microbial metabolism of choline results in the production of trimethylamine, which, upon intestinal absorption is converted into the pro-atherogenic molecule trimethylamine-N-oxide (TMAO) in the liver. In this study we investigated if additional endogenous plasma metabolites were modulated by increased choline intake.

Methods: Eight weeks old ApoE-KO female mice (n=20/group) were fed for 16 weeks on standard rodent diets containing low (0.09%) or high concentration (1.2%) choline. At sacrifice, atherosclerosis was evaluated, and a targeted metabolomics of plasma was performed.

Results: The boost of dietary choline caused a worsening of atherosclerosis development at the aortic sinus. As expected, the increased choline intake was accompanied by a significantly increased plasma concentration of TMAO. Less obviously, in the group of mice that received high-dose choline, an increased plasma concentration of carnitine, a branched non-essential amino acid endogenously synthesized in kidney and liver that plays a role in energy metabolism, was detected. Similarly, in the same mice, an increased plasma concentration of the amino acids serine, glycine, methionine and sarcosine with a concomitantly reduced concentration of homocysteine was observed, suggesting an impairment in several interrelated metabolic pathways such as the methionine cycle, folate cycle, sarcosine pathway and transsulfuration pathway.

Conclusions: Our results indicate that, in addition to increasing TMAO, dietary choline supplementation leads to increased plasma concentration of several amino acids with key roles in different metabolic pathways. Such alterations may reveal further choline-mediated deleterious effects predisposing to atherosclerosis.

058

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

LIVER FIBROSIS DEVELOPMENT AFFECTS TISSUE AND SOLUBLE ENDOGLIN IN MICE

POSTER VIEWING SESSION

Samira Eissazadeh[1], Fatemeh Alaei Faradonbeh[2], Ivone A. Igreja Sá[1], Ivana Němečková[1], Katarína Tripská[1], Martina Vašinová[1], Barbora Vitverová[1], Jana Rathouská[1], Petr Nachtigal*[1]
[1]Department Of Biological And Medical Sciences, Charles University, Faculty of Pharmacy in Hradec Kralove, Hradec Kralove, Czech Republic, [2]Department Of Pharmacology, Charles University, Faculty of Medicine in Hradec Králové, Hradec Kralove, Czech Republic

Background and Aims : Endoglin (CD105) is a 180 kDa transmembrane glycoprotein and a coreceptor for binding to TGFβ1 superfamily existing in two forms, namely membrane endoglin (Eng) and soluble endoglin (sEng) circulating in the blood. It has been demonstrated that Eng might play an important role in the process of liver fibrosis, inflammation, and endothelial dysfunction. However, the precise impact of Eng expression and signalling changes and sEng levels during liver disorders are still unknown. We aimed to analyse the expression of Eng and sEng levels with respect to biomarkers of inflammation, fibrosis and endothelial dysfunction in mouse model of liver injury.

Methods: The liver damage was induced in three-month-old C57BL/6 female mice by DDC diet (3,5-diethoxycarbonyl-1,4-dihydrocollidine diet) while control animals were received standard chow diet, following by sacrificing the mice after four weeks with subsequent blood collection and molecular analysis of liver samples.

Results: The liver impairment and fibrosis in DDC mice were confirmed by significant increase in the level of ALT, ALP, AST, total bilirubin as well as α-SMA and CRIP2 expression. Although DDC diet significantly increased sEng levels and MMP-14 expression, there was a significant reduction in the expression of Eng in liver.

Conclusions: We suggest that DDC treatment results in cleavage of Eng by MMP-14 leading to high levels of sEng. Thus, sEng might be considered a circulating biomarker of liver damage after DDC treatment. However, the precise role of Eng expression changes with respect to the inflammation, fibrosis and endothelial dysfunction is currently under investigation in our lab.

059

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

ISFAHAN TWIN COHORT: A TEN YEARS' LONGITUDINAL PROSPECTIVE STUDY BASED ON A TWIN REGISTRY

POSTER VIEWING SESSION

Mojgan Gharipour
Genetics, Isfahan University of Medical Sciences, Isfahan, Iran

Background and Aims : Given the complex etiology of non-communicable diseases(NCD) , an understanding of the origins of NCD requires an in-depth analysis of the interplay between genetic variation and environment, preferably over time. For decades, twin studies have played a key role in understanding such traits. Their strength lies in the ability to disentangle genetic and environmental factors that contribute to a phenotype. This is done by comparing genetically identical monozygotic (MZ) with dizygotic twins, who share on average 50% of genetic variation, or by comparing MZ twins within a pair. This study aims to determine the relative contributions of genes and environment in the incidence of NCD.

Methods: The Isfahan Twin Cohort (ITR) recruited 1005 twins and multiples, with will follow-up them to 10 years. Data collection will be undertaken at five points. Demographic information, twin similarities, lifestyle, and past medical history are collected using validated questionnaires. Anthropometric measurements and blood pressure are measured by health professionals. Hematology panel, fasting blood sugar, cholesterol, LDL, HDL, AST, ALT and CRP are measured.

Results: We will continue to follow the twins who have been recruited in our cohort and will design matched case-control and cohort studies in disease/lifestyle-discordant twin pairs.

Conclusions: We will continue to follow the twins who have been recruited in our cohort and will design matched case-control and cohort studies in disease/lifestyle-discordant twin pairs.

060

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

AGE-DEPENDENT DIFFERENCES IN CORONARY ATHEROSCLEROSIS BETWEEN WOMEN AND MEN WHO DIED SUDDENLY OUT-OF-HOSPITAL

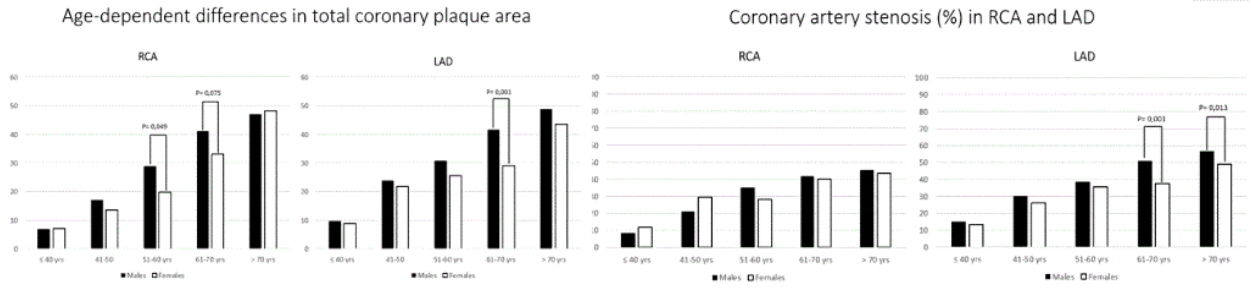
POSTER VIEWING SESSION

Emma Hakamaa[1], Pekka Karhunen[2,3], Sirkka Goebeler[4], Mika Martiskainen[4], Anne-Mari Louhelainen[4], Katja Ahinko[5], Terho Lehtimäki[3]
[1]Faculty Of Medicine, Semmelweiss University, Budapest, Hungary, [2]Medicine And Health Technology, Tampere University, Tampere, Finland, [3]Faculty Of Medicine And Health Technology, Tampere University, Tampere, Finland, [4]Forensic Medicine, Finnish Institute for Health and Wellfare, Helsinki, Finland, [5]Department Of Gynaegology And Obstetrics, Tampere University Hospital, Tampere, Finland

Background and Aims : Women have thought to be protected from coronary heart disease up to menopause, after which their morbidity and mortality from CHD reach the level of men in the same age-group. Possible gender differences in the severity of atherosclerosis have never been measured exactly at the vessel wall level.

Methods: We measured stenosis percentage and surface area of atherosclerotic lesions using computer-assisted planimetry in the left anterior descending coronary artery (LAD) and right coronary artery (RCA) in 10-year age-groups of 185 Caucasian white women and 515 men comprising the Tampere Sudden Death Study. This prospective series comprising individual aged 16 - 96 years represent a cross section of the general population.

Results: Women were in mean 7 years older than men (p<0,0001). In age-adjusted analysis, there were no differences in the total plaque area or stenosis percentage in RCA or LAD between premenopausal women (< 50 years) and men in the same age-group. However, in postmenopausal women aged 51-60 years the plaque area remained on average 24% smaller, and in women aged 61-70 years, 25% smaller compared to men. In the oldest postmenopausal group (>70 years), the total plaque area reached the level of men. Coronary artery stenosis percentage showed no gender difference in RCA, whereas in LAD women had statistically significantly smaller stenosis than men in all age groups over 60 years.



Conclusions: The severity of atherosclerosis among premenopausal women did not differ from men. However, it seems that in postmenopausal women the progression of atherosclerosis is slower compared to men.

061

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

INVESTIGATION OF THE ANTIOXIDANT AND ANTI-INFLAMMATORY POTENCY OF ECHINACEA ANGUSTIFOLIA EXTRACT

POSTER VIEWING SESSION

Konstantina Karavasili[1], Despoina Pantazi[1], Louisa Pechlivani[1], Eirini Maria Bata[2], Panagiotis Stathopoulos[2], Alexios-Leandros Skaltsounis[2], Alexandros D. Tselepis[1]
[1]Department Of Chemistry, Atherothrombosis Research Centre/Laboratory of Biochemistry, Ioannina, Greece, [2]Department Of Pharmacy, Nkua, Division of Pharmacognosy & Natural Products Chemistry, Athens, Greece

Background and Aims : Echinacea is known for its potent antioxidant properties. We studied the effect of 2 different extracts of Echinacea angustifolia on low-density lipoprotein (LDL) oxidation and on the expression of the adhesion molecule ICAM-1, on endothelial cells (HUVECs) activated with the tumor necrosis factor-alpha (TNF-α).

Methods: We prepared an aqueous and an isopropanol/water (1/1v/v) extract of the aerial parts of Echinacea angustifolia. Both extracts were treated with XAD-7 adsorbent resin. Using HPLC-DAD and LC-HRMS, the biologically active substances found were rosmarinic, chlorogenic and chicoric acid and kaempferol-3-O-glucoside. The inhibitory activity of all extracts (5-200μg/mL) towards the oxidative modification of LDL (100μg/mL) was studied and the threshold concentration (the minimum concentration with the maximum antioxidant activity) was determined. To study their possible anti-inflammatory activity these extracts were incubated for 1h with HUVECs following by cell activation with TNF-α (0,5ng/mL) for 6h. Cell activation was assessed by the membrane expression of ICAM-1 by flow cytometry.

Results: All extracts inhibited LDL oxidation, the extract with the strongest antioxidant activity being the isopropanol/water extract treated with XAD-7, exhibiting a threshold concentration of 10μg/mL. At the range of concentrations studied all extracts did not inhibit the ICAM-1 expression in activated HUVECs.

Conclusions: The isopropanol/water extract of Echinacea angustifolia is a potent antioxidant but it does not inhibit the inflammatory activation of HUVECs. Further studies are necessary to investigate the compound(s) responsible for this activity and the underlying mechanisms.

062

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

ANTIOXIDANT AND ANTI-INFLAMMATORY EFFECTS OF ROSMARINUS OFFICINALIS AND MELISSA OFFICINALIS ETHANOLIC EXTRACTS

POSTER VIEWING SESSION

Ioannis K. Koutsaliaris[1], Iraklis C. Moschonas[1], Christina D. Papaemannouil[2], Aikaterini N. Tsouka[1], Andreas G. Tzakos[2], Alexandros D. Tselepis[1]
[1]Department Of Chemistry, Atherothrombosis Research Centre, Ioannina, Greece, [2]Department Of Chemistry, Laboratory of Organic Chemistry, Ioannina, Greece

Background and Aims : Oxidized LDL, endothelial dysfunction and neutrophil extracellular trap formation (NETs) play a central role in atherosclerosis. The aim of the present study was to investigate the effect of *Rosmarinus officinalis* (ROe) and *Melissa officinalis* (MOe) ethanolic extracts on LDL oxidation, intercellular adhesion molecule-1 (ICAM-1) expression on endothelial cells (HUVECs) and NET formation.

Methods: Ethanolic extraction of whole plants was performed for 72h. Phytochemical analysis was performed using NMR-spectroscopy. LDL (d=1.019-1.063g/mL) was isolated by sequential ultracentrifugation of plasma from healthy volunteers and oxidized (100μg protein/mL) by 5μM $CuSO_4$, in the presence of ROe or MOe, for 6h. HUVECs were pre-incubated with various extract concentrations for 1h and treated with 0.5ng/mL TNF-α for 6h or 8U/mL thrombin for 24h. ICAM-1 expression was determined by flow cytometry. Neutrophils (2×10^5) were isolated, pre-incubated with the extracts for 5min and activated with 100nM PMA for 4h at 37℃, 5% CO_2. NETs were isolated and quantitated using ELISA kit.

Results: The main compounds identified in ROe and MOe are shown in Table 1. ROe and MOe significantly inhibit LDL oxidation, the ROe being significantly more potent than MOe. ROe inhibited inflammatory HUVECs activation and NETs formation, exhibiting a maximum inhibition at 50μg/mL, while MOe was inactive at any concentration studied (Table

2).

Table 1. Phytochemical analysis of *Rosmarinus officinalis* and *Melissa officinalis* ethanolic extracts using NMR-spectroscopy.

Compound	*Rosmarinus Officinalis*	*Melissa Officinalis*
Luteolin	+	-
Luteolin Glycoside	+	-
Apigenin	+	+
Apigenin Glycoside	+	+
Rosmarinic acid	+	+
Caffeic acid	+	+
Carnosic acid	+	-
Rosmadial	+	-
Ursolic acid	+	+
Oleanolic acid	-	+
Betulinic acid	+	+
Eriodictyol	-	+
3,5,7-dihydroxy-4′,7-dimethoxyflavone	+	-
5,6-dihydroxy-3′,4′,7-trimethoxyflavone	+	-
Hydroxylated flavones	-	+

+ Present in ethanolic extract

- Not present in ethanolic extract

Table 2. Effect of *Rosmarinus officinalis* and *Melissa officinalis* ethanolic extracts on LDL oxidation, ICAM-1 expression and NETs formation.

LDL oxidation			
Extract	**Threshold concentration (µg/mL)**	**IC_{50} (µg/mL)**	
ROe	15.0±4.3*	8.8±2.4*	
MOe	20.0±7.6	13.4±4.9	
ICAM-1 expression			
Extract	**Concentration (µg/mL)**	**% Inhibition**	
		Thrombin	TNF-α
ROe	50	95.9±2.5	97.4±2.6
MOe	50	-	-
NET formation			
Extract	**Concentration (µg/mL)**	**% Inhibition**	
ROe	50	81.0±27.0	
MOe	50	-	

*P<0.05 compared with MOe

Conclusions: ROe and MOe share many similarities in their phytochemical profile, however ROe exhibits more potent antioxidant activity than MOe and anti-inflammatory activities that are not present in MOe. Further ongoing studies will shed light into the active compounds of ROe and their specific mechanisms of action.

063

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

VEGF-A LEVELS AND G634C GENE POLYMORPHISM AS A PREDICTOR OF ADVERSE OUTCOMES IN PATIENTS WITH STEMI

POSTER VIEWING SESSION

Inna Kutya[1], Iulia Rodionova[1], Mykola Kopytsya[2], Yaroslava Hilova[1]
[1]Department Of Prevention And Treatment Of Emergency Conditions, Government Institution “I.t.malaya Therapy National Institdepartment Of Prevention And Treatment Of Emergency Conditions, Kharkiv, Ukraine, [2]Department Of Prevention And Treatment Of Emergency Conditions, GI "LT Malaya National Therapy Institute of the NAMSU", Kharkiv, Ukraine

Background and Aims : was to assess the role of the VEGF-A gene polymorphism in the prediction of outcomes in patients with STEMI after successful revascularization during 6 month

Methods: 135 STEMI patients. The selected group of patients who reached the combined endpoint included 29 (21.5%) patients (group 1). The second group consisted of 106 (78.5%) people and was without cardiovascular events (group 2). The combined endpoint included cardiovascular death, recurrent myocardial infarction, the occurrence/progression of heart failure that required hospitalization

Results: The patients from the group 1 had significantly elevated VEGF-A levels compared to group 2 (217.40 [102.54-473.78] pg/ml; 311.45 [204.20-680.86] pg/ml; p=0.046).Significantly higher levels of VEGF-A in the acute period of the disease were in carriers of the GG genotype (314.01 [159.94-627.66] pg / ml) compared with G634C + C634C genotype (221,28 [77.58-440.82] pg / ml, p = 0.045). The carriers of the G634G genotype had a lower accumulation of the combined endpoint compared to G634C + C634C genotypes after 6 month follow up (p = 0.020). Multivariate linear regression analyses demonstrated that polymorphism G634C (rs2010963) of VEGF-A gene (G634C+C634C) β = 0.808, CI [1.191 to 5.649] p=0.0465; decreased level of VEGF-A in the acute period β =-0.0054, CI [1.007 to 1,010] p=0.024, and LVEF < 50.60% β = 0.049 CI [0.918 to 0.988], p=0.0096 are significantly associated with negative outcomes

Conclusions: STEMI patients with G634C+C634C polymorphism of VEGF-A gene, with lower levels of VEGF-A and with LVEF<50.60% have greater chances for adverse outcomes.

064

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

EXTRACELLULAR VESICLES ENRICHED IN PCSK9 ARE INDICATIVE OF PRO-ATHEROGENIC PHENOTYPE - IN VITRO AND IN VIVO EVIDENCE

POSTER VIEWING SESSION

Chiara Macchi[1], Maria Francesca Greco[1], Marco Cafora[2], Cristina Banfi[3], Cesare R. Sirtori[1], Alberto Corsini[4], Anna Pistocchi[2], Nicola Ferri[5], Valentina Bollati[6], Massimiliano Ruscica[1]
[1]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Department Of Medical Biotechnology And Translational Medicine, Università degli Studi di Milano, Milan, Italy, [3]Unità Di Ricerca Proteomica Cardiovascolare, Centro Cardilogico Monzino, Milano, Italy, [4]Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milano, Italy, [5]Department Of Medicine, University of Padua, Padova, Italy, [6]Dipartimento Di Scienze Cliniche E Di Comunità, Università degli Studi di Milano, Milano, Italy

Background and Aims : Extracellular vesicles (EVs) are secreted into the extracellular space by several cell types. EVs carry proteins, lipids, and nucleic acids. EVs play a significant role in the process of atherosclerotic cardiovascular diseases (ASCVD). In the pathophysiology of ASCVD, proprotein convertase subtilisin/kexin type 9 (PCSK9) appears to play a crucial role, e.g., PCSK9 influences vascular smooth muscle cells (SMC) differentiation, migration and proliferation. Aim: To unveil the impact of EVs derived from human SMC overexpressing PCSK9 on the inflammatory milieu in in vitro (THP-1 and derived-macrophages) and in vivo (zebrafish) models.

Methods: EVs isolated from hSMC overexpressing or not PCSK9 (EVs^{PCSK9} and EVs^{CTR});flow cytometry, Western blot; nanoparticle tracking analysis; transmission electron microscopy; proteomic analysis; mitochondrial respiration; LDL uptake; transgenic zebrafish model of inflammation.

Results: EVs^{CTR} and EVs^{PCSK9} express tetraspanins (CD9, CD63), Alix and b1-Integrin. No differences were found in the concentrations, size and morphology between EVs^{CTR} and EVs^{PCSK9} ($1.2*10^{10}$ and $1.3*10^{10}$ particles/ml, respectively and 152.3 nm and 160.7 nm, respectively). EVs^{PCSK9} carry a higher amount of PCSK9. In THP-1 and derived-macrophages, 24-h exposure to EVs^{PCSK9}: (i) raised the gene expression of MCP-1 (27 fold), IL-1α and -b (both 28 fold), IL-6 (94 fold), and IL-8 (4 fold); (ii) raised thephosphorylation of STAT3 and decreased that of SOCS3; (iii) raised the uptake of oxLDL; (iv) decreased the mitochondrial respiration; (v) increased the migratory capacity. Local injection of EVs^{PCSK9} in the hindbrain ventricle of the *Tg(mpx:GFP)* zebrafish led to a local recruitment of neutrophil/macrophage.

Conclusions: EVs enriched in PCSK9 appear to favor a pro-atherogenic inflammatory phenotype.

065

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

COVID-19 AND CARDIOVASCULAR SYSTEM: NOT ONLY HEART BUT ALSO VASCULAR. THE EFFECTS OF THE INFECTION ON ARTERIAL STIFFNESS

POSTER VIEWING SESSION

Alessandro Maloberti, Elena Gualini, Sara Scarpellini, Michela Algeri, Marco Biolcati, Enzo Grasso, Chiara Tognola, Antonella Moreo, Cristina Giannattasio
Cardiologia 4, ospedale niguarda, milano, Italy

Background and Aims : SARS-CoV-2 determines a framework of multi-organ dysfunction that can involve the cardiovascular system creating damages of different nature. Among these, endothelial damage could play a key role in increasing arterial stiffness and thus the cardiovascular risk of infected patients. The aim of this study is to evaluate the Pulse Wave Velocity (PWV) of a population of patients after recovery from infection and to compare them with those of a group affected by arterial hypertension.

Methods: This prospective observational monocentric study involved 143 patients with previous diagnosis of Covid-19 who undergone PWV measurement during the follow-up at a median time of 3.8 months after the infection. These patients were compared to a population of 143 patients with hypertension matched by age, sex, Systolic Blood Pressure values and Body Mass Index.

Results: PWV values were higher in Covid-19 group comparing to hypertension group (10.5 ± 3.0 m/s VS 8.9 ± 2.5 m/s). Furthermore, there is a correlation between higher PWV values and lower values of SpO2% at time of admission at the Emergency Department. ($R= -0.302$; $p<0.001$).

Conclusions: SARS-CoV-2 infection seems related to increased PWV values. Moreover, higher arterial stiffness seems correlated to a worse oxygen saturation in Emergency Department. More studies with longer follow-up time are necessary to establish whether the vascular damage is reversible and whether it correlates with an increase of long-term cardiovascular risk.

066

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

MIR-210-3P MEDIATES THE UP-REGULATION OF NADPH OXIDASE EXPRESSION IN THE ATHEROSCLEROTIC AORTA OF HYPERCHOLESTEROLEMIC APOLIPOPROTEIN E-DEFICIENT MICE; POTENTIAL IMPLICATIONS FOR HUMAN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Simona-Adriana Manea[1], Mihaela Loredana Vlad[2], Alexandra G. Lazar[2], Adrian Manea[1]
[1]Molecular And Cellular Pharmacology - Functional Genomics Laboratory, Institute of Cellular Biology and Pathology 'Nicolae Simionescu', Bucharest, Romania, [2]Functional Genomics Laboratory, Institute of Cellular Biology and Pathology Nicolae Simionescu, Bucharest, Romania

Background and Aims : Reactive oxygen species overproduction driven by up-regulated NADPH oxidase (Nox) plays a major role in atherosclerosis. Hypoxia-induced miR-210-3p has been largely implicated in human malignancies as key regulator of oncogenic mechanisms. The role of miR-210-3p in atherogenesis is yet to be discovered. This study aimed at investigating the potential role of miR-210-3p in mediating Nox up-regulation in atherosclerosis.

Methods: Human non-/atherosclerotic arterial specimens, ApoE-/- mice, and human THP-1 monocytes (Mon) were studied. Male ApoE-/- mice fed a normal or atherogenic diet were randomized into four experimental groups to receive (i.p.) PBS or 10 mg/kg negative control/miR-210-3p LNA inhibitor, once per week, for 6 weeks. Resting macrophages (M0-Mac) were transfected with negative control/miR-210-3p LNA inhibitor and subjected to polarization into pro-inflammatory (M1) or anti-inflammatory (M2) phenotype. Real-time PCR, Western blot, and high-resolution fluorescence imaging were employed.

Results: Significant increases in miR-210-3p levels were detected in human carotid atherosclerotic lesions, mice atherosclerotic aorta and in M1-Mac. Bioinformatics analysis predicted that miR-210-3p targets negative regulators of NF-κB signaling (TNIP1, SOCS1). Biodistribution studies confirmed the efficient uptake of FAM-labeled miRNA control inhibitor in the atherosclerotic aorta/liver of mice. Inhibition of miR-210-3p suppressed the up-regulation of Nox1-4 expression in atherosclerotic aorta of mice and Nox1-5 subtypes in cultured human M1-Mac.

Conclusions: In experimental atherosclerosis, miR-210-3p controls the up-regulation of Nox subtypes potentially by targeting negative regulators of NF-kB-related signaling pathways. These data point to miR-210-3p as prospective therapeutic target to reduce oxidative stress in human atherosclerosis. **Acknowledgements:** Work supported by PN-III-P4-ID-PCE-2020-1898, PN-III-P2-2.1-PED-2019-2497, PN-III-P2-2.1-PED-2019-2512.

067

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

LYSINE-SPECIFIC HISTONE DEMETHYLASE 1A MEDIATES OXIDATIVE STRESS, INFLAMMATION, AND ATHEROGENESIS IN APOLIPOPROTEIN E-DEFICIENT MICE; PROSPECTIVE IMPLICATIONS FOR HUMAN ATHEROSCLEROSIS

POSTER VIEWING SESSION

Adrian Manea[1], Simona-Adriana Manea[1], Mihaela Loredana Vlad[2], Alexandra G. Lazar[2], Horia Muresian[3], Maya Simionescu[1]
[1]Molecular And Cellular Pharmacology - Functional Genomics Laboratory, Institute of Cellular Biology and Pathology 'Nicolae Simionescu', Bucharest, Romania, [2]Functional Genomics Laboratory, Institute of Cellular Biology and Pathology Nicolae Simionescu, Bucharest, Romania, [3]Cardiovascular Surgery, University Hospital of Bucharest, Bucharest, Romania

Background and Aims : Epigenetic mechanisms play a major role in the pathophysiology of cardiovascular diseases. The implication of histone methylation-based regulatory mechanisms in atherosclerosis remains poorly understood. We aimed at investigating the potential role of lysine-specific histone demethylase 1A (KDM1A) in the regulation of key down-stream molecular effectors and pathways linked to atherosclerotic plaque formation.

Methods: Human non-atherosclerotic superior thyroid artery and atherosclerotic carotid artery specimens, aorta of ApoE-/- mice, and in vitro polarized human/mouse M1/M2-macrophages (Mac) were examined. Male ApoE-/- mice fed a normal or atherogenic diet were randomized to receive via intraperitoneal injection 5 mg/kg GSK2879552, a selective KDM1A inhibitor, or its vehicle, for 4 weeks. Resting and M1/M2-Mac were cultured (24 hours) in the absence/presence of GSK2879552. Real-time PCR, Western blot, and microscopy were employed.

Results: The mRNA and protein levels of KDM1A were found significantly elevated in human carotid atherosclerotic lesions, atherosclerotic aorta of ApoE-/- mice, and in pro-inflammatory human/mouse M1-Mac. Treatment of hypercholesterolemic ApoE-/- mice with GSK2879552 significantly reduced the extent of atherosclerotic lesions and the aortic expression of NADPH oxidase (Nox1-4) subtypes, 4-hydroxynonenal-protein adducts, and markers of immune cell infiltration, inflammation and vascular remodeling (CD68/80/86, TLR2/4, NOS2, MMP2/9). Inhibition of KDM1A significantly down-regulated the expression of oxidative stress- and pro-inflammatory genes associated with M1-Mac phenotype.

Conclusions: In experimental atherosclerosis, KDM1A mediates the up-regulation of molecular effectors linked to oxidative stress, inflammation, and vascular remodeling. Histone methylation-oriented pharmacological interventions could become a significant supportive therapeutic strategy in atherosclerosis. **Acknowledgements:** Work supported by PN-III-P4-ID-PCE-2020-1898, PN-III-P2-2.1-PED-2019-2497, PN-III-P2-2.1-PED-2019-2512.

068

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

RESTRING: A SOFTWARE TO MANAGE FUNCTIONAL ENRICHMENT OF COMPLEX EXPERIMENTAL DESIGNS

POSTER VIEWING SESSION

Stefano Manzini[1], Marco Busnelli[2], Alice Colombo[1], Elsa Franchi[1], Pasquale Grossano[3], Giulia Chiesa[2]
[1]Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milan, Italy, [2]Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milano, Italy, [3]-, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Background and Aims : Functional enrichment analysis is an analytical method popularized by the ever-growing application of high-throughput techniques to provide biological insights. It tackles the problem of putting overall analyte abundance changes into a broader biological context which represents a daunting task for the average wet-biology researcher. To enable all researchers to explore more easily their data sets, we developed reString, a cross-platform software.

Methods: reString (https://github.com/Stemanz/restring), is an open-source software that seamlessly retrieves from STRING functional enrichments from multiple user-supplied gene sets, without any need for specific bioinformatics skills. With a few clicks, it aggregates multiple findings into human-readable table summaries, and user-customizable, publication-grade clustermaps and bubble plots. Everything is managed through reString's straightforward graphical user interface in just a few clicks and seconds of processing times. The software is backed with a comprehensive online documentation, YouTube installation tutorials, sample input files, online support, and a Scientific Reports publication.

Results: To demonstrate reString features, we profiled RNAseq data from aorta samples of double knockout Apoe/Apoa1 (DKO) mice, and DKO expressing human APOA1. Eight-weeks old mice were fed with normal laboratory diet (NLD) or WD for either 6 or 22 weeks. All possible diet, genotype and time comparisons were processed with reString.

Conclusions: We developed reString, a cross-platform software with a graphical user interface, written in Python, to enable all researchers the possibility of broadening the exploration of their RNAseq or high-throughput proteomics datasets, effortlessly automating a series of tasks that would be otherwise daunting if performed by hand.

069

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

ATHEROSCLEROSIS AND RECURRENT PREGNANCY LOSSES: COMMON BIOMARKERS INVOLVED ?

POSTER VIEWING SESSION

Sarah Mohamad[1], Maryam Salim[2], Claire Crampes[3], Stephane Claverol[4], Nawaf Jurdi[5], Gisèle Clofent-Sanchez[1], Iman El Hajj Dib[2], Marie-Josée Jacobin-Valat[1]
[1]Cnrs Umr 5536, university of bordeaux, bordeaux, France, [2]Nord, Lebanese university, tripoli, Lebanon, [3]Aquitaine, ENSTBB, Bordeaux, France, [4]Aquitaine, CGFB, Protéome pole, Bordeaux, France, [5]Riad El-solh, american univerity of beirut, beirut, Lebanon

Background and Aims : The occurrence of recurrent pregnancy losses (RPL) in women patients can be due to placental lesions such as atherosis (ATS), a vascular change similar to atherosclerosis (ATH). Women vulnerable to RPL are at higher risk of ATH and women with a family history of ATH have a predisposition to have pregnancy loss. These data underline the existence of potential common biomarkers to these two pathologies. Thus, the aim of this study is to identify the biomarkers of RPL linked to ATH in order to understand the vascular molecular processes of RPL and to offer personalized therapy in the future.

Methods: A human monoclonal antibody named P3, selected for its specificity against the galectin 3 protein (Gal3) over expressed in atheroma, was tested on human placental biopsies from RPL and compared with a control group of placentas obtained from normal childbirth. For the histological characterization of placental lesions, placental biopsies were stained with hematoxylin and eosin. The bio-reactivity of P3 was tested by immunohistochemistry and the staining was quantified using imageJ software. To identify P3 target in placental protein extracts, immunoprecipitations were performed and the eluates were analyzed by western blot followed by proteomics studies to validate gal3 as the placental P3 target.

Results: highlight P3 bio-reactivity on placenta with a staining 3.8-fold higher in pathological placentas compared to controls.

Conclusions: These results hold great promise for the choice of galectin 3 as biomarker for atherosis and the use of P3 antibody for the prevention and therapy of recurrent pregnancy losses

070

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

A NOVEL NEUTROPHIL-LIKE IN VITRO MODEL FOR THE STUDY OF HUMAN NEUTROPHIL POLARIZATION

POSTER VIEWING SESSION

Sinziana Popescu, Mihai A. Publik, Bogdan M. Preda
Regenerative Medicine, Institute of Cellular Biology and Pathology "Nicolae Simionescu", Bucharest, Romania

Background and Aims : Neutrophils are key players in the activation and regulation of innate and adaptive immunity. As mediators of the inflammatory response in cardiovascular diseases, the polarity of neutrophils towards pro- and anti-inflammatory phenotypes has recently been advanced. Considering that their lifespan is very limited and long-term in vitro studies are challenging, our aim was to develop and characterize a representative model of human neutrophil-like cells.

Methods: Human HL-60 promyeloblasts were cultured for 5 days in complete media supplemented with 1.3% DMSO, then assessed for proliferation, nuclear segmentation by cytochemistry, expression of cell-surface markers by flow cytometry and differentiation markers by qPCR. Polarization of the neutrophil-like cells was induced for 48h towards the pro-inflammatory phenotype (N1) in the presence of LPS and IFNγ, whereas IL-4 was used for the anti-inflammatory phenotype (N2), then assessed for viability and gene expression.

Results: Promyeloblasts differentiation was confirmed by down-regulation of TERT expression, strong FPR1 and Integrinβ3 induction (~300-fold and ~25-fold over control, respectively) and cell surface expression of CD11b and CD18. Equally, neutrophil-like cells exhibited nuclear segmentation, decrease in proliferation and maintained similar viability in culture. Polarization towards N1 phenotype was confirmed by up-regulation of pro-inflammatory genes MCP-1, IL-1β, TNFα and IRF7, whereas N2 markers CD206 and TGM2 were highly induced following IL-4 stimulation. Cellular viability remained comparable under both treatments.

Conclusions: Promyeloblast differentiation by DMSO generates neutrophil-like cells that can be polarized towards N1/N2 phenotypes. These resemble subsets of native neutrophils and can be employed for long-term in vitro studies.

071

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

SERUM DIPEPTIDYL PEPTIDASE-4 LEVELS AND DPP4 RS17574 POLYMORPHISM IN SUBCLINICAL ATHEROSCLEROSIS INDIVIDUALS WITH AND WITHOUT FATTY LIVER. THE GEA MEXICAN STUDY.

POSTER VIEWING SESSION

Rosalinda Posadas-Sánchez, Adrián Hernández-Díaz Couder, Fausto S.-M. Sánchez-Muñoz, Gilberto Vargas-Alarcón
Endocrinology, Instituto Nacional de Cardiologia, Ciudad de Mexico, Mexico

Background and Aims : Dipeptidyl peptidase-4 (DPP4) levels are related to non-alcoholic fatty liver (NAFLD/NASH), and this condition is associated with subclinical atherosclerosis (SA). On the other hand, the association of *DPP4* gene polymorphisms with cardiovascular disease has been suggested. The present study aimed to establish whether DPP4 levels and the *DPP4* rs17574 polymorphism are associated with fatty liver (FL) in individuals with SA.

Methods: In 390 individuals with SA, 145 with and 245 without FL belonging to the GEA Mexican study control group. DPP4 serum levels were quantified using a Bioplex system. The *DPP4* rs17574 polymorphism was genotyped using TaqMan assays. The associations were evaluated using logistic regression analyses adjusted for potential confounders.

Results: DPP4 serum levels were similar in FL and non-FL individuals (128 [105-165] vs 123 [98-152], p=0.067). Under the recessive model, the *DPP4* rs17574 *GG* genotype was associated with an increased risk of FL in individuals with SA (OR=4.186, p=0.037). Non-statistical significance was observed when DPP4 levels in the whole sample were analyzed stratifying for *DPP4* rs17574 genotypes. When the same analyses were done separately in both groups, significant differences were observed in the FL group; subjects with *AA* genotype had the highest DPP4 levels (134[106-175] ng/mL) compared with *AG* (128[114-149] ng/mL) and *GG* genotypes (80[71-117 ng/mL], p=0.019).

Conclusions: Our data suggest that the *DPP4* rs17574*GG* genotype could be envisaged as a genetic risk marker for FL in SA. In FL individuals, the rs17574*GG* genotype was associated with the lowest DPP4 levels. CONACyT CB-2016-01-286065

072

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

MITOCHONDRIAL DNA CRISPR/CAS9 EDITING: AN APPROACH TO ESTABLISHING THE ROLE OF MITOCHONDRIAL MUTATIONS IN ATHEROGENESIS

POSTER VIEWING SESSION

Vasily N. Sukhorukov, Vladislav A. Kalmykov, Victoria A. Khotina, Andrew V. Omelchenko, Varvara Orekhova, Alexander N. Orekhov
Unit 21, Institute for Atherosclerosis Research, Moscow, Russian Federation

Background and Aims : We have previously found an association of some mitochondrial mutations with asymptomatic atherosclerosis in the carotid arteries of patients. The most direct way to elucidate the role of these mutations in atherogenesis is by editing the mitochondrial genome. The aim of this work was to develop an approach to eliminate mitochondrial mutations from mitochondrial DNA (mtDNA).

Methods: The mitoCAS9 vector was used to produce RNA complex, consisting of Cas9 nuclease linked to sgRNA. Mannose liposomes were used to deliver RNA complex in the THP-1 cells. The THP-1 cybrid cells that carried Cytb G15059A mutation. The efficiency of mutation elimination was assessed by T7E1, qPCR, and ddPCR.

Results: The elimination of Cytb G15059A mutation by MitoCas9 RNA complex was successfully confirmed by T7E1, ddPCR, and sequencing. We found that the MitoCas9-RNA complex can cleave up to 92% mtDNA, and the heteroplasmy level was reduced up to 3.7% from 68%. Moreover, we found that some double-strand breaks were repaired by the mechanism of microhomology-mediated end joining (MMEJ). The possible matrix for MMEJ was a part of the mitoCas9 vector, that was delivered to mitochondria together with the RNA complex. This mechanism might be used to incorporate mitochondria mutations of interest in “healthy” mitochondria.

Conclusions: The method to eliminate mitochondrial mutations was created. It might be possible to create a novel approach of mtDNA editing via the MMEJ mechanism. This study was supported by Russian Science Foundation, Grant # 22-15-00064

073

Topic: *ASA01 - PATHOGENESIS OF ATHEROSCLEROSIS / ASA01-12 Other*

IL-37 POLYMORPHISMS ARE ASSOCIATED WITH CARDIOVASCULAR RISK FACTORS IN INDIVIDUALS WITH SUBCLINICAL ATHEROSCLEROSIS. THE GEA MEXICAN STUDY.

POSTER VIEWING SESSION

Gilberto Vargas-Alarcón[1], Fabiola López-Bautista[2], Rosalinda Posadas-Sánchez[3]
[1]Research Direction, Instituto Nacional de Cardiología Ignacio Chávez, Mexico, Mexico, [2]Molecular Biology, Instituto Nacional de Cardiología Ignacio Chávez, Mexico, Mexico, [3]Endocrinology, Instituto Nacional de Cardiologia, Ciudad de Mexico, Mexico

Background and Aims : Interleukin 37 (IL-37) is an anti-inflammatory cytokine that belongs to the interleukin 1 family. This cytokine is involved in the regulation of cholesterol homeostasis and has been associated with the presence of atherosclerosis. The aim of the present study was to evaluate the association of the *IL-37* polymorphisms with subclinical atherosclerosis (SA), and with cardiovascular risk factors.

Methods: Seven *IL-37* polymorphisms (rs2708965, rs2708962, rs2708961, rs2708960, rs2708958, rs2708947, and rs2723192) were determined by TaqMan assays in a group of 341 individuals with SA and 951 healthy controls belonging to the Cohort of the GEA Mexican Study. The associations were evaluated by logistic regression using inheritance models adjusted by confounding variables.

Results: *IL-37* polymorphisms were not associated with the presence of SA. However, under codominant model, these polymorphisms were associated with high risk of fatty liver [rs2708965 (OR = 2.36, p = 0.045), rs2708960 (OR = 2.38, p = 0.047), rs2708947 (OR = 2.63, p = 0.039), and rs2723192 (OR = 3.46, p = 0.012)], HOMA-IR [rs2708965 (OR = 3.65, p = 0.023), rs2708962 (OR = 3.62, p = 0.032), rs2708960 (OR = 3.51, p = 0.028), and rs2723192 (OR = 4.00, p = 0.032)], T2DM [rs2708961 (OR = 3.49, p = 0.029), rs2708958 (OR = 2.42, p = 0.041), and rs2708947 (OR = 2.42. p = 0.042)].

Conclusions: The *IL-37* polymorphisms were not associated with the risk of SA. However, an association of the polymorphisms with a high risk of fatty liver, T2DM, and high levels were observed. CONACYT 286659

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

LIPOPROTEIN(A) AND PREVALENT ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN PATIENTS WITH TYPE 2 DIABETES

POSTER VIEWING SESSION

Fotios Barkas[1], Ad Koutsogianni[1], Petros Adamidis[1], Georgia Anastasiou[1], Sisi-Fotini Sakkou[1], Konstantina Kyrili[1], George Liamis[1], Evangelos Liberopoulos[2]
[1]Department Of Internal Medicine, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannnina, Greece, [2]1st Propaideutic Department Of Medicine, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Background and Aims : Type 2 diabetes (T2D) and increased lipoprotein (a) [Lp(a)] are associated with elevated risk of atherosclerotic cardiovascular disease (ASCVD). We aimed to investigate the joint effect of hyperLp(a) and T2D on ASCVD prevalence.

Methods: This was a case control study including adult patients with dyslipidemia followed-up at the outpatient Lipid Clinic of Ioannina University General Hospital, Greece. HyperLp(a) was defined as Lp(a) level ≥30 mg/dL. Independent and joint effects of hyperLp(a) and T2D on ASCVD prevalence were determined using regression models adjusted for traditional cardiovascular risk factors.

Results: Among 941 subjects [49 years, 47% males, 7% with T2D, 36% with hyperLp(a)], 13% (n=124) were diagnosed with ASCVD. A higher ASCVD prevalence was found in patients with both T2D and hyperLp(a) (OR: 2.48, 95% CI: 1.05-5.89, n=39) compared with the group of non-diabetic patients with Lp(a) <30 mg/dL (n=536). No significant differences were found for other comparisons (OR: 0.63, 95% CI: 0.20-1.97 for those with T2D and Lp(a) <30 mg/dL, n=31; OR: 1.33, 95% CI: 0.84-2.10 for those without T2D, but Lp(a) ≥30 mg/dL, n=335). Among patients with T2D, hyperLp(a) multiplied the risk of prevalent ASCVD (OR: 4.77, 95% CI: 1.23-18.50).

Conclusions: HyperLp(a) increases the risk of prevalent ASCVD in patients with T2D. This finding may have implications regarding treatment intensity.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

JOINT EFFECT OF FAMILIAL HYPERCHOLESTEROLEMIA AND HYPERLIPOPROTEINEMIA(A) ON THE RISK OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

POSTER VIEWING SESSION

Fotios Barkas[1], Georgia Anastasiou[1], Petros Adamidis[1], Ad Koutsogianni[1], Chrysa Styla[1], Christos Rizos[1], Konstantina Kyrili[1], George Liamis[1], Evangelos Liberopoulos[2]
[1]Department Of Internal Medicine, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannnina, Greece, [2]1st Propaideutic Department Of Medicine, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Background and Aims : Familial hypercholesterolemia (FH) and elevated lipoprotein(a) (Lp[a]) are associated with increased risk of atherosclerotic cardiovascular disease (ASCVD). We aimed to investigate the joint effect of FH and hyperLp(a) on the risk of prevalent ASCVD.

Methods: This was a cross-sectional study including adult patients with dyslipidemia followed-up at the outpatient Lipid Clinic of Ioannina University General Hospital, Greece. FH diagnosis was based on the Dutch Clinic Lipid Network Criteria (score ≥5), while hyperLp(a) levels was defined as Lp(a)>30 mg/dL. Independent and joint effects of FH and hyperLp(a) with ASCVD prevalence were determined using binary logistic regression models adjusted for traditional cardiovascular risk factors.

Results: Among 941 participants (49 years, 47% males, 54% with FH, 36% with hyperLp[a]), the prevalence of ASCVD was 12.9% (n=121). Compared with subjects without FH and non-elevated Lp(a) (n=296), those with both FH and hyperLp(a) had the highest ASCVD prevalence (adjusted OR: 2.13; 95% CI: 1.14-3.96, n=195). Among FH patients, hyperLp(a) tripled the risk of prevalent ASCVD (adjusted OR: 2.83, 95% CI: 1.39-5.78). Likewise, among patients with hyperLp(a), FH was associated with a 3-fold increase in the risk of prevalent ASCVD (adjusted OR: 3.23, 95% CI: 1.47-7.13).

Conclusions: FH and hyperLp(a) have synergistic effects on ASCVD prevalence. This finding may have therapeutic implications regarding treatment intensity.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

LIPIDOMIC PROFILING AND OXLDL MEASUREMENT FOR RISK STRATIFICATION IN PATIENTS WITH ELEVATED LP(A) WITH AND WITHOUT ESTABLISHED ASCVD

POSTER VIEWING SESSION

Moritz Ferch[1], Lisa M. Poindl[1], Paul Fellinger[1], Thomas Koller[2], Reinhold Innerhofer[2], Birgit Reiter[2], Christoph J. Binder[2], Thomas Stimpfl[2], Alexandra Kautzky-Willer[1], Yvonne Winhofer-Stöckl[1]
[1]Department Of Internal Medicine Iii, Division Of Endocrinology And Metabolism, Medical University Vienna, Vienna, Austria, [2]Department Of Laboratory Medicine, Medical University Vienna, Vienna, Austria

Background and Aims : Lipoprotein(a) has been recognized as heritable, major, independent and probably causal driver of residual cardiovascular risk. Distinct lipid species, such as ceramides and oxidized phospholipids on apolipoprotein-B-containing lipoproteins (oxPL/apoB) have previously been identified as major mediators of the atherogenicity of plasma profiles. Therefore, comparing the lipidome of cohorts of hyperlipoproteinemia(a) patients with established ASCVD to those spared from ASCVD might elucidate pathophysiological implications of these constituents and aid in further cardiovascular risk stratification in hyperlipoproteinemia(a) patients.

Methods: With our single-center, longitudinal dyslipidemia registry and biobank facilitating the provision of samples, lipidomic analyses on ceramide species as well as measurements of oxPL/apoB and high-sensitivity C-reactive protein (hs-CRP) will be performed in cohorts with elevated (>75 nmol/L) lipoprotein(a) with and without established ASCVD, matched for age, BMI and sex.

Results: Patients (n=102) with and without ASCVD do not significantly differ in age (53.2±12.7 vs 49.5±12.0, p=0.122), BMI (27.3±5.0 vs 28.0±5.2, p=0.461), or sex (52.9% males). Lipoprotein(a) levels (nmol/L) are higher in the ASCVD cohort (235.0 (182.0 - 323.0) vs 199.0 (145.0 - 291.0), p=0.022) while LDL-C levels (mg/dL) are lower (56.4 (33.8 - 71.8) vs 133.6 (87.0 - 168.8), p<0.001), due to higher use of lipid-lowering therapy (lipid apheresis 15.7% vs 0%, p=0.01; PCSK9 inhibitors 33.3% vs 2.0%, high-intensity statins 56.9% vs 11.8%, ezetimibe 62.7% vs 13.7%, p<0.001). Results of lipidomic analyses are pending at submission deadline and will be presented at the meeting.

Conclusions: Results of the lipidomic measurements might provide insights in previously unidentified markers for cardiometabolic risk stratification specific in hyperlipoteinemia(a) patients.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

BIOCHEMICAL ROLE OF LIPOPROTEIN SCREENING IN PATIENTS WITH PREMATURE MIOCARDIAL INFARCTION AND ELITE ATHLETES

POSTER VIEWING SESSION

Fabio Fimiani[1], Felice Gragnano[2,3], Arturo Cesaro[2,3], Andrea Vergara[2,3], Antonio De Pasquale[2,3], Ettore Blasi[2,3], Paolo Calabro'[2,4]
[1]Unit Of Inherited And Rare Cardiovascular Diseases, AORN Dei Colli "V. Monaldi" , Napoli, Italy, Naples, Italy, [2]Division Of Clinical Cardiology, AORN "Sant'Anna e San Sebastiano", Caserta, Italy, [3]Department Of Cardiothoracic And Respiratory Sciences, Division of Cardiology, Department of Cardiothoracic and Respiratory Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy, [4]Department Of Cardiothoracic And Respiratory Sciences, Division of Cardiology, Department of Cardiothoracic and Respiratory Sciences, University of Campania "Luigi Vanvitelli", Caserta, Italy

Background and Aims : Elevated concentrations of lipoprotein(a) [Lp(a)] represent a well-established risk factor for atherosclerotic disease. However, its role in patients with premature coronary artery disease remains unclear. Moreover, physical activity has been shown to improve lipoprotein metabolism and reduce the risk of coronary artery disease. We investigated the role of Lp(a) screening in patients with premature myocardial infarction and elite athletes to assess its impact on clinical decision-making and the influence of physical activity on Lp(a) profile.

Methods: We prospectively evaluated Lp(a) in 105 consecutive patients (age <50 years) admitted for premature myocardial infarction and 30 healthy elite basket athletes (age <28 years). Lp(a) was measured with ELISA at baseline and during follow-up in stable clinical conditions. Lp(a) ≥30 mg/dL was considered as elevated.

Results: In our premature myocardial infarction population, Lp(a) was elevated (≥30 mg/dL) in 28.5% (n=30) of cases (mean follow-up: 9.6 months). Moreover, 12.3% (n=13) of patients had Lp(a) ≥70 mg/dL, with clinical indications to Lp(a) apheresis. All patients with high levels of Lp(a) were on optimal medical therapy according to the European guidelines. In our elite athletes population, Lp(a) was elevated (≥30 mg/dL) in 20% (n=3) of cases, and 13% (n=4) of subjects had Lp(a) ≥70 mg/dL.

Conclusions: Elevated Lp(a) levels are highly prevalent in young patients presenting with myocardial infarction. In this pilot study, we also found elevated levels of Lp(a) in elite athletes. Systematic screening of Lp(a) levels might be helpful to intensify the control of risk factors in young patients and elite athletes.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

THE EFFECT OF THE LPA VARIANT P.THR3888PRO ON LIPOPROTEIN(A) AND CORONARY ARTERY DISEASE IS MODIFIED BY THE LPA KIV-2 SPLICE SITE VARIANT 4925G>A

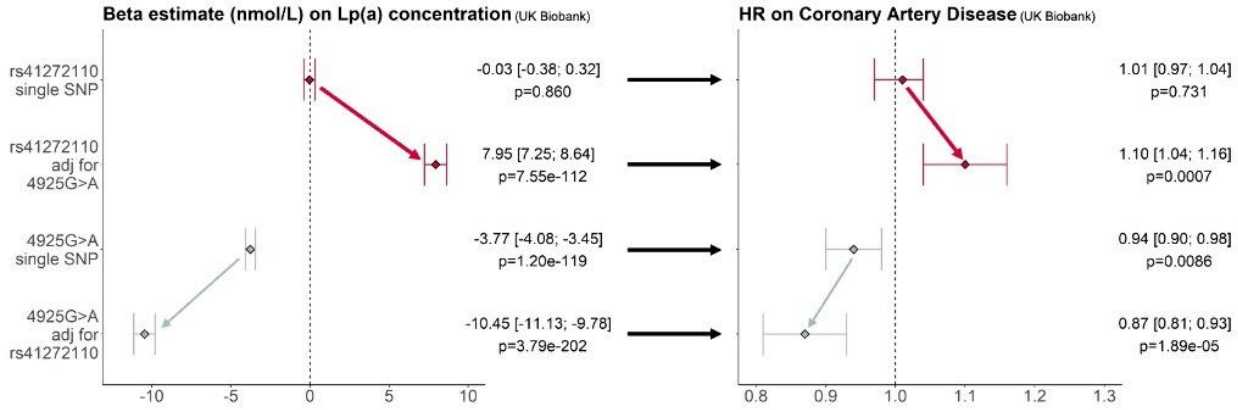
POSTER VIEWING SESSION

Rebecca Grüneis[1], Claudia Lamina[1], Silvia Di Maio[1], Sebastian Schönherr[1], Peter Zöscher[1], Lukas Forer[1], Annette Peters[2,3], Christian Gieger[2,3,4], Anna Köttgen[5,6], Florian Kronenberg[1], Stefan Coassin[1]
[1]Institute Of Genetic Epidemiology, Medical University of Innsbruck, Innsbruck, Austria, [2]Institute Of Epidemiology, Helmholtz Zentrum München, Neuherberg, Germany, [3]German Center For Diabetes Research (dzd), Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany, [4]Research Unit Of Molecular Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany, [5]Institute Of Genetic Epidemiology, University of Freiburg, Freiburg, Germany, [6]German Chronic Kidney Disease Study, University Hospital Erlangen, Erlangen, Germany

Background and Aims : Lipoprotein(a) [Lp(a)] plasma concentrations are mainly regulated by the *LPA* gene. Besides the KIV-2 repeat (a complex copy number variation), multiple SNPs pronouncedly modify Lp(a) levels (e.g. the recently described KIV-2 variant 4925G>A). However, little is known about non-linear and/or epistatic mechanisms and SNP interactions. Thus, we investigated the impact of the interaction between the largely investigated *LPA* variant p.Thr3888Pro (rs41272110) and the KIV-2 variant 4925G>A on Lp(a) concentration and CAD risk.

Methods: The effect of the interaction between rs41272110 and 4925G>A on Lp(a) was analyzed by quantile regression in the German Chronic Kidney Disease (GCKD), KORA-F3 and KORA-F4 studies (total=10,405, female: 45.6%). Effect on CAD risk was investigated by survival analysis in UK Biobank (n=186,088).

Results: We found a partial linkage disequilibrium (LD) between rs41272110 and 4925G>A (R^2=0.836-0.872, D'=0.984-0.985). Rs41272110 alone had no effect on Lp(a) (β=-0.06, [-0.79;0.68], p=0.879). However, adjusting rs41272110 for 4925G>A revealed a pronounced Lp(a)-increasing effect of rs41272110 (β=+9.40 mg/dL, [6.45;12.34], p=4.07E-10), which at population scale was masked by the Lp(a)-lowering SNP 4925G>A. Adjustment of apolipoprotein(a) isoforms further modified the effect estimates. Consistent with the effect on Lp(a), rs41272110 alone showed no effect on CAD (HR=1.01, [0.97;1.04], p=0.731), but a joint model with both SNPs reveals significantly higher CAD risk (HR=1.10, [1.04;1.16], p=6.9e-04) in rs41272110- carriers not carrying 4925G>A (4% of the population).



Conclusions: The *LPA* gene contains complex LD structures with pronounced SNP-SNP interactions. This emphasizes the importance of including SNP interactions into Lp(a) association studies to improve genetic prediction of Lp(a) and CAD.

079

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

ASSOCIATION OF LPA AND LEVELS OF HBA1C IN PATIENTS WITH DIABETES MELLITUS TYPE 2

POSTER VIEWING SESSION

Styliani Lagou, Alexandra Sianni, Kyparissia Sitara, Marina Tzanni, Euaggelia Mougkaraki, Evangelia Nikoli, Sofia Miliou, Nikolaos Fytrakis, Zoitsa Zachariadou, Archontoula Fragkou
2nd Department Of Internal Medicine, Elpis General Hospital of Athens, Athens, Greece

Background and Aims : Lipoprotein(a) [Lp(a)], is a well-recognized cardiovascular risk factor. Emerging data support a correlation between elevated levels of Lp(a) and the development of diabetes mellitus type 2. To investigate whether there is correlation between Lp(a) levels and HbA1c, in diabetic patients type 2.

Methods: We enrolled 108 patients(47.2% males,52.7% females),mean aged 78.2±10 years with Diabetes Mellitus type 2, under treatment with either insulin and/or oral medication. Follow up visits was at 3,9 and 12 months. In each visit, total cholesterol, triglycerides, HDL, LDL, Lp(a) and HbA1c was measured. We divide the diabetic patients into 2 groups. Group A(n=48) had a baseline HbA1c 6,50–7,50% and Group B(n=60) with baseline HbA1c>7,50%. Diet and/or drug modification was made in all patients in order to optimize regulation of diabetes mellitus.

Results: Group A: Lpa=25.92±1.98 mg/dl (3.4<Lpa<42.1) in 3 months, Lpa=24.33±1.87 mg/dl (3.3<Lpa<41.2) in 9 months (p=0.0565), Lpa=24.07±1.87 mg/dl (3.1<Lpa<42) in 12 months(p= 0.0336), HbA1c = 6.96%±0.1(5.50%<HbA1c<7.40%) in 3 months, HbA1c = 6.65% ±0.1 (5.30%<HbA1c<7.1%) in 9 months (p=0.026), HbA1c=6.37±0.09 (5.1%<HbA1c<6.9%) in 12 months (p=0.0001). Group B: Lpa=27.69±1.95 (4.43<Lpa<48) in 3 months, Lpa =24.46±1.68 mg/dl (4<Lpa<45) in 9 months (p=0.0004), Lpa=22.16±1.4 mg/dl 4<Lpa<40.6) in 12 months (p<0.0001), HbA1c=8.44%±0.19 (7.60%<HbA1c<11.30%) in 3 months, HbA1c=8.07%±0.2 (7.20%<HbA1c<11.00%) in 9 months (p=0.013), HbA1c=7.81%±0.2 (6.90%<HbA1c<10.70%) in 12 months(p=0.0001).

Conclusions: Our data support an association between high Lp(a) HbA1c in patients with diabetes mellitus type 2. Optimization of diabetes therapeutic strategy reflects in a reduction of Lp(a). The reduction of Lp(a) in combination with lower HbA1c levels may lower the cardiovascular risk of diabetic patients.

080

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

TYPE 2 DIABETES SIGNIFICANTLY MODULATES THE POWER OF LIPOPROTEIN(A) TO PREDICT CARDIOVASCULAR EVENTS AND MORTALITY IN YOUNG CORONARY ARTERY DISEASE PATIENTS

POSTER VIEWING SESSION

Arthur Mader[1], Maximilian Maechler[1], Barbara Larcher[1], Lukas Sprenger[1], Valentin Grabher[2], Andreas Leiherer[2], Axel Muendlein[2], Alexander Vonbank[1], Heinz Drexel[3], Christoph H. Saely[4]
[1]Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria, [2]Academic Teaching Hospital Feldkirch, Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria, [3]Internal Medicine, County Hospital Bregenz, Bregenz, Austria, [4]Medical Sciences, Private University of the Principality of Liechtenstein, Triesen, Liechtenstein

Background and Aims : Lipoprotein(a) [Lp(a)] is an important cardiovascular risk factor especially in young individuals. The power of Lp(a) to predict cardiovascular events in young coronary artery disease (CAD) patients with type 2 diabetes (T2DM) however is unclear and is addressed in the present study.

Methods: Lp(a) was measured in a cohort of 731 patients with angiographically proven CAD who were aged <65 years. Vascular events were recorded over a mean follow-up of 6.6±3.2 years.

Results: At baseline, 216 patients had T2DM, and 515 did not have diabetes. During follow-up, 30.2% of our patients suffered cardiovascular events. Lp(a) proved to be a strong and independent predictor of vascular events in the total study cohort (standardized adjusted HR=1.30 [1.07-1.56]; p=0.007). In subgroup analyses by diabetes status, Lp(a) significantly predicted vascular events in non-diabetic patients (standardized adjusted HR= 1.39 [1.12-1.74]; p=0.003) but not in diabetic patients (standardized adjusted HR=0.93 [0.63-1.38]; p=0.731). An interaction term Lp(a)xT2DM was significant (p=0.002), indicating that T2DM significantly modulated the power of Lp(a) to predict cardiovascular events.

Conclusions: We conclude that type 2 diabetes significantly modulates the power of Lp(a) to predict cardiovascular events in CAD patients <65 years.

081

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

PCSK-9 INHIBITORS AND THE REDUCTION OF SERUM LIPOPROTEIN (A) LEVELS: EXPERIENCE OF THE REFERENCE CENTER

POSTER VIEWING SESSION

Dunja Leskovar, Dražen Perica, Nediljko Šućur, Ana Godan Hauptman, Ivan Pećin, Željko Reiner
Internal Medicine, Divison For Metabolic Diseases, University Hospital Centre Zagreb, Zagreb, Croatia

Background and Aims : Lipoprotein (a) is an LDL-like lipid particle that represents a great risk factor for cardiovascular disease, therefore, its reduction is of great importance. So far, the only lp(a) lowering therapy available is PCSK-9 inhibitors that reduce lp(a) levels by 25-30%. Although the mechanism of how pcsk-9 inhibitors reduce lp(a) levels is unclear, some studies show that at lower LDL-cholesterol levels, lp(a) levels decrease more with the assumption of better competence for LDL-receptor site.

Methods: We compared 51 patients on pcsk-9 inhibitor therapy (>3 months) with elevated lp(a) (>75 nmol/L, >0,5 g/L).

Results: The average age of our patients was 52,74 years with an almost equal distribution of male and female gender (53%, 47%). The overall percentage in reduction of lp (a) levels during 3 months was 30.78% (max: 72%, min: 5%). T-test of paired samples revealed a statistically significant difference (t = 5,2015; p = 0.00000156) at serum lp (a) concentrations before (M = 127.05, SD = 133.93) and after pcsk-9 inhibitor therapy (M = 82.29, SD = 81.06). The maximum observed reduction of 72% was observed in a patient who was previously on the statin therapy at the maximum dosage.

Conclusions: Our experience confirms previous research in which pcsk-9 inhibitors reduce lp (a) concentration by 30%. Comparing targeted concomitant therapy, we have observed a trend of greater reduction in lp (a) levels with pcsk-9 inhibitor therapy in patients who are previously on the maximum statin dose, suggesting possible metabolism of the particle itself via the LDL receptor by the mechanism of competition.

082

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

CARDIOVASCULAR DISEASE IN PATIENTS WITH ELEVATED LP(A) – REAL WORLD DATA FROM A SPECIALIST LIPID CLINIC IN SCOTLAND.

POSTER VIEWING SESSION

Christina Kanonidou, Maurizio Panarelli
Glasgow Royal Infirmary, Nhs Greater Glasgow And Clyde, Lipid Clinic/Department of Clinical Biochemistry, Glasgow, United Kingdom

Background and Aims : The 2019 ESC/EAS Guidelines acknowledge the substantial lifetime atherosclerotic cardiovascular disease (ASCVD) risk conferred by very high inherited Lp(a) levels. The UK Biobank data demonstrated a linear gradient in risk across the Lp(a) distribution, without a threshold effect. As this risk is lifelong, early diagnosis and intervention may yield significant benefits for CVD prevention. We studied the characteristics of patients with hyperlipoproteinaemia(a) and ASCVD.

Methods: We conducted a retrospective audit of patients who attended our clinic from 01/01/2019-18/06/2021 and had a Lp(a) measurement. We focused on those with raised Lp(a) and documented ASCVD. Since the Lp(a) threshold determining risk is debatable, we included patients with Lp(a) ≥70 mg/dL, which is unequivocally associated with increased risk.

Results:

Table 1. Characteristics of patients with Lp(a) ≥70 mg/dl and ASCVD (N=15).

Age at the time of Lp(a) testing, years	62.6 ± 11.2
Male	4 (27)
Race	
White	14 (93.3)
South Asian	1 (6.7)
Form of ASCVD	
Coronary heart disease	15 (100)
Cerebrovascular disease	1 (6.7)
Peripheral vascular disease	3 (20)
Aortic stenosis	1 (6.7)
Age at the time of ASCVD diagnosis, years	55.8 ± 9.9
Personal history of premature ASCVD	12 (80)
Definite FH (genetically confirmed)	1 (6.7)
Diabetes	4 (27)
Hypertension	7 (46.7)
Obesity	7 (46.7)
Smoking (active smoker or <5 years from cessation)	6 (40)
Family history of ASCVD in first degree relative	15 (100)
Family history of premature ASCVD	11 (73.3)
Positive personal and family history of premature ASCVD	8 (53.3)
Lp(a), mg/dL	109.8 (97.1 – 116.1)
Pre-treatment LDL-C, mmol/L	4.8 (4.5 - 6.1)
On lipid-lowering medication at the time of Lp(a) testing	
Low-intensity LDL-lowering therapy	3 (20)
Moderate-intensity LDL-lowering therapy	4 (26.6)
High-intensity LDL-lowering therapy	8 (53.3)
LDL-C while on treatment, mmol/L	2.8 (2.4 - 4.0)
Lp(a)-corrected LDL-C while on treatment, mmol/L*	1.9 (1.5 - 3.3)

Values are: Mean ± SD, N (%), Median (interquartile range)
ASCVD: atherosclerotic cardiovascular disease; FH: heterozygous familial hypercholesterolaemia
*Lp(a)-corrected LDL-C (mmol/L) = LDL-C (mmol/L) – [Lp(a) (mg/dL) x 0.0078]

Fifteen of 88 patients with Lp(a) ≥70 mg/dL (17%) had ASCVD. Table 1 presents their characteristics. The median Lp(a) level of this group was 109.8 mg/dL. Twelve patients (80%) had personal and 11 (73.3%) family history of premature ASCVD (<60 years of age). All had ≥2 ASCVD risk factors. Four subjects (26.6%) suffered recurrent CVD events, proved fatal in 2 of them. Despite being on maximally tolerated treatment, 93.3% of patients failed to achieve the recommended LDL-C goal of <1.4 mmol/L; this percentage was 80% when the Lp(a)-corrected LDL-C level was evaluated.

Conclusions: Among patients with Lp(a) ≥70mg/dL, 1 in 6 (15/88) had ASCVD, while 1 in 11 (8/88) had positive personal and family history of premature ASCVD. This study underscores the need for early identification and CVD risk management of patients with hyperlipoproteinaemia(a) and for targeted treatments.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

EXTREME LIPOPROTEIN(A) LEVELS AND SUB-CLINICAL ATHEROSCLEROTIC DISEASE: A DESCRIPTIVE CASE-CONTROL STUDY (THE LP(A)EXTRAVASC STUDY)

POSTER VIEWING SESSION

Jean-François Perregaux, Eric Bruckert, Antonio Gallo
Paris, Cardiovascular prevention unit, Pitié-Salpêtrière Hospital, AP-HP, PARIS, France

Background and Aims : Lipoprotein(a) [Lp(a)] contributes to atherogenesis, reduces fibrinolysis leading to thrombogenesis and increases pro-inflammatory response. Extreme levels of Lp(a) are associated with an increased risk of cardiovascular mortality, coronary heart disease, peripheral artery disease and stroke in primary prevention. Whether extreme Lp(a) is associated with sub-clinical atherosclerotic cardiovascular disease (sASCVD) has not been described yet. The aim of this study was to assess sASCVD in patients with extreme Lp(a) levels in primary prevention.

Methods: 65 patients with Lp(a) > 130 mg/dl and 79 with Lp(a) < 30 mg/dl without any cardiovascular events were recruited in this retrospective case-control study. We investigated sASCVD through coronary artery calcium (CAC) and carotid and femoral Doppler ultrasonography. Wilcoxon-Mann-Whitney and Chi-2 statistical tests were used for comparisons.

Results: Main characteristics of the study population are shown in Table 1. Age and sex distribution was similar for both groups. There was no difference between both groups for total CAC (high Lp(a): 34.1 (0.0-133.3) HU vs. low Lp(a): 68.3 (0.0-195.1) HU, p=0.497), prevalence of carotid atherosclerosis (65.8% vs. 67.7%, p=0.813, respectively), and prevalence of femoral atherosclerosis (62.0% vs. 70.8%, p=0.270,

respectively).

Table 1: Characteristics of the study population

		Control (n=79)	Case (n=65)	P value
Sex (female)	n (%)	44 (55.7)	45 (69.2)	0.096
Age	years	61 (50-66)	61 (54-68)	0.571
BMI	kg/m^2	25.1 (22.7-29.1)	25.6 (23.7-30.1)	0.143
Waist-to-hip ratio	ratio	0.92 (0.84-0.98)	0.92 (0.87-0.98)	0.655
SBP	mmHg	116 (109-128)	114 (105-123)	0.226
DBP	mmHg	67 (62-73)	65 (60-75)	0.445
Fasting glucose	mmol/l	5.00 (4.80-5.55)	5.10 (4.80-5.55)	0.721
HbA1c	%	5.8 (5.6-6.1)	5.9 (5.7-6.2)	0.161
Creatinine	µmol/l	78 (64-89)	72 (65-87)	0.716
CRP	mg/L	1.1 (0.6-2.6)	1.5 (0.7-3.6)	0.164
Total Cholesterol	mg/dl	224 (190-266)	239 (213-288)	0.022
LDL-C	mg/dl	142 (115-172)	155 (127-201)	0.054
Corrected LDL-C	mg/dl	138 (107-168)	102 (74-151)	0.001
HDL-C	mg/dl	57 (44-70)	59 (47-69)	0.515
TG	mg/dl	102 (74-152)	103 (84-132)	0.747
Lp(a)	mg/dl	12 (9-21)	171 (156-195)	0.001
Apo A1	mg/dl	159 (141-182)	164 (142-186)	0.759
Apo B	mg/dl	107 (95-125)	121 (105-144)	0.003
Apo B/Apo A1	ratio	0.67 (0.58-0.77)	0.75 (0.57-0.97)	0.031
Diabetes	n (%)	8 (10.1)	7 (10.8)	0.900
Hypertension	n (%)	36 (45.6)	29 (44.6)	0.909
Smoking habit	n (%)	6 (7.6)	10 (15.4)	0.154
Use of antidiabetic drugs	n (%)	5 (6.3)	7 (10.8)	0.563
Use of antihypertensive drugs	n (%)	36 (45.6)	30 (46.2)	0.251
Use of statin	n (%)	41 (51.9)	39 (60.0)	0.635
Use of ezetimibe	n (%)	6 (7.6)	14 (21.5)	0.056
Use of statin and ezetimibe	n (%)	5 (6.3)	13 (20.0)	0.046
Use of antiplatelet drug	n (%)	12 (15.2)	11 (16.9)	0.786

BMI: body mass index ; SBP: systolic blood pressure ; DBP: diastolic blood pressure
Corrected LDL-C: LDL - [0,30 x Lp(a)] ; Lp(a): lipoprotein(a) ; Apo: apolipoprotein

Conclusions: Lp(a) is a surrogate of increased cardiovascular risk by means of atherosclerosis, plaque quality changes and thrombosis. This study suggests that these two latter phenomena, currently not explored by conventional non-invasive cardiovascular imaging, may be driving factors in Lp(a)-induced cardiovascular disease.

084

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

SEX DIFFERENCES OF LIPOPROTEIN(A) LEVELS AND ASSOCIATED RISK OF MORBIDITY AND MORTALITY BY AGE: THE COPENHAGEN GENERAL POPULATION STUDY

POSTER VIEWING SESSION

Sofie B. Simony[1,2,3], Martin B. Mortensen[1,2,3,4], Anne Langsted[1,2,3], Shoaib Afzal[1,2,3], Pia R. Kamstrup[1,3], Børge G. Nordestgaard[1,2,3]
[1]Department Of Clinical Biochemistry, Herlev and Gentofte Hospital, Copenhagen University Hospital, Herlev, Denmark, [2]Department Of Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen N, Denmark, [3]Department Of Clinical Biochemistry, The Copenhagen General Population Study, Herlev, Denmark, [4]Department Of Cardiology, Aarhus University Hospital, Aarhus N, Denmark

Background and Aims : Lipoprotein(a) is a well-known causal risk factor for cardiovascular morbidity and mortality. Little is known about the effect of age and sex on lipoprotein(a) levels, and it is largely unknown if the same elevation in lipoprotein(a) confer the same increase in risk of morbidity and mortality in women and men. We hypothesized that lipoprotein(a) levels and lipoprotein(a) associated risk of morbidity and mortality by age are similar in women and men.

Methods: We included 37,545 women and 32,497 men from the Copenhagen General Population Study.

Results: Plasma lipoprotein(a) increased with age and in women we found an additional increase around age 50 (age by sex interaction $P=4\cdot10^{-7}$). In women, levels were 22% higher after menopause ($P=1\cdot10^{-57}$) and 12% lower during hormone replacement therapy ($P=2\cdot10^{-19}$). Adjustment for eGFR (estimated Glomerular Filtration Rate) in both sexes and plasma estradiol in women resulted in attenuated sex differences in lipoprotein(a) levels. In sex and age stratified multivariable adjusted models, lipoprotein(a) >40 mg/dL(83 nmol/L) versus <10 mg/dL(18 nmol/L) was associated with increased risk of myocardial infarction, ischemic heart disease, aortic valve stenosis, and heart failure (men only), but not statistically significant with risk of ischemic stroke, cardiovascular mortality, or all-cause mortality.

Conclusions: Lipoprotein(a) levels increase around age 50 selectively in women; however, risk of morbidity and mortality for high lipoprotein(a) was similar in women and men above age 50. This implies that elevated lipoprotein(a) above age 50 is a relatively more common cardiovascular risk factor in women, pointing toward repeat measurement in women above age 50.

085

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

HIGH LIPOPROTEIN(A) IS ASSOCIATED WITH MAJOR ADVERSE LIMB EVENTS AFTER FEMORAL ARTERY ENDARTERECTOMY

POSTER VIEWING SESSION

Maarten C. Verwer[1], Farahnaz Waissi[1], Joost M. Mekke[1], Mirthe Dekker[1], Erik S. Stroes[2], Gert J. De Borst[1], Jeffrey Kroon[3], Constantijn E.V.B. Hazenberg[1], Dominique P.V. De Kleijn[1]
[1]Department Of Vascular Surgery, University Medical Center Utrecht, Utrecht, Netherlands, [2]Department Of Vascular Medicine, Amsterdam Cardiovascular Sciences, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands, [3]Experimental Vascular Medicine, Amsterdam UMC - Location AMC, Amsterdam, Netherlands

Background and Aims : Elevated lipoprotein(a) (Lp[a]) has been identified as a causal risk factor for cardiovascular disease including peripheral arterial disease (PAD). Although Lp(a) is associated with the diagnosis of PAD, it remains elusive whether there is an association of Lp(a) with cardiovascular and limb events in patients with severe PAD.

Methods: Preoperative plasma Lp(a) levels were measured in 384 consecutive patients that underwent femoral endarterectomy and were included in the Athero-Express biobank. Our primary objective was to assess the association of Lp(a) levels with Major Adverse Limb Events (MALE). Our secondary objective was to relate Lp(a) levels to Major Adverse Cardiovascular Events (MACE) and femoral plaque composition that was acquired from baseline surgery.

Results: During a median follow-up time of 5.6 years, a total of 225 MALE were recorded in 132 patients. Multivariable analysis, including history of peripheral intervention, age, diabetes mellitus, end stage renal disease and Fontaine stages, showed that Lp(a) was independently associated with first (HR of 1.36 (95% CI 1.02-1.82) p =.036) and recurrent MALE (HR 1.36 (95% CI 1.10 – 1.67) p =.004). Lp(a) levels were not associated with MACE (HR 0.88 (95% CI 0.63-1.23); p = .45). A higher presence of smooth muscle cells was seen in atherosclerotic plaque of patients with higher Lp(a) levels, although this was not associated with endpoints.

Conclusions: Plasma Lp(a) is independently associated with first and consecutive MALE after femoral endarterectomy. Consequently, Lp(a) could be considered as a biomarker to improve risk stratification in patients undergoing femoral endarterectomy.

086

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-01 Lp(a)*

RELATIONSHIP BETWEEN LIPOPROTEIN (A) AND CORONARY ARTERY DISEASE IN PATIENTS WITH VERY HIGH LDL LEVEL

POSTER VIEWING SESSION

Ece Yurtseven[1], Dilek Ural[1], Berkay O. Cunedioglu[1], Erol Gursoy[1], Saide Aytekin[1], Vedat Aytekin[1], Kemal Baysal[2]
[1]Cardiology, Koc University, İstanbul, Turkey, [2]Biochemistry, Koc University, İstanbul, Turkey

Background and Aims : Adults who have low density lipoprotein (LDL) cholesterol levels of more than 190 mg/dl are classified in very high-risk group for major cardiovascular events. The data about the impact of Lp(a) on coronary artery disease (CAD) in patients with very high LDL levels is insufficient. We aimed to investigate the relationship of Lp(a) level with CAD in patients with very high LDL levels.

Methods: We retrospectively analyzed the data of 247 patients whose LDL levels were equal to or higher than 190mg/dl and who had Lp(a) measurements. Lipid profile, co-morbidities, cardiovascular diseases, blood pressure, body mass index, eGFR and smoking status were assessed. The relationship between Lp(a) levels and CAD was analyzed.

Results: A total of 247 patients whose 50.4% were female, 22.6% diabetic and 36.7% hypertensive, 19% had coronary artery disease were included in the analysis. Patients with CAD had higher levels of Lp (a) (median 16 mg/dl vs 23 mg/dl p= 0.024). Age [odds ratio (OR), 1.060; 95% confidence interval (CI): 1.020-1.101; p = 0.003], sex (OR, 6.29; 95% CI:2.604-15.198; p = 0.000) and Lp(a) level (OR, 1.011; 95% CI: 1.001-1.021; p = 0.035) were independently related with CAD. ROC curve analyses demonstrated that Lp(a) level of 19.5mg/dl was the cut-off value for CAD in patients with very high LDL level (AUC:0.6, p=0.023).

Conclusions: In our study, we found increased Lp(a) level as a risk factor for CAD in patients with very high LDL levels. Furthermore, our results demonstrate that Lp(a) is the independent predictor of CAD in this patient group.

087

Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

PEMAFIBRATE IMPROVED POSTPRANDIAL TG, REML-C AND APOB48 IN PATIENTS WITH TYPE 2 DIABETES (T2D) AND HYPERTRIGLYCERIDEMIA: A POST-HOC ANALYSIS OF THE PHASE 3 CLINICAL TRIAL

POSTER VIEWING SESSION

Hidenori Arai[1], Shizuya Yamashita[2], Koutaro Yokote[3], Eiichi Araki[4], Neil Hounslow[5], Kenichiro Ikeda[6], Toshiaki Nojima[7], Hideki Suganami[7], Shun Ishibashi[8]
[1]President, National Center for Geriatrics and Gerontology, Obu, Japan, [2]Department Of Cardiology, Rinku General Medical Center, Izumisano, Japan, [3]Department Of Endocrinology, Hematology And Gerontology, Chiba University Graduate School of Medicine, Chiba, Japan, [4]Department Of Metabolic Medicine, Faculty Of Life Sciences, Kumamoto University, Kumamoto, Japan, [5]Medical Affairs, Kowa Pharmaceutical Europe Co. Ltd., Wokingham, United Kingdom, [6]Medical Affairs Department, Kowa Company, Ltd., Tokyo, Japan, [7]Clinical Data Science Department, Kowa Company, Ltd., Tokyo, Japan, [8]Division Of Endocrinology And Metabolism, Department Of Internal Medicine, Jichi Medical University School of Medicine, Shimotsuke, Japan

Background and Aims : Postprandial increase in TG-rich lipoproteins is a risk factor for atherosclerosis. Pemafibrate, a selective PPARα modulator (SPPARMα), causes profound TG reduction and HDL increase in patients with hypertriglyceridemia. However, there is limited data available about postprandial lipid parameters under pemafibrate treatment in patients with T2D and hypertriglyceridemia. The aim of this study was to examine the effect of pemafibrate on postprandial lipid parameters in this population.

Methods: This was a post-hoc analysis of a pemafibrate phase 3 clinical trial in Japanese patients with T2D and hypertriglyceridemia. Participants were randomly assigned to one of the following three arms, PEM0.2 (pemafibrate 0.2 mg/day for 52 weeks), PEM0.4 (pemafibrate 0.4 mg/day for 52 weeks), and PBO/PEM0.2 (placebo for 24 weeks and pemafibrate 0.2 mg/day for 28 weeks). Meal tolerance test (592 kcal) was conducted at week 0, 24 and 52. The blood sampling was conducted at 0, 1, 2, 4.5 and 6.5 h after taking the test meal (N=68).

Results: In the PEM0.2 and PEM0.4 groups, TG, RemL-C and ApoB48 were significantly decreased at all time points after taking the test meal at week 24 and 52, compared with week 0. These significant reductions were also found in PBO/PEM0.2 at week 52. $AUC_{0\text{-}6.5h}$ in TG, RemL-C and ApoB48 were significantly decreased in PEM0.2 and PEM0.4 at week 24 and 52, compared with week 0. These significant reductions of $AUC_{0\text{-}6.5h}$ were also observed in PBO/PEM0.2 at week 52.

Conclusions: Pemafibrate significantly reduced postprandial TG, RemL-C, ApoB48 and their $AUC_{0\text{-}6.5h}$ in patients with T2D and hypertriglyceridemia.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

LIPID PROFILE OF PATIENTS WITH DYSLIPIDEMIA DEPENDS ON THEIR GLYCEMIC STATUS

POSTER VIEWING SESSION

Fotios Barkas[1], Evangelos Rizos[1], Georgia Anastasiou[1], Petros Adamidis[1], Ad Koutsogianni[1], Eliza Christopoulou[1], Matilda Florentin[1], George Liamis[1], Evangelos Liberopoulos[2]
[1]Department Of Internal Medicine, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannnina, Greece, [2]Internal Medicine, Laiko Hospital, NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS, ATHENS, Greece

Background and Aims : To record lipid profile of patients with dyslipidemia in association with their fasting plasma glucose (FPG) levels and the presence of type 2 diabetes (T2D).

Methods: A retrospective observational cohort including 1602 adults with dyslipidemia followed-up at the outpatient Lipid Clinic of Ioannina University General Hospital, Greece. Normoglycemia was defined as FPG <100 mg/dL, prediabetes as FPG 100-125 mg/dL, and diabetes as meeting the diagnostic criteria or being on antidiabetic therapy.

Results: Of the 1602 patients, 1081 were not receiving lipid-lowering therapy at baseline visit: 63% and 26% of those were normoglycemic and prediabetic, whereas 11% had T2D. Patients with T2D had lower levels of total, high-density and low-density-lipoprotein cholesterol, apolipoprotein B and lipoprotein (a) compared with the normoglycemic and prediabetic subjects. Respectively, prediabetic and diabetic subjects had higher triglyceride levels, but lower high-density-lipoprotein cholesterol levels compared with normoglycemic ones. **Table** Lipid profile of patients with dyslipidemia depending on their glycemic status.

	FPG <
Total Cholesterol,mg/dL	260(23
Triglycerides,mg/dL	122(90
High-density-lipoprotein cholesterol,mg/dL	53(46-
Low-density-lipoprotein cholesterol,mg/dL	174(15
non-high-density-lipoprotein cholesterol,mg/dL	206(18
Apolipoprotein A-I,mg/dL	147(13
Apolipoprotein B,mg/dL	121(10
Apolipoprotein E,mg/dL	47(38-
Lipoprotein (a),mg/dL	10.5(5.

***** p<0.05 for the comparison with the patients with T2D ¥ p<0.05 for the comparison with the patients with prediabetes

Conclusions: T2D patients are characterized by atherogenic dyslipidemia, but exhibit lower levels of low-density-liporotein cholesterol, non-high-density-liporotein cholesterol, apolipoprotein B and lipoprotein (a) compared with normoglycemic and prediabetic patients with dyslipidemia.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

THE BIOCHEMISTRY PART IN THE DIAGNOSIS OF CHYLOTHORAX AND CHYLE EFFUSION.

POSTER VIEWING SESSION

Pierre Gres[1], Bertrand Lefrere[1], Mehdi Sakka[1], Julie Coiffard[1], Belkacem Zenati[1], Zoé Guilbert[1], Thomas Audon[1], Corinne Cherfils[1], Valérie Fesel-Fouquier[1], Randa Bittar[1,2], Dominique Bonnefont-Rousselot[1,3]
[1]Biochimie Métabolique, Unité fonctionnelle de Biochimie des Maladies cardiométaboliques, Paris, France, [2]Ican, UMRS_1166, Paris, France, [3]Utcbs, Cnrs, Inserm, Université de Paris, Paris, France

Background and Aims : Background Chylothorax and chyle effusion are rare lymphatic disorders which characterize by an abnormal circulation of lymph fluid in the pleural, pericardia and peritoneal cavities. They commonly occur in neonatal period and after surgery cut in the thoracic duct. Aim: We developed a biological decision tree for the diagnosis of chylothorax and chyle effusion, based on the aspect of the liquid, the assays of triglycerides (TG), total cholesterol (TC) and glycerol and the lipidogram (LPG) that separates the different lipoproteins depending on their electrophoretic charge, and allows to detect the presence of chylomicrons.

Methods: We selected 178 patients from January to October 2021; were excluded purulent or viscous liquids, liquids with analytical interferences (n=5), and redundant liquids that were collected several times for clinical follow-up (n=48). We performed on the remaining liquids (n=125) lipid parameters and lipidogram .

Results: Among the 125 liquids, we detected 69 liquids with the presence of chylomicron via the lipidogram (LPG+) and 56 liquids without chylomicrons (LPG-). When we compared the two groups, we observed in the LPG(+) group, 44 male, with a median for TG 2.64 mmol/L ***(p<0.0001)***, for TC 1.37 mmol/L (*p=0.06*), only 3 patients have a glycerol >0.5 mmol/L, and the chylomicron fraction in LPG represented 12.30 % **(p<0.0001)**

Conclusions: Conclusion: Chylothorax and chyle effusions are rare lymphatic disorders, requiring rapid diagnosis based on biological process including lipid parameters as triglycerides assays and lipidogram as a confirmation test. Early biological detection of chylomicrons, allows a successful follow-up and treatment.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

TREATMENT OF VOLANESORSEN IN A PATIENT WITH FAMILIAL CHYLMICRONAEMIA SYNDROME (FCS) DUE TO HOMOZYGOUS C.337T>C(P.TRP113ARG) - MUTATION AND IMPACT OF DIETARY INCOMPLIANCE: A CASE REPORT

POSTER VIEWING SESSION

Charlotte De Gier, Gabriele Skacel, Nina-Katharina Walleczek, Julia Lischka, Margot Baumgartner, Susanne Greber-Platzer
Department Of Pediatrics And Adolescent Medicine, Medical University of Vienna, Vienna, Austria

Background and Aims : FCS is an extremely rare genetic disease resulting in severe chylomicronaemia and high risk of recurrent pancreatitis in early childhood. Genes causing the disease include LPL, APOA5, APOC2, LMF1, and GPIHBP1.

Methods: We report the case of a 19-year-old with FCS caused by a homozygous c.337T>C (p.Trp113Arg) mutation in the LPL gene.

Results: The patient was diagnosed at the age of two months showing plasma triglyceride levels above 30.000 mg/dL. The treatment consisted of a restricted low-fat diet supplemented with medium-chain triglycerides. Medical initiatives with fibrates and omega-3-fatty-acids showed no effect. Due to severe hypertriglyceridemia, the patient suffered from acute pancreatitis at the age of six. To prevent comorbidities, the patient's family established an extreme activity program resulting in intense training sessions as a professional handball player. At the age of 18 years, we started pharmacotherapy with Volanesorsen, an Apo-C-III inhibitor, that is approved for adult patients with FCS and risk of pancreatitis, with subcutaneous (s.c.) injections of Volanesorsen 285 mg weekly. After 8 weeks, triglycerides declined significantly up to -85%. Nevertheless, the triglyceride levels were volatile, ranging from 295 to 4400 mg/dL. The overall mean reduction was -20%. There was a significant correlation with dietetic incompliance during extreme physical activity and training camps. As known side effect, thrombocytes decreased persistently <140 G/L after 18 weeks of therapy. After recovery of thrombocytopenia during a five-week pause, a biweekly s.c.-injection was continued.

Conclusions: Significant correlations with diet incompliance were observed and indicate the need for continued restriction of fat intake during therapy with Volanesorsen.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

ASSOCIATION OF TRIGLYCERIDE AND CHOLESTEROL CONTENT IN FOURTEEN LIPOPROTEIN SUBFRACTIONS WITH CORONARY HEART DISEASE: A MENDELIAN RANDOMISATION ANALYSIS.

POSTER VIEWING SESSION

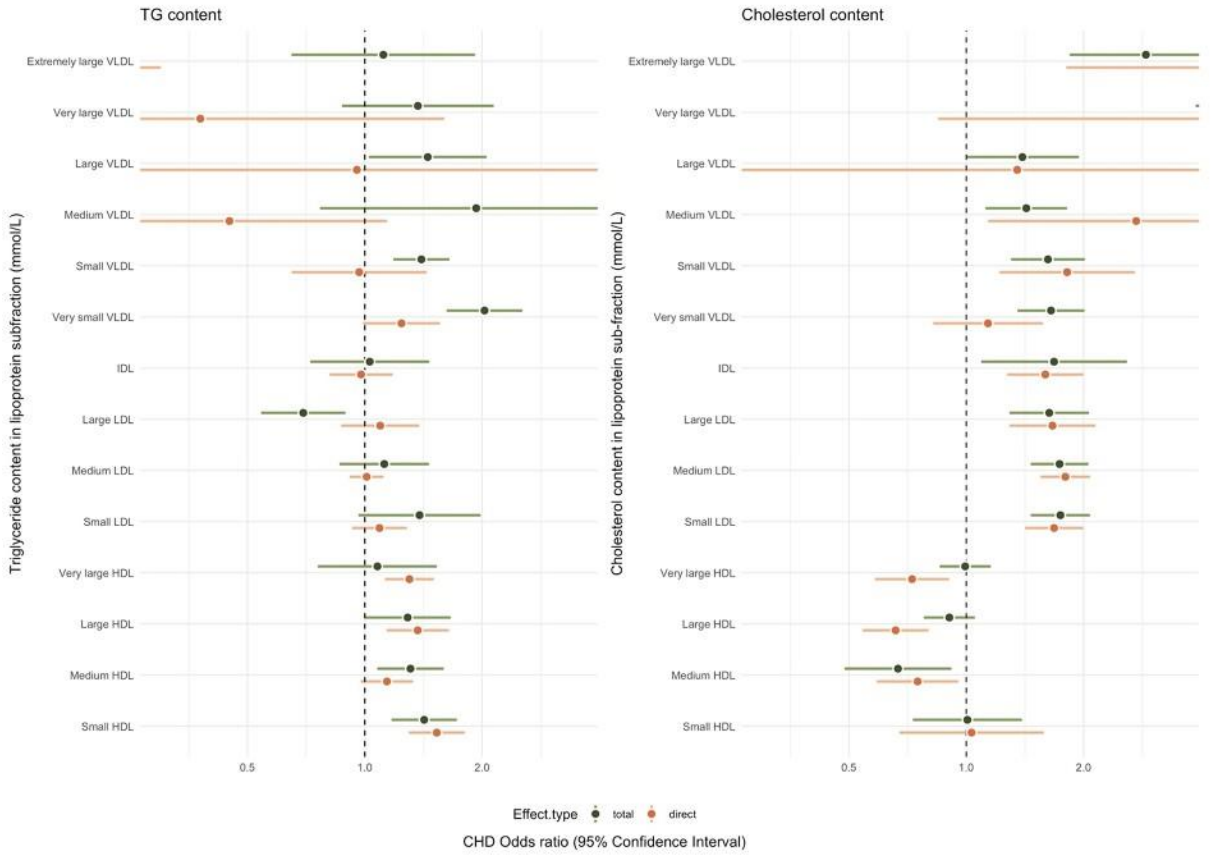
Roshni Joshi[1], Goya Wannamethee[1], Jorgen Engmann[1], Tom Gaunt[1], Deborah Lawlor[2], Jackie Price[3], Theresa Tillin[1], Nishi Chaturvedi[4], Mika Kivimaki[1], Alun Hughes[4], Andrew Wong[1], Aroon D. Hingorani[1], Amand F. Schmidt[1]
[1]Institute Of Cardiovascular Sciences, University College London, London, United Kingdom, [2]Bristol Medical School, University of Bristol, Bristol, United Kingdom, [3]Usher Institute, University of Edinburgh, Edinburgh, United Kingdom, [4]Population Science & Experimental Medicine, University College London, London, United Kingdom

Background and Aims : The causal relevance of the cholesterol and triglyceride (TG) content of lipoproteins other than low-density lipoproteins (LDL-C) in coronary heart disease (CHD) is uncertain.

Methods: We identified genetic instruments for the TG and cholesterol content of 14 lipoprotein subfractions and used two-sample Mendelian randomisation (MR) to explore their potential causal relevance for CHD. We used univariable-MR to estimate the total effect of TG and cholesterol on CHD and multivariable-MR (MVMR) to estimate the direct effect of TG or cholesterol content in each subfraction, conditioning on its cholesterol or TG content, respectively. A model selection framework determined when Egger adjustment was required in the presence of pleiotropy.

Results:

Figure 1 Univariable and MVMR association of triglyceride and cholesterol content in fourteen lipoprotein subfractions with CHD



N.B. Univariable estimates (green) MVMR estimates (orange)

Univariable MR indicated a causal association with CHD of the TG content of six lipoprotein subfractions and the cholesterol content of 10 lipoprotein subfractions. In MVMR analysis, the TG content of four subfractions displayed associations with CHD independently of the cholesterol content in the same subfraction, while the cholesterol content of 10 subfractions displayed a causal association with CHD independent of the TG content of the corresponding subfractions. The cholesterol but not the triglyceride content in subfractions referred to as triglyceride-rich lipoproteins (TRL) displayed the largest association with CHD (MVMR odds ratio [OR] 2.73 to 14.31 per 1 SD increase in the subfraction), though the large effect estimates may reflect model instability.

Conclusions: The cholesterol and TG content of certain lipoprotein subfractions other LDL may contribute to risk of CHD and may be relevant risk factors to target in drug development.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

TREATMENT OF TYPE V DYSLIPOPROTEINEMIA: A RARE PHENOTYPE OF LIPID DISORDERS

POSTER VIEWING SESSION

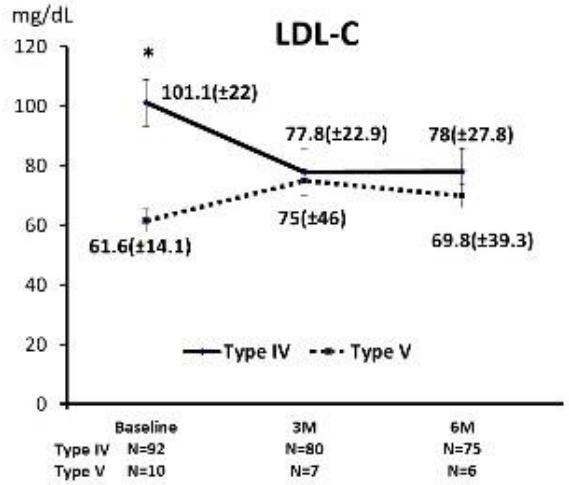
Chao-Feng Lin[1], Chih-Hung Liang[2], Jen-Yu Chuang[2], Dai-Yi Lin[1], Chia-Ling Tsai[1], Yi-Han Chen[3], Hung-I Yeh[1], Ya-Hui Chang[4]
[1]Department Of Cardiology, MacKay Memorial Hospital, Taipei, Taiwan, [2]Department Of Medical Education, MacKay Memorial Hospital, Taipei, Taiwan, [3]School Of Public Health, College Of Public Health, Taipei Medical University, Taipei, Taiwan, [4]Department Of Pharmacy, MacKay Memorial Hospital, Taipei, Taiwan

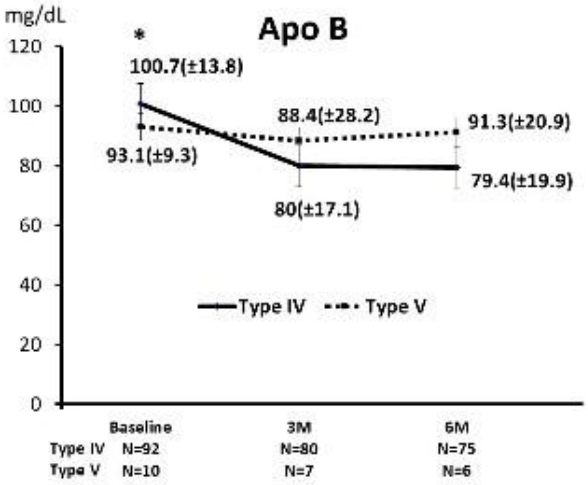
Background and Aims : Despite Type IV (T4DL) and Type V (T5DL) dyslipidemia are both characterized by hypertriglyceridemia (HTG), T5DL is specifically characterized by a rare phenotype of lipid disorders and the presence of fasting plasma chylomicrons. The present study was aimed to report our experience on treatment of T5DL in a tertiary medical center.

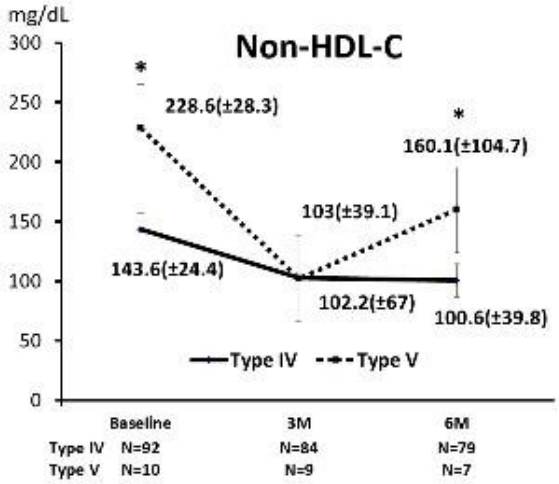
Methods: Between July 2018 and May 2021, 102 patients with HTG (>150 mg/dL) and low serum apolipoprotein B (apo B) (<120 mg/dL) were divided into T4DL and T5DL groups by using apo B diagnostic algorithm and lipoprotein electrophoresis. The patients' demographic data and lipid profiles (i.e., total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), and apo B) were recorded and compared between groups at 6-month follow-up.

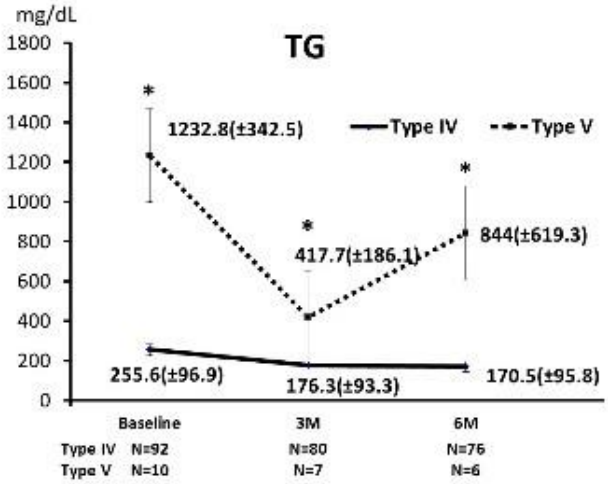
Results: Patients with T5DL were younger (46.1±11.9 vs. 57.0±9.9 years), had more histories of pancreatitis (30% vs. 0%), and had higher baseline TG (1232.8±342.4 vs. 255.6±96.8 mg/dL) and lower baseline LDL-C (61.6±14.1 vs. 101.1±22.0 mg/dL) levels compared with patients with T4DL. At 6-month follow-up, the serum TG levels of patients with T5DL were still much higher and fluctuated compared with those of patients with T4DL (844.0±619.3 vs. 170.5±95.8 mg/dL). The serum LDL-C levels of patients with T5DL did not decline with treatment (61.6±14.1 to 69.8±39.3 mg/dL), while those of patients with T4DL declined with treatment (101.1±22.0 to 78.0±27.8 mg/dL). These results were consistent irrespective of baseline lipid-lowering medication

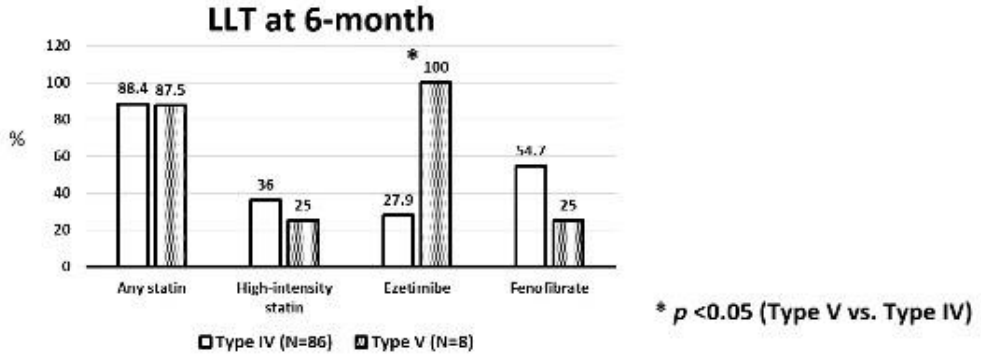
use.











Conclusions: Our findings highlight unmet medical needs among patients with T5DL, including lack of treatment guidelines and novel TG-lowering medications.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-02 TG rich lipoproteins metabolism and lipases*

ALBUMIN AFFECTS THE STABILITY, OLIGOMERIZATION AND LIGAND INTERACTIONS OF LIPOPROTEIN LIPASE

POSTER VIEWING SESSION

Robert Risti[1], Kathryn H. Gunn[2], Kristofer Hiis-Hommuk[3], Naatan Seeba[1], Ly Villo[1], Marko Vendelin[3], Saskia B. Neher[2], Aivar Lõokene[1]
[1]Department Of Chemistry And Biotechnology, Tallinn University of Technology, Tallinn, Estonia, [2]Biochemistry And Biophysics, The University of North Carolina at Chapel Hill, Chapel Hill, United States of America, [3]Department Of Cybernetics, Tallinn University of Technology, Tallinn, Estonia

Background and Aims : Lipoprotein lipase (LPL), a crucial enzyme in the intravascular hydrolysis of triglyceride-rich lipoproteins, is a potential drug target for the treatment of hypertriglyceridemia. Previous studies have shown that LPL can appear in various oligomeric states and its activity is influenced by a complex ligand network. The aim of the current study was to investigate how plasma, the natural environment of the LPL action, influences its oligomerization, stability and ligand interactions.

Methods: The investigations were performed by a combined use of isothermal titration calorimetry, surface plasmon resonance, negative stain transmission electron microscopy (TEM) and fluorescence correlation spectroscopy (FCS).

Results: Our data showed that albumin formed a complex with LPL and had a specific effect on its stability, which could not solely be reproduced by macromolecular crowding or non-specific protein-protein interactions. TEM and FCS measurements revealed that albumin and heparin induced reversible oligomerization of LPL. Interestingly, while heparin and albumin both alone induced LPL oligomerization, their combined effect on LPL resulted in dissociation of oligomers into active LPL. Finally, our data also suggested that the formation of the oligomers protected LPL from inactivation by its physiological regulator ANGPTL4.

Conclusions: The interplay between albumin and heparin could provide an additional mechanism for ensuring the dissociation of HSPG-bound LPL oligomers into active LPL upon secretion. Additionally, great consideration into LPL concentration and buffer environment should be taken in studies to distinguish between irreversible inactivation or aggregation and reversible LPL oligomer formation, which might affect interactions with various ligands and drugs.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

REPURPOSING THE ANTI-CANCER DRUG DOCETAXEL FOR THE PREVENTION AND TREATMENT OF ATHEROSCLEROSIS

POSTER VIEWING SESSION

Hong Y. Choi, Shiwon Choi, Isabelle Ruel, Jacques Genest
Cardiology, The Research Institute of the McGill University Health Centre, Montreal, Canada

Background and Aims : We have identified that a negative regulator of high-density lipoprotein (HDL) biogenesis, desmocollin 1 (DSC1) contributes to cholesterol accumulation in the atherosclerotic plaque. With screening of 10 million small molecules, the FDA-approved chemotherapy drug docetaxel was identified to inhibit the DSC1 activity and promote HDL biogenesis. To test whether docetaxel reduces atherosclerosis in an animal model, apoE-null mice were fed a high-fat diet to promote dyslipidemia.

Methods: After 2 weeks on the diet, one third of the mice were sacrificed as a baseline group. The rest were divided into two groups for subcutaneous implantation of an osmotic pump loaded with either 1 μg/μl of docetaxel or vehicle. The implanted mice were fed the high-fat diet for 6 weeks. At the end of 2 weeks (baseline group) and 8 weeks (docetaxel- and vehicle-treated groups), the mice were sacrificed for the analysis of blood and tissue samples.

Results: Blood test results showed anti-dyslipidemic effects of docetaxel: docetaxel reduced the levels of triglycerides, non-esterified fatty acids, glucose, total cholesterol, LDL- and HDL-cholesterol. Docetaxel decreased all cholesterol, but increased the HDL-/total cholesterol ratio, which is consistent with docetaxel promoting HDL biogenesis. Measurement of the aortic surface area covered by lipid-laden atherosclerotic lesions showed anti-atherosclerotic effects of docetaxel: small lesions were observed in the baseline group and markedly increased in the vehicle group, but significantly reduced by docetaxel treatment.

Conclusions: These results demonstrate that docetaxel reduces atherosclerosis caused by dyslipidemia by decreasing atherogenic lipids (triglycerides, LDL- and total cholesterol), while increasing the HDL-/total cholesterol ratio in the blood.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

HDL LEVELS DO NOT IMPACT ON THE EXPRESSION OF GENES PLAYING A PIVOTAL ROLE IN INTESTINAL LIPID METABOLISM IN APOLIPOPROTEIN E-KNOCKOUT MICE

POSTER VIEWING SESSION

Alice Colombo, Stefano Manzini, Marco Busnelli, Elsa Franchi, Giulia Chiesa
Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milan, Italy

Background and Aims : We investigated the impact of genetic manipulation of apoA-I/HDL levels on plasma lipids, atherosclerosis development and expression of genes with a pivotal role in lipid metabolism in the three segments of the small intestine.

Methods: Mice with extremely low plasma HDL levels, deficient for both murine apoA-I and apoE (DKO), were compared with mice characterized by elevated HDL, deficient for both apoA-I/apoE, but overexpressing human apoA-I (DKO/hA-I). Eight-week-old mice (n=8-16) were fed chow diet for 16 weeks. Plasma lipids were evaluated and atherosclerosis development at the aortic sinus quantified. Intestinal gene expression was analyzed by qPCR.

Results: DKO mice had almost three-fold lower total cholesterol levels than DKO/hA-I and almost negligible HDL-cholesterol levels, which were strongly elevated in DKO/hA-I mice. In the aortic sinus, DKO developed plaques that were over 16 times larger than those in DKO/hA-I. In both genotypes, Abca1 gene expression peaked in the jejunum; the same trend was seen for Abcg5/Abcg8. Cd36 and Npc1l1 had similar expression levels along the length of the small intestine. Mttp expression was dramatically lower in the ileum, whereas that of Srebf2 and of the ileal sodium/bile acid cotransporter Slc10a2 peaked in the last portion of the small intestine. Despite their opposite phenotypes, the expression of all genes analyzed was not different between DKO and DKO/hA-I.

Conclusions: Although different levels of apoA-I/HDL dramatically affect the plasma lipid profile and the atherosclerosis development, they did not seem to affect the expression of genes with a relevant role in intestinal lipid metabolism.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

HIGH DENSITY-LIPOPROTEIN FUNCTIONALITY SCORE PREDICTS CARDIOVASCULAR RISK ESTIMATES AND SUBCLINICAL ATHEROSCLEROSIS IN BRAZILIAN INDIVIDUALS

POSTER VIEWING SESSION

Nagila R.T. Damasceno[1], Maria Camila P. De Freitas[2]
[1]Department Of Nutrition, University of São Paulo, sao paulo, Brazil, [2]Department Of Nutrition, University of São Paulo, São Paulo, Brazil

Background and Aims : Current studies have not presented association between high density-lipoprotein cholesterol (HDL-C) increase, induced by drugs or genetic mutations, and coronary events reduction. HDL plays different functional cardioprotective role. Here, our goal was to develop a HDL functionality score (HFS) and to assessment its association with predictive cardiovascular risk algorithms and subclinical atherosclerosis outcomes in Brazilian subjects.

Methods: This is a cross-sectional study based in two steps. In the first step, the HFS predictor of cardiovascular risk disease (HFS-CVR) was developed and validated on CARDIONUTRI study subsample (n=354). In second step the HFS predictor of subclinical atherosclerosis (HFS-SA) was developed and validated on ELSA-Brasil study subsample (n=4549). CARDIONUTRI study evaluated PON1 and CETP activity, APOAI concentration, HDL antioxidant capacity, and HDL subfractions. ELSA-Brasil study evaluated the size of HDL and subfractions by Vertical Auto Profile (VAP) and Nuclear Magnetic Resonance (NMR) method, and the diagnosis of subclinical atherosclerosis by computed tomography, quantifying coronary artery calcification (CAC) and CAC score.

Results: Large HDL presented consistent association with cardiovascular risk (OR=0.797;p<0.001). The HFS-CVR showed satisfactory performance (AUC=0.899;p<0.001) by Framingham risk score, Reynolds risk score (AUC=0.722; p <0.001) and Adult Treatment Panel III/2013 escore (AUC=0.864;p<0.001). In addition, HFS-CVR presented reproducibility and was associated with subclinical atherosclerosis on ELSA-Brasil sample using large HDL measurements by VAP method (AUC=0.864;p<0.001;r=0.252;p<0.001) or the NMR method (AUC=0.876;p<0.001;r=0.277;p<0.001). HFS-AS based in HDL size showed consistent association with subclinical atherosclerosis (OR=0.549;p<0.001). HFS-AS demonstrated satisfactory performance (AUC=0.769;p<0.001).

Conclusions: The large HDL reveals a promising future as an adjunct marker in the estimation of cardiovascular risk.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

HISTOLOGICAL ASSESSMENT OF LIPID DEPOSITION IN PERIPHERAL TISSUES FROM GENETICALLY MODIFIED MICE WITH DEFICIENCY OR OVEREXPRESSION OF APOA-I

POSTER VIEWING SESSION

Elsa Franchi, Marco Busnelli, Stefano Manzini, Alice Colombo, Giulia Chiesa
Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milano, Italy

Background and Aims : The reverse cholesterol transport is a multistep process whereby excess cholesterol is transported by HDL from the peripheral tissues to the liver for excretion. In this study, the impact of genetic manipulation of HDL/apoA-I levels on lipid deposition in liver and kidney was investigated.

Methods: ApoE/apoA-I double deficient (DKO) mice and DKO mice overexpressing human apoA-I (DKO/hA-I), both females and males, were fed a standard rodent diet until one year of age. Plasma lipids were quantified by enzymatic methods. Liver and kidney histology were evaluated by light microscopy on frozen sections.

Results: Plasma total cholesterol concentration in DKO mice was comparable with that of wild type mice and 3-fold lower than that observed in DKO/hA-I mice. Plasma HDL-C was almost absent in DKO mice and strongly elevated in DKO/hA-I mice. The H&E-stained sections did not reveal the presence of steatosis in liver parenchyma as well as of foam cells in renal glomeruli of both genotypes. The neutral lipid-specific staining with Oil Red O showed instead interesting differences. In the hepatic parenchyma, an increased accumulation of lipids around the centrilobular vein was observed only in DKO/hA-I mice. In addition, within the glomeruli of DKO/hA-I mice, lipid accumulation was significantly higher than in DKO, both in females and males ($p<0.05$).

Conclusions: Although DKO mice are almost completely devoid of HDL and prone to atherosclerosis development, they do not exhibit steatosis or other signs of abnormal lipid accumulation in the liver and do not develop glomerular lipidosis.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

CHOLESTEROL EFFLUX CAPACITY OF HIGH-DENSITY LIPOPROTEIN PARTICLES IS IMPAIRED IN AGE-RELATED MACULAR DEGENERATION PATIENTS WITH HIGH PLASMA HDL-C LEVELS

POSTER VIEWING SESSION

Yanlin Li[1,2,3], Marcella Palumbo[4], Leonie Van Der Zee-Van Vark[2], Adrie Verhoeven[2], Franco Bernini[4], Caroline Klaver[1,5], Maria Pia Adorni[4], Francesca Zimetti[4], Pieter J.M. Leenen[3], Magda Meester-Smoor[1,5], Monique T. Mulder[2]
[1]Department Of Ophthalmology, Erasmus University Medical Center, Rotterdam, Netherlands, [2]Department Of Internal Medicine, Laboratory Of Vascular Medicine, Erasmus University Medical Center, Rotterdam, Netherlands, [3]Department Of Immunology, Erasmus University Medical Center, Rotterdam, Netherlands, [4]Department Of Food And Drug, University of Parma, Parma, Italy, [5]Department Of Epidemiology, Erasmus University Medical Center, Rotterdam, Netherlands

Background and Aims : Age-related macular degeneration (AMD) is a blinding disease initiated by the formation of fat globules, so-called drusen, in the retina. Epidemiological studies demonstrated an association between elevated plasma high-density lipoprotein-cholesterol (HDL-c) levels and AMD. This is in contrast to the risk of cardiovascular disease that is negatively associated with HDL-c levels. Among the genes linked with AMD, ABCA1, CETP, LIPC and APOE are related to the role of HDL in mediating cholesterol efflux from cells and consequently in reverse cholesterol transport. In accordance, we hypothesized that the cholesterol efflux capacity (CEC) of HDL is impaired in AMD patients, consequently leading to cholesterol accumulation underneath retinal pigment epithelium (RPE) cells, facilitating drusen formation.

Methods: To approach this, the capacity of HDL isolated from 30 AMD patients and 30 controls to mediate cellular cholesterol efflux from [^{3}H]-cholesterol-loaded ARPE-19 cells was assessed by measuring the percentage of [^{3}H]-cholesterol secreted into the culture medium.

Results: We found no differences in cholesterol efflux capacity between AMD patients and controls when comparing HDL isolated from 1 ml of plasma of each individual. However, HDL from AMD patients with high, but not low plasma HDL-c levels, showed a decreased cholesterol efflux capacity per HDL particle as compared to healthy controls.

Conclusions: Together, our data suggest that functional impairment of HDL is not causal for AMD pathogenesis but may be a result of other metabolic dysfunctions of AMD patients. Elevated plasma HDL-c levels in AMD patients might compensate for the decreased CEC of HDL per particle.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

DIFFERENT IMPACT OF AIR POLLUTION ON HDL FUNCTIONALITY IN HEALTHY AND IN OBESE SUBJECTS

POSTER VIEWING SESSION

Alice Ossoli[1], Chiara Favero[2], Silvana Frascarelli[1], Laura Calabresi[1], Valentina Bollati[2], Monica Gomaraschi[1]
[1]Dipartimento Di Scienze Farmacologiche E Biomolecolari, Università degli Studi di Milano, Milano, Italy, [2]Dipartimento Di Scienze Cliniche E Di Comunità, Università degli Studi di Milano, Milano, Italy

Background and Aims : The exposure to air pollution is associated with an increase of cardiovascular risk. Interestingly, obese subjects seem to be particularly susceptible to air pollution. Air pollutants trigger an inflammatory reaction and oxidative stress; thus, the exposure to particulate matter (PM) may lead to HDL dysfunction as observed in other inflammatory conditions. Aim of the study was to investigate whether exposure to air pollutants affects HDL functionality.

Methods: Forty-one apparently healthy subjects with normal BMI and 50 obese subjects were enrolled within the SPHERE study in the Milan area. Individual exposure to PM_{10}, $PM_{2,5}$ and NO_2 was evaluated during the 24 hours before blood sampling. HDL ability to promote nitric oxide (NO) release by endothelial cells and to remove cholesterol from macrophages was evaluated.

Results: Healthy and obese subjects were comparable for age and gender distribution. HDL from healthy subjects were more efficient than those from obese ones in promoting NO release by endothelial cells and in reducing the cholesterol content of macrophages. In healthy subjects, HDL function was positively correlated with the exposure to both PM_{10} and $PM_{2.5}$ after adjustment for age, gender, smoking habits, plasma lipids and inflammatory parameters. On the contrary, in obese subjects a tendency towards a negative correlation was found.

Conclusions: In healthy subjects, the exposure to PM triggers a compensatory protective response leading to an increased HDL function; this compensation was not observed in obese subjects. These data could help explaining why obese subjects seem more susceptible to the effect of air pollutants.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

ASSOCIATION BETWEEN HIGH HDL CHOLESTEROL LEVELS AND MORTALITY IN WELL-CONTROLLED DIABETIC PATIENTS TYPE 2.

POSTER VIEWING SESSION

Alexandra Sianni, Styliani Lagou, Marina Tzanni, Konstantinos Tentolouris, Alkistis Patsaki, Styliani Michailidou, Sofia Miliou, Nikolaos Fytrakis, Dimitrios Syrigos, Archontoula Fragkou
2nd Department Of Internal Medicine, Elpis General Hospital of Athens, Athens, Greece

Background and Aims : Elevated levels of High-density lipoprotein cholesterol (HDL cholesterol) seem to protect against atheromatosis and its clinical sequelae, including myocardial infraction and stroke in diabetic patients type 2. To investigate whether high HDL cholesterol correlates with mortality rate in well controlled patients with Diabetes Mellitus.

Methods: Six hundred sixteen (n=616) patients, with mean age 74+-18 years and with Diabetes Mellitus type 2, included in the study group. All subjects had well controlled glucose levels as reflected in HbA1c levels (6.5<HbA1c<7). 57,1% were males (n=352) and 42,9% were females (n=264). The duration of study was 3 years and HbA1c, total cholesterol, LDL cholesterol, and triglycerides levels were measured in all follow-up visits (at 3, 6, 12, 18, 24, 36 months). During the study 9 subjects died (6 males, mortality rate 17/1000, 3 females mortality rate 11/1000).

Results: HDL cholesterol levels of dead males were counted among 95-125 mg/dl whereas HDL cholesterol levels were 115-142mg/dl. Risk ratio for males was 1,35 for HDL levels 95-115mg/dl and 2,01 for HDL levels >116 mg/dl. Risk ratio for women was 1,1 for HDL levels 115-135 and 1,7 for HDL levels>135.

Conclusions: Elevated levels of HDL cholesterol correlated with higher mortality in well controlled diabetic patients type 2.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

ENRICHMENT OF HIGH-DENSITY LIPOPROTEINS WITH PHOSPHATIDYLETHANOLAMINE (36:5) IMPAIRS THEIR PROTECTIVE BIOLOGICAL ACTIVITIES AND IS ASSOCIATED WITH ATHEROSCLEROSIS IN WOMEN.

POSTER VIEWING SESSION

Malik Taradeh[1], Veronica Dahik[1], Marie Lhomme[2], Sophie Galier[1], Lise Hardy[1], Eric Frisdal[1], Hervé Durand[1], Anatol Kontush[1], Eric Bruckert[1], Philippe Giral[1], Maryse Guerin[1], Isabelle Guillas[1], Wilfried Le Goff[1]
[1]Inserm Umr_s1166 Ican, Faculté de Médecine Sorbonne Université, PARIS, France, [2]Institute Of Cardiometabolism And Nutrition (ican), Pitié-Salpêtrière hospital, Paris, France

Background and Aims : Circulating concentrations of high-density lipoprotein-Cholesterol (HDL-C) are inversely associated to cardiovascular diseases (CVD) which reflect the atheroprotective activities of HDL. Phospholipidome of HDL is a major determinant of their activities and alterations of HDL phospholipidome and functions are common features of CVD patients. Plasma lipidome analyses reported that phosphatidylethanolamine (PE) (36:5) is associated with cardiovascular diseases. The objective of the present study was to determine if such association results in part from an impairment of the protective functions of HDL.

Methods: Reconstituted HDL (rHDL) enriched with PE (36:5)

Results: PE (36:5) rHDL exhibited a reduced capacity to promote cholesterol efflux from human THP-1 macrophages as compared to control rHDL. Moreover, the anti-inflammatory property of rHDL on the expression of some cytokines and chemokines was abolished upon enrichment of PE (36:5) in human THP-1 macrophages stimulated with LPS. Circulating PE (36:5) content of HDL2 isolated from 86 metabolically healthy women was significantly and positively correlated with carotid intima-media thickness in both univariate (β=0.359, p=0.0008) and multivariate (β=0.255, p=0.0116) regression analyses after adjustment for CVD risk factors. Moreover, unadjusted analyses revealed significant associations between the highest tertile (Ter3) of PE (36:5) in HDL2 and both the presence of atherosclerotic plaques in carotid arteries (OR : 3.93; 95%CI: 1.26-12.3, p = 0.0277 for Ter3 vs Ter1) and with coronary artery calcification score >100 (OR : 4.23; 95%CI: 1.16-15.4, p = 0.0379; Ter1 vs Ter3).

Conclusions: Our study demonstrates that PE (36:5) content of HDL2 is a predictor of dysfunctional HDL and CVD in women.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

PCSK9 IS DIFFERENTIALLY DISTRIBUTED AMONG HDL SUBPOPULATIONS

POSTER VIEWING SESSION

Aikaterini N. Tsouka[1], Ioannis Dafnis[2], Constantinos C. Tellis[1], Christina Gkolfinopoulou[2], Angeliki Chroni[2], Alexandros D. Tselepis[1]
[1]Department Of Chemistry, University Of Ioannina, Atherothrombosis Research Centre, Ioannina, Greece, [2]National Center For Scientific Research "demokritos, Institute of Biosciences and Applications, Athens, Greece

Background and Aims : PCSK9 plays a crucial role to LDL-R binding in hepatocytes, LDL-R regulation, and increased plasma LDL levels. Plasma PCSK9 is associated with LDL and Lp(a), whereas a recent study showed that PCSK9 is mostly carried by HDL. The aim of this study was to determine the PCSK9-HDL association.

Methods: Plasma from healthy volunteers was treated with Dextran/Mg2+ to precipitate ApoB lipoproteins and ApoB-depleted plasma (ApoB-DP) was isolated. Total plasma was subjected to non-denaturing PAGE, using the Lipoprint System and HDL particles were isolated by size Large-HDL, Intermediate-HDL, and Small-HDL, (L-HDL, I-HDL, and S-HDL), and were subjected to SDS-PAGE and immunoblotting using anti-PCSK9. ApoB-DP was subjected to native PAGE, two-dimensional nondenaturing agarose-PAGE and immunoblotting using anti-apoA-I and anti-PCSK9. PCSK9 levels were determined by ELISA, whereas HDL-associated PCSK9 was measured using coated plates with anti-HDL.

Results: Total plasma contains 344±94ng/ml PCSK9 whereas ApoB-DP contains 111±35ng/ml, showing that 32.3±10.3% of total PCSK9 is found in ApoB-DP. ApoB-DP contains both mature and furin-cleaved forms of PCSK9 but only 6.18±2.11% is bound to HDL. The majority of PCSK9 in ApoB-DP is not bound on HDL. Importantly, L-HDL and I-HDL contain only furin-cleaved PCSK9 containing the slow migrating forms of apoA-I, whereas S-HDL contains only mature PCSK9, present in α3/α4 HDL particles.

Conclusions: The present study demonstrates a heterogenous distribution of PCSK9 among HDL subclasses, while both forms are associated with HDL. The presence of mature PCSK9 in S-HDL subfraction, especially in small α3/α4 HDL subpopulations, may contribute to the elevated cardiovascular risk associated with these HDL particles.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-03 HDL*

LIPOPROTEIN METABOLISM IN ALZHEIMER'S DISEASE: CSF AND PLASMA HDL CHARACTERIZATION IN AN ITALIAN COHORT

POSTER VIEWING SESSION

Marta Turri[1], Chiara Pavanello[1], Francesco Gastoldi[1], Elisa Conti[2], Davide Emide[3], Alberto Barbiroli[3], Lucio Tremolizzo[2], Laura Calabresi[1]
[1]Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Neurobiology Laboratory, School Of Medicine And Surgery, University of Milano-Bicocca, Monza, Italy, [3]Department Of Food, Environmental And Nutritional Sciences, University of Milan, Milan, Italy

Background and Aims : A growing number of evidence indicates a strong inverse association between the risk of developing Alzheimer's disease (AD) and plasma HDL-C levels. The mechanism by which plasma HDL could influence the pathogenesis and progression of AD is still unsolved. It has been suggested a direct involvement of plasma HDL on brain cholesterol homeostasis, given the ability of specific HDL subfractions to cross the BBB. Despite this consistent evidence, a qualitative analysis of plasma and cerebrospinal fluid (CSF) HDL is still lacking.

Methods: 42 AD (19M/23F, 75±7 y.o.) and 5 cognitively-intact control subjects (3M/2F, 75±10 y.o.) were recruited at the San Gerardo hospital. A complete plasma lipid-lipoprotein profile was determined using a Roche Cobas c311 analyzer. CSF total cholesterol (TC) and unesterified cholesterol (UC) content have been measured by HPLC. HDL subclasses have been characterized in plasma and CSF by non-denaturing two-dimensional (2D)-electrophoresis.

Results: In AD plasma HDL-C levels are normal and interestingly HDL-C levels are inversely associated to cognitive decline (measured with Mini-Mental State Exam). HDL subclass distribution is analogous to that of healthy controls. CSF apoE-containing lipoproteins showed only α-migrating particles. Curiously CSF apoA-I and apoA-II-containing lipoproteins are very similar to plasma HDL in AD. UC/TC ratio in AD CSF (0.51±0.13) is higher than controls (0.40±0.12), suggesting a defect in esterification process.

Conclusions: This qualitative characterization of HDL supports the hypothesis of a direct role of plasma HDL in brain cholesterol homeostasis.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-04 Lipoprotein receptors*

SILENCING OF PCSK9 BY SIRNA-FUNCTIONALIZED RHDL AS TOOL TO UPREGULATE LDLR EXPRESSION IN HEPATOCYTES

POSTER VIEWING SESSION

Asier Larrea[1], Shifa Jebari Benslaiman[2], Unai Galicia-Garcia[2], Kepa B. Uribe[3], Asier Benito-Vicente[2], Cear Martin[1]
[1]Biochemistry And Molecular Biology, Biofisika Institute, Leioa, Spain, [2]Biochemistry And Molecular Biology, Biofisika Institutua, LEJONA, Spain, [3]Nanomedicine, Center for Cooperative Research in Biomaterials (CIC biomaGUNE), Donostia, Spain

Background and Aims : Cardiovascular disease (CVD) is the leading cause of death worldwide and is often related to high plasma concentrations of low-density lipoprotein cholesterol (LDL-c). Many approaches have been carried out to deal with high cholesterol levels in plasma, statins and antibodies targeting PCSK9 among others. Although the use of antibodies has been proven to be an efficient treatment against PCSK9 effect, they are not effective for GOF variants with intracellular activity. Recently, the use of siRNA that impair the PCSK9 synthesis has been proposed as an alternative to antibodies. Therefore, the aim of this work has been to develop a new therapeutic strategy based on siRNA delivery within recombinant HDL (rHDL) to downregulate PCSK9 expression.

Methods: siRNA targeting PCSK9 was incorporated onto rHDL. Uptake of the nanoparticles, their effect on LDL uptake and LDLr expression was determined by flow cytometry. *PCSK9* mRNA levels were determined by qPCR. PCSK9 expression was measured by western blot and ELISA

Results: siRNA targeting PCSK9 delivered by rHDL significantly reduces *PCSK9* mRNA levels and PCSK9 expression, as well as increases *LDLR* expression and LDL uptake.

Conclusions: The inhibition of PCSK9 by rHDL-mediated delivery of siRNA is an effective method to reduce the deleterious effect of PCSK9 *in vitro*. This approach could also useful against PCSK9 variants with intracellular activity.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 Cholesterol efflux and reverse cholesterol transport*

MIR-125B DOWNREGULATES MACROPHAGE SCAVENGER RECEPTOR TYPE B1 AND REVERSE CHOLESTEROL TRANSPORT

POSTER VIEWING SESSION

Raquel Griñán[1,2], Miguel Hueso[3,4], Adrián Mallen[3], Estanislao Navarro[3], Elvira Purqueras[5], Montse Gomá[5], Fabrizio Sbraga[6], Arnau Blasco-Lucas[6], Giovanna Revilla[2], David Santos[7], Marina Canyelles[2], Josep Julve[2,7], Joan C. Escolà[2,7], Noemi Rotllan[2,7]
[1]Department Of Biochemistry And Molecular Biology, Autonomous University of Barcelona (UAB), Cerdanyola del Vallès, Spain, [2]Pathophysiology Of Lipid Related Diseases, Biomedical Research Institute Sant Pau (IIB-Sant Pau), Barcelona, Spain, [3]Department Of Nephrology, Hospital Universitari Bellvitge and Bellvitge Research Institute (IDIBELL), L'Hospitalet de Llobregat, Spain, [4]Experimental Nephrology Lab, Institutd'Investigació Biomèdica de Bellvitge-IDIBELL, L'Hospitalet de Llobregat, Spain, [5]Department Of Pathology, Hospital Universitari Bellvitge and Bellvitge Research Institute (IDIBELL), L'Hospitalet de Llobregat, Spain, [6]Department Of Cardiac Surgery, Hospital Universitari Bellvitge and Bellvitge Research Institute (IDIBELL), L'Hospitalet de Llobregat, Spain, [7]Department Of Biochemistry, CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Barcelona, Spain

Background and Aims : We aim to evaluate the role of miR-125b in regulating scavenger receptor type B1 (SR-B1)-mediated macrophage cholesterol efflux to HDL particles *in vitro* and the entire reverse cholesterol transport pathway *in vivo*.

Methods: *In situ* hybridization (AISH) assay was performed in 8 mm fresh-frozen sections from human aortas samples using 5' fluorescein Cy5 probes (25nM AntagomiR-125b or 25 nM AntagomiR Cel-miR-67 scrambled control). Consecutive sections were stained for CD68. Human monocytic (THP-1) and mouse macrophages (J774A.1 and RAW264.7) cells were used for different experiments. To determine whether the SCARB-1 3'UTR activity was specifically regulated by miR-125b, dual luciferase assay were performed. 40nM of control mimic or hsa-miR-125b-5p mimic were used for 48h transfection experiments. *In vitro* cholesterol efflux assays and *in vivo* macrophage-specific reverse cholesterol transport were also performed.

Results: We demonstrated that miR-125b is up-regulated in human aortas of patients with CAD and is located in macrophages. We identified *SCARB1* as a direct target of miR-125b by repressing the activity of the *SCARB1* 3'UTR reporter construct. Moreover, the overexpression of miR-125b in both human and mouse macrophages was found to downregulate the expression of the *SCARB1* gene and impaired α-HDL-mediated macrophage cholesterol efflux *in vitro*. The *in vivo* RCT rate from macrophages transfected with miR-125b to faeces was also found to be decreased when compared with that of control mimic-transfected macrophages.

Conclusions: Together, these results provide evidence that miR-125b downregulates *SCARB1* and SR-B1 in both human and mouse macrophages, thereby impairing macrophage cholesterol efflux *in vitro* and the whole RCT pathway *in vivo*.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 Cholesterol efflux and reverse cholesterol transport*

GENOME-WIDE FUNCTIONAL GENETIC APPROACHES TO IDENTIFY NOVEL REGULATORS OF NIEMANN PICK TYPE C1 (NPC1)

POSTER VIEWING SESSION

Klevis Ndoj
Medical Biochemistry, Amsterdam UMC Locatie AMC, Amsterdam, Netherlands

Background and Aims : Mammalian cells acquire exogenous cholesterol via the LDL-receptor-pathway. LDL is carried to the late endosome/lysosome (Le/Ly) compartment. Egress of free cholesterol from this compartment depends on the Nieman Pick type 1 and 2 proteins. Accordingly, mutations in these genes are the cause of Niemann-Pick type C disease, a lysosomal storage disease resulting in accumulation of lysosomal cholesterol that leads to progressive neurological disorders and premature death. Most patients carry mutation in NPC1 (~95%), of which 70% are missense mutations which lead to misfolding of the nascent protein and its subsequent proteasomal degradation. Interestingly, many mutants retain some degree of function, and blocking proteasomal degradation is able to increase delivery of the mutant protein to the Le/Ly, and counter lysosomal cholesterol accumulation. Hence, identification of genes affecting endogenous NPC1 trafficking and stability may inform on new therapeutic strategies for treating NPC disease.

Methods: Our group recently applied genome-wide functional genetic screens to interrogate cellular lipid metabolism. We therefore propose to apply a genome-wide functional genetic screen to identify genes genetic modifiers of NPC1 abundance and function.

Results: Using CRISPR/Cas9 based genome editing we have developed mammalian cells in which the endogenous NPC1 is tagged with the fluorescent protein mNeon. These cells faithfully report on NPC1 abundance and localization and allows the study of endogenous NPC1 in real time at a single cell resolution.

Conclusions: We have developed an experimental system to interrogate genetic modifiers of NPC1 pathway. Results from our screening effort will be presented.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 Cholesterol efflux and reverse cholesterol transport*

INHIBITION OF PCSK9 AFFECTS SERUM LIPOPROTEIN FUNCTIONS IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Marcella Palumbo[1], Maria Pia Adorni[2], Francesca Zimetti[1], Chiara Pavanello[3], Antonina Giammanco[4], Angelo Baldassare Cefalù[4], Davide Noto[4], Salvatore Piro[5], Antonino Di Pino[5], Maurizio Averna[4], Laura Calabresi[3], Franco Bernini[1], Francesco Purrello[5], Roberto Scicali[5]
[1]Department Of Food And Drug, University of Parma, Parma, Italy, [2]Department Of Medicine And Surgery, Unit Of Neuroscience, University of Parma, Parma, Italy, [3]Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [4]Department Of Health Promotion, Mother And Child Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy, [5]Medicine Department, ARNAS GARIBALDI NESIMA, Catania, Italy

Background and Aims : PCSK9, beyond regulating plasma cholesterol levels, exerts several pleiotropic effects modulating lipid metabolism in extrahepatic cells, including macrophages. Macrophage cholesterol homeostasis strictly depends on serum lipoprotein functions, including the HDL capacity to promote cell cholesterol efflux (cholesterol efflux capacity, CEC) and the serum capacity to promote cell cholesterol accumulation (cholesterol loading capacity, CLC). The aim of the present study was to evaluate potential changes in HDL-CEC and serum CLC after six-month of treatment with PCSK9 inhibitors in Familial Hypercholesterolemia (FH) subjects.

Methods: N = 31 patients with a diagnosis of heterozygous FH have been recruited. Blood was collected and serum isolated at baseline and after six months of treatment with PCSK9 inhibitors (evolocumab/alirocumab). HDL-CEC through the main pathways was evaluated with a radioisotopic cell-based assay. Serum CLC was assessed fluorimetrically in human monocyte-derived macrophages THP-1.

Results: After treatment with PCSK9 inhibitors, total cholesterol, LDL-c and HDL-c significantly decreased. Total HDL-CEC was not different between subjects before and after treatment. Conversely, HDL-CEC by aqueous diffusion significantly increased by 7,8%, while ABCA1 HDL-CEC decreased by 10,6% after treatment. Moreover, treatment significantly increased ABCG1 HDL-CEC by 22,15%. All the HDL-CEC changes occurred independently of HDL-c levels variations. Serum CLC significantly decreased after treatment (-7,8% p=0,0258), partly due to the reduction of LDL-c levels.

Conclusions: Treatment with PCSK9 inhibitors had a positive impact on both quantitative and functional lipid profile as it increased aqueous diffusion and ABCG1 HDL-CEC and reduced the serum proatherogenic potential.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-07 Lipidomics*

ICOSAPENT ETHYL SUPPLEMENTATION RAPIDLY AND TRANSIENTLY ALTERS THE COMPOSITION AND FUNCTIONALITY OF CIRCULATING LIPOPROTEINS IN HUMANS

POSTER VIEWING SESSION

Lauri Äikäs[1,2], Martin Hermansson[1], Minna Holopainen[2,3], Hanna Ruhanen[3], Reijo Käkelä[2,3], Petri T. Kovanen[1], Katariina Öörni[1,2]
[1]Atherosclerosis Unit, Wihuri Research Institute, Helsinki, Finland, [2]Molecular And Integrative Biosciences, Faculty Of Biological And Environmental Sciences, University of Helsinki, Helsinki, Finland, [3]Helsinki University Lipidomics Unit (hilipid), Helsinki Institute of Life Science (HiLIFE) and Biocenter Finland, Helsinki, Finland

Background and Aims : Icosapent ethyl-supplementation has postulated benefits in improving cardiovascular health. Total circulating eicosapentaenoic acid (EPA) correlates negatively with cardiovascular disease (CVD) risk and total mortality. Here we assessed how EPA-supplementation affects the lipidome and proatherogenic properties of plasma lipoproteins.

Methods: 39 healthy, normolipidemic volunteers received a 4 g daily dose of icosapent ethyl for 4 weeks. VLDL, LDL, and HDL were isolated from blood samples collected prior, during, and after the supplementation, and their fatty acid and lipid compositions were assessed by lipidomics, LDL aggregation propensity and proteoglycan-binding of the plasma lipoproteins were also determined.

Results: Total plasma EPA increased 5-fold within the first week of supplementation and returned to baseline level 1 week after the supplementation. Among the lipoprotein fractions, 53 lipid species were significantly increased and 31 significantly decreased. Lipids containing n-3 fatty acids were increased, while those containing n-6 fatty acids were decreased, resulting in a reduction of plasma n-6/n-3 ratio from 7.9 to 2.8. Changes were qualitatively similar in all lipoprotein classes. Largest changes were observed in cholesteryl esters, followed by phosphatidylcholines and triacylglycerols. Icosapent ethyl-supplementation decreased lipoprotein binding to proteoglycans, and LDL aggregation decreased in individuals having the most aggregation-prone LDL.

Conclusions: Icosapent ethyl-supplementation leads to a rapid but transient increase in total circulating EPA, a reduction of the n-6/n-3 fatty acid ratio of lipoprotein lipids, and a reduction in proteoglycan-binding of plasma lipoproteins. EPA-containing lipids fluctuate equally in all main lipoprotein classes. Reduced proteoglycan-binding of plasma lipoproteins may partly explain the known icosapent ethyl-induced reduction in CVD risk.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-07 Lipidomics*

IN-SITU LIPID ALTERATIONS OF AORTIC ATHEROSCLEROSIS IN LDLR-DEFICIENT MICE USING MASS SPECTROMETRY IMAGING

POSTER VIEWING SESSION

Marta Martin-Lorenzo[1], Jianhua Cao[2], Kim Van Kuijk[3], Marion J. Gijbels[3], Britt S.R. Claes[2], Ron M.A. Heeren[2], Judith Sluimer[3], Gloria Alvarez-Llamas[1], Benjamin Balluff[2]
[1]Immunology, FIIS- Fundación Jiménez Díaz, Madrid, Spain, [2]Maastricht Multimodal Molecular Imaging Institute (m4i), Maastricht University, Maastricht, Netherlands, [3]Pathology Department, Cardiovascular Research Institute Maastricht (carim), Maastricht UMC+, Maastricht, Netherlands

Background and Aims : We aim to characterize the in-situ lipid alterations associated with atherosclerosis in mice aortic roots.

Methods: Lipidomic non-targeted analysis by mass spectrometry imaging was performed of aortic roots obtained from low-density lipoprotein receptor deficient (*ldlr*$^{-/-}$) mice fed with high fat diet (n=11), in comparison to a control group fed with normal diet (n=11) during 8 weeks. Additionally, targeted mass-spectrometry was performed in human plasma samples of patients at CV-risk (n=27) and controls (n=27) to investigate a potential translation of the tissue-based lipid alterations to a biological fluid with diagnostic potential.

Results: We found 362 *m/z* values significantly altered between control and atherosclerosis mice (p-value≤0.05; log2-fold-change≥1.5). In cardiomyocytes, a decreased trend in lysolipids and heptanoylcarnitine and an imbalance in phospholipids were found. In the aortic region, an accumulation of glycerophospholipids was observed in all three arterial layers. N-stearoyl-glutamine, lysoPI(20:3) and SM(d18:0/15:0) were increased in the intima in agreement with a potential role for SMs and lysolipids in the progression of atherosclerosis. In human plasma, Trimethylamine N-oxide and carnitine were found at higher levels and heptanoylcarnitine at reduced levels in subjects with CV-risk. The combination of these three molecules into a panel showed a promising performance as diagnostic markers (area-under-the-curve=0.916; CI: 0.842-0.990).

Conclusions: This study indicates an altered phospholipid metabolism occurring in atherosclerosis, which affects both, the aorta as well as the adjacent cardiomyocyte area. Some of the in-tissue lipidic changes identified are reflected in human plasma and show diagnostic potential.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-07 Lipidomics*

SMALL LDL SUBFRACTIONS ARE ASSOCIATED WITH CORONARY ATHEROSCLEROSIS

POSTER VIEWING SESSION

Julie C. Sæther[1,2], Anja Bye[1,2], Marie Klevjer[1,2], Tone F. Bathen[1], Guro Giskeødegård[1], Erik Madssen[1,2], Elisabeth Vesterbekkmo[1,2], Rune Wiseth[1,2], Sigrid Gjære[1], Marthe Myhra[1], Bruna Gigante[3]
[1]Department Of Circulation And Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway, [2]Clinic Of Cardiology, St. Olavs University Hospital, Trondheim, Norway, [3]Department Of Cardiovascular Epidemiology, Karolinska Institute, Stockholm, Sweden

Background and Aims : Limitation in the ability to predict risk of coronary artery disease (CAD) have led to an increased clinical interest in identifying novel risk markers and to improve measures of the traditional risk factors. With the advances in lipidomic technology, research show that lipoprotein subfractions may provide us with more detailed information regarding future risk of CAD compared to conventional lipid measures. We aim to investigate whether lipoprotein subfractions are associated with coronary atherosclerosis in patients without prior cardiovascular disease.

Methods: Fasting serum samples from 60 patients with suspected CAD were collected before coronary angiography and analysed by nuclear magnetic resonance (NMR) spectroscopy. The presence and severity of coronary atherosclerosis was quantified by the Gensini Score (<20.5= normal arteries, 20.6-30.0= non-significant CAD, >30.1= significant CAD). Differences in lipoprotein subfractions between the groups were assessed by two-way ANOVA, adjusted for statin use.

Results: Despite no difference in the conventional lipid measures, patients with significant CAD had an increased number of small and dense LDL-5 particles and increased levels of cholesterol, triglycerides, phospholipids, and apo-B within LDL-5 compared to the those with non-significant CAD and normal arteries.

Conclusions: NMR revealed a significant increase in the small and dense LDL-5 subfractions in patients with significant CAD. Our results suggest that small and dense LDL subfractions are associated with coronary atherosclerosis and may represent a promising risk marker for CAD.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-08 Cellular lipid metabolism and lipid droplets*

SIZE, FATTY ACID AND PROTEIN CHARACTERIZATION OF DIFFERENT POPULATIONS OF EXTRACELLULAR VESICLES OBTAINED BY SEQUENTIAL CENTRIFUGATION. AN USEFUL TOOL TO DISSECT THEIR BIOLOGICAL PROPERTIES?

POSTER VIEWING SESSION

Felice Maria Accattatis[1], Sara Mazza[2], Francesca Bordonaro[2], Agnese Granata[2], Elisabetta Vergani[3], Monica Rodolfo[3], Laura Bianchi[4], Fabrizio Francomano[4], Alfonso Carleo[5], Stefano Bellosta[2], Alberto Corsini[2], Lorenzo Arnaboldi[2]
[1]Department Of Pharmacy, Health And Nutritional Sciences, Università della Calabria, Arcavacata di Rende, Italy, [2]Dipartimento Di Scienze Farmacologiche E Biomolecolari, Università degli Studi di Milano, milano, Italy, [3]Immunotherapy Of Human Tumors Department Of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy, [4]Dept. Of Life Sciences, Università di Siena, Siena, Italy, [5]Dpt. Of Pulmonology, Medizinische Hochschule Hannover, Fraunhofer-Institut für Toxikologie und Experimentelle Medizin, Hannover, Germany

Background and Aims : Extracellular vesicles (EVs), by transferring their cargo from cell to cell, participate to pathophysiological processes. Unfortunately, unproper separation and characterization methods impair the comprehension of their functions.Therefore, we set up an ultracentrifugation method to separate by size different EV populations derived from a melanoma cell line, according to the algorithm developed by Livshits (Sci Rep. 2015;14:1).

Methods: Next we characterized them by transmission electron microscopy (TEM), tracking analysis (nanosight) and dynamic light scattering (Zetasizer). We also obtained EV fatty acid (FA) and protein profiles by gas-chromatography and label-free quantitative mass spectrometry (MS) proteomic approach, respectively.

Results: Size analysis confirmed not only the existence of different EVs populations, but also the theoretical sizes calculated by the algorithm. Gas-chromatography revealed a continuous percentage increase in saturated FAs ranging from parental cells to smaller EVs (33.61% to 64.79%), suggesting different origin and membrane properties among different populations. Mass spectrometry identified up to 2000 proteins differentially distributed among the populations or even unique for each fraction. Finally, Ingenuity Pathway and MetaCore net analyses delineated specific pathways and protein-cross-talks that differential protein cargo may establish in the different vesicle-fractions.

Conclusions: In conclusion, lipid and protein differences detected among the EV fractions may translate into distinct biological relevance for each of them. Therefore, the here proposed separation method, which may be applied to any cell line, may be helpful in defining the role of specific EV populations in cell pathophysiology and in finding new pharmacological treatments able to modulate EV functions. *Supported by EXTRALIPO Bando SEED–PSR 2019.*

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-08 Cellular lipid metabolism and lipid droplets*

PHARMACOLOGICAL MODULATION OF LIPID METABOLISM IN A HUMAN CELL LINE ALTERS PROTEIN CONTENT AND SIGNALLING OF SECRETED EXTRACELLULAR VESICLES

POSTER VIEWING SESSION

Sara Mazza[1], Felice Maria Accattatis[2], Francesca Bordonaro[1], Agnese Granata[1], Laura Bianchi[3], Fabrizio Francomano[3], Alfonso Carleo[4], Elisabetta Vergani[5], Monica Rodolfo[5], Stefano Bellosta[1], Alberto Corsini[1], Lorenzo Arnaboldi[1]
[1]Dipartimento Di Scienze Farmacologiche E Biomolecolari, Università degli Studi di Milano, milano, Italy, [2]Department Of Pharmacy, Health And Nutritional Sciences, Università della Calabria, Arcavacata di Rende, Italy, [3]Dept. Of Life Sciences, Università di Siena, Siena, Italy, [4]Dpt. Of Pulmonology, Medizinische Hochschule Hannover, Fraunhofer-Institut für Toxikologie und Experimentelle Medizin, Hannover, Germany, [5]Immunotherapy Of Human Tumors Department Of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

Background and Aims : Extracellular Vesicles (EVs) are an attractive pharmacological target due to their involvement in cell-cell communications. From a lipid point of view, EVs are composed by phospholipids and cholesterol. The latter, together with the phospholipid bis-monoacylglycerophosphate (BMP), plays a pivotal role in EVs fate, since their balance drives late endosomes towards secretion or lysosomal recycling. Based on these premises, we decreased cholesterol biosynthesis with the HMG-CoA reductase inhibitor simvastatin and BMP degradation by KT182 in a melanoma cell line and we evaluated the effects on secreted EVs and their potential functional alterations.

Methods: After ultracentrifugation, we characterized separated microvesicles (10K) and exosomes (100K) by size (Nanosight), fatty acid (FA; gas-chromatography) and protein content (mass spectrometry). MS identified proteins were functionally processed by applying Ingenuity and MetaCore pathway analysis.

Results: The pharmacological treatments neither affected cell proliferation, nor EVs size, FA composition and number. Simvastatin (0.1µM) and KT182 (50nM) alone or combined, decreased cell cholesterol biosynthesis. while KT182 concentration-dependently increased it. Intriguingly, confocal microscopy analysis showed that KT182 affects cell BMP distribution and lysosome compartmentalization. Several proteins were detected changing in abundance after the treatments, both in 100K and 10K fractions. Their functional processing showed that treatments affect specific cellular pathways, which suggest altered EVs biological functions.

Conclusions: In conclusion, cholesterol and BMP modulation of parental cells significantly affects the protein content of released EVs, possibly leading to altered EVs functionality, suggesting the potential of a lipid modulation in cell-released EVs, in the light of new therapeutic approaches. *Support: EXTRALIPO Bando SEED–PSR2019.*

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-08 Cellular lipid metabolism and lipid droplets*

SPRING1 IS REQUIRED FOR PROPER FUNCTIONING OF SREPB MEDIATED LIPID SYNTHESIS.

POSTER VIEWING SESSION

Sebastian Hendrix[1], Noam Zelcer[2]
[1]Medical Biochemistry, Amsterdam UMC location AMC, Amsterdam, Netherlands, [2]Medical Biochemistry, Amsterdam UMC, locatie AMC, Amsterdam, Netherlands

Background and Aims : Disturbed lipid metabolism is a key contributor to development of cardiovascular diseases. We identified SPRING1 as a new determinant of sterol regulator element-binding protein (SREBP) mediated transcriptional activation of cholesterol and fatty acid synthesis. SPRING1 encodes a Golgi-resident, glycosylated membrane protein that is ubiquitously expressed. In this study we aim to further investigate and characterize this previously unknown regulator of lipid metabolism.

Methods: To elucidate the role of SPRING1 *in vivo* we are studying the consequences of hepatic loss of SPRING1 expression in mice by means of dietary studies coupled with various omics approaches. To understand its mechanism of action, we investigated levels and interactions of SPRING1 and other SREBP-related proteins and its influence on lipid-associated pathways in SPRING1 deficient cells.

Results: Ablation of SPRING1 impairs SREPB target gene expression and therefore cholesterol biosynthesis and lipoprotein uptake in response to sterol depletion. This is dependent on an intricate interaction between SPRING1 and Site1 protease (S1P). This interaction leads to activation of S1P and to processing of SPRING1. Mechanistic studies in cells demonstrate that S1P activation requires SPRING1. The significance of SPRING1 processing by S1P is being currently investigated.

Conclusions: Our data further establish the role of SPRING1 as a novel regulator of the SREBP pathway and thereby may help to develop mechanism-based strategies to treat dysregulated lipid metabolism.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-08 Cellular lipid metabolism and lipid droplets*

THE ROLE OF IL7 AND ITS RECEPTOR IN CHOLESTEROL ACCUMULATION IN MONOCYTE-DERIVED HUMAN MACROPHAGES

POSTER VIEWING SESSION

Vasily N. Sukhorukov[1,2], Victoria A. Khotina[1,2], Maryam Bagheri Ekta[1], Andrey V. Omelchenko[1], Igor A. Sobenin[3], Alexander N. Orekhov[1]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Angiology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation, [3]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation

Background and Aims : Cholesterol accumulation is a primary outcome of atherosclerosis at the arterial cell level. We used the transcriptome analysis and the bioinformatics approach to determine genes that change their expression in monocyte-derived human macrophages exposed to native and atherogenic LDL. Our aim was to evaluate the role of revealed genes in cellular cholesterol accumulation

Methods: Monocyte-derived human macrophages (MDMs)were cultured with native human LDL as well as modified LDL for 24 hours, and then RNA-seq libraries were prepared using a NEBNext Ultra RNA library kit. Libraries were sequenced on an Illumina HiSeq 1500. To identify genes showing differential expression we used the edgeR package. Cholesterol accumulation was evaluated in MDMs with genes knocked-downed by siRNA.

Results: The transcriptome from macrophages incubated with native LDL was compared with the transcriptome from macrophages incubated with modified LDLs. As a result, 5 genes related to cholesterol accumulation were identified: IL7, IL7R, CXCL8, DUSP1, and TIGIT. We performed knock-down of these genes to assess their role in cholesterol accumulation in MDMs. The knock-down of IL7 and IL7R augmented cholesterol accumulation compared to the control cholesterol accumulation in the cells without the knock-down. The knock-down of CXCL8, DUSP1, and TIGIT genes haven’t affected cellular cholesterol accumulation.

Conclusions: IL7 and its receptor (IL7R) may play role in cellular cholesterol accumulation.
This work was supported by Russian Science Foundation (Grant # 22-25-00274).

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

CONSISTENCY OF FRIEDEWALD, MARTIN/HOPKINS AND SAMSON FORMULAS FOR LDL-C CALCULATION IN HIGH AND VERY HIGH CARDIOVASCULAR RISK PATIENTS

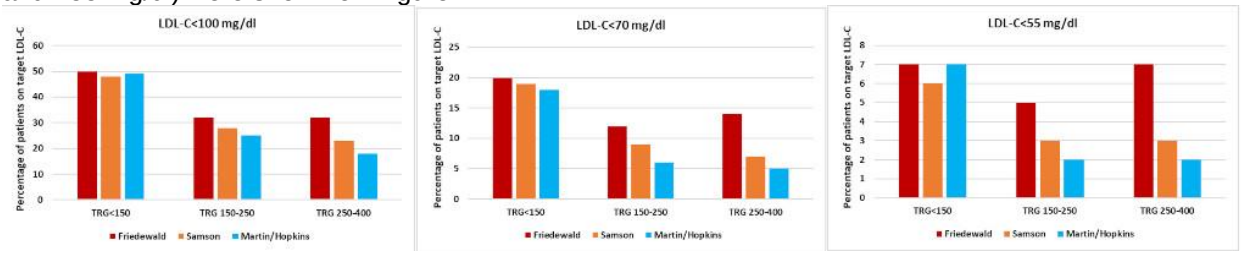
POSTER VIEWING SESSION

Ozcan Basaran[1], Volkan Dogan[1], Oguzhan Celik[1], Cem Cil[2], Bulent Ozlek[2], Eda Ozlek[2], Ibrahim H. Ozdemir[3], Ibrahim Rencuzogullari[4], Fatma Karadeniz[5], Mehmet Tekinalp[6], Lutfu Askin[7], Selami Demirelli[5], Erkan Gencer[8], Murat Biteker[1], Meral Kayikcioglu[9]
[1]Cardiology, Mugla Sitki Kocman University, Mugla, Turkey, [2]Cardiology, Mugla Sitki Kocman University Education And Research Hospital, Mugla, Turkey, [3]Cardiology, Nizip State Hospital, Gaziantep, Turkey, [4]Cardiology, Kars University, Kars, Turkey, [5]Cardiology, Erzurum education and research hospital, Erzurum, Turkey, [6]Cardiology, Necip Fazıl State Hospital, Kahramanmaras, Turkey, [7]Cardiology, Adiyaman University, Adiyaman, Turkey, [8]Cardiology, Kilis State Hospital, Kilis, Turkey, [9]Cardiology, Ege University School of Medicine, Izmir, Turkey

Background and Aims : Friedewald formula is the most common used equation to calculate LDL-C levels. However, its accuracy has been questioned recently. We aimed to investigate the consistency of Friedewald (F), Martin/Hopkins (M) and Samson (S) formulas for calculated LDL-C levels, and the effect on target goal attainment for different LDL-C targets.

Methods: The lipid parameters of EPHESUS study (multicenter, observational study conducted on high and very high CVD risk patients) participants were used to calculate LDL-C values according to three (F,M,S) formulas. Correlation was assessed by Pearson's correlation coefficient among these formulas. The patients grouped according to triglyceride (TG) levels of <150 mg/dl, 150-250 mg/dl, and 250-400 mg/dl. Goal attainment rates at different LDL-C targets (<100 mg/dl, <70 mg/dl, and <55 mg/dl) were than compared.

Results: Of the 1810 patients, correlation coefficients among formulas were 0.998, 0.996, and 0.991 for F&S, M&S, and F&M respectively (p<0.001). When patients were grouped according to TG levels 884 (48.9%) had <150 mg/dl, 663 (36.7%) had 150-250 mg/dl, and 261 (14.4%) had 250-400 mg/dl. A comparison of those patients according to different LDL-C target attainment rates (<100 mg/dl, <70 mg/dl, and <55 mg/dl) were shown on Figure.



Conclusions: Although there was a good correlation among all formulas Friedewald formula tended to underestimate LDL-C values in patients with high triglyceride levels. Furthermore, the risk underestimation was highest for lower LDL-C levels. Hence it might be reasonable to use new formulas for LDL-C calculation in high and very high cardiovascular risk patients especially if their LDL-C values were close to targets.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

FAMILIAL HYPERCHOLESTEROLEMIA WITHIN CARDIOLOGY PRACTICE - SINGLE-CENTER EXPERIENCE

POSTER VIEWING SESSION

Edin Begić[1], Nedim Begić[2], Ada Đozić[3], Emina Karavelić[1], Nadira Zatrić[4], Adela Sinančević[4], Alen Džubur[5], Amina Šahbaz[6], Esma Hasanagić[6]
[1]Department Of Cardiology, General Hospital "Prim. dr. Abdulah Nakaš", Sarajevo, Bosnia and Herzegovina, [2]Pediatric Cardiology, Pediatric Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina, [3]Internal Medicine, General Hospital "Prim. dr. Abdulah Nakaš", Sarajevo, Bosnia and Herzegovina, [4]Family Medicine, Health Care Center, Sarajevo, Bosnia and Herzegovina, [5]Department Of Cardiology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina, [6]Sarajevo Medical School, Sarajevo School Of Science And Technology, Sarajevo Medical School, Sarajevo School of Science and Technology, Sarajevo, Bosnia and Herzegovina, Sarajevo, Bosnia and Herzegovina

Background and Aims : To evaluate familial hypercholesterolemia (FH) in our centre, and to increase awareness of this disorder.

Methods: The research had cross-sectional, descriptive and analytical character, and included 6881 patients hospitalized in the Clinic for Heart, Blood Vessel and Rheumatic Diseases, Clinical Center University of Sarajevo, in the period from January 2019 to January 2021. LDL values were analyzed, and patients with LDL> 4 mmol/L were included in the study.

Results: A total of 74 patients had LDL ≥ 4 mmol/L. Indication for hospitalisation in 44.60% of patients was a STEMI, hypertension 14.87% and angina pectoris 14.87%. In 29.7% of the patients, there were no indications for coronary angiography or patient refuse to do it, while in 4.1% of patients coronarography was without significant stenosis. Single-vessel disease was found in 24.32% (n=18) of patients, two-vessels disease in 13.51% (n=10), and triple-vessels in 28.38% (n=21) of patients. According to the results, patients under the age of 65 have higher Dutch Lipid Score compared to the patients above the age of 65, regardless of male or female. Correlational analysis indicated a positive significant relationship between Dutch Lipid Score and level of cholesterol and LDL. In the first model, non-modifiable risk factors explained 25.5% of the variance of the criteria variable. The obtained results of the hierarchical regression analysis showed that the final model explained 50.8% of the variance of the Dutch Lipid Score and diagnosis of FH.

Conclusions: Screening for the existence of FH in clinical practice has to be a daily clinical practice, along with monitoring of LDL values.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

IDENTIFICATION OF THE TRANSCRIPTION FACTOR ATF3 AS A NEW REGULATOR OF THE LDLR

POSTER VIEWING SESSION

Jana Eigenmann[1], Sabine Bauer[2], Julia Fleig[1], Yuqi Zhao[3], Heribert Schunkert[1], Moritz Von Scheidt[1]
[1]Department Of Cardiology, German Heart Centre Munich, Munich, Germany, [2]Experimental Cardiology, German Heart Centre Munich, München, Germany, [3]Integrative Biology And Physiology, Quantitative and computational Biosciences, Los Angeles, United States of America

Background and Aims : Coronary artery disease (CAD) is a globally leading cause of death and brought about by atherosclerosis prompted by a multifactorial interplay of genetic and lifestyle factors. Mechanisms resulting in CAD can be grouped into different pathways. However, characterization and regulation of these tissue specific functional networks is far from being complete. We aimed to experimentally study the regulatory capacities of promising targets and identify new therapeutical concepts to decrease CAD risk.

Methods: We built this work on two distinct resources. First, genes identified to affect atherosclerosis in mouse and human and second, transcriptome analysis in several atherosclerosis relevant tissues. Based on an established workflow candidate genes of interest, should be validated based on experimental work.

Results: One top ranked key driver orchestrating a liver network was the transcription factor *ATF3* (FDR $3.89e^{-6}$; Fold enrichment 14.05). Most interestingly, implementing directionality based on expression data, *LDLR* was predicted to be a direct downstream target of *ATF3*. *In vivo* data from human and mouse confirmed co-regulation patterns. To confirm the role of *ATF3* orchestrating the predicted regulatory liver network human Hep3b cells were used. siRNA knockdown of *ATF3* showed consistent and significant upregulation of the *LDLR* expression ($p<0.001$), as well as significant perturbation of the neighbor-genes *MAFF* ($p<0.001$) and *SERPINE1* ($p<0.001$).

Conclusions: We show for the very first time, that liver specific downregulation of *ATF3* causes significant upregulation of the *LDLR* and speculate that therapeutical downregulation of *ATF3* might be a novel approach to treat hypercholesterolemia and reduce CAD risk.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

LIPOPROTEIN SUBFRACTIONS IN PATIENTS WITH VARIOUS CARDIOVASCULAR RISK

POSTER VIEWING SESSION

Elena A. Utkina[1], Nadezhda V. Artemieva[2], Marat V. Ezhov[2], Olga I. Afanasieva[1], Sergey N. Pokrovsky[1]
[1]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation, [2]Atherosclerosis Department, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Russian Federation

Background and Aims : To analyze lipoproteins subfractions in subjects with various cardiovascular risk and cardiovascular disease (CVD).

Methods: We included 91 patients (66 men, mean age 57±10 years; 25 women, mean age 61±11 years) with one or more atherosclerosis risk factors, with and without CVD. All patients were on hypolipidemic therapy with statins. Lipid parameters were determined by the enzymatic method, the quantitative determination of lipoprotein subfractions was carried out using the Lipoprint® Quantimetrix system (USA).

Results: All patients were divided into three groups: moderate risk (group 1, n = 13), high risk (group 2, n = 12), and very high risk with diagnosed CVD (group 3, n = 66). There were no statistically significant differences between the groups in lipids and lipoproteins subfractions, excepting small dense low-density lipoprotein (sdLDL) particles in the group 1 and 3 (median [25%; 75%]: 0.0 [0.0; 2.0] mg/dL and 2.0 [0.0; 3.0] mg/dL, respectively, $p<0.05$). We found that cardiovascular risk was positively associated with age ($r = 0.325$; $p <0.01$), the levels of subfractions of intermediate-density lipoproteins (IDL-C, $r = 0.225$; $p = 0.032$) and sdLDL ($r = 0.216$; $p < 0.039$). An inverse relationship was demonstrated with small subfractions of IDL (IDL-A, $r = -0.210$; $p = 0.046$). According to multivariate analysis only association of sdLDL with higher cardiovascular risk was remained ($p = 0.022$).

Conclusions: Patients with high and very high cardiovascular risk have increased levels of sdLDL particles.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

WHOLE EXOME/GENOME SEQUENCING JOINT ANALYSIS IN A FAMILY WITH OLIGOGENIC FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Youmna Ghaleb[1], Sandy El Bitar[2], Anne Philippi[3], Petra El Khoury[1], Yara Azar[1], Miangaly Andrianirina[1], Alexia Loste[1], Yara Abou-Khalil[1], Gaël Nicolas[4], Marie Le Borgne[1], Philippe Moulin[5], Mathilde Di Filippo[5], Sybil Charriere[5], Michel Farnier[6], Cécile Yelnik[7], Valérie Carreau[8], Jean Ferrières[9], Jean-Michel Lecerf[10], Alexa Derksen[11], Geneviève Bernard[12], Marie-Soleil Gauthier[13], Benoit Coulombe[13], Dieter Luetjohann[14], Bertrand Finn[15], Anne Boland[15], Robert Olaso[15], Jean-François Deleuze[15], Jean-Pierre Rabès[16], Catherine Boileau[1], Marianne Abifadel[1], Mathilde Varret[1]
[1]Laboratory For Vascular Translational Science (lvts), INSERM, Paris, France, [2]Bichat Hospital, Laboratory for Vascular Translational Science (LVTS), National Institute for Health and Medical Research (INSERM) U1148, Paris, France, [3]Institut Cochin, INSERM U1016, Paris, France, [4]Centre De Recherche Sur L'inflammation, INSERM U1149, CNRS ERL 8252, Paris, France, [5]Inserm U1060, Université Lyon 1, Inrae U1397, Laboratoire CarMen, Oullins, France, [6]No, Université de Bourgogne Franche-Comté, CHU Dijon Bourgogne, DIJON, France, [7]Département De Médecine Interne Et D'immunologie Clinique, Université de Lille, INSERM UMR 1167 RID-AGE, CHU Lille, LILLE, France, [8]Paris, Cardiovascular prevention unit, Pitié-Salpêtrière Hospital, AP-HP, PARIS, France, [9]Department Of Cardiology And Inserm Umr 1295, Toulouse Rangueil University Hospital, Toulouse, France, [10]Nutrition Department, Institut Pasteur de Lille, Lille, France, [11]Translational Proteomics Laboratory, Institut de Recherches Cliniques de Montréal, Montréal, Montréal, Canada, [12]Department Of Neurology And Neurosurgery, McGill University, Montréal, Canada, [13]Translational Proteomics Laboratory, Institut de Recherches Cliniques de Montréal, Montréal, Canada, [14]Institute Of Clinical Chemistry And Clinical Pharmacology, University Clinics Bonn, Bonn, Germany, [15]Centre National De Recherche En Génomique Humaine, Université Paris-Saclay, Evry, France, [16]Department Of Biochemistry And Molecular Genetics, Ambroise Paré University Hospital, Boulogne-Billancourt, France

Background and Aims : Autosomal Dominant Hypercholesterolemia (ADH) is a genetic disorder caused by pathogenic variants in *LDLR*, *APOB*, *PCSK9* and *APOE* genes. We sought to identify a new candidate gene responsible of the ADH phenotype in patients with no pathogenic variants in known ADH causing genes.

Methods: We performed linkage analysis, whole exome and whole genome sequencing in one French family, with affected and non-affected members presenting a high ADH polygenic risk score (wPRS). We also performed functional studies in HEK293T cells of the four *LRP6* mutants.

Results: Linkage analysis, whole exome and whole genome sequencing in one French family, with affected and non-affected members presenting a high ADH polygenic risk score (wPRS) allowed us to identify p.(Pro398Ala) in *CYP7A1*, p.(Val1382Phe) in *LRP6* and p.(Ser202His) in *LDLRAP1*. Six other variants were identified in 6 from 160 unrelated ADH probands: p.(Ala13Val) and p.(Aps347Asn) in *CYP7A1*, p.(Tyr972Cys), p.(Thr1479Ile) and p.(Ser1612Phe) in *LRP6* and p.(Ser202LeufsTer19) in *LDLRAP1*. All these six probands presented a moderate wPRS. Serum analysis of carriers of p.(Pro398Ala) variant in *CYP7A1* showed no differences in bile acids synthesis when compared to non-carriers serums. Functional studies in HEK293T cells of the four *LRP6* mutants showed contradictory results. None of the family members heterozygous carriers of the *LDLRAP1* p.(Ser202His) variant alone presented ADH.

Conclusions: Altogether, each variant alone does not seem to contribute sufficiently to the elevation of LDL-C and it is the oligogenic combination of two or three variants that is necessary to reveal the ADH phenotype.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

GENETIC AND CLINICAL CHARACTERISTICS OF HETEROZYGOUS AND HOMOZYGOUS LPL DEFICIENCY: CASE SERIES

POSTER VIEWING SESSION

Tatiana M. Marusic[1], Barbara Jenko Bizjan[2,3], Urša Šuštar[2], Matija Cevc[4], Matej Mlinarič[1], Jernej Kovač[1], Hijab Batool[5], Iqbal Khan[6], Tadej Battelino[1,3], Fouzia Sadiq[6], Urh Groselj[1]
[1]Department Of Endocrinology, Diabetes, And Metabolic Diseases, University Children's Hospital, UMC Ljubljana, Ljubljana, Slovenia, [2]Clinical Institute For Special Laboratory Diagnostics, University Children's Hospital, UMC Ljubljana, Ljubljana, Slovenia, [3]Faculty Of Medicine, University of Ljubljana, Ljubljana, Slovenia, [4]Division Of Medicine, Centre For Preventive Cardiology, University Medical Centre Ljubljana, Ljubljana, Slovenia, [5]Department Of Clinical Chemistry And Immunology, Chugtai Institute of Pathology, Lahore, Pakistan, Lahore, Pakistan, [6]Directorate Of Research, Shifa Tameer-e-Millat University, Islamabad, Pakistan, Islamabad, Pakistan

Background and Aims : To characterize cohort of patients with Lipoprotein Lipase (LPL) deficiency from Slovenia and Pakistan.

Methods: We investigated the genetic and clinical characteristics of 4 patients with primary hypertriglyceridemia from the Slovenian registry and those who were previously diagnosed at our institution. We followed up 3 Slovenian patients (an 8 years old female, an 18 years old man and a 57 years old female) and 1 male aged 59 years from Pakistan.

Results: Two Slovenian patients were diagnosed at birth and at 2 years old, with triglyceride (TG) values of 16 and 20 mmol/L, respectively; they stayed asymptomatic with good control of their TG values. In both of them, a heterozygous mutation c.[984G<T] in the exon 6 of the LPL gene was detected. The patient from Pakistan had a presenting TG value of 36.8 mmol/L, asymptomatic. He had confirmed a heterozygous mutation in exon 5 of LPL:c.[724G>A]. With medication and diet, his TG levels dropped to 12.7 mmol/L. On the other hand, the Slovenian homozygous LPL patient was diagnosed after the first episode of pancreatitis at the age of 18 with a TG value of 34 mmol/L. She recurred with seven episodes of pancreatitis and with a pancreatic cyst. A mutation in both alleles of LPL:c.[337T>C] was confirmed.

Conclusions: This publication presents four patients with severe hypertriglyceridemia: three were heterozygous and one was homozygous for LPL deficiency. Although all patients presented with highly elevated TG levels at the onset, clinical findings and prognosis were worse in the homozygous LPL deficiency.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

ENERGY METABOLISM HORMONES AND LIPID PROFILES IN TRANSGENDER INDIVIDUALS: CROSS-SECTIONAL PILOT STUDY

POSTER VIEWING SESSION

Michael Frenkel[1], Natalie Cusano[1], Eugenia Gianos[1], Tung Ming Leung[2], Karina Ziskovich[1], Dimitar Avtanski[1], Radoslav Stojchevski[1], Sadiya Thermidor[1], Marwen Hassan Eid[1], Leonid Poretsky[1]
[1]Endocrinology, Northwell Health, New York, United States of America, [2]Biostatistics, Northwell Health, New York, United States of America

Background and Aims : Energy metabolism is closely related to lipid profiles and sex hormones. Gender affirming hormone therapy (GAHT) can increase adiponectin and leptin levels in transgender females, while resistin levels are unaffected by GAHT. GAHT also increases triglycerides (TG) and total cholesterol (TC) in transgender females and males (Auer, JCEM 2018; Ott; J. Sex. Med. 2011). We examined the relationships among resistin, leptin, adiponectin, testosterone, estradiol, TC, HDL, LDL and TG within 4 gender identity groups.

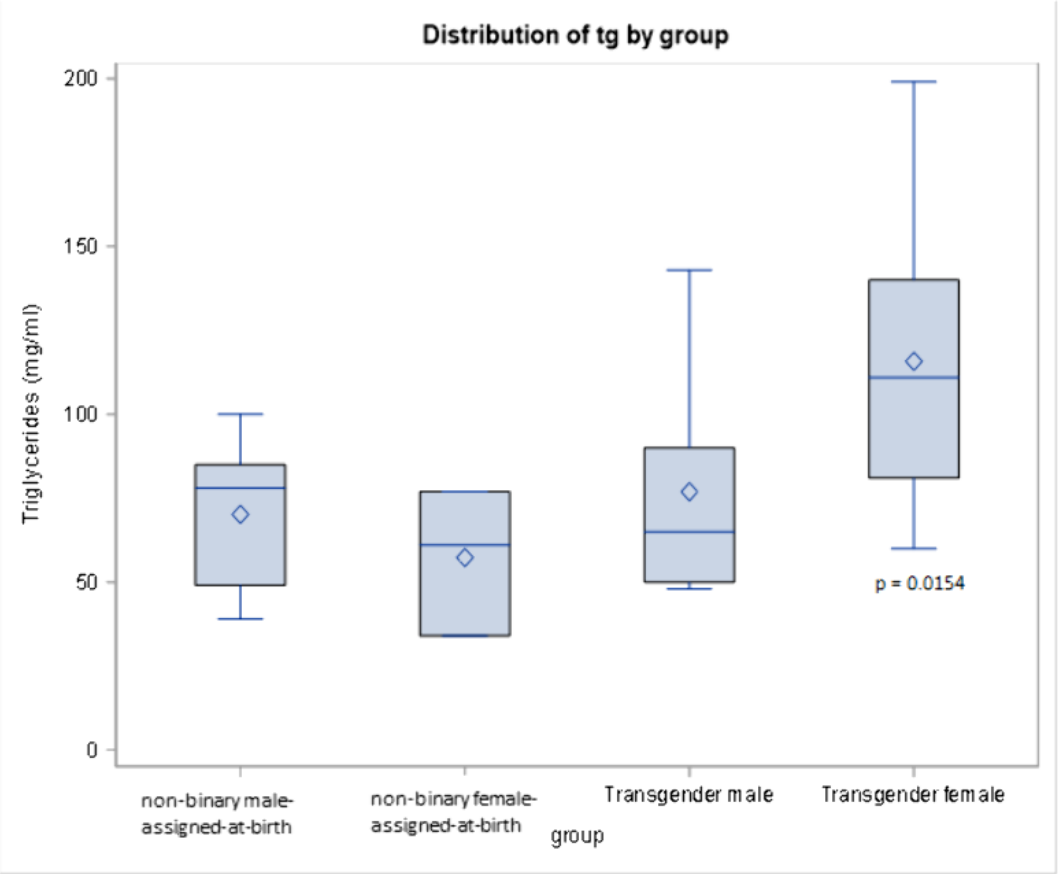
Methods: 38 subjects were recruited from a prospective transgender registry and classified into 4 groups (Table 1). Kruskal-Wallis tests and Spearman correlation analysis were carried out.

Table 1: Demographics

				Race					
Group	N	median age	median bmi	White or Caucasian	Black or African-American	Asian	Native American or Alaskan Native	Other	Multi-racial
Assigned-at-birth-males, non-binary, NOT on GAHT	5	21.43	26.03	2	2	0	0	0	1
Assigned-at-birth-females, non-binary, NOT on GAHT	3	22.56	26.17	1	0	0	0	2	0
Transgender males or non-binary on GAHT-testosterone	15	22.65	23.62	8	3	0	1	2	1
Transgender females or non-binary on GAHT- estrogen, spirinolactone	15	34.99	28.57	13	0	1	0	1	0

Results: The only statistically significant difference among the groups was for circulating triglyceride levels (higher in transgender females, p=0.0154) [Figure 1].

Figure 1: Triglyceride Distribution (Box Plots)



Significant correlations between energy metabolism hormones and other examined parameters persisted for the cohort and within the four groups. Resistin levels were not significantly different among the groups and did not correlate with BMI or other examined parameters (Table

2).

Table 2: Correlation for variables (entire cohort)

Spearman Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	leptin	adiponectin	resistin	bmi	testosterone	Estradiol	hdl_c	ldl_c	tc	tg
leptin	1.00000 37	-0.23661 0.1586 37	0.06211 0.7150 37	0.66453 <.0001 37	-0.23025 0.1902 34	0.12928 0.4959 30	-0.24986 0.1417 36	0.28864 0.0878 36	0.22647 0.1841 36	0.28156 0.0962 36
adiponectin	-0.23661 0.1586 37	1.00000 37	0.11735 0.4891 37	-0.55524 0.0004 37	0.02246 0.8997 34	-0.07788 0.6825 30	0.40013 0.0156 36	-0.27551 0.1039 36	-0.15463 0.3679 36	-0.50029 0.0019 36
resistin	0.06211 0.7150 37	0.11735 0.4891 37	1.00000 37	-0.04339 0.7987 37	0.01879 0.9160 34	-0.02893 0.8794 30	0.16949 0.3230 36	-0.03643 0.8329 36	-0.01970 0.9092 36	0.04236 0.8062 36
bmi	0.66453 <.0001 37	-0.55524 0.0004 37	-0.04339 0.7987 37	1.00000 38	-0.20476 0.2380 35	0.15003 0.4205 31	-0.42478 0.0088 37	0.48212 0.0025 37	0.38077 0.0201 37	0.63864 <.0001 37
testosterone	-0.23025 0.1902 34	0.02246 0.8997 34	0.01879 0.9160 34	-0.20476 0.2380 35	1.00000 35	-0.55495 0.0012 31	-0.13261 0.4547 34	0.18783 0.2874 34	0.01437 0.9357 34	-0.23477 0.1814 34
Estradiol	0.12928 0.4959 30	-0.07788 0.6825 30	-0.02893 0.8794 30	0.15003 0.4205 31	-0.55495 0.0012 31	1.00000 31	-0.10568 0.5783 30	-0.32862 0.0762 30	-0.19032 0.3138 30	0.44373 0.0140 30
hdl_c	-0.24986 0.1417 36	0.40013 0.0156 36	0.16949 0.3230 36	-0.42478 0.0088 37	-0.13261 0.4547 34	-0.10568 0.5783 30	1.00000 37	-0.10248 0.5461 37	0.26350 0.1151 37	-0.33638 0.0418 37
ldl_c	0.28864 0.0878 36	-0.27551 0.1039 36	-0.03643 0.8329 36	0.48212 0.0025 37	0.18783 0.2874 34	-0.32862 0.0762 30	-0.10248 0.5461 37	1.00000 37	0.88548 <.0001 37	0.39420 0.0158 37
tc	0.22647 0.1841 36	-0.15463 0.3679 36	-0.01970 0.9092 36	0.38077 0.0201 37	0.01437 0.9357 34	-0.19032 0.3138 30	0.26350 0.1151 37	0.88548 <.0001 37	1.00000 37	0.42145 0.0094 37
tg	0.28156 0.0962 36	-0.50029 0.0019 36	0.04236 0.8062 36	0.63864 <.0001 37	-0.23477 0.1814 34	0.44373 0.0140 30	-0.33638 0.0418 37	0.39420 0.0158 37	0.42145 0.0094 37	1.00000 37

Legend
Correlation Coefficient
P-value
N

Limitations of Study: Small sample size. Data prior to the initiation of GAHT were unavailable.

Conclusions: Because expected gender differences for leptin and adiponectin were absent for transgender individuals on GAHT, it is possible that GAHT affected levels of energy metabolism hormones. In individuals on GAHT, leptin and adiponectin maintained their positive and negative associations respectively with BMI. GAHT affects TG levels in transgender females. Larger controlled prospective studies are needed to examine the relationships among energy metabolism hormones and lipid profiles in transgender individuals.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

CHANGES IN LIPOPROTEINS ASSOCIATED WITH PHARMACOLOGICAL STRATEGIES IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Zahra Lotfollahi[1], Ana Paula D.Q. Mello[2], Francisco A.H. Fonseca[3], Luciene O. Machado[1], Andressa F. Mathias[1], Maria C. Izar[3], Nagila R.T. Damasceno[4], Cristiano L.P.D. Oliveira[1], Antonio M. Figueiredo Neto[1]
[1]Physics, Unversity of Sao Paulo, Sao Paulo, Brazil, [2]Faculdade De Saúde Pública, Centro Universitário São Camilo, Sao paulo, Brazil, [3]Department Of Medicine, Discipline Of Cardiology, Federa University of Sao Paulo, Sao paulo, Brazil, [4]Department Of Nutrition, University of São Paulo, sao paulo, Brazil

Background and Aims : Despite lipid-lowering and antiplatelet therapy, the pattern of residual lipoproteins seems relevant to long-term cardiovascular outcomes. This study aims to evaluate the effects of combined therapies, commonly used in subjects with acute myocardial infarction, in the quality of LDL particles.

Methods: Prospective, open-label trial, included patients with acute myocardial infarction. Patients were randomized to antiplatelet treatment (ticagrelor or clopidogrel) and subsequently to lipid-lowering therapy (rosuvastatin or simvastatin/ezetimibe) and were followed up for six months. Nonlinear optical properties of LDL samples were examined by Gaussian laser beam (Z-scan) to verify the oxidative state of these lipoproteins, small angle X-ray scattering (SAXS) to analyze structural changes on these particles, dynamic light scattering (DLS) to estimate the particle size distribution, UV-visible spectroscopy to evaluate the absorbance at wavelength 484 nm (typical from carotenoids), and polyacrylamide gel electrophoresis (Lipoprint) to analyze the LDL subfractions.

Results: Simvastatin/ezetimibe with either clopidogrel or ticagrelor was associated with less oxidized LDL, and simvastatin/ezetimibe with ticagrelor to lower cholesterol in the atherogenic subfractions of LDL, while rosuvastatin with ticagrelor was the only combination associated with increase in LDL size.

Conclusions: The quality of LDL particles was influenced by the antiplatelet/lipid-lowering strategy, with ticagrelor being associated with the best performance with both lipid-lowering therapies.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

EGYPTIAN ASSOCIATION FOR VASCULAR BIOLOGY AND ATHEROSCLEROSIS (EAVA) CONSENSUS ON THE USE OF INCLISIRAN IN CLINICAL PRACTICE

POSTER VIEWING SESSION

Ashraf Reda[1], Ahmed Shawky[2], Ahmed Elkersh[1], Atef Elbahry[3], Elsayed Farag[4], Mohamed Ashraf[5], Ahmed Bendary[6]
[1]Cardiology, Menoufia University, Shebin Elkom, Egypt, [2]Cardiology, Ain Shams University, Cairo, Egypt, [3]Cardiology, Port Fouad cardiac center, Pot Fouad, Egypt, [4]Cardiology, Zagazing University, Zagazig, Egypt, [5]Cardiology, National Heart Institute, Giza, Egypt, [6]Cardiology, Benha University, Benha, Egypt

Background and Aims : Small interfering RNA molecules (siRNA) e.g., Inclisiran represent an attractive alternative to monoclonal antibodies for Proprotein convertase subtilisin/kexin type 9 (PCSK9) lowering. These molecules offer profound lowering of (intra- and extracellular) PCSK9 at a lower-dose frequency and potentially at a lower cost. Inclisiran has undergone phase 1, 2, and 3 evaluation all within the context of the ORION trials, with good efficacy and safety. Considering that Egypt is a middle-income country with a burdened economy, concerns are raised on which patients would benefit from this expensive medication. Therefore, the Egyptian Association for Vascular biology and Atherosclerosis (EAVA) took the responsibility of providing the 1st Egyptian consensus on the use of Inclisiran in clinical practice.

Methods: EAVA analyzed the data that would enable us to obtain clear indications for the use of Inclisiran.

Results: Dyslipidemia represents a major atherosclerotic risk factor in Egypt. Among Egyptian patients with acute coronary syndromes, it has been estimated that the prevalence of dyslipidemia is 48%, and that of ‘at-least-possible’ FH is 17%. Reaching low-density lipoprotein cholesterol (LDL-C) goals is difficult as well.

Conclusions: We recommend the use of Inclisiran in addition to statins ± ezetimibe in patients with either [1]. established ASCVD or [2]. FH with one of the following: another major risk factor, eGFR < 30 ml/min,or very-high risk DM, who didn’t reach LDL-C goals and/or with true statin intolerance.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-09 Lipid and lipoprotein metabolism*

NORMALIZING EFFECTS OF BACTERIAL SERUM OPACITY FACTOR ON PLASMA LIPIDS, TISSUES, AND ATHEROSCLEROSIS

POSTER VIEWING SESSION

Dedipya Yelamanchili[1], Baiba K. Gillard[1], Henry J. Pownall[1], Antonio M. Gotto[2], Corina Rosales[1]
[1]Bioenergetics, Houston Methodist Research Institute, Houston, United States of America, [2]Pathology, Weill Cornell Medicine, New York, United States of America

Background and Aims : Although plasma HDL-C levels negatively correlate with atherosclerotic cardiovascular disease (ACVD), attempts to reduce ACVD risk by raising plasma HDL have disappointed. Thus, hypotheses about salutary HDL effects have shifted from higher-is-better to function-is-more-important. The $SRB1^{-/-}$ mouse is an extreme model of HDL dsyfunctionality; compared to WT mice, $SRB1^{-/-}$ mice have higher plasma HDL levels and an HDL surface that is free cholesterol (FC)-rich (60 vs. 15 mol%). This would be expected to increase HDL-FC bioavailability to cytotoxic levels. HDL dysfunctionality among $SRB1^{-/-}$ mice is associated with multiple metabolic abnormalities—impaired cell membrane structure and function and atherosusceptibility, despite having high plasma HDL-C levels; moreover, female $SRB1^{-/-}$ mice are infertile. Liver-specific SRB1 expression in $SRB1^{-/-}$ mice normalizes HDL size and FC content. Thus, the $SRB1^{-/-}$ mouse phenotype is due to lack of hepatic clearance of lipids from dysfunctional HDL. Our studies used the $SRB1^{-/-}$ mouse model to determine the effects of SOF on plasma and tissue lipids, as well as atheroregression or atheroprevention in high-fat fed mice.

Methods: The AAV-SOF was delivered by IP injection leading to the endogenous expression of SOF. Mice were fed a Cocoa Butter Diet (Envigo) for 18 weeks before being administered AAV-SOF for atheroregression study, while AAV was given jointly with diet for the atheroprevention study.

Results: Preliminary results show there was no significant difference in total average plaque area of the treated mice vs. controls. However, when grouped by gender, males had less plaque burden than female mice.

Conclusions: SOF treatment reduced plasma lipid levels compared to controls.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-10 Modified lipoproteins*

PLASMA SMALL-DENSE LDL MODULATION IN PATIENTS WITH THYROID DYSFUNCTION: ROLE OF OBESITY AND TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Saoussen Medfai[1], Rim Cherif[1], Rihab Ben Jemaa[1], Eya Tlich[1], Amel Lazzezm[2], Mohsen Sakly[1], Nebil Attia[1]
[1]Live Sciences, RLM17ES02, Res Lab Integrated Physiology, Faculty of Sciences of Bizerte, Carthage University, Tunisia, Jarzouna-Bizerte, Tunisia, [2]Lab Department, CNSS Polyclinic, Bizerte, Tunisia

Background and Aims : To associate plasma small-dense LDL (sdLDL) to thyroid dysfunctions with and without Type 2 diabetes mellitus (T2DM) and obesity.

Methods: Our cross-sectional study included 87 patients, divided into 69 hypothyroid patients and 18 hyperthyroid patients. SdLDL and large LDL were separated by a selective precipitation method.

Results: The comparison of the lipid profile between the two groups showed a significant difference in favor of hyperthyroid patients, since hypothyroidism induces hyercholesterolemia (increased LDL-C) with a predominance of sdLDL. Whereas dyslipidemia in hyperthyroid patients is characterized by an increase of high-density lipoproteins (HDL) and large LDL. Pearson's correlation test reveals a closed correlation between the hormonal status and plasma sdLDL in hypothyroid patients ($p<0.01$). However, in hyperthyroid patients, we noted a positive correlation of thyroid hormonal status with plasma large LDL ($p<0.05$). Multiple linear regression shows that correlations with sdLDL are maintained only when the thyroid dysfunction coexists with obesity and T2DM. However, large LDL is associated with hyperthyroidism independently of obesity and diabetes

Conclusions: Our data suggest that dyslipidemia, mainly increased sdLDL, is associated to hypothyroidism rather than hyperthyroidism and that obesity and T2DM interfere in this association.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-10 Modified lipoproteins*

DEVELOPMENT OF "HOMEMADE" OXLDL AND CHARACTERIZATION ON HEAD AND NECK CANCERS CELLS.

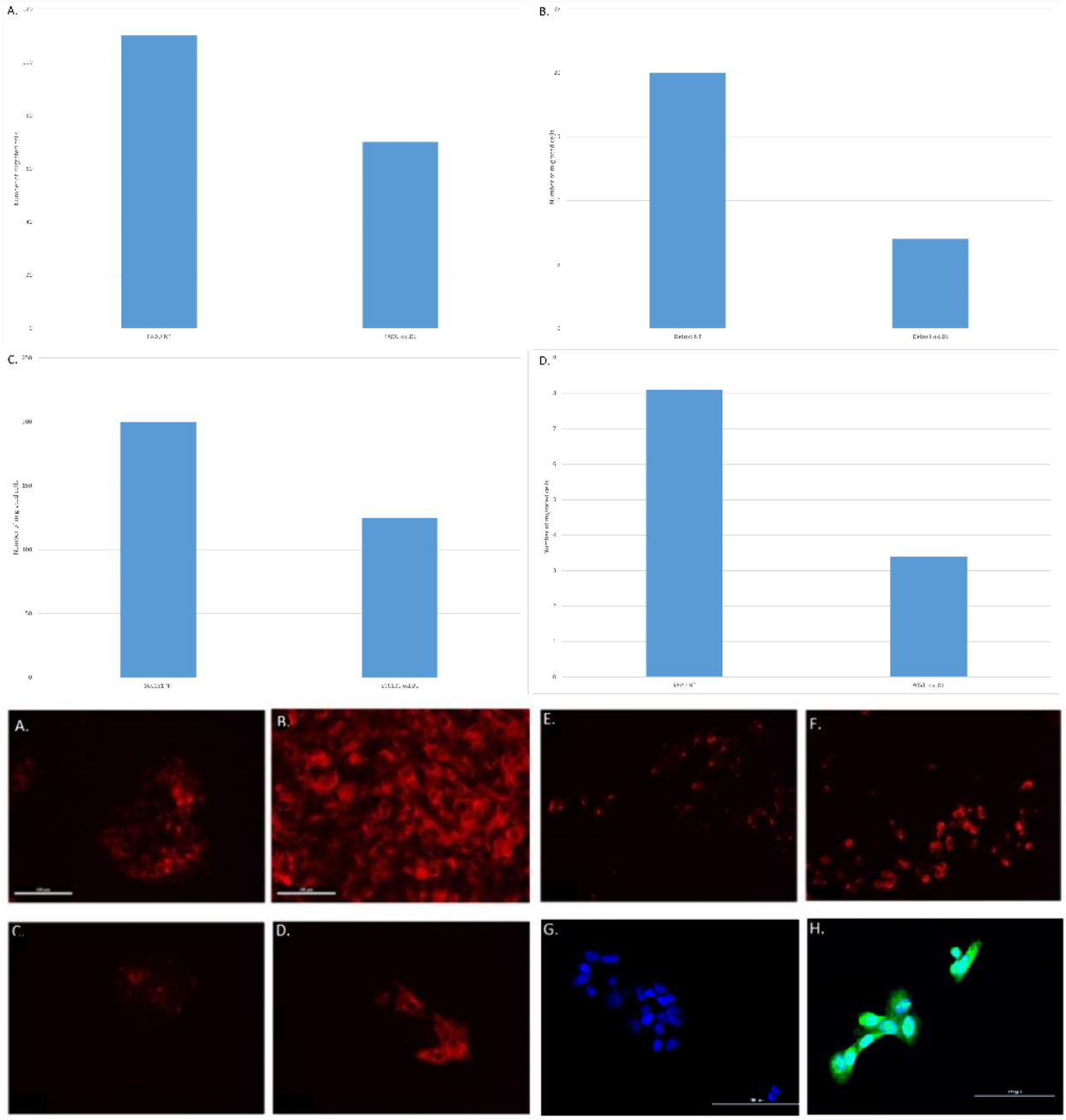
POSTER VIEWING SESSION

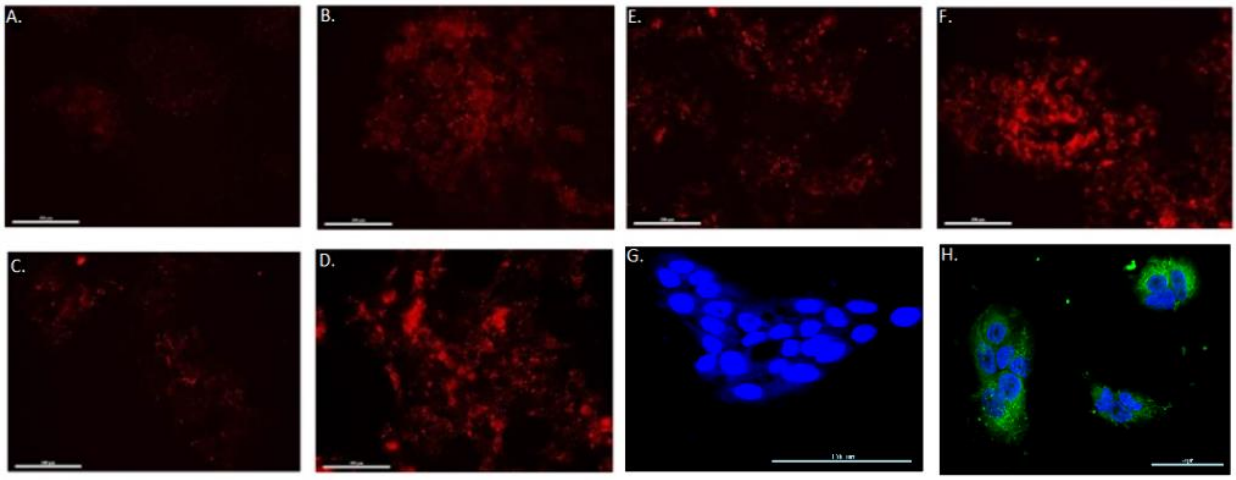
Alessandro Scalia[1], Nadège Kindt[2], Anne Trelcat[1], Amandine Nachtergael[3], Pierre Duez[3], Stéphane Carlier[1]
[1]Cardiology, CHU Ambroise Paré, Mons, Belgium, [2]Laboratoire D'anatomie Humaine Et Oncologie Expérimentale, Institut Jules Bordet, Bruxelles, Belgium, [3]Chemistry, CHU Ambroise Paré, Mons, Belgium

Background and Aims : Cardiovascular diseases and cancers are the two main causes of death worldwide, sharing many comorbidities and risk factors. Inflammatory process, neoangiogenesis and oxidative stress seems to be the cornerstone linking them, while initiation and progression of atherosclerotic plaque are mainly caused by oxidized low-density lipoproteins(oxLDL). We sought to study the effect of oxLDL on cancer cells.

Methods: We developed "home-made"oxLDL by applying a commercial purification kit to isolate LDL and VLDL from human plasma. LDL were isolated by gel permeation chromatography, then oxidized by incubation with 5µM CuSO4 for 20h, the reaction being stopped with 0.2mM EDTA. We used three negative-HPV head and neck cancer cell lines (HNCC)(FaDu, Detroit-562 and UPCI-SCC-131) and one positive-HPV HNCC (93VU-147T). We have analyzed cell proliferation after 48h oxLDL exposition (5-50µg/mL) by Crystal Violet and cell migration after 48h oxLDL exposition (0-20-30µg/mL) by Boyden chamber and analyzed the Wnt/ß-catenin pathway by WesternBlotting. We also analyzed the expression of two oxLDL receptors, LOX-1 and CD36, by immunofluorescence, after exposition, or not, with oxLDL.

Results:





We observed: a) an increased proliferation of HNCC with oxLDL exposition from 5 to 30µg/mL, b)a decreased migration in parallel to inhibition of ß-catenin pathway resulting in an increase of ß-catenin phosphorylation, c) an increase of CD36 and LOX-1 expression in all HNCC.

Conclusions: We successfully produced oxLDL to assess their involvement in cancer progression. Our results demonstrate increased HNCC proliferation and an increased expression of LOX1 and CD36 after oxLDL exposition. β-catenin pathways are inhibited after oxLDL treatment in both negative- and positive-HPV HNCC.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

INCREASED DNL AND PNPLA3 EXPRESSION BY LIQUID FRUCTOSE ARE ESSENTIAL IN THE PRODUCTION OF FATTY LIVER AND HYPERTRIGLYCERIDEMIA IN A NON-OBESE HFD-FED RAT MODEL

POSTER VIEWING SESSION

Roger Bentanachs Raset[1], Ana M. Velázquez[1,2], Aleix Sala-Vila[3], Iolanda Lázaro[3], Jose Rodríguez-Morató[3,4,5], Rosa M. Sánchez[1,2,4], Marta Alegret[1,2,4], Núria Roglans[1,2,4], Juan Carlos Laguna[1,2,4]
[1]Department Of Pharmacology, Toxicology And Therapeutic Chemistry, School Of Pharmacy And Food Science, University of Barcelona, Barcelona, Spain, [2]Institute Of Biomedicine, University of Barcelona, Barcelona, Spain, [3]Imim, Hospital del Mar Medical Research Institute, Barcelona, Spain, [4]Spanish Biomedical Research Centre In Physiopathology Of Obesity And Nutrition (ciberobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain, [5]Department Of Experimental And Health Sciences, Universitat Pompeu Fabra (CEXS-UPF), Barcelona, Spain

Background and Aims : To delineate the contribution of saturated fatty acids (FA) of dietary origin *vs* DNL to fatty liver and hypertriglyceridemia development.

Methods: 24 female rats were randomly assigned to 3 groups (n=8 each) and maintained for 3 months in: (1) standard rodent chow (control, CT); (2) High-fat diet (rich in palmitic and stearic FA, HFD) and (3) HFD with 10% w/v fructose in drinking water (HFHFr). Zoometric parameters, plasma biochemistry, and liver ORO stain, lipidomics and expression of proteins involved in FA metabolism were analyzed at the end of the treatment.

Results: Both dietary interventions increased the calories ingested without modifying body weight. HFD increase in liver TGs (x1.8 vs CT), was further enhanced in HFHFr livers (x11.0 vs CT), and accompanied by hypertriglyceridemia (x1.7 vs CT/HFD) and reduced liver FA β-oxidation (x0.7 vs CT). TGs of HFHFr livers showed increased concentrations of several FA (palmitic x6.3, stearic x13.9, oleic x17.6, and palmitoleic acid x39.2 vs CT). While HFD livers showed a higher content of ceramides, HFHFr samples showed unchanged ceramides, and an increase in diacylglycerols. Only the HFHFr diet led to a marked increase in the expression of enzymes and proteins involved in FA synthesis and TG metabolism, such as ChREBPβ, a transcription factor that regulates DNL, and PNPLA3, a lipase that mobilizes TGs stored in lipid droplets for VLDL formation and secretion.

Conclusions: Fructose, increasing DNL and PNAPLA3 expression, and reducing FA catabolism, is determinant in the production of liver steatosis and hypertriglyceridemia.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

BEMPEDOIC ACID INDUCES PNPLA3 EXPRESSION IN THE LIVER OF FEMALE RATS FED A HIGH-FAT DIET SUPPLEMENTED WITH LIQUID FRUCTOSE

POSTER VIEWING SESSION

Roger Bentanachs Raset[1], Ana M. Velázquez[1,2], Núria Roglans[1,2,3], Rosa M. Sánchez[1,2,3], Juan Carlos Laguna[1,2,3], Marta Alegret[1,2,3]
[1]Department Of Pharmacology, Toxicology And Therapeutic Chemistry, School Of Pharmacy And Food Science, University of Barcelona, Barcelona, Spain, [2]Institute Of Biomedicine, University of Barcelona, Barcelona, Spain, [3]Spanish Biomedical Research Centre In Physiopathology Of Obesity And Nutrition (ciberobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain

Background and Aims : Bempedoic acid (BemA) reduces LDL-cholesterol levels in humans, but plasma triglyceride (TG) levels remains unaffected. We studied BemA effects on plasma TG in a diet-induced rat model of hepatic steatosis, and explored the mechanisms involved.

Methods: Female Sprague-Dawley rats were randomly distributed into 3 groups (n=8): (1) control (CT; standard rodent chow); (2) high-fat diet with 10% w/v fructose in drinking water (HFHFr); (3) HFHFr plus BemA at 30 mg/Kg/day (BemA). Rats were fed the diets for three months, and group (3) was treated orally with BemA for the last month. Plasma and hepatic triglycerides and gene/protein expression in hepatic tissue were determined.

Results: The hypertriglyceridemia induced by the HFHFr diet was not reversed by Bem A, but hepatic triglyceride accumulation was reduced significantly in BemA-treated rats. The gene and protein expression of LDL and VLDL receptors, as well as the mRNA levels of *Psck9*, were not modified by the diet or Bem A. Protein levels of microsomal triglyceride transfer protein were increased similarly in the HFHFr and the BemA groups compared to CT. In contrast, the mRNA and protein levels of patatin like phospholipase domain-containing protein 3 (PNPLA3) were significantly increased by HFHFr diet and further increased by BemA treatment.

Conclusions: Induction of PNPLA3 by BemA, leading to an increase of its lipase activity on hepatic lipid droplets and inducing VLDL formation and export, is a key event in the BemA-mediated reduction of hepatic triglycerides, explaining also the lack of effect of this drug on plasma TG levels.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

KETOHEXOKINASE INHIBITION BY BEMPEDOIC ACID REDUCES FRUCTOSE CONSUMPTION IN FEMALE RATS FED A HIGH-FAT DIET

POSTER VIEWING SESSION

Roger Bentanachs Raset[1], Ana M. Velázquez[1,2], Núria Roglans[1,2,3], Rosa M. Sánchez[1,2,3], Juan Carlos Laguna[1,2,3], Marta Alegret[1,2,3]
[1]Department Of Pharmacology, Toxicology And Therapeutic Chemistry, School Of Pharmacy And Food Science, University of Barcelona, Barcelona, Spain, [2]Institute Of Biomedicine, University of Barcelona, Barcelona, Spain, [3]Spanish Biomedical Research Centre In Physiopathology Of Obesity And Nutrition (ciberobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain

Background and Aims : Fructose supplementation induces ketohexokinase (KHK), the first enzyme in its hepatic metabolism, promoting DNL and fatty liver. In the context of a study designed to examine the effects of bempedoic acid (BemA) on liver and plasma lipids in rats fed a high-fat diet supplemented with liquid fructose, we focused on the effects of BemA on KHK expression.

Methods: Female Sprague-Dawley rats were randomly distributed into 3 groups (n=8): (1) control (CT); (2) high-fat diet with 10% w/v fructose in drinking water (HFHFr); (3) HFHFr plus BemA 30 mg/Kg/day. Rats were fed the diets for three months, and group (3) was treated orally with BemA during the last month. Food, liquid intake and corporal weight were determined, as well as gene/protein expression in liver.

Results: BemA-treated rats exhibited lower body weight and adiposity at the end of the study, and reduced weight gain in the third month of the procedure. Solid food consumption was unchanged, but fructose consumption was significantly reduced during the third month. KHK expression was significantly induced by the HFHFr diet, and treatment with BemA reduced its expression below control values. The expression of ChREBP, which controls KHK expression, was induced by the HFHFr diet and this effect was attenuated by BemA treatment.

Conclusions: BemA reduces liver KHK expression, probably in part by inhibiting ChREBP transcriptional activity. This results in a lower consumption of fructose, as described in KHK-deficient mice, contributing to the reduction in body weight and adiposity caused by BemA administration

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

ANGPTL3 AND PCSK9 INTERACT AND SHOW COORDINATED METABOLIC REGULATION IN VITRO.

POSTER VIEWING SESSION

Simone Bini, Valeria Pecce, Laura D'Erasmo, Alessia Di Costanzo, Ilenia Minicocci, Marcello Arca
Department Of Translational And Precision Medicine, Sapienza University of Rome, Roma, Italy

Background and Aims : ANGPTL3 and PCSK9 are known regulators of lipoprotein metabolism. Patients harboring homozygous loss of function mutations in the *ANGPTL3* gene show reduced levels of circulating PCSK9, indicating a possible coordinate regulation of these two proteins. This study aimed to establish whether the two proteins can cross-regulate in different conditions of nutritional availability.

Methods: To better study the interaction between ANGPTL3 and PCSK9, we overexpressed (OE) *ANGPTL3*, *PCSK9*, or both genes in HepG2 cells cultured in *fasting* (low-glucose medium) or *feeding* (high-glucose medium) conditions. In addition, we performed Co-immunoprecipitation (Co-IP) to verify protein-protein interaction and western-blotting for protein quantification both intracellularly and in the culture medium.

Results: The Co-IP showed a direct interaction between ANGPTL3 and PCSK9 in the HepG2 total protein extract; the same interaction was not detected in the culture medium. The *ANGPTL3* OE cells presented in *fasting* and *feeding* 1.5-fold higher total PCSK9, predominantly in immature form. Conversely, in *PCSK9* OE cells higher intracellular ANGPTL3 expression (1.5-fold as control) was observed only in *fasting*. Although intracellular PCSK9 increase was detected in *feeding* (9-fold CTRL) and *fasting* (5-fold CTRL), its levels in the culture medium did not increase. In the cells overexpressing both genes, we found increased ANGPTL3 and PCSK9 in culture media in *feeding* and *fasting* conditions (up to 2-fold as compared to CTRL medium).

Conclusions: ANGPTL3 and PCSK9 are in close intracellular interaction. ANGPTL3 intracellular accumulation, predominant in *fasting* favors PCSK9 proteolytic maturation. The two proteins are transcriptionally cross-regulated and respond to changes in glucose availability *in vitro*.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

CHOLESTEROL TRAPPING BY SOAT1 INDUCES MITOCHONDRIAL CHOLESTEROL ACCUMULATION AND DECREASE OXIDATIVE METABOLISM

POSTER VIEWING SESSION

Lorenzo Da Dalt[1], Matteo Pedrelli[2], Camilla Pramfalk[2], Giuseppe Danilo Norata[1], Paolo Parini[3]
[1]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Department Of Laboratory Medicine, Karolinska Institutet, Huddinge, Sweden, [3]Dept. Of Laboratory Medicine, Karolisnka University Hospital Huddinge, Huddinge, Sweden

Background and Aims : Normal hepatocytes in-vivo express only Sterol O-Acyltransferase2 (SOAT2), whereas in pathologic conditions (cancer) acquire SOAT1 expression. Hepatocytes mainly use mitochondrial oxidative metabolism for energy production, whereas cancer cells rely more on glycolysis for energy production. Currently, it is not known how cholesterol in mitochondria affects their metabolism, and whether SOAT2 and SOAT1 could play a role. Thus, we studied HepG2 cells and a unique cell model in which SOAT1 was genetically depleted: SOAT2-only-HepG2 cells.

Methods: HepG2 and SOAT2-only-HepG2 cells were cultured with fetal bovine serum (FBS), 10% f.c., or with human serum (HS), 2% f.c. Quantitative PCR, mitochondrial isolation and characterization, flow-cytometry analysis, and metabolic profiling by Seahorse were performed.

Results: In SOAT2-only-HepG2 cells treated with HS mitochondrial fusion and fission genes, as well as mitophagy genes, were significantly increased. Interestingly, SOAT2-only-HepG2 cells, cultured in HS, increased the mass of active mitochondria, and increased oxygen consumption and ATP production, compared to HepG2 treated with FBS. Moreover, mitochondria of HS treated SOAT2-only-HepG2 contained less free cholesterol compared to those of wild-type HepG2 cells cultured with both HS and FBS. Inhibition of cholesterol esterification by Sandoz 58-035 (5µg/ml f.c.) prevented cholesterol enrichment of mitochondria especially in HS SOAT2-only-HepG2, which became more dependent on oxidative metabolism.

Conclusions: Despite HS modulates mitochondrial activity by itself, SOAT2-only-HepG2 showed an increase in mitochondrial metabolism, suggesting that SOAT1 impairs cellular oxidative metabolism. Our studies contribute to the understanding of how cholesterol metabolism affects lipid accumulation and oxidation in hepatocytes.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

IMPACT OF IRON STATUS ON NON-ALCOHOLIC FATTY LIVER DISEASE: A MENDELIAN RANDOMIZATION STUDY

POSTER VIEWING SESSION

Nooshin Ghodsian[1], Jérôme Bourgault[1], Benoit J. Arsenault[1,2]
[1]Quebec Heart And Lung Institute, Laval University, Quebec City, Canada, [2]Department Of Medicine, Faculty of Medicine, Laval University, Québec, Canada

Background and Aims : Iron is an essential element for various physiological processes and metabolic pathways. However, observational studies revealed an impact of iron overload on several metabolic disorders such as obesity and type 2 diabetes. Iron accumulation might damage the liver, but whether there is a causal relationship between iron overload and non-alcoholic fatty liver disease (NAFLD) is unknown. Using Mendelian randomization (MR), we evaluated how genetically-predicted iron status affected NAFLD risk.

Methods: A two-sample MR analysis was used to obtain causal estimates between four biomarkers of systemic iron status (serum iron, ferritin, transferrin saturation and transferrin) and NAFLD. We selected the top genetic variants associated ($P < 5\times10^{-7}$) and linkage disequilibrium (R2=0.01) with these biomarkers in a study involving 48,972 participants of European ancestry included in the Genetics of Iron Status Consortium. The study outcome included genome-wide association meta-analysis summary statistics from three cohorts (UK biobank, FinnGen and eMERGE; 4315 cases and 580,060 controls).

Results: Genetically-predicted serum iron metabolites were associated with NAFLD with beta [95% CI] = 0.246 [0.39 – 0.04]; and P-value = 0.018 for iron, 0.5571 [0.76–0.11] and P-value = 0.014 for ferritin, 0.23 [0.95–0.36] and P-value = 0.0007 for transferrin saturation, respectively. In contrast, genetically-predicted transferrin, which is a marker of reduced iron status, was inversely associated with NAFLD with beta [95% CI] = -0.15 [-0.03– -0.2661] and P-value=0.013.

Conclusions: Our study supports a causal link between iron overload and higher NAFLD risk. The pathobiological mechanisms underlying these associations may need further investigation.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

METABOLIC ASSOCIATED FATTY LIVER DISEASE IS HIGHLY PREVALENT IN THE POST-ACUTE COVID SYNDROME

POSTER VIEWING SESSION

Paolo Raggi[1], Sara Barbieri[2], Jovana Milic[3], Licia Gozzi[2], Alberto Brigo[2], Bianca Beghe'[4], Alessia Verduri[4], Enrico Clini[4], Cristina Mussini[3], Giada Sebastiani[5], Giovanni Guaraldi[6]
[1]Medicine-cardiology, University of Alberta, Edmonton, Canada, [2]Medicine, University of Modena and Reggio Emilia, Modena, Italy, [3]Infectious Diseases, University of Modena and Reggio Emilia, Modena, Italy, [4]Pneumology, University of Modena and Reggio Emilia, Modena, Italy, [5]Gastroenterology, McGill University, Montreal, Canada, [6]Infectious Diseases, Universita' di Modena e Reggio Emilia, Modena, Italy

Background and Aims : Recently a proposal has been advanced to change the traditional definition of Non-Alcoholic Fatty Liver Disease to Metabolic Associated Fatty Liver Disease (MAFLD), to reflect the cluster of metabolic abnormalities that may be more closely associated with cardiovascular risk. Long COVID is a smoldering inflammatory condition, characterized by a number of symptom clusters. This study aims to determine the prevalence of MAFLD in patients with post-acute COVID syndrome (PACS) and its association with other PACS-cluster phenotypes.

Methods: We included 235 patients followed at a single university outpatient clinic. The diagnosis of PACS was based on ≥1 cluster of symptoms: respiratory, neurocognitive, musculoskeletal, psychological, sensory, dermatological. The outcome was prevalence of MAFLD detected by transient elastography during the first post-discharge follow-up outpatient visit. The prevalence of MAFLD at the time of hospital admission was calculated retrospectively using the hepatic steatosis index.

Results: Of 235 patients, 162 (69%) were men (median age 61). The prevalence of MAFLD was 55.3% at follow-up and 37.3% on admission (P<0.001). Insulin resistance (OR=1.5, 95%CI: 1.14-1.96), body mass index (OR=1.14, 95%CI: 1.04-1.24), and the metabolic syndrome (OR=2.54, 95%CI: 1.13-5.68), were independent predictors of MAFLD. The number of PACS clusters was inversely associated with MAFLD (OR=0.86, 95%CI: 0.76-0.97). Thirty-one patients (13.2%) had MAFLD with no other associated PACS clusters. All correlations between MAFLD and other PACS clusters were weak.

Conclusions: MAFLD was highly prevalent after hospital discharge and may represent a specific PACS-cluster phenotype, with potential long-term metabolic and cardiovascular health implications.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

A RARE GENETIC VARIANT IN THE MANGANESE TRANSPORTER SLC30A10 AND ELEVATED LIVER ENZYMES IN THE GENERAL POPULATION

POSTER VIEWING SESSION

Anne-Sofie Seidelin[1], Børge G. Nordestgaard[2,3], Anne Tybjaerg-Hansen[3,4], Hanieh Yaghootkar[5,6], Stefan Stender[1,7]
[1]Department Of Clinical Biochemistry, Copenhagen University Hospital, Copenhagen, Denmark, [2]Department Of Clinical Biochemistry, Herlev and Gentofte Hospital, Copenhagen University Hospital, Herlev, Denmark, [3]Department Of Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen N, Denmark, [4]Department Of Clinical Biochemistry, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [5]Research Centre For Optimal Health, School Of Life Sciences, University of Westminster, London, United Kingdom, [6]Genetics Of Complex Traits, University Of Exeter Medical School, University of Exeter, Exeter, United Kingdom, [7]Department Of Clinical Biochemistry, Bispebjerg And Frederiksberg Hospital, Copenhagen University Hospital, Copenhagen, Denmark

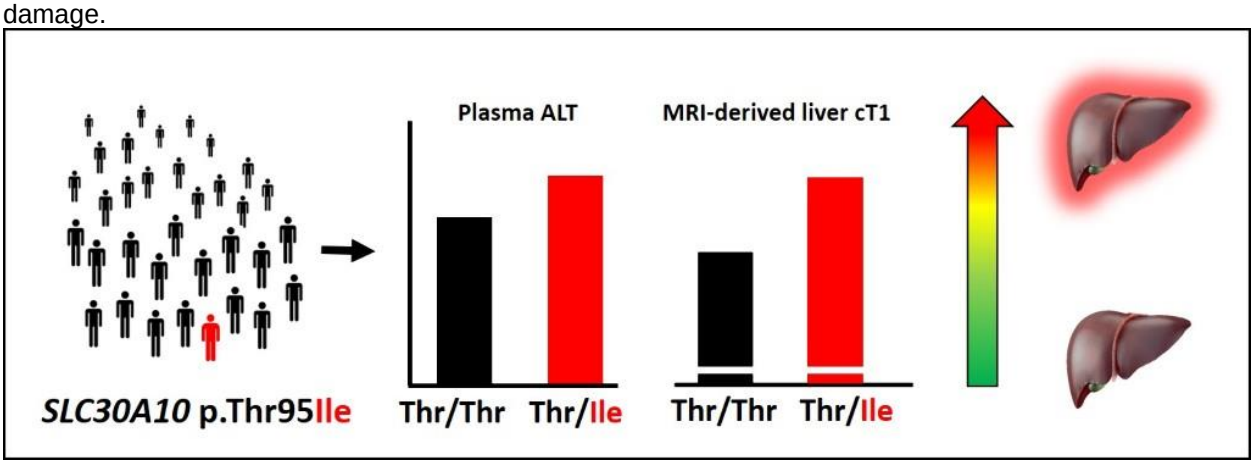
Background and Aims : *SLC30A0* encodes a manganese transporter which effluxes manganese from hepatocytes to the bile. Individuals homozygous for loss-of-function variants in *SLC30A10* accumulate manganese in the liver and have severe phenotypes including liver cirrhosis. A genetic variant in *SLC30A10* (rs188273166, p.Thr95Ile) associated with increased plasma alanine transaminase (ALT) in a recent GWAS in the UK Biobank (UKB). The aims of the present study were to validate the association of rs188273166 with ALT in an independent cohort, and to test clinical, hepatic and biochemical phenotypes associated with the variant.

Methods: We included n=334,886 white participants from the UKB, including 14,462 with hepatic magnetic resonance imaging (MRI), and n=113,612 individuals from the Copenhagen City Heart Study and the Copenhagen General Population Study combined. Associations with continuous and categorical outcomes were tested using linear and logistic regression, respectively.

Results: Genotyping *SLC30A10* p.Thr95Ile identified 816 heterozygotes in the UKB and 111 heterozygotes in the Copenhagen cohort. Compared to non-carriers, heterozygotes had 4 U/L and 5 U/L higher levels of plasma ALT in the UKB ($P=9\times10^{-19}$) and Copenhagen cohort (P=0.02), respectively, and 3 U/L higher plasma aspartate transaminase ($P=1\times10^{-13}$) and gamma glutamyl-transferase ($P=3\times10^{-4}$) in the UKB. Heterozygotes also had higher corrected T1 on liver MRI, a marker of hepatic inflammation ($P=4\times10^{-7}$), but no change in MRI-quantified steatosis (P=0.57).

Conclusions: *SLC30A10* p.Thr95Ile was associated with elevated liver enzymes in two large general population cohorts, and with MRI-quantified hepatic inflammation. We hypothesize that Thr95Ile heterozygosity associates with a mild form of hepatic manganese accumulation leading to liver

damage.


Plasma ALT
MRI-derived liver cT1
SLC30A10 p.Thr95Ile
Thr/Thr
Thr/Ile
Thr/Thr
Thr/Ile

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-11 Liver metabolism and steatosis*

THE IMPACT OF ASGR1 DEFICIENCY ON LIPID AND LIPOPROTEIN METABOLISM DURING ATHEROGENESIS

POSTER VIEWING SESSION

Monika Svecla[1], Annalisa Moregola[1], Lorenzo Da Dalt[1], Patrizia Uboldi[1], Alessandra Idini[1], Fabrizia Bonacina[1], Alberico L. Catapano[1,2], Giuseppe Danilo Norata[1,3]
[1]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Irccs, Multimedica Hospital, Sesto San Giovanni, Italy, [3]Bassini Hospital, Center SISA, Cinisello Balsamo, Italy

Background and Aims : LOF mutation on ASGR1 is associated with lower non-HDL cholesterol and reduced incidence of CVD. The beneficial effect of ASGR1 deficiency goes beyond the achieved reduction in non-HDL cholesterol levels a call for lipid unrelated effects. This project aims to investigate the molecular mechanism of ASGR1 to impact dyslipidemia and CVD outcome.

Methods: Plasma, aorta, and liver were isolated from 6-months old ApoEdeficient mice and ASGR1$^{-/-}$ /ApoE$^{-/-}$ (DKO mice), male and female, fed for 16 weeks on a western-type diet (WTD, 40% Kcal fat + 0.2% total cholesterol). We have performed histology and proteomics in the liver, histology in the aorta, and lipid profile in plasma.

Results: The lipid profile of DKO mice presents a significant decrease ($p<0.05$) in total cholesterol, both in male and female, compared to ApoE deficient mice (male ApoE$^{-/-}$ 971.1± 155.8, DKO 841.4±128.2 female ApoE$^{-/-}$ 833.3±69.4, DKO 630.2±116.7). Liver proteomics reveals an increased lipid uptake (z-score 2.66) coupled with an improvement of mitochondrial functionality (z-score 2.4). No change is observed in histology on the liver section. Aortic root in DKO male mice does not change while in females present a reduction in the atherosclerotic plaque (ApoE$^{-/-}$ 706954±139383, DKO 459092±104015, $p=0.01$) compared with ApoE deficient mice.

Conclusions: Our data suggest that ASGR1 is altering cholesterol metabolism by increasing mitochondrial functionality within the liver. These findings suggest that inhibiting ASGR1 can be a potential strategy to reduce circulation cholesterol content.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-12 Adipose tissue biology and pathology*

COMPARISON OF ADIPOCYTE SIZE IN TWO RELATED FAT DEPOTS AND THEIR ASSOCIATION TO CARDIOVASCULAR RISK FACTORS

POSTER VIEWING SESSION

Hana Bartuskova[1,2], Sona Kauerova[2], Ivana Kralova Lesna[2], Jiri Fronek[3], Libor Janousek[3], Rudolf Poledne[2]
[1]Faculty Of Science, Charles University, Prague, Czech Republic, [2]Atherosclerosis Research Laboratory, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [3]Transplantation Surgery Department, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Background and Aims : Metabolic syndrome is connected to adipose tissue inflammation and dysfunction. Adipocyte size is used as a surrogate marker of adipose tissue dysfunction. Data regarding adipocyte size in perivascular adipose tissue in human are scarce. We therefore analyzed human perivascular adipose tissue in living kidney donors and compared our data to perirenal visceral depot.

Methods: Seventy-nine living kidney donors (57 women) completed a standardized questionnaire and underwent a body composition analysis to establish the presence of cardiovascular risk factors. Lipid and other biochemical parameters were measured in plasma. Samples of visceral and perivascular adipose tissue were obtained during during retroperitoneoscopic nephrectomy. Both tissues were processed for flow cytometric and histological analyses to measure proportion of macrophages and adipocyte size respectively. Spearman correlation and Student's t-test were used for statistical analysis.

Results: Adipocyte size was significantly higher in the perirenal depot ($p < 0.01$). Both visceral and perivascular adipocyte size correlated positively with waist circumference, BMI and HDL/TC ratio and negatively with basal metabolic rate/kg. Positive correlations with triglyceride levels in plasma and also with markers of inflammation (CRP and TNF-α levels in plasma and the proportion of CD14+CD16+CD36high macrophages in adipose tissue) were found only in perivascular adipose tissue. A strong negative correlation with HDL-C levels was also found only in this depot.

Conclusions: Adipocyte size was compared in two adipose tissue depots. Despite their proximity, marked differences were found in adipocyte size and its association with different cardiovascular risk factors. Especially perivascular adipose tissue could be prone to pro-inflammatory changes and tissue dysfunction.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

INTERPLAY BETWEEN S1P RECEPTORS AND SR-BI IN ATHEROSCLEROSIS RELEVANT CELLS: NEW INSIGHT FROM TRANSGENIC ANIMALS

POSTER VIEWING SESSION

Mattia Dessena[1], Manuela Simoni[2], Jerzy-Roch Nofer[3], Arnold Von Eckardstein[4], Francesco Potì[1]
[1]Department Of Medicine And Surgery - Unit Of Neurosciences (pharmacology), University of Parma, Parma, Italy, [2]Unit Of Endocrinology, Department Of Biomedical, Metabolic And Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy, [3]Central Laboratory Facility, University Hospital of Münster, Münster, Germany, [4]Institute Of Clinical Chemistry, University of Zurich and University Hospital of Zurich, Zurich, Switzerland

Background and Aims : Sphingosine 1-phosphate (S1P), traveling in plasma mainly bound to high-density lipoproteins (HDL), fulfills several tasks in immune and cardiovascular systems by binding to its G protein-coupled receptors ($S1P_{1-5}$). SR-BI, an HDL receptor, is widely expressed in different cell types, including endothelial cells and macrophages, and plays key roles in cholesterol homeostasis and lipoprotein metabolism. Recent evidence showed that HDL-bound S1P stimulates the transient interaction between SR-BI and S1PRs, activating S1PRs. We generated peculiar animal models overexpressing S1PRs in a tissue-specific manner, and tried clarifying the interplay between S1PRs and SR-BI.

Methods: S1PR overexpression in endothelium and myeloid cells was achieved through Cre-LoxP technology. Animals overexpressing $S1P_1$ in the endothelium ($S1P_1$-iECKI) were sacrificed, their aortas isolated and processed for immunofluorescence imaging through confocal laser microscopy. Mice overexpressing $S1P_3$ in myeloid cells ($S1P_3$-LyzMCre) were intraperitoneally injected with thioglycolate broth, sacrificed and their peritoneal macrophages (MPMs) isolated and cultivated under cholesterol normal or loading (acetylated LDL, AcLDL) conditions. Gene and protein expression of target molecules in MPMs were evaluated by real time RT-PCR and Western blot.

Results: Confocal microscopy interestingly showed a higher expression of SR-BI in the aortic endothelium of $S1P_1$-iECKI mice, compared to controls. In addition, in $S1P_3$-LyzMCre macrophages, SR-BI expression increased at both mRNA and protein levels, as detected by qPCR and Western blot, respectively. Treatment with S1PR-modulators also affected SR-BI expression, regardless of AcLDL stimulation.

Conclusions: Our preliminary observations suggest that the modulation of S1PRs may affect the expression of SR-BI in atherosclerosis-relevant cells.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

ESTIMATING THE CAUSAL EFFECTS OF CARDIOMETABOLIC FACTORS ON CORONARY ARTERY DISEASE IN BRITISH PAKISTANIS AND BANGLADESHIS: A TRANS-ANCESTRY MENDELIAN RANDOMISATION STUDY

POSTER VIEWING SESSION

Diana Dunca
Ucl Genetics Institute, UCL, London, United Kingdom

Background and Aims : British people with South-Asian ancestry have a higher risk of coronary artery disease (CAD) than other ancestry groups. Statistical power can be the limiting factor when extending Mendelian Randomisation (MR) to non-European populations because ancestry-matched GWAS for risk factors (RFs) of interest might not be sufficiently large.

Methods: We compared different strategies for trans-ancestry MR to assess the causal effect of cardiometabolic RFs (BMI, triglycerides, HDL-cholesterol, LDL-cholesterol, systolic and diastolic blood pressure) on the risk of CAD in 22,000 British Pakistani and Bangladeshi (BPB) individuals from the Genes&Health cohort. We used an ancestry-matched sample to derive instruments in a two-sample MR of CAD in G&H, with summary statistics for RF from the UK Biobank BPB group. However, insufficient numbers of genome-wide significant instruments were identified in the UK Biobank BPB population. Therefore, we used a less stringent p-value threshold ($p<5x10^{-5}$) for selecting instruments, incorporated results from large European GWASs, and used a subset of loci with evidence of transferability.

Results: We found that most of the associations were not significant in the ancestry-matched MR. We found a risk increasing effect for LDL-cholesterol and risk decreasing effect for HDL-cholesterol when using the variants from the large European GWAS as instruments, and also for the subset of loci that were transferable. The association of BMI with CAD was significant only for transferable loci.

Conclusions: We showed that incorporating findings from large European GWAS can increase power for MR in other ancestry groups. We demonstrated the importance of considering transferability of RF loci to ensure causal inference.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

STATIN THERAPY IS NOT ASSOCIATED WITH INSULIN RESISTANCE IN CHILDREN AND ADOLESCENTS WITH FAMILIAL HYPERCHOLESTEROLAEMIA

POSTER VIEWING SESSION

Urh Groselj[1], Jaka Šikonja[1], Matej Mlinarič[2], Primoz Kotnik[2], Tadej Battelino[1,2], Joshua W. Knowles[3]
[1]Faculty Of Medicine, University of Ljubljana, Ljubljana, Slovenia, [2]Department Of Endocrinology, Diabetes, And Metabolic Diseases, University Children's Hospital, UMC Ljubljana, Ljubljana, Slovenia, [3]Cardiovascular Medicine, Cardiovascular Institute, Prevention Research Center, Diabetes Research Center, Department Of Medicine, Stanford University, palo alto, United States of America

Background and Aims : Statins are first line therapy for lowering atherogenic low-density lipoprotein cholesterol (LDL-C) in patients with familial hypercholesterolaemia (FH). Statins were associated with an increased insulin resistance and the risk for type 2 diabetes. We aimed to assess the effect of statins on insulin resistance in children.

Methods: We performed a prospective study of children with FH who were introduced rosuvastatin 5 mg daily. Twenty-six participants that had LDL-C reduction of ≥20% from initial visit (baseline), were included. All patients were White/European. Their median age was 10.0 years, 46% were female, median body mass index (BMI) Z-score 0.49 at baseline. All had a second exam at a median of 8 months after the statin first introduction. HOMA-IR was calculated. Wilcoxon signed-rank test was used to compare the characteristics between visits.

Results: Baseline total cholesterol (7.3 mmol/L) and LDL-C (5.4 mmol/L) reduced by 31% and 39% ($p < 0.001$ for both) while on rosuvastatin. Changes in BMI Z-score were insignificant (median change –0.03; $p = 0.74$). Compared to baseline, rosuvastatin did not increase fasting glucose (4.6 vs. 4.6 mmol/L; $p = 0.87$), fasting insulin (7.6 vs. 6.8 mU/L; $p = 0.75$) and HOMA-IR (1.5 vs. 1.3; $p = 0.83$). HbA1c levels remained unchanged (5.2 vs. 5.2%; $p = 0.89$).

Conclusions: Rosuvastatin therapy was not associated with an increase of insulin resistance markers in paediatric patients with FH.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

APO E MUTATIONS AS A CAUSE OF FAMILIAR HYPERCHOLESTEROLEMIA IN NORTH-EAST MORAVIA REGION

POSTER VIEWING SESSION

Pavla Jadrníčková, Jan Václavík
Interní A Kardiologické Klinika, Fakultní nemocnice Ostrava, Ostrava, Czech Republic

Background and Aims : Familiar hypercholesterolemia (FH) is a collective term for a set of genetically linked diseases that cause increased plasma LDL-C levels by various mechanisms, thereby increasing an individual's cardiovascular risk. FH is most frequently caused by one of the three following mechanisms: the absence or reduction of the number and thereby decreased function of LDL-receptors, the defect in apolipoprotein B or increased function of the PCSK9 enzyme.We recently encountered a remarkable occurrence of patients with mutations in Apo E lipoprotein. The goal of this study was to assess the incidence of Apo E mutation patients in our outpatient clinics.

Methods: We retrospectively reviewed hospital records of outpatients tested for clinically suspected familial hypercholesterolaemia. Apo E isomers were determined in collaboration with the department of clinical genetics. The DNA isolation was made from peripheral blood using the MagNA Pure Compact NA Isolation Kit (f, Roche). Polymerism in the Apo E gene was detected by reverse hybridization using the APoETM Stripassay kite (ViennaLabGmbH).

Results: 420 patients undewent detailed laboratory testing in our outpatient lipidology clinic between 2006 and 2021. Of these, 34 patients (8%) have been identified to have pathological ApoE isoforms of Apo E2 or E4.

Conclusions: An appreciable proportion of our patients was shown to have one of pathological isoforms of ApoE. These mutations are associated with increased plasma LDL-C levels, and thus with increased cardiovascular risk. Unfortunately, at this time, these mutations are not included in the classification of familial hypercholesterolemia, and therefore we cannot provide them therapeutic options available for other FH patients.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

THERAPEUTIC PLASMA EXCHANGE FOR HYPERTRIGLYCERIDEMIA: A RETROSPECTIVE STUDY.

POSTER VIEWING SESSION

Kaspars Kivlenieks[1], Evita Skrula[1], Dace Trumpika[2], Eva Bormane[1], Anda Grigane[1], Julija G. Voicehovska[2]
[1]Kidney Diseases, RAKUS, Riga, Latvia, [2]Internal Diseases, Riga Stradins university, Riga, Latvia

Background and Aims : Acute hypertriglyceridemia has got sever causes and manifests itself with serious clinical consequences. Therapeutic plasma exchange (TPE) is one of treatment options for lowering plasma triglycerides and possibly decreasing morbidity and mortality. However, clinical data regarding its effectiveness are limited.

Methods: We retrospectively examined the clinical data and outcomes of 12 consecutive episodes of hypertriglyceridemia in which TPE was employed to reduce plasma triglycerides during a 8-month period. The TPE was initiated at a median of 12 hours from the time of presentation. We performed 1.5 volume TPEs with 5% albumin 500ml and 1000ml Gelaplasma as the replacement fluid.

Results: After3-5 TPE procedure, the mean plasma triglycerides values decreased from average 61.3mmol/l (7 patients, 6 had hilose serum) patients to 4.70 mmol/l with a reduction of 13 times 1300.4 % All 12 patients survived with a mean length of hospital stay of 8.3 days. There were no complications related to TPE.

Conclusions: One TPE procedure is an effective method for reducing plasma triglycerides and possibly decreases the length of hospital stay in patients admitted with hypertriglyceridemia. Further prospective studies are necessary to evaluate TPE efekts regarding hypertrigliceridemia-associated complications like cardiovascular events and rehospitalization.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

EICOSAPENTAENOIC ACID (EPA) COMBINED WITH HIGH-INTENSITY STATINS REDUCE LIPID OXIDATION IN MODEL MEMBRANES COMPARED TO DOCOSAHEXAENOIC ACID (DHA)

POSTER VIEWING SESSION

Samuel C.R. Sherratt[1,2], Peter Libby[3], Deepak L. Bhatt[3], Preston Mason[1,3]
[1]Lab, Elucida Research, Beverly, United States of America, [2]Department Of Molecular, Cellular, And Biomedical Sciences, University of New Hampshire, Durham, United States of America, [3]Department Of Medicine, Cardiovascular Division, Brigham & Women's Hospital, Boston, United States of America

Background and Aims : Lipid oxidation leads to endothelial dysfunction and promotes foam cell formation during atherogenesis. Treatment with icosapent ethyl, a formulation of highly-purified omega-3 fatty acid (O3FA) EPA, reduced cardiovascular (CV) events in REDUCE-IT unlike trials using DHA-containing formulations in statin-treated patients. We compared the effects of EPA and DHA on lipid oxidation in membranes in combination with high-intensity statins.

Methods: The dose-dependent effects of EPA and DHA (5.0 and 10.0 µM) on rates of lipid oxidation were measured with equimolar levels of atorvastatin (active metabolite, ATM) and rosuvastatin (rosuva) at 1.0 µM during autoxidation for 96 hr. Membrane vesicles were prepared with cholesterol and dilinoleoylphosphatidylcholine (DLPC) at a 0.5:1 mole ratio. Lipid hydroperoxide (LOOH) levels were determined from triiodide (I_3^-) formation.

Results: After 96 hr, membranes underwent oxidation with LOOH levels measured at 2049 µM. EPA, and to a lesser extent DHA, significantly reduced lipid oxidation in a dose-dependent fashion in the presence of either ATM or rosuva. At 10 µM, the combination of EPA/ATM and EPA/rosuva reduced lipid oxidation by 86 and 75%, respectively (p<0.001). The EPA/statin combinations had significantly greater antioxidant activity than DHA/statin combinations at both O3FA concentrations; at 10 µM, EPA/ATM and EPA/rosuva inhibited LOOH formation by 52% and 66% compared to the cognate DHA/statin combinations (p<0.01).

Conclusions: EPA significantly reduced lipid oxidation in the presence of high-intensity statins compared to DHA. Differences in antioxidant benefits for EPA compared to DHA may inform mechanisms of discordant findings in clinical trials that used different O3FA formulations.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

BROWN SEAWEEDS ACTIVATING LIVER X RECEPTORS: POTENTIAL ROLE IN THE PREVENTION OF NEURODEGENERATIVE AND CARDIOMETABOLIC DISEASES

POSTER VIEWING SESSION

Monique T. Mulder[1], Nikita Martens[1], Na Zhan[1,2], Gardi Voortman-Minderman[1], Hongbing Liu[2], Folkert Kuipers[3], Hans Jonker[3], Dieter Luetjohann[4], Tim Vanmierlo[5]
[1]Internal Medicine, Erasmus MC University Medical Center, Rotterdam, Netherlands, [2]Key Laboratory Of Marine Drugs, Ocean University of China, Qingdao, China, [3]Pediatrics, UMCG, Groningen, Netherlands, [4]Institute Of Clinical Chemistry And Clinical Pharmacology, University Clinics Bonn, Bonn, Germany, [5]Neuroscience - Biomedical Research Institute, Hasselt University, Diepenbeek, Belgium

Background and Aims : Liver X receptors (LXRa/β) are transcription factors that are key in the regulation of cholesterol homeostasis and inflammatory processes. LXR are a therapeutical target for cardiometabolic and neurodegenerative diseases, including Alzheimer's disease (AD). AD is a progressive neurodegenerative disorder for which no effective therapy is available yet. We reported that activation of LXR by synthetic agonists restores cognitive decline in AD mice. Because of the hepatosteatosis and hypertriglyceridemia, induced by synthetic agonists, we are testing LXR-activating phytosterols that do not induce such side effects. We demonstrated that a lipophilic-extract of the Asian brown seaweed *Sargassum fusiforme,* containing the LXR-activating oxyphytosterol 24(S)-saringosterol, prevents cognitive decline in AD mice. We aimed at identifying European and Dutch brown seaweeds with LXR-activating capacities.

Methods: The LXR-activating capacity of lipophilic-extracts from different brown European and Dutch seaweeds was determined using a dual luciferase assay, using HEK cells and different brain cell lines. The LXR-activating capacity was related to the oxyphytosterol content. QPCR and western blotting was used for gene and protein expression.

Results: Positive effects for LXRa- and LXRβ-activation were observed for *Himanthalia elongata, Saccharina latissima, Alaria esculenta, Fucus vesiculosus and Sargassum muticum. Himanthalia elongata* extracts upregulated the expression of the LXR-targets ABCA1, ABCG1 and APOE and their protein expression.

Conclusions: Local seaweeds contain LXR-activating lipophilic compounds similar to *Sargassum fusiforme*. Seaweed may provide sustainable and affordable compounds for the prevention of a disease afflicting thousands of Dutch and global citizens, Alzheimer's disease and for other neurodegenerative or cardiometabolic diseases.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

CYCLODEXTRIN DIMERS FOR THE REMEDIATION OF ATHEROSCLEROTIC PLAQUE

POSTER VIEWING SESSION

Matthew S. Oconnor, Daniel Clemens
Underdog Pharmaceuticals, Underdog Pharmaceuticals, Mountain view, United States of America

Background and Aims : The world's biggest killer today is cardiovascular disease (CVD). Current treatments for CVD are failing to deliver the results required to beat this deadly and complex family of diseases. New approaches that go far beyond controlling LDL are needed.

Methods: Underdog Pharmaceuticals has developed a novel class of cyclodextrin (CD) molecules for the encapsulation of toxic oxidized cholesterol. Oxidized cholesterol accumulates over time and causes dysfunction in many cell types, linking it to several age-related diseases including atherosclerosis. Presently, treatments for atherosclerosis are invasive, expensive, and/or show limited benefits. CDs are cyclic glucose oligomers, utilized to capture small, hydrophobic molecules. Here, a combination of in silico, in vitro, and ex vivo methods are used to implement a synergistic rational drug design strategy for developing CDs to remove atherogenic oxidized cholesterol from cells and tissues.

Results: UDP-003 can both prevent and reverse the formation of foam cells in-vitro and shrink plaques in ApoE-/- HF diet mice. UDP-003 binds and clears 7KC from in-vivo and ex-vivo systems selectivity, and it has an excellent safety profile. UDP-003 has been awarded the Innovative Licensing and Access Pathway (ILAP) Innovation Passport by the UK MHRA, which is accelerating Underdog's path to clinic and will facilitate rapid and innovative clinical trials.

Conclusions: Targeted removal of 7KC from plaque with proprietary cyclodextrin compounds has the potential to prevent and reverse the formation of atheroscloertic plaques. This innovation represents the first disease-modifying therapeutic approach to treating atherosclerosis.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

ANTI-INFLAMMATORY EFFECT OF APOLIPOPROTEIN J IN DB/DB MICE FED ATHEROGENIC DIET

POSTER VIEWING SESSION

Núria Puig[1,2], Andrea Rivas-Urbina[1], Jose Rives[3], Laura Rabanal[1], Josep Julve[4], Noemi Rotllan[4], Jose Luis Sánchez-Quesada[1,5], Sonia Benitez[1]
[1]Cardivascular Biochemistry, Biomedical Research Institute Sant Pau (IIb-St Pau), Barcelona, Spain, [2]Biochemistry And Molecular Biology, Universitat Autònoma de Barcelona, Cerdanyola del Vallès, Spain, [3]Biochemistry, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [4]Pathophysiology Of Lipid Related Diseases, Biomedical Research Institute Sant Pau (IIb-St Pau), Barcelona, Spain, [5]Ciber Of Diabetes And Metabolic Diseases (ciberdem), CIBER, Madrid, Spain

Background and Aims : Patients with obesity and type 2 diabetes mellitus (T2DM) show a chronic low grade inflammatory state and an abnormal lipoprotein function. Apolipoprotein J (ApoJ) is a secreted glycoprotein with cardiovascular protective role. We aimed to assess the putative anti-inflammatory action of apoJ treatment in the db/db murine model of obesity and T2DM.

Methods: Female leptin receptor-deficient (db/db) mice were fed an atherogenic diet for 8 weeks. ApoJ-treated mice (n=7) were given a dose of 90 µg apoJ once a week, whereas an untreated group (n=7) was used as control. Animals were sacrificed and gene expression in liver, white adipose tissue (WAT), heart and kidney was evaluated by real-time qPCR. Plasma concentrations of leptin and adiponectin were measured by ELISA, and 9 inflammatory cytokines by Multiplex assay. To analyze the anti-inflammatory capacity of mouse HDL against human oxidized LDL (oxLDL), both lipoproteins were added to THP1 monocytes for 24 h, and MCP1 and IL1β were measured in supernatants by ELISA.

Results: Inflammatory cytokines increased and adiponectin decreased in plasma of mice compared to baseline levels; however, no difference was found between animals treated or not with apoJ. On the other hand, apoJ administration down-regulated *Mcp-1, CD68,* and *IL-1β* expression in WAT. In addition, HDL from apoJ-treated db/db mice was more protective against oxLDL-induced inflammation than HDL from untreated mice.

Conclusions: *ApoJ might contribute to diminish the inflammatory state associated with obesity and T2DM by eliciting an anti-inflammatory action in WAT and improving the anti-inflammatory action of HDL.*

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

MAPPING OF FAMILIAL HYPERCHOLESTEROLEMIA BASIC INFRASTRUCTURE IN PAKISTAN

POSTER VIEWING SESSION

Fouzia Sadiq[1], Saeed Shafi[2], Madeeha Khan[1], Quratul Ain[1], Iqbal Khan[3], Habibur Rehman[4], Jaka Šikonja[5], Matej Mlinarič[6], Samuel Gidding[7], Urh Groselj[6]
[1]Directorate Of Research, Shifa Tameer-e-Millat University, Islamabad, Pakistan, Islamabad, Pakistan, [2]Department Of Anatomy, Shifa College Of Medicine, Shifa Tameer-e-Millat University, Islamabad, Pakistan, Islamabad, Pakistan, [3]Department Of Vascular Surgery, Shifa International Hospital, Islamabad, Pakistan, Islamabad, Pakistan, [4]Directorate Of Cardiology, Shifa International Hospital, Islamabad, Pakistan, Islamabad, Pakistan, [5]Faculty Of Medicine, University of Ljubljana, Metlika, Slovenia, [6]Faculty Of Medicine, University of Ljubljana, Ljubljana, Slovenia, [7]Geisinger, Geisinger Health, PA, United States of America

Background and Aims : Globally, less than 10% of the Familial Hypercholesterolemia (FH) population is diagnosed and treated partly due to the lack of general awareness of FH among the public and medical community. We launched a survey to map activities to identify FH patients and to assess the national situation regarding available infrastructure that could be applied to systematically identify FH patients.

Methods: An online questionnaire was administered to 110 clinicians across Pakistan, mainly from two most-populous provinces (accounting for 72% of Pakistan's population): Punjab (62%) and Sindh (19%); and responders comprised of specialists in cardiology (34%), pediatrics (27%), internal medicine (13%) and general medicine (10%).

Results: Respondents did not frequently encounter FH patients; 85% of them had seen less than 10 children and 72% seen less than 50 adults with FH over the last 5 years. Around 70% of them estimated that less than 10% adults and children have free access to cholesterol measurement whereas 40% and 46% stated that cholesterol measurement is available to less than 1% of adults and children, respectively. Statins alone or in combination with ezetimibe are accessible to 94% adults and 78% of children with FH. Out-of-pocket was the only possible payment option for FH patients of 57% of clinicians for lipid lowering therapy.

Conclusions: The estimated low availability of cholesterol measurements in the country and low awareness likely explains why the respondents had seen a considerably low number of patients with FH over the 5-year study period. Statins are generally accessible to FH patients but are financially unattainable.

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Topic: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-13 Other*

TRANSIENT ELEVATION OF HUMORAL RESPONSES AGAINST APOLIPOPROTEIN A-1 FOLLOWING COVID-19 AND ITS ASSOCIATION WITH SYMPTOMS PERSISTENCE

POSTER VIEWING SESSION

Arnaud G. L'Huillier[1], Sabrina Pagano[1], Stephanie Baggio[2], Benjamin Meyer[3], Diego O. Andrey[1], Mayssam Nehme[4], Idris Guessous[4], Christiane S. Eberhardt[3], Angela Huttner[5], Klara M. Posfay-Barbe[6], Sabine Yerly[1], Claire-Anne Siegrist[3], Laurent Kaiser[1,5], Nicolas Vuilleumier[1]
[1]Department Of Diagnostics And Of Medical Specialties, Geneva University Hospital, Geneva, Switzerland, [2]Division Of Prison Health, Geneva University Hospitals and Geneva University, Geneva, Switzerland, [3]Centre For Vaccinology, Department Of Pathology And Immunology, University of Geneva, Geneva, Geneva, Switzerland, [4]Division Of Primary Care Medicine, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland, [5]Division Of Infectious Diseases, Geneva University Hospitals, Geneva, Switzerland, [6]Pediatric Infectious Diseases Unit, Department Of Woman, Child And Adolescent Medicine, Geneva University Hospitals and Geneva University, Geneva, Switzerland

Background and Aims : Auto-antibodies against apolipoprotein A-1 (AAA1) develop during SARS-CoV-2 infection and could be of concern as mediators of symptoms in the later stages of infection. We aimed at determining i) the duration and kinetics of AAA1 response over 12 months after a SARS-CoV-2 infection, and ii) whether AAA1 were associated with COVID-19 symptoms persistence.

Methods: All serologies were measured by immunoassays at one, three, six, and twelve months in 193 COVID-19 positive hospital employees. LGM, ROC curve and LRM analyses were used to assess the clinical determinants of AAA1 levels and kinetics, their prognostic accuracy and the association between AAA1 levels and patient-reported COVID-19 symptoms persistence respectively.

Results: AAA1 positivity rate was 92% declining to 14.5% at 12 months after infection. Significant correlation were retrieved between SARS-CoV-2 anti-S, anti-N and AAA1 IgG levels. Age was the only independent factor modulating AAA1 initial levels. Persistent symptoms at 12 months were observed in 45.1 % of participants, with a predominance of neurological (28.5 %), followed by general (15%) and respiratory symptoms (9.3%). AAA1 levels at 3 months after the infection, displayed significant prognostic accuracies and were independently associated with respiratory symptoms persistence (AUC ranging between 0.72 to 0.74; $p<0.001$; adjusted OR varying between 4.81-4.94; $p=0.02$), while anti-S and anti-N antibodies levels were not.

Conclusions: SARS-CoV-2 infection induces a marked though transient AAA1 response, independently predicting one-year persistence of respiratory symptoms from the third month after infection. If and how AAA1 levels assessment could be of use for COVID-19 risk stratification remains to be determined.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

IDENTIFICATION AND FOLLOW-UP OF POPULATION WITH FAMILY HYPERCHOLESTEROLEMIA AND HIGH CARDIOVASCULAR RISK

POSTER VIEWING SESSION

Larissa B. Pellegrino[1], Renato J. Alves[2,3]
[1]Cardiologia, Hospital Santa Casa de Misericórdia de São Paulo, São Paulo, Brazil, [2]Cardiology, Santa Casa de Misericordia de Sao Paulo Hospital, São Paulo, Brazil, [3]Cardiology, Santa Casa de Sao Paulo School of Medical Sciences, Sao Paulo, Brazil

Background and Aims : Background: Family Hypercholesterolemia (FH) is related to cardiovascular events.The gold standard test for the diagnosis is genetic analysis, but when it's not available, the Dutch Lipid ClinicNetwork Score (DLCNS) criterion is used as an alternative to classify and diagnose these individuals. Aim: To evaluate the incidence of cardiovascular disease in a FH's population and reduction on the incidence of cardiovascular events after diagnosis and optimized clinical treatment.

Methods: The patients were selected according to the DLCNS criterion and classified according to the score. The follow-up period of the population was 3 years, on average. Inclusion criteria were: age above 18 years and LDL-c > 190 mg/dL. Patients with secondary dyslipidemia were excluded.

Results: Were 71 patients, mean age of 55 years. The mean DLCNS of the studied population was 6 (probable FH). The incidence of previous cardiovascular events at the beginning of follow-up was 25% (95% acute myocardial infarction). The main risk factors: positive family historyfor early cardiovascular disease (79%), hypertension(51%), smoking (35%) and diabetes mellitus (20%). The mean concentrations of basal total cholesterol (TC) andLDL-c were 326 mg/dL and 255 mg/dL, respectively. After the three-year period with treatment of high-potency statins the values of TC and LDL-c increased to 221mg/dL and 135mg/dL. The target of 50% reduction of basal LDL-c was reached by 59% and 10% the LDL-c target < 70 mg/dL.

Conclusions: Conclusion: Early diagnosis and optimized treatment with high-potency statins reduce serum levels of TC and LDL, directly impacting on the reduction of events and, consequently, mortality form cardiovascular causes.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

CARDIOVASCULAR OUTCOMES ACCORDING TO RISK CATEGORY: RESULTS OF A RETROSPECTIVE DATABASE STUDY

POSTER VIEWING SESSION

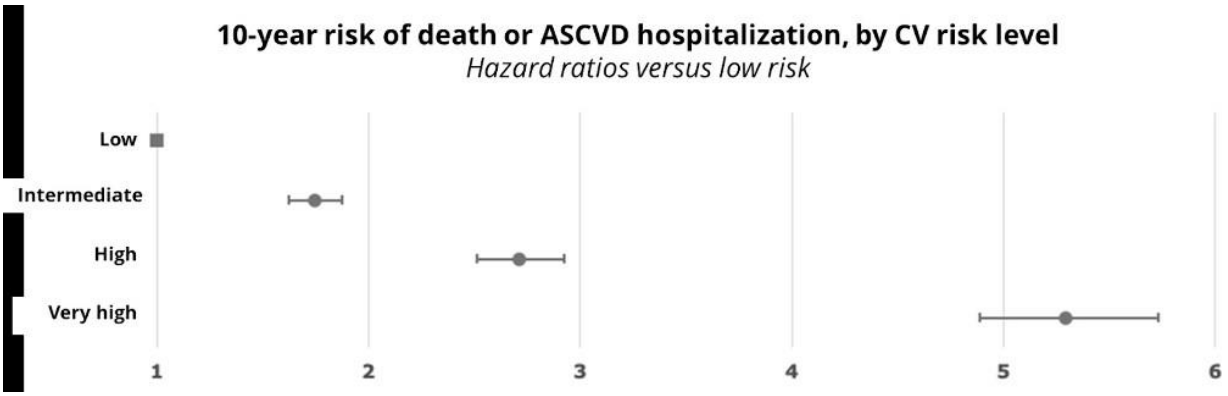
Francisco Araújo[1,2], Daniel Seabra[3], Marta Afonso-Silva[4], Diana Grangeia[5], Tiago Taveira-Gomes[6,7,8,9,10], Cristina Gavina[2,3,11,12]
[1]Internal Medicine, Hospital Lusíadas, Lisbon, Portugal, [2]Sociedade Portuguesa De Aterosclerose, SPA, Lisboa, Portugal, [3]Cardiology, Hospital Pedro Hispano, Matosinhos, Portugal, [4]Heor / Rwe, Novartis Farma - Produtos Farmacêuticos SA, Porto Salvo, Portugal, [5]Medical Affairs, Novartis Farma - Produtos Farmacêuticos SA, Porto Salvo, Portugal, [6]Departmento De Medicina Da Comunidade, Informação E Decisão Em Saúde, Faculdade de Medicina, Universidade do Porto, Porto, Portugal, [7]Faculdade De Ciências Da Saúde, Universidade Fernando Pessoa, Porto, Portugal, [8]Instituto Universitário De Ciências Da Saúde, Cooperativa de Ensino Superior Politécnico e Universitário, Porto, Portugal, [9]Centro De Investigação Em Tecnologias E Serviços De Saúde, CINTESIS, Porto, Portugal, [10]Magalhães & Taveira-gomes Sociedade Médica, MTG, Porto, Portugal, [11]Departmento De Medicina, Faculdade de Medicina, Universidade do Porto, Porto, Portugal, [12]Unic, Faculdade de Medicina, Universidade do Porto, Porto, Portugal

Background and Aims : This study aims to analyze the 10-year risk of death or hospitalization for atherosclerotic cardiovascular disease (ASCVD) by cardiovascular (CV) risk level.

Methods: Retrospective population-based study using data from a Local Health Unit in Portugal. New patients in each CV risk category (defined according to the ESC/EAS 2019 guidelines) and ≥1 General Practice appointment in the three years prior to the date of inclusion (date of entry into the respective risk category) were analyzed. This analysis focused on the composite endpoint of 10-year risk of death (from any cause) or ASCVD hospitalization, by CV risk level. Death and hospitalization data were obtained from the corresponding ICD-9-CM and ICD-10-CM codes. Cox regression, sex- and age-adjusted, clustered per patient was used.

Results: The total cohort consisted of 78,459 patients (low risk=32.6%, intermediate=28.8%, high=21.6%, very high=17.0%). Sociodemographic and clinical characteristics by CV risk, at the time of entry into the risk category, are depicted in Table1. The 10-year risk of death or hospitalization for ASCVD was 1.7 times higher in intermediate-risk patients, 2.7 times higher in high-risk and 5.3 times higher in very high-risk compared to patients with low risk
(Figure1).

Table 1 – Sociodemographic and clinical characteristics by CV risk, at the time of entry into the risk category				
	Low risk	***Intermediate risk***	***High risk***	***Very high risk***
Age, years (median (IQR))	33.0 (18.0)	57.0 (11.0)	65.0 (16.0)	70.0 (18.0)
Males (%)	41.3	45.7	49.3	55.0
Most common comorbidities (%)				
Hypercholesterolemia	10.8	49.2	56.9	57.2
Hypertension	1.7	20.0	27.6	47.3
Type II DM	0.5	5.0	25.3	49.2
CKD	0	0	19.1	28.2
Intermediate CV risk criteria (%)				
SCORE [1, 5[%	-	97.0	-	-
Healthy T2DM	-	3.0	-	-
Young T1DM	-	0	-	-
High CV risk criteria (%)				
GFR 30-60%	-	-	19.1	-
Unhealthy T2D	-	-	24.9	-
HTN G3	-	-	1.9	-
High TC	-	-	3.7	-
Familial Hypercholesterolemia	-	-	0.5	-
High LDL-C	-	-	18.3	-
SCORE [5, 10[%	-	-	37.2	-
Very high CV risk criteria (%)				
Severe Kidney Function	-	-	-	12.3
ASCVD	-	-	-	23.0
Damaged DM	-	-	-	20.1
T2D and 3+ Major Risk Factors	-	-	-	24.4
Unhealthy FH	-	-	-	3.0
SCORE > 10%	-	-	-	21.5
Long T1DM	-	-	-	0
Risk enhancers AHA 18 (%)				
Early Heart Disease	0	0	0	2.1
LDL-C [160, 190[, mg/dL	1.8	13.3	7.7	10.3
HDL-C [190, 220[, mg/dL	1.4	12.0	10.5	10.3
Metabolic Syndrome	32.0	91.8	93.5	95.9
eGFR]15, 60] mL/min	0	0	19.1	26.6
Menopause < 40y	0	0	0	0
Preeclampsia	0	0	0.1	0.1
Hypertriglyceridemia, Primary	1.0	4.2	6.0	8.4
Lipid lowering treatment (LLT) (%)				
Any LLT	5.2	38.7	43.6	57.1
Low intensity statin	0.5	4.5	5.5	6.9
Moderate intensity statin	3.9	30.9	34.5	45.8
High intensity statin	0.1	0.8	0.8	1.5
Ezetimibe	0.2	1.8	2.0	3.0
Fibrates	1.2	6.3	7.4	10.7
Lipid panel (mean (SD))				
LDL-C, mg/dL	116.8 (43.0)	127.0 (45.0)	136.0 (70.7)	125.0 (48.0)
HDL-C, mg/dL	44.0 (15.0)	48.0 (16.5)	48.0 (17.0)	45.0 (16.0)
non HDL-C, mg/dL	140.0 (49.0)	152.3 (51.7)	161.0 (69.0)	154.0 (51.0)
TC, mg/dL	185.1 (50.0)	202.0 (55.0)	211.0 (69.0)	201.6 (53.0)
TG, mg/dL2	98.0 (70.0)	108.0 (69.0)	119.0 (79.0)	121.0 (80.0)



Conclusions: These real-world evidence show an increased risk of death or ASCVD hospitalization in patients in higher CV risk categories, independently of sex and age, reinforcing the need of more effective disease management as patients' CV risk increases. This corroborates the recommendations put forward by the ESC guidelines.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

ASSESSMENT OF STATIN ADHERENCE IN PATIENTS WHO UNDERWENT PERCUTANEOUS CORONARY INTERVENTION

POSTER VIEWING SESSION

Sevda Aygun[1], Mert Dogan[1], Yusuf Ziya Şener[2], Ahmet Hakan Ateş[3], Kudret Aytemir[3], Lale Tokgözoğlu[4]
[1]Cardiology Department, Hacettepe University Faculty of Medicine, Turkey, Turkey, [2]Cardiology Department, Beypazarı State Hospital, Ankara, Turkey, [3]Cardiology, Hacettepe University Hospital, Ankara, Turkey, [4]Cardiology, Hacettepe University Medical Faculty, Ankara, Turkey

Background and Aims : Statin therapy is one of the cornerstone part of coronary artery disease treatment. Current guidelines recommends high intensity statin treatment for primary and secondary prevention of CV events and in daily clinical pratice, discontuniation of statins is a frequent problem.We aimed to evaluate the status and associated factors of statin adherence in patients underwent percutaneous coronary intervention (PCI).

Methods: All cases who underwent index PCI between January and July 2019 in Hacettepe University Hospital were screened. Patients with previous PCI history and patients who died during follow-up were excluded. Datas were obtained from electronic database of the hospital.

Results: A total of 187 patients were included. Baseline characteristics were presented in Table-1. During follow-up; staying at statin treatment at the end of 1 year was 84,2%. The most common cause of statin discontinuation was patient's own request. Elevation of liver enzymes, myalgia and pruritus were the following reasons. Multivariate Cox regression analysis showed that hypertension (HR:2,82; p=0.010) and diabetes (HR:0,27; p=0.006) were associated with statin discontinuation (parameters with a p value<0,200 in univariate analysis were included) (Table-2).

Table-1. Baseline Characteristics of the patients (n=187)	
Age, years	63,3 ± 11,0
Female, n (%)	52 (27,8 %)
Current smoking, n (%)	84 (44,9 %)
Comorbidities, n (%);	
Hypertension	102 (54,5%)
Diabetes mellitus	60 (32,1 %)
CKD	11 (5,9 %)
Atrial fibrillation	6 (3,2 %)
Cerebrovascular disease	5 (2,7 %)
Follow-up, months, median	14 (6-22)
LDL, mg/dL, median (25-75 percentile)	
Baseline	135 (101-160)
Last visit	100 (85-124)
Statin type, n (%);	
Atorvastatin	153 (81,8 %)
Rosuvastatin	34 (18,2 %)
Statin dose intensity, n (%);	
Low	100 (53,5 %)
Moderate	72 (38,5 %)
High	15 (8 %)
Statin discontiuation, n (%)	49 (26,2 %)
Cause of statin discontinuation, n (%);	
Doctor recommendation (Due to low LDL level)	12 (6,4 %)
Elevated liver enzymes	5 (2,6 %)
Myalgia	7 (3,7 %)
Pruritus	1 (0,5 %)
Own request	24 (12,8 %)
Coronary angiography datas;	
Indication, (Acute coronary syndrome)	61 (32,6 %)
Number of stents, median	1 (1-2)
Percent maximum stenosis	80 (70-95)
PCI performed vessel;	
-LMCA	3 (1,6 %)
-LAD	101 (54,0 %)
-Cx	33 (17,6 %)
-RCA	64 (34,2 %)
Abbreviations; CKD: Chronic kdiney disease; LDL: Low density lipoprotein; PCI: Percuatneous coronary intervention; LMCA: Left main coronary artery; LAD: Left anterior descending artery; Cx: Circumflex artery; RCA: Right coronary artery	

Table-2. Factors associated with statin discontinuation				
	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1,02 (0,99-1,05)	0,129	1,02 (0,99-1,05)	0,179
Hypertension	2,49 (1,17-5,27)	0,017	2,82 (1,27-6,2)	0,010*
Diabetes mellitus	0,39 (0,16-0,96)	0,041	0,27 (0,11-0,69)	0,006*
Abbreviations: CI: Confidence interval; * p values < 0.05 were defined as statistically significant				

Conclusions: It's still an important proportion of patients don't adhere to statin treatment. Patient's pereference is the most common cause of statin discontinuation. Diabetes is associated with statin adherence and it must be due to strict follow-up of patients with both cardiolgists and endocrinologists. On the contrary, hypertension is associated with statin discontinuation and this could be explained with possible polypharmacy as many patients with hypertension uses more than one drug for blood pressure control.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

LONG-TERM IMPACT OF DIFFERENT TRIPLE ANTIHYPERTENSIVE DRUG TREATMENTS ON BLOOD PRESSURE CONTROL, METABOLIC PATTERN AND INCIDENT EVENTS: DATA FROM THE BRISIGHELLA HEART STUDY

POSTER VIEWING SESSION

Arrigo F.G. Cicero, Federica Fogacci, Elisabetta Rizzoli, Sergio D'Addato, Claudio Borghi
Medical And Surgical Sciences Department, University of Bologna, Bologna, Italy

Background and Aims : Aim of this study was to comparatively evaluate clinical, laboratory and hemodynamic effects on the long term of different triple combination antihypertensive medications in a well-characterized population cohort.

Methods: We considered data of a subset of Brisighella Heart Study participants who were consecutively evaluated in three epidemiological surveys between 2012 and 2020. We excluded normotensive subjects, patients treated with <3 or ≥3 high blood pressure (BP) medications without taking angiotensin-converting enzyme (ACE) inhibitors, angiotensin-II receptor blockers (ARBs), calcium-channel blockers (CCB) and/or thiazide/thiazide-like diuretics. Remaining participants were divided into three groups depending on whether they were treated with ACE-inhibitors/CCBs/Thiazide, ARBs/CCBs/Thiazide or Perindopril/Amlodipine/Indapamide, either with separate drugs or fixed pill combinations. A further group of age- and sex-matched volunteers was selected as control and included patients receiving other antihypertensive medications. Long term effects of different antihypertensive medications were compared among the pre-defined groups.

Results: On long-term, combination treatment with renin-angiotensin system (RAS) modulators, CCBs and thiazide/thiazide-like diuretics was associated with better control of diastolic BP and lipids than other triple combination antihypertensive medication. Patients treated with Perindopril/Amlodipine/Indapamide did not experience any age-related increase in total cholesterol. Moreover, during the follow-up they neither developed type 2 diabetes nor had a need for a greater number of antihypertensive drugs to improve BP control.

Conclusions: Combination treatment with RAS modulators, amlodipine and thiazides/thiazide-like diuretics is more effective than other combination antihypertensive medications for lowering the diastolic BP and has a better impact on lipids. Perindopril/amlodipine/indapamide is associated with better lipids' profile than any other considered combination antihypertensive medication.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

THE MANAGEMENT OF PATIENTS WITH CHRONIC CARDIOVASCULAR THERAPIES IN LOMBARDY REGION: THE IMPACT OF THE COVID-19 PANDEMIC

POSTER VIEWING SESSION

Federica Galimberti[1], Elena Olmastroni[2], Alberico L. Catapano[3], Elena Tragni[4], Manuela Casula[5]
[1]., IRCCS MultiMedica, Milan, Italy, [2]Department Of Pharmacological And Biomolecular Sciences, Epidemiology and Preventive Pharmacology Service (SEFAP), Milan, Italy, [3]Department Of Pharmacological And Biomolecular Sciences, University of Milan and Multimedica IRCCS, Milan, Italy, [4]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Epidemiology and Preventive Pharmacology Service (SEFAP), Milan, Italy, [5]Epidemiology And Preventive Pharmacology Service (sefap) - Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy

Background and Aims : The COVID-19 pandemic has posed major challenges to healthcare systems and public policies. We aimed to investigate its impact on the management of chronic cardiovascular therapies using administrative databases of Lombardy Region.

Methods: The study period between January and June 2020 was compared with the control period January-June 2019. For all adult patients (≥40 years) with at least one prescription of the selected drugs, the percentage change in drug consumption, adherence to therapy and access to healthcare services (blood tests, diagnostic investigations, or specialist visits for disease monitoring) was evaluated.

Results: A total of 911,566 patients on lipid-lowering therapy, 2,147,386 on antihypertensives, 392,678 on antidiabetics and 621,976 on anticoagulants were enrolled and compared with 879,881, 2,128,334, 381,752, and 601,204 controls, respectively. Overall, there was a small change in the number of dispensed packages (+3.8%, -1.8%, -5.9%, -5.2%, respectively); however, in all the cohorts, a slight increase was observed in the first two bimesters, with a sharp decrease in May-June (-6.7%, -11.4%, -21.3%, -22.6%, respectively). Likewise, adherence to treatments showed an increase in March-April, and a reduction during the following two months. Conversely, there was a dramatic drop in healthcare services utilization in each patient cohort, with a negative spike in March/April (-65.2%, -66.0%, -63.5%, -53.9%, respectively).

Conclusions: The COVID-19 pandemic has negatively affected the access to healthcare services by patients with chronic cardiovascular diseases. We observed a tendency to accumulate medicines at the beginning of the lock-down, and a decreased use of health services for disease monitoring compared to the control period.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

COMPARISON OF CORONARY ARTERY CALCIUM SCORE AND ITS DETERMINANTS IN PATIENTS WITH FAMILIAL COMBINED HYPERLIPIDEMIA AND TYPE 2 DIABETES, IN PRIMARY CARDIOVASCULAR PREVENTION

POSTER VIEWING SESSION

Zoé Henry[1], Oriane Marmontel[2,3], Laetitia Balaire[1], Charlotte Marsot[1], Mathilde Di Filippo[2,3], Philippe Moulin[1,3,4], Sybil Charriere[1,3,4]
[1]Service D'endocrinologie, De Diabétologie Et Des Maladies Métaboliques, Hôpital Louis Pradel, Bron cedex, France, [2]Laboratoire De Biologie Médicale Multi-sites, Hcl, Service de Biochimie et Biologie moléculaire Grand Est, Bron, France, [3]Inserm U1060, Université Lyon 1, Inrae U1397, Laboratoire CarMen, Oullins, France, [4]Université Lyon 1 Claude Bernard, Faculté de Médecine Lyon Est, Lyon, France

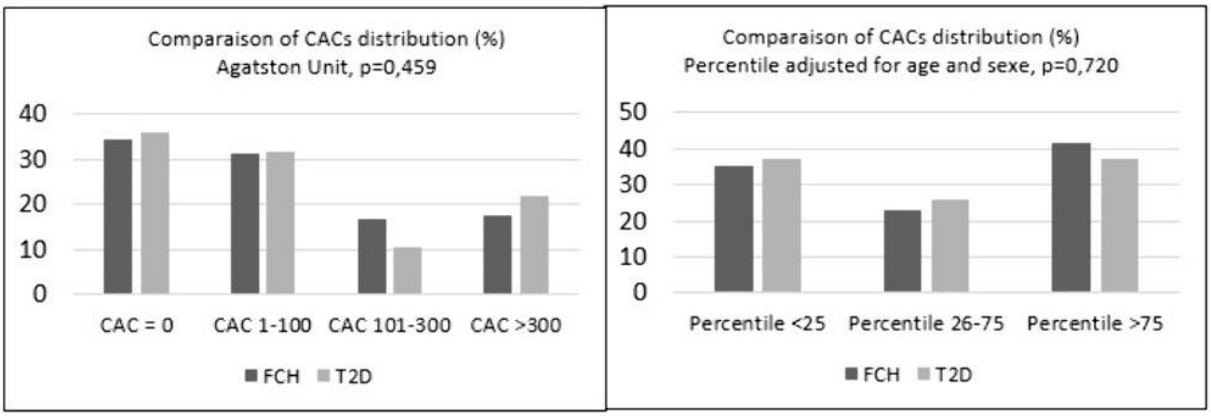
Background and Aims : Familial combined hyperlipidemia (FCH) is a frequent dyslipidemia often associated with metabolic syndrome (MetS). The magnitude of the atherosclerotic cardiovascular disease (ASCVD) risk increase in FCH is not clearly established. We used coronary artery calcium score (CAC) as a surrogate of the intensity of coronary atherosclerosis and as a strong predictor of MACE and compared its results in FCH versus T2D (type 2 diabetes) patients (a control group with a well-established high ASCVD risk).

Methods: This monocentric, observational, retrospective cohort study included 96 FCH (without diabetes) and 192 T2D. Patients were matched 1:2 on gender and age. Inclusion criteria were: age >40, cardiovascular (CV) primary prevention and CAC performed between Dec-2011 and Nov-2020. Traditional CV risk factors, biomarkers of lipid and carbohydrate metabolisms, hepatic function were retrospectively recorded in electronic medical files.

Results: Median CAC score (46.5 AU [IQ168] vs 22.0 AU [IQ242], p=0.532), prevalence of CAC>300 AU or CAC>75th percentile were similar for both FCH and T2D patients. Age, male sex, MetS, hypertension and high fibrosis-4 score were significantly associated with CAC>300 AU in FCH patients, whereas only age and diabetes duration were significant covariates in T2D patients. In multivariate analysis, MetS only remained an independent factor of CAC>75th PAS in

FCH.

Figure 1 – Comparison of CACs distribution in absolute and relative values



FCH: familial combined hyperlipidemia; T2D: type 2 diabetes

Conclusions: This study showed a similar CAC distribution for FCH and T2D patients. MetS was strongly associated with CAC leading to the identification of a subgroup of FCH patients who need an intensification of their CV prevention.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

DIGITAL TWINS FOR PREDICTION OF ATHEROSCLEROSIS PROGRESSION AND STROKE

POSTER VIEWING SESSION

Tilda Herrgårdh, Christian Simonsson, Kajsa Tunedal, Gunnar Cedersund
Department Of Biomedical Engineering, Imt, Linköpings universitet, Linköping, Sweden

Background and Aims : The etiology behind atherosclerosis is complex, involving many different processes, and develops over several years, often without symptoms, before it leads to more acute conditions such as stroke. One way of dealing with this complexity is through mathematical modelling. There already exist models for relevant organs and sub-systems. However, none have combined these models for different sub-systems and personalized them into digital twins.

Methods: The mathematical models describe physiological processes over time in a multi-level (intracellular biochemistry to whole-body) and multi-timescale (seconds to years) description. The sub-models are trained and validated on in vitro, in vivo, and clinical population data, and the interconnected model is personalized by validating on individual data.

Results: The digital twins describes both development of risk factors for development of atherosclerosis - dyslipidemia, high plod pressure, and diabetes –, the build-up of plaque and an increased risk of ruptures, and the subsequent thrombosis and increased risk of a stroke. The different sub-models are developed on different types of data and each sub-model provides input for the next.

Conclusions: Our digital twin for atherosclerosis progression can be used to simulate the evolution of relevant biomarkers given certain scenarios, e.g. different medications, diet and exercise. Simulating scenarios can be used to evaluate different health scenarios and thus aid in prevention or treatment of atherosclerosis and its precursors. The model will be tested in clinical usage, in the health conversation: a preventive examination, where we hope to increase doctor-patient communication, patient compliance, and preventive actions.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

THE EFFECT OF SEDENTARY TIME ON BLOOD LIPIDS AND ANTHROPOMETRIC PARAMETERS IN HEALTHY PHYSICALLY ACTIVE PEOPLE.

POSTER VIEWING SESSION

Maryna Vovchenko[1], Anna Isayeva[1], Olga Petyunina[2]
[1]Department Of Chronic Non-communicable Disease Prevention, The Government Institution “National Institute of Therapy named by L.T. Malaya of National Ukrainian Academy of Medical Science”,, Kharkov, Ukraine, [2]Department Of Prevention And Treatment Of Emergency Conditions, The Government Institution “National Institute of Therapy named by L.T. Malaya of National Ukrainian Academy of Medical Science”,, Kharkov, Ukraine

Background and Aims : The aim was to analyze the effect of the duration of a sedentary lifestyle on blood lipids and anthropometric parameters in people engaged in regular strength training.

Methods: A cross sectional study included 169 subjects without cardiovascular disease, white caucasian people, female 82 (48 %), male 87 (52 %). Participants practiced resistance training two-three times per week for at least 12 months prior to study commencing. Anthropometric parameters, body composition (bioelectrical impedance method), muscle strength, blood pressure, blood lipids and glucose were assessed. The International Questionnaire on long Physical Activity (IPAQ) to assess physical activity and sedentary time was used. IBM® SPSS® Statistics 19 was used for statistical analysis.

Results: Participants were divided into four groups according to their sitting time: 1st group 21.05 [14.00÷21.25] hours per week; 2nd group 28 hours [25.0÷28.7]; 3rd group 38.5 hours [35.0÷42.0]; 4th group 56 [49.0÷56.7]. In the 4th group proportion of muscle tissue was lower than in 1st and 2nd groups (p_{1-4} = 0.052; p_{2-4} = 0.008). Median of high-density cholesterol progressively decreased from the 1st to the 4th group, ANOVA test; p=0.003. High density cholesterol in the 1st group corresponded to 1,620 [1,45÷1,75] mmol/l; in the 2nd group - 1,52 [1,39÷1,67] mmol/l; in the 3rd group - 1,50 [1,41÷1,64] mmol/l, and was the lowest in the 4th group - 1,310 [1,12÷1,38] mmol/l. Participants from 4th group had larger waist and hip circumference.

Conclusions: Although active regular resistance training, long duration sitting time negatively influence HDL cholesterol and anthropometric parameters.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

STATUS OF PREMATURE CORONARY ARTERY DISEASE IN VIETNAM AND ITS ASSOCIATED RISK FACTORS

POSTER VIEWING SESSION

Thanh Huong Truong[1], Ngoc Thanh Kim[1], Hong Phu Vu[2], Mai Ngoc T. Nguyen[2], Doan Loi Do[1], Thanh Tung Le[2], Hong An Le[2]
[1]Department Of Cardiology, Hanoi Medical University, Hanoi, Viet Nam, [2]Vietnam National Heart Institute, Bach Mai Hospital, Hanoi, Viet Nam

Background and Aims : Knowledge about premature coronary artery disease (PCAD) is still limited in Vietnam. This study aims to describe status of coronary artery lesion and its associated risk factors in these patients.

Methods: A cross sectional study of 177 patients aged ≤55 years for men and ≤60 for women undergoing coronary angiography was conducted, from 2018 to 2019 in Vietnam.

Results: Most of PCAD patients was acute coronary syndrome (83.1%). The most common cardiovascular risk factor was smoking (63.3%). Complex lesions were common in PCAD patients, including long lesion, (44.6%), diffuse lesion (18.6%), chronic total occlusion (12.4%), bifurcation lesion (12.4%), ostial lesion (5.6%) and SYNTAX score ≥22 (27.9%). Multivariate logistic regression analysis showed that serum low density lipoprotein cholesterol (LDL-C) level was independently related to the presence of moderate-severe coronary artery disease (SYNTAX score ≥22) with Odds ratio as 1.706.

Conclusions: PCAD patients had significant rates of complex lesions. Elevated serum LDL-C level was independent risk factor related to mordeate-severe coronary artery disease in these patients.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

LONGITUDINAL MULTIVARIABLE TRAJECTORY RISK CLUSTERS AND SEX-SPECIFIC ASSOCIATION WITH MRI-DERIVED CARDIAC FUNCTION AND STRUCTURE IN A POPULATION-BASED SAMPLE

POSTER VIEWING SESSION

Roberto Lorbeer[1], Susanne Rospleszcz[2], Christopher Schlett[3], Sophia Rado[4], Barbara Thorand[2], Christa Meisinger[2], Wolfgang Rathmann[5], Margit Heier[2], Ramachandran Vasan[6], Fabian Bamberg[3], Annette Peters[2], Wolfgang Lieb[7]
[1]Department Of Radiology, Klinikum der LMU, München, Germany, [2]Institute Of Epidemiology, Helmholtz Zentrum München, Neuherberg, Germany, [3]Department Of Diagnostic And Interventional Radiology, University Freiburg, Freiburg, Germany, [4]Department Of Diagnostic And Interventional Radiology, Eberhard Karl University Tübingen, Tübingen, Germany, [5]Institute For Biometrics And Epidemiology, German Diabetes Center, Düsseldorf, Germany, [6]Preventive Medicine & Epidemiology Section, Boston University School of Medicine and Framingham Heart Study, Boston, United States of America, [7]Institute Of Epidemiology, Kiel University, Kiel, Germany

Background and Aims : This study aimed to relate longitudinal trajectory clusters of multiple cardiovascular risk factor levels from different examination cycles to MRI-measures of cardiac structure and function of the left and right ventricle in women and men of a population-based cohort.

Methods: Risk factor levels were measured in 349 participants (143 women; aged 25-59 years) at three examination cycles (baseline, 7-years follow-up, 14-years follow-up) of the KORA S4 cohort. We investigated longitudinal multivariable risk clusters including systolic and diastolic BP, waist circumference, HbA1c and LDL-cholesterol in relation to various cardiac MRI-measures obtained at the last examination separately in women and men.

Results: Longitudinal multivariable trajectory risk clusters were associated with subclinical alterations of cardiac function and structure independently of recently obtained risk factor levels and sex. The high-risk cluster was stronger associated with reduced left and right volume parameters in men (e.g. LV stroke volume β=-7.73 ml/m^2, 95%CI -12.73;-2.73, p=0.003 compared to the low risk cluster) than in women. Only men of the high-risk cluster showed lower LV diastolic filling rate (β=-92.5ml/s, 95%CI -150.4; -34.5, p=0.002). In contrast, the high-risk cluster was associated with higher myocardial mass only in women (β=12.9g, 95%CI 3.88; 22.0, p=0.005). Positive associations between trajectory risk clusters and cardiac fat were similar in both sexes.

Conclusions: Longitudinal multivariable trajectory risk clusters, based on a time period of 14 years, were associated with recently MRI-derived measures of cardiac structure and function in a population-based sample with a greater explanation of cardiac structure differences in women and cardiac function differences in men.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

ACHIEVING THE LDL-C GOAL IN INDIAN PATIENTS OF ACUTE CORONARY SYNDROME WITH HIGH INTENSITY STATIN

POSTER VIEWING SESSION

Jps Sawhney[1], Jigneshkumar G. Vanani[2], Kushal Madan[2], Manish K. Sharma[2], Kavita Tyagi[2], Bhuwanesh Kandpal[2], Ashwani Mehta[2]
[1]Cardiology, Sir Ganga Ram Hospital, New Delhi, India, [2]Department Of Cardiology, Sir Ganga Ram hospital, New delhi, India

Background and Aims : High dose statin therapy is recommended to achieve the LDL-C goal<55mg/dL or >50% reduction from baseline. The aim of this pilot study is to investigate the time taken for achieving the LDL-C goal <55mg/dL and the proportion of ACS patients who could achieve the LDL-C goal with high intensity statins.

Methods: Statin naive >18 years old ACS patients were included in this prospective observational study. All patients were given guidelines based standard care for ACS along with oral atorvastatin 80mg/day. Before starting the high dose statin, LDL-C was measured at baseline, on Day 3,7,14 and 28. An additional measurement was done on day 42 in those patients who did not attain the goal within 28 days.

Results: 100 consecutive ACS patients were included. Total 460 lipid profiles were done within the period of 4-6 weeks.

Mean LDL-C at baseline (n=100)	Day 3 (n=93)	Day 7 (n=80)	Day 15 (n=74)	Day 28 (n=100)
141.6 mg/dL	114.7 mg/dL	86.6 mg/dL	57.0 mg/dL	41.7 mg/dL
%reduction in LDL-c	19.0%	40.7%	59.7%	70.6%
%of patients who attained the LDL-C goal	0	1%	47%	87%

The mean LDL-C at baseline was 141.6 mg/dL and there was a trend of reduction in LDL-c in all follow up measurements .13% patients did not achieve the LDL-C target even on Day 42

Conclusions: High dose statin in ACS patients leads to rapid lowering of LDL-C, which is maximum (70%) within 28 days. 87% patients achieved LDL-C goal (<55mg/dL). Beyond 28 days there was no further reduction in LDL-C.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

CREATION OF CYBRID CULTURE WITH ANTIATHEROGENIC MITOCHONDRIAL GENOME MUTATION M.13513G>A (GENE MT-ND5)

POSTER VIEWING SESSION

Margarita A. Sazonova[1], Vasily V. Sinyov[2], Anastasia I. Ryzhkova[1], Marina D. Sazonova[1], Tatiana V. Kirichenko[3], Natalya A. Doroshchuk[1], Alexander N. Orekhov[3], Igor A. Sobenin[4]
[1]Laboratory Of Angiopathology, FSBSI “Institute of General Pathology and Pathophysiology”, Moscow, Russian Federation, [2]Laboratory Of Medical Genetics, FSBI «National Medical Research Center of Cardiology» Ministry Of Health products RF, Moscow, Russian Federation, [3]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation, [4]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation

Background and Aims : The aim of the present study was to create cybrid lines with mtDNA mutation m.13513G>A. In our previous studies, it was found that, after reaching the threshold level of heteroplasmy, mutation m.13513G>A had a protective effect in atherosclerosis (33,5%).

Methods: The cybrid lines were obtained by fusing rho0-culture cells of monocytic origin THP-1 and thrombocytes from study participants containing mitochondria with mtDNA mutation m.13513G>A. The heteroplasmy level of mtDNA mutation was measured with the use of an original method of M.A. Sazonova with colleagues on the basis of pyrosequencing technology.

Results: During the study cybrid culture with heteroplasmy level of 21,8% for mutation m.13513G>A. was created using mitochondria from a study participant with atherosclerotic plaque in the carotid artery. In addition, a cybrid culture with platelets of a conditionally healthy study participant was created, in which the threshold level of heteroplasmy of this mutation was 36,4%. A native cell culture THP-1 was a control group.

Conclusions: In the course of the present investigation, we obtained two cybrid cultures, containing antiatherogenic mutation of mtDNA m.13513G>A. Cybrid culture, obtained with the use of mitochondria from a patient with atherosclerotic plaques in carotid arteries had a low level of heteroplasmy by mutation m.13513G>A. Cybrid culture, obtained with the use of mitochondria from a conditionally healthy study participant, had a high heteroplasmy level by mutation m.13513G>A. The obtained cybrid cultures can be used to work out methods of gene therapy of atherosclerosis. This study was supported by Russian Science Foundation (Grant # 20-15-00364).

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

DIRECT AND INDIRECT EFFECTS OF SARS-COV-2 PANDEMIC IN SUBJECTS WITH FAMILIAL HYPERCHOLESTEROLEMIA: A SINGLE LIPID-CENTER REAL-WORLD EVALUATION

POSTER VIEWING SESSION

Roberto Scicali, Viviana Ferrara, Salvatore Piro, Francesco Purrello, Antonino Di Pino
Medicine Department, ARNAS GARIBALDI NESIMA, Catania, Italy

Background and Aims : We evaluated the impact of direct and indirect effects of SARS-CoV-2 infection in subjects with familial hypercholesterolemia (FH).

Methods: In this observational, retrospective study, 260 FH subjects had a telephone survey concerning lipid profile values, lipidologist and cardiologist consultations, and vascular imaging evaluation during the 12 months before and after the Italian lockdown. The direct effect was defined as SARS-CoV-2 infection; the indirect effect was defined as the difference in one of the parameters evaluated by the telephone survey before and after lockdown.

Results: Among FH subjects, the percentage of the lipid profile evaluation was lower after lockdown than before lockdown (56.5% vs 100.0%, $p < 0.01$), HDL-C was significantly reduced (47.78 ± 10.12 vs 53.2 ± 10.38 mg/dL, $p < 0.05$) and a significant increase of Non-HDL-C was found (117.24 ± 18.83 vs 133.09 ± 19.01 mg/dL, $p < 0.05$). The proportions of lipidologist and/or cardiologist consultations and/or vascular imaging were lower after lockdown than before lockdown (for lipidologist consultation 33.5% vs 100.0%, $p < 0.001$; for cardiologist consultation 22.3% vs 60.8%, $p < 0.01$; for vascular imaging 19.6% vs 100.0%, $p < 0.001$); the main cause of missed lipid profile analysis and/or health care consultation was the fear of SARS-CoV-2 contagion. The percentage of FH subjects affected by SARS-CoV-2 was 7.3%.

Conclusions: In conclusion, a lower percentage of FH subjects performed a lipid profile analysis as well as lipidologist and cardiologist consultations and vascular imaging evaluation after SARS-CoV-2 Italian lockdown.

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POLYMORPHIC ASSESSMENT OF PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) VARIANT RS11591147 IN CORONARY ARTERY DISEASE SUBJECTS FROM PAKISTAN

POSTER VIEWING SESSION

Dr Shabana, Saleem U. Shahid
Institute Of Microbiology And Molecular Genetics, University of the Punjab, Lahore, Pakistan

Background and Aims : Coronary artery disease (CAD) is the narrowing of the lumen of coronary arteries due to deposition of plaque. Extensive research has identified a large number of genetic markers predisposing to CAD. Proprotein convertase subtilisin/kexin type 9 is an enzyme that degrade LDL receptors which results in decreased LDL clearance from blood, however loss of function mutations in its gene do the reverse. One such loss of function PCSK9 variant is rs11591147 also known as G137T or R46L. The polymorphic allele of this SNP is protective and more common in White population.

Methods: We aimed to investigate the frequency and effect of this variant on CAD in Pakistani subjects. 625 subjects (405 CAD cases and 225 controls) were genotyped by KASPar allelic discrimination assay. The lipid profile of study cohort was determined using spectrophotometric techniques.

Results: The risk alle (G) frequency was slightly higher in cases (0.999) than controls (0.995) but the difference was statistically insignificant (p=0.252). it also did appear to be associated with CAD risk (p 0.29). The SNP was checked for effect on the lipid parameters and appeared to affect LDL only. The mean increase (mg/dL) (Se) in LDL-C per risk allele was 14.81(15.8) and the mean increase in TC for each risk allele held was 9.9(30.4) but was not statistically significant.

Conclusions: In conclusion, the direction of variant effect is similar to that observed in White population therefore larger studies should be done to investigate the true relationship of the PCSK9 rs11591147 and CAD.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

RISK FACTORS MANAGEMENT IN CORONARY ARTERY DISEASE PATIENTS

POSTER VIEWING SESSION

Svetlana Stoica, Andreea Rus, Dan Gaita
Cardiology, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

Background and Aims : SURF II was developed as a simple audit tool during routine clinic visits aimed to assess risk factors and guideline adherence in daily practice. Our country was an active participant in this survey **Aim**: The purpose of this study was to evaluate risk factors in patients with coronary artery disease undergoing secondary prevention and to assess their adherence to treatment and guideline recommendations.

Methods: We have enrolled 136 consecutive patients with coronary artery disease attending routine out-patient clinic check-ups between May 2019 and July 2020. All patients had been diagnosed with acute coronary syndrome or stable angina pectoris. Laboratory analyses were recently drawn before the current visit as part of the local standard of care.

Results: Most patients (81%) were males with the mean age 61.7 years old. 93.4% of the patients had undergone PCI and 4.4 % had coronary artery by-pass graft (CABG). Only 17.6% of the patients had had a hospital admission in the last year due to coronary heart disease. Regarding risk factors, 25% were current smokers, while 50% former smokers and mean BMI value was 29.9 (±6.07). While most patients (80.1%) revealed no previous history of dyslipidaemia, 62.5% no previous history of arterial hypertension and 84.6% no previous history of diabetes mellitus, mean LDL cholesterol levels after a major coronary event remained 93.55 (±43.52) mg/dl, mean HbA1c levels were 7.86 (±1.40) % and mean systolic blood pressure was 129 (±14.9) mmHg.

Conclusions: Risk factor control in secondary prevention requires tighter patient adherence to guideline recommendations.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-01 Epidemiology of cardiovascular diseases and risk factors*

NO INCREASED RISK OF STROKE IN GENETICALLY VERIFIED FAMILIAL HYPERCHOLESTEROLEMIA: A PROSPECTIVE MATCHED COHORT STUDY

POSTER VIEWING SESSION

Karianne Svendsen[1,2], Thomas Olsen[2], Kathrine J. Vinknes[2], Liv J. Mundal[1], Kirsten B. Holven[2,3], Martin P. Bogsrud[4], Jannicke Igland[5,6], Kjetil Retterstøl[1,2]
[1]Lipid Clinic, Oslo University Hospital, Oslo, Norway, [2]Nutrition, University of Oslo, Oslo, Norway, [3]National Advisory Unit On Familial Hypercholesterolemia, Oslo University Hospital, Oslo, Norway, [4]Unit For Cardiac And Cardiovascular Genetics,, Oslo University Hospital, Oslo, Norway, [5]Global Public Health And Primary Care, University of Bergen, Bergen, Norway, [6]Health And Social Sciences, Western Norway University of Applied Sciences, Bergen, Norway

Background and Aims : Risk of ischemic stroke is associated with elevated concentrations of LDL-C, which is severely elevated in subjects with familial hypercholesterolemia (FH). The risk of hemorrhagic stroke is however unknown. Aim was to investigate risk of incident stroke (ischemic and hemorrhagic combined) in individuals with genetically verified FH compared with age and sex matched controls. Further, to examine the relationship between cumulative statin exposure [daily defined doses (DDD)] and risk of stroke in FH.

Methods: Risk is presented as Hazard Ratio (HR) from Cox proportional hazard model. Statin exposure was categorized as: 0-5000 DDD (“low”), 5000-10 000 DDD (“intermediate”) and >10 000 DDD (“high”). Data were available from Norwegian health registries in the period 2008-18.

Results: There were no excess risk of incident stroke in individuals with FH (102 cases in FH and 1610 controls) [HR = 1.12 (95%CI: 0.9-1.4)], and no excess risk for ischemic stroke. An association between FH and hemorrhagic stroke was observed but after adjusting for antithrombotic medication, the risk was strongly attenuated [HR 1.25 (95% CI: 0.8, 1.9)]. in FH 70% had high statin exposure compared to 30% in controls. There were no association between statin use and risk of stroke for intermediate vs. low DDD [HR: 0.69 (95% CI: 0.3, 1.5)] or for high vs. low DDD [HR 0.83 (95% CI: 0.4, 1.7)].

Conclusions: Individuals with genetically verified FH did not have higher risk of incident stroke nor ischemic or hemorrhagic stroke than age and sex matched controls. Cumulative statin exposure was not associated with stroke risk among individuals with FH.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

DISTRIBUTION OF CARDIOVASCULAR RISK AMONG PATIENTS WITH DYSLIPIDEMIA IN TURKEY: RESULTS FROM A DELPHI PANEL

POSTER VIEWING SESSION

Mehmet B. Yilmaz[1], Ozlem Cinar[2], Baris Gungor[3], Meral Kayikcioglu[4], Tuba K. Oz[5], Oner Ozdogan[6], Umit Y. Sinan[7], Ahmet Temizhan[8], Uygar C. Yuksel[9], Lale Tokgözoğlu[10]
[1]Cardiology, Dokuz Eylul University, Medical Faculty, Izmir, Turkey, [2]Medical, Novartis Pharma, Ankara, Turkey, [3]Department Of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, Istanbul, Turkey, [4]Cardiology, Ege University School of Medicine, Izmir, Turkey, [5]Cardiology, Istinye University Liv Hospital Ulus, Istanbul, Turkey, [6]Cardiology, University of Health Sciences, Izmir Faculty of Medicine, Izmir, Turkey, [7]Cardiology, Institute of Cardiology, Istanbul University, Istanbul, Turkey, [8]Cardiology, Ankara City Hospital, Ankara, Turkey, [9]Cardiology, Gülhane Training and Research Hospital, Ankara, Turkey, [10]Cardiology, Hacettepe University Medical Faculty, Ankara, Turkey

Background and Aims : Determining the risk groups of dyslipidemia patients under follow-up is important to reach LDL-C treatment goals.

Methods: Delphi Panel Methodology was used to seek out information from 9 cardiologists in Turkey to describe the proportion of individuals regarding cardiovascular risk among patients with dyslipidemia.

Results: Cardiovascular (CV) risk distribution of patients with dyslipidemia on follow up yielded that 43% had very high CV risk, 25.6% had high CV risk, 18.7% had moderate CV risk and 12.8% had low CV risk. Among those with very high CV risk, 76.4% belonged to secondary prevention arm of CV disease (VHR-SP) whereas 23.6% belonged to primary prevention (VHR-PP). Hence, 32.9% of all patients with dyslipidemia were allocated to very high CV risk group on secondary prevention (VHR-SP) along with 12.1% of them having recurrent CV events. Of this VHR-SP group of patients, the proportion of patients with LDL-C level of less than 55 mg/dl was 5.1%. Of note, among patients with VHR-SP and recurrent CV events, 6% had LDL-C level of less than 55 mg/dl. Of the group with VHR-PP, the proportion of patients with LDL-C level of less than 55 mg/dl was 1.7%.

Conclusions: Patients with very high CV risk represent significant proportion of patients with dyslipidemia, three fourths of these patients were categorized in secondary prevention and most of the VHR-PP and VHR-SP patients do not reach the LDL-C level goals.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

MANAGEMENT OF SECONDARY PREVENTION PATIENTS WITH LDL-CHOLESTEROL LEVELS < 70MG/DL (1.8MMOL/L): AN ANALYSIS BASED ON DELPHI PANEL APPROACH

POSTER VIEWING SESSION

Meral Kayikcioglu[1], Ahmet Temizhan[2], Baris Gungor[3], Mehmet B. Yilmaz[4], Oner Ozdogan[5], Ozlem Cinar[6], Tuba K. Oz[7], Umit Y. Sinan[8], Uygar C. Yuksel[9], Lale Tokgözoğlu[10]
[1]Cardiology, Ege University School of Medicine, Izmir, Turkey, [2]Cardiology, Ankara City Hospital, Ankara, Turkey, [3]Department Of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, Istanbul, Turkey, [4]Cardiology, Dokuz Eylul University, Medical Faculty, Izmir, Turkey, [5]Cardiology, University of Health Sciences, Izmir Faculty of Medicine, Izmir, Turkey, [6]Medical, Novartis Pharma, Ankara, Turkey, [7]Cardiology, Istinye University Liv Hospital Ulus, Istanbul, Turkey, [8]Cardiology, Institute of Cardiology, Istanbul University, Istanbul, Turkey, [9]Cardiology, Gülhane Training and Research Hospital, Ankara, Turkey, [10]Cardiology, Hacettepe University Medical Faculty, Ankara, Turkey

Background and Aims : Current guidelines recommend at least 50% LDL-C reduction from baseline levels in patients with atherosclerotic cardiovascular disease in addition to getting the LDL-C goal of <55 mg/dL. We sought to determine how secondary prevention patients with LDL-C levels <70 mg/dL (1.8 mmol/L) are managed.

Methods: Delphi Panel Methodology was used to figure out the approach to patients with LDL-C <70mg/dL. Nine expert cardiologists replied to the questionnaire to generate a consensus on how high-risk patients were treated in Turkey.

Results: Treatment-naïve secondary prevention patients with LDL-C<55mg/dL are left untreated in 75.6%, only 18.3% are considered for low to moderate doses of statins and 6.1% for high doses of statins. For those with LDL-C levels of 55-69mg/dL, are left untreated in 50.9%, considered for low-moderate dose statin therapy in 40%, and 29.4% high doses of statins. For patients with recurrent cardiovascular events and LDL-C<55mg/dL these proportions were 75.6%, 18.3%, and 6.1%, respectively. For those with recurrent events but LDL-C levels ranging 55-69mg/dL were 50.9%, 32.2%, and 9.1%, respectively.

Conclusions: According to expert cardiologists' consensus, only one-fourth of secondary prevention patients with LDL-C levels <55mg/dL or 55-69mg/dL will be considered for antilipid therapy in Turkey. However, patients should be targeted to at least 50% LDL-C reduction from baseline levels on top of getting to LDL-C goals according to current guidelines. Our results may imply that awareness of current guideline recommendation of at least 50% LDL-C reduction in secondary prevention is extremely low among cardiologists.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

MANAGEMENT OF PATIENTS WITH LDL-CHOLESTEROL LEVELS >190MG/DL (4.9MMOL/L) IN TURKEY: AN ANALYSIS BASED ON DELPHI PANEL APPROACH

POSTER VIEWING SESSION

Meral Kayikcioglu[1], Uygar C. Yuksel[2], Mehmet B. Yilmaz[3], Ahmet Temizhan[4], Umit Y. Sinan[5], Oner Ozdogan[6], Tuba K. Oz[7], Mesut Kuş[8], Baris Gungor[9], Lale Tokgözoğlu[10]
[1]Cardiology, Ege University School of Medicine, Izmir, Turkey, [2]Cardiology, Gülhane Training and Research Hospital, Ankara, Turkey, [3]Cardiology, Dokuz Eylul University, Medical Faculty, Izmir, Turkey, [4]Cardiology, Ankara City Hospital, Ankara, Turkey, [5]Cardiology, Institute of Cardiology, Istanbul University, Istanbul, Turkey, [6]Cardiology, University of Health Sciences, Izmir Faculty of Medicine, Izmir, Turkey, [7]Cardiology, Istinye University Liv Hospital Ulus, Istanbul, Turkey, [8]Medical, Novartis Pharma, Istanbul, Turkey, [9]Department Of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, Istanbul, Turkey, [10]Cardiology, Hacettepe University Medical Faculty, Ankara, Turkey

Background and Aims : Patients with severe hypercholesterolemia (low-density lipoprotein-cholesterol (LDL-C) ≥190mg/dL) have a significantly increased risk of cardiovascular disease (CVD). We sought to determine how these high-risk patients managed in terms of lipid lowering therapy (LLT) either in primary or secondary prevention.

Methods: Delphi Panel Methodology was used to figure out the approach to patients with LDL-C≥190 mg/dL. Nine expert cardiologists replied to the questionnaire to generate a consensus on how high-risk patients were treated in Turkey.

Results: Treatment-naïve patients on secondary prevention with LDL-C>190mg/dL are left untreated in 3.8%, are put on low to moderate dose statin therapy in 30.6%, receive only high doses of statins in 47.7%, maximally tolerated statin plus ezetimibe in 16%, considered for statin plus PCSK9 inh 1.4%, statin, ezetimibe, and PCSK9 combination in 1.4% and only PCSK9-inh in 2.2%. These proportions for those on primary prevention with very high cardiovascular risk are 13%, 30.3%, 38.9%, 16.9%, 0.8%, 01%, and 0.89% respectively. For those with high cardiovascular risk the same ratios are worser as follows, 17.8%, 29.8%, 47.4%, 4.7%, 0.2%, 0.1%, and 0.33%, respectively. The approach to patients with LDL-C>190mg/dL already on LLT did not differ from treatment naïve patients.

Conclusions: The expert cardiologists agree that the treatment approach to patients with LDL-C≥190 mg/dL either on LLT or treatment naïve are far from the guideline recommendations. Almost one-third is receiving only low to moderate dose of statins, half only high-dose statin and <20% is receiving ezetimibe whereas <3% is considered for PCSK9-inh in current practice.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

FIRST DIAGNOSIS AND FOLLOW UP FEATURES OF PATIENTS WITH DYSLIPIDEMIA IN TURKEY

POSTER VIEWING SESSION

Oner Ozdogan[1], Baris Gungor[2], Meral Kayikcioglu[3], Tuba K. Oz[4], Koray Ozcan[5], Umit Y. Sinan[6], Ahmet Temizhan[7], Mehmet B. Yilmaz[8], Uygar C. Yuksel[9], Lale Tokgözoğlu[10]
[1]Cardiology, University of Health Sciences, Izmir Faculty of Medicine, Izmir, Turkey, [2]Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, Istanbul, Turkey, [3]Cardiology, Ege University School of Medicine, Izmir, Turkey, [4]Cardiology, Istinye University Liv Hospital Ulus, Istanbul, Turkey, [5]Medical, Novartis Pharma, Istanbul, Turkey, [6]Cardiology, Institute of Cardiology, Istanbul University, Istanbul, Turkey, [7]Cardiology, Ankara City Hospital, Ankara, Turkey, [8]Cardiology, Dokuz Eylul University, Medical Faculty, Izmir, Turkey, [9]Cardiology, Gülhane Training and Research Hospital, Ankara, Turkey, [10]Cardiology, Hacettepe University Medical Faculty, Ankara, Turkey

Background and Aims : Background and Aims: It is important to know where and how patients with dyslipidemia are first diagnosed to amplify preventive efforts and to decrease cumulative LDL-C load early.

Methods: Methods: Delphi Panel Methodology was used to seek out information from 9 cardiologists in Turkey in order to generate a consensus on the first diagnosis and follow up features of dyslipidemia.

Results: Results: Half of the patients with dyslipidemia are first diagnosed during assessment of atherosclerotic cardiovascular diseases and/or diabetes; diagnosis during routine check-up is less common. Dyslipidemia is first diagnosed in outpatient clinics in 2/3 of patients, while the rest of the diagnosis is made during the hospital stays. In 35.9% of the patients, the first diagnosis is made by the Cardiologist. Once diagnosed, 61.9% of the routine follow-up is also in the Cardiology departments due to the rarity of lipid clinics. The remaining patients (53.7%) are diagnosed with dyslipidemia in internal medicine, endocrinology, and family medicine departments.

Conclusions: Conclusion: Most of the patients with dyslipidemia are diagnosed while being treated because of atherosclerotic cardiovascular diseases and/or diabetes. Screening policies should be developed for earlier diagnosis of dyslipidemia before these patients develop atherosclerotic vascular disease for preventive efforts to be more successful.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

HOSPITALIZATION FEATURES AND MORTALITY RATES OF VERY HIGH-RISK PATIENTS WITH DYSLIPIDEMIA IN TURKEY

POSTER VIEWING SESSION

Oner Ozdogan[1], Baris Gungor[2], Meral Kayikcioglu[3], Tuba K. Oz[4], Koray Ozcan[5], Umit Y. Sinan[6], Ahmet Temizhan[7], Mehmet B. Yilmaz[8], Uygar C. Yuksel[9], Lale Tokgözoğlu[10]
[1]Cardiology, University of Health Sciences, Izmir Faculty of Medicine, Izmir, Turkey, [2]Department Of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, Istanbul, Turkey, [3]Cardiology, Ege University School of Medicine, Izmir, Turkey, [4]Cardiology, Istinye University Liv Hospital Ulus, Istanbul, Turkey, [5]Medical, Novartis Pharma, Istanbul, Turkey, [6]Cardiology, Institute of Cardiology, Istanbul University, Istanbul, Turkey, [7]Cardiology, Ankara City Hospital, Ankara, Turkey, [8]Cardiology, Dokuz Eylul University, Medical Faculty, Izmir, Turkey, [9]Cardiology, Gülhane Training and Research Hospital, Ankara, Turkey, [10]Cardiology, Hacettepe University Medical Faculty, Ankara, Turkey

Background and Aims : Background: In patients with dyslipidemia, hospitalization features and mortality rates due to recurrent cardiovascular (CV) events may vary according to the patient's risk levels and management.

Methods: Methods: Delphi Panel Methodology was used to seek out information from 9 cardiologists in Turkey to generate a consensus on the frequency and duration of hospitalization and the mortality rates due to CV events in patients with dyslipidemia with different clinical risk factors in different hospital settings.

Results: Results: Very high-risk patients with recurrent CV events and familial hypercholesterolemia with diabetes were considered to be associated with more frequent hospitalizations due to CV events in the 10-year period. (7.1 times/year and 5.1times/year, respectively) According to the panel; as with hospitalization, CV interventions were also more frequently performed in secondary prevention patients with recurrent CV events and in diabetic patients with familial hypercholesterolemia (FH). Besides acute coronary events, both acute cerebral and limb ischemic events were reported to be higher in patients with recurrent CV events and in diabetic patients with FH (11.4%, 12.3% and 10.2%, 11.4%, respectively). Mortality rates were also predicted to be high in patients with recurrent CV events and in diabetic patients with FH (19.1% and 13.1%, respectively).

Conclusions: Conclusion: Since secondary prevention patients with recurrent CV events and primary prevention patients with FH and diabetes have the highest risk of mortality and hospitalization due to coronary, cerebrovascular, and peripheral vascular events, improvements can be considered in the follow-up of these patients to ensure that they reach appropriate treatment strategies.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

GENETICALLY CONFIRMED FH CASES DISTRIBUTION BY AGE AND GENDER IN VILNIUS UNIVERSITY HOSPITAL SANTAROS KLINIKOS IN 2019-2021

POSTER VIEWING SESSION

Viktoras Sutkus[1], Žaneta Petrulionienė[2,3], Odeta Kinčinienė[2,4], Vilija Černiauskienė[2,4], Egle Skiauteryte[2,3], Urtė Aliošaitienė[2,3], Rimantė Čerkauskienė[1,2]
[1]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Paediatrics Centre, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Background and Aims : Familial hypercholesterolemia (FH) is one of the main causes of atherosclerotic cardiovascular diseases. Due to lack of research and systematic patient search, exact prevalence of FH in Lithuania is unknown. There are also no recommendations for pediatric or familial screening in Lithuania. By the end of 2019 families at high risk for FH were invited for genetic screening in Vilnius University Hospital Santaros Klinikos. The aim of this study was to review the distribution of screened FH patients by age and gender.

Methods: Patients with suspected diagnosis of FH who were referred to Vilnius University Hospital Santaros Klinikos were invited to participate in the genetic screening for FH. Those who agreed had their blood sample taken on a dried blood spot card which was then sent to a genetics laboratory. Next generation sequencing was used to identify FH causing mutations (LDLR, APOB, PCSK9, LDLRAP1).

Results: A total of 126 patients have been screened for FH: 71 female (aged 2-69 years; median 48 years) and 55 male (age 2-79 years; median 35 years). 50 (39,7%) have had FH diagnosis confirmed genetically (26 female, 24 male). Median age of FH patients at the time of genetic screening was 37 years (2-79 years). Median age of female patients was 46 years (6-68 years) and of male patients 22 years (2-79 years).

Conclusions: Results of this study show that screening of families at high risk for FH may confirm diagnosis for patients of various ages. Screening also helps to find family members, not at risk for FH.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-02 Epidemiology of dyslipidemias*

IMPLEMENTATION OF A BIOCHEMICAL AND CLINICAL PLAN TO SCREEN FOR FAMILIAL HYPERCHOLESTEROLEMIA IN 25 CENTERS IN SPAIN: THE ARIAN PROJECT.

POSTER VIEWING SESSION

Teresa Arrobas Velilla[1], Angel Brea Hernando[2], Pedro Valdivielso Felices[3]
[1]Clinical Biochemistry. Hospital Universitario Virgen Macarena De Sevilla, servicio andaluz de Salud, SEVILLA, Spain, [2]Medicina Interna, Hospital San Pedro de Logroño, Logroño, Spain, [3]Medicina Interna, Hospital Virgen de la Victoria, MALAGA, Spain

Background and Aims : Familial hypercholesterolemia (FH) is underdiagnosed and undertreated. The aim of this study was to analyse the feasibility to screen for FH through the collaboration of Clinical Laboratories and Lipid Units in Spain.

Methods: Participaron en el estudio veinticinco centros de todo el país. Todos los análisis de suero entre enero, 1 st , 2017 y diciembre, 31 st , 2018 fueron revisados y pacientes con colesterol LDL> 250 mg / dl fueron identificados. Una vez descartadas las causas secundarias, se contactó a los médicos prescriptores y se les aconsejó que remitieran a los pacientes a la Unidad de Lípidos, donde se clasificaba a los pacientes según la puntuación de la Red de Clínicas de Lípidos Holandesa para la HF; a los que tenían una puntuación ≥ 6 se les ofreció una prueba genética.

Results: Among 3,827,513 serum samples analysed, 3,015 subjects were included with a cLDL > 250 mg/dL after secondary causes were excluded. Among them, only 1,205 patients could be contacted and only 635 patients referred to Lipid Units. In 153 patients a genetic test was ordered and in 69 subjects a pathogenic variant was found, mainly in the *LDLR* gene.

Conclusions: Despite its limitations, the systematic collaboration between the Clinical Laboratory and the Lipid Units allows to identify a substantial number of patients with phenotypic or genetic diagnosis of FH, which should reduce the burden of arteriosclerosis disease. This activity should be part of usual care.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

THE EFFECT OF METFORMINE PROLONGED PROTECTION TITLETING ON THE LIPIDIC PROFILE OF PATIENTS WITH TYPE 2 DIABETES (SD2)

POSTER VIEWING SESSION

Adamantios Bourdakis[1], Stamatis Papadatos[2], Georgia Filli[2]
[1]Diabetes & Lipid-obesity Unit, TRIKALA GENERAL HOSPITAL, TRIKALA, Greece, [2]Diabetes &lipid-obesityunit, TRIKALA GENERAL HOSPITAL, TRIKALA, Greece

Background and Aims : PURPOSE: Patients with SD2 often have dyslipidemia. The target of LDL is defined more and more strictly. The aim of this study was to evaluate the effect of the titrated metformin prolonged dose (Met-XR) at 2000 mg on the lipid profile and glycemic control of patients with SD2.

Methods: MATERIAL AND METHOD: 41 patients with primary diagnosis of SD2 were studied. The 19 e received immediate release metformin (Met-IR) and the 22 Met-XR up to a titration of 2000mg daily. For 6 months the patients were monitored every 3 months by measuring Glu fasting, HbA1c, LDL, HDL, TGs. There was no change in the hypolipidemic treatment they were receiving as it was within the LDL target according to the latest guidelines. There were no differences in gender, age, GFR, and statin intake between the groups that continued on Met-IR and those who received Met-XR. Everyone followed a diet and exercise program.

Results: RESULTS: Met-XR intake was well tolerated. Met-IR securitization was equally well tolerated. No patients discontinued treatment. Over a period of 6 months, all patients showed improvement in glycemic parameters and BMI without statistically significant differences (P> 005). Patients receiving Met-XR showed a statistically significant decrease in LDL (ΔLDL = 12mg / dl, P = 0.041) compared with those receiving Met-IR.

Conclusions: CONCLUSIONS: In this small-scale study, a decrease in LDL and a decrease in TG was seen in patients receiving Met-XR. Larger-scale prospective studies are required for the effect of prolonged-release metformin on the lipid profile of patients with SD2

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

ASSESSMENT OF THERAPEUTIC TARGETS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND CARDIOVASCULAR DISEASE

POSTER VIEWING SESSION

Elena-Daniela Grigorescu[1], Cristina-Mihaela Lăcătușu[1], Alina Onofriescu[1], Georgiana Diana Cazac[2], Alexandr Ceasovschih[3], Sorina-Nicoleta Drăgoi[4], Alexandra-Georgeta Grigorescu[1], Laurențiu Șorodoc[3], Bogdan-Mircea Mihai[1]
[1]Diabetes, Nutrition And Metabolic Diseases, Grigore T. Popa University of Medicine and Pharmacy Iasi, Iasi, Romania, [2]Diabetes, Nutrition And Metabolic Diseases, “Sf. Spiridon” County Clinical Emergency Hospital, Iasi, Romania, [3]Internal Medicine, Grigore T. Popa University of Medicine and Pharmacy Iasi, Iasi, Romania, [4]Diabetes, Nutrition And Metabolic Diseases, Faculty of Medicine “Iuliu Hațieganu” University of Medicine and Pharmacy, Cluj-Napoca, Cluj, Romania

Background and Aims : Cardiovascular disease (CVD) affects approximately one third of type 2 diabetes mellitus (T2DM) patients. We aimed to evaluate treatment targets of T2DM patients with CVD.

Methods: This retrospective study included 469 T2DM patients attending a Diabetes Center before COVID-19 (08.2016-12.2019). Data regarding diabetes history, complications and comorbidities, anthropometric parameters, metabolic profile were collected from medical records.

Results: The patients’ mean age was 62.27±9.98 and 48.8% were men. The mean diabetes duration was 6.81±7.04 years and the metabolic parameters were: BMI 31.78±5.32 kg/m^2, HbA_{1c} 7.5±1.47%, glycaemia 159.96±49.31 mg/dl, LDL-cholesterol 99.60±42.68 mg/dl, triglycerides 200.33±143.37 mg/dl. 203 patients had atherosclerotic CVD (angina, cardiac ischemic disease, peripheral arterial disease). A comparative analysis revealed higher values in CVD patients for age, diabetes duration, abdominal circumference, glycaemia, urinary albumin to creatinine ratio (ACR), $p < 0.05$. Diabetes duration and ACR seemed to be predictive factors for CVD (AUC=0.579, $p < 0.01$, CI=0.52 – 0.63, respectively AUC=0.607, $p < 0.01$, CI=0.52 – 0.68). Regarding treatment targets of CVD patients, 45.5% had systolic blood pressure <130 mmHg, 14.8% had LDL-cholesterol <55 mg/dl, and 26.6% had HbA_{1c} <7%.

Conclusions: In clinical practice, some T2DM patients fail to achieve cardio-metabolic control even if managed according to the latest ESC recommendations.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

EFFECT OF SEMAGLUTIDE ON LIPOPROTEIN SUBFRACTIONS AND CHEMERIN LEVELS IN TYPE 2 DIABETIC PATIENTS

POSTER VIEWING SESSION

Ferenc Sztanek, Áron András Jakab, Ágnes Molnár, Anita Szentpéteri, Hajnalka Lőrincz, Gyorgy Paragh, Mariann Harangi
Department Of Internal Medicine, University of Debrecen Faculty of Medicine, Debrecen, Hungary

Background and Aims : There are strong associations between obesity, cardiovascular complications, and lipid abnormalities in type 2 diabetes (T2DM). Once-weekly administration of semaglutide lowers the blood glucose level in a glucose-dependent manner and has a beneficial effect on lipid levels. Small and dense LDL particles play a pivotal role in the development of atherosclerosis and cardiovascular diseases. Chemerin, a previously described adipokine, is associated with insulin resistance associated with obesity and lipoprotein abnormalities. To date, the effect of semaglutide treatment on chemerin and lipoprotein subfraction levels are currently unclear.

Methods: We enrolled 11 T2DM patients on metformin monotherapy who received 1 mg semaglutide per week add-on therapy. We assessed the changes in body weight, lipoprotein subfractions, adiponectin, leptin and chemerin levels after six months. LDL and HDL subfractions were detected using non-gradient polyacrylamide gel electrophoresis.

Results: Body mass index and HbA1c were significantly reduced. Among the lipid subfractions, a significant decrease in small dense LDL ratio and concentration were found ($p<0.001$ and $p<0.01$, respectively). Serum chemerin levels were significantly lower in T2DM patients after six months of semaglutide treatment ($p<0.01$). We found a positive correlation between the change in the ratio of small dense LDL subfraction and the change in the level of chemerin ($p<0.05$).

Conclusions: Semaglutide treatment reduces body weight in obese T2DM patients and may have a beneficial effect on lipid parameters. Chemerin may be involved in the regulation of lipoprotein metabolism in T2DM patients treated with semaglutide.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

LOWER MIR-21/ROS/HNE LEVELS ASSOCIATE WITH LOWER GLYCEMIA AFTER HABIT-INTERVENTION: DIAPASON STUDY 1-YEAR LATER

POSTER VIEWING SESSION

Lucia La Sala[1], Elena Tagliabue[2], Simona Mrakic-Sposta[3], Anna Chiara Uccellatore[4], Pamela Senesi[5], Ileana Terruzzi[5], Luigi Rossi Bernardi[6], Livio Luzi[7]
[1]Endocrinology, Nutrition And Metabolic Diseases, IRCCS MultiMedica, Milan, Italy, [2]Biostatistica, IRCCS MULTIMEDICA, milan, Italy, [3]Institute Of Clinical Physiology, National Research Council CNR, Milan, Italy, [4]Istituto Clinici Città Studi, ICCS, Milan, Italy, [5]Endocrinology, Nutrition And Metabolic Diseases, IRCCS MULTIMEDICA, MILAN, Italy, [6]Direzione Scientifica, IRCCS MULTIMEDICA, milan, Italy, [7]Endocrinology, Nutrition And Metabolic Diseases,, IRCCS MULTIMEDICA,, milan, Italy

Background and Aims : The prevalence of prediabetes is increasing in the global population and its metabolic derangements may expose to a higher risk to develop type 2 diabetes (T2D) and its cardiovascular burden. Lifestyle modifications might have considerable benefits on ameliorating metabolic status. Alternative biomarkers, such as circulating miR-21, has been recently discovered associated with dysglycemia. Current evidences have demonstrated that miRs may predict the progression from pre-diabetic to diabetes state. Here we evaluated, in a longitudinal cohort of dysglycemic population the relation between the circulating miR-21/ROS/HNE levels and the lifestyle changes after 1 year of follow-up.

Methods: 1506 subjects from DIAPASON study were screened on the basis of the Findrisc score. 531 subjects with Findrisc ≥9 were selected for dysglycemia (ADA criteria) and tested for circulating miR-21, ROS and HNE levels, as damaging-axis. 207 dysglycemic subjects were re-evaluated after a habit-intervention (HI), 1-year later. Repeated measures tests were used to evaluate changes\. Furthermore, linear regression and logistic regression models were implemented to evaluate association between glycemic parameters and miR-21/ROS/HNE.

Results: We observed, after HI,significant reduction of miR-21/ROS/HNE axis in dysglycemic subjects, concomitantly with ameliorating of metabolic parameters.Significant positive interaction was observed between miR-21 axis with glycaemic parameters after HI. Lower miR-21 levels after HI, strongly associated with reduction of glycemic damaging-axis, in particular within subjects with values of 2hPG<200 mg/dL.

Conclusions: Our findings demonstrated that HI influenced the epigenetic changes related to miR-21 axis. These data support the usefulness of novel biological approaches for monitoring glycemia as well as provide a screening tool for preventive programmes.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

DEVELOPMENT OF A NEUROPATHY MODEL IN PRE-DIABETIC MICE

POSTER VIEWING SESSION

Guillaume Rastoldo, Ali K. Jaafar, Aurelie Paulo-Ramos, Steeve Bourane
Cyroi, UMR Inserm U1188 - Université de La Réunion Diabète athérothrombose Thérapies Réunion Océan Indien, Sainte Clotilde, France

Background and Aims : Diabetic peripheral neuropathy (DPN) is the most common complication of both type 1 and 2 diabetes. In Reunion Island the prevalence of type 2 diabetes is twice as high as in metropolitan France and the associated excess mortality is 3.5 times higher. In order to study DPN and to propose new therapeutic approaches, we have developed a neuropathy model in pre-diabetic mouse.

Methods: We used C57Bl6 male fed with a high-fat diet (HFD: 45 kcal% fat) during 16 weeks. We evaluated DPN by performing sensory tests (Von Frey, Hargreaves, Brush, and Pinprick), electromyography (sciatic nerve conduction velocity), immunohistochemistry (Intraepidermal Nerve Fiber Density, (IENFD)) and blood analysis (HbA1c, Oral Glucose Tolerance Test (OGTT) and lipid assay).

Results: Our preliminary results showed a mechanical hyposensitivity (17% decrease in the sensitivity threshold; $p < 0.001$) as well as a thermal hypersensitivity (45% increase; $p < 0.0001$) in HFD mice compared to control mice (Normal Diet (n=10) vs. HFD (n=10)). Sensory nerve conduction velocity tended to decrease without reaching significance after 16 weeks diet. IENFD quantification and lipid assay are still under analysis. HbA1c in the HFD group appeared to increase slightly after 16 weeks of diet (ND vs. HFD: 4.7% and 5%) while the area under the curve of OGTT increased in these same mice (ND vs. HFD: 29904 and 41047 cm^2; $p < 0.001$).

Conclusions: Similar to human with pre-diabetes, HFD-fed mice recapitulates the phenotypes observed in clinics and, therefore, are a suitable model for better understanding DPN and its evolution over time.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

ADIPOSITY AND INSULIN RESISTANCE LINKED TO NON-HDL CHOLESTEROL AND APOLIPOPROTEIN B-100: A CROSS-SECTIONAL STUDY IN A HYPERTENSIVE POPULATION

POSTER VIEWING SESSION

Riccardo Sarzani[1,2], Federico Giulietti[1,2], Simone Biondini[1], Elisabetta Fausti[1], Massimiliano Allevi[1], Francesco Spannella[1,2]
[1]Department Of Clinical And Molecular Sciences, University “Politecnica delle Marche”, Ancona, Italy, Ancona, Italy, [2]Internal Medicine And Geriatrics, IRCCS INRCA, Ancona, Italy, Ancona, Italy

Background and Aims : Non-HDL cholesterol (non-HDLc) and apolipoprotein B (ApoB) indirectly measure all potentially atherogenic circulating lipoproteins. In patients with essential hypertension, atherogenic dyslipidemia and insulin resistance (IR) due to overweight/obesity are highly prevalent. Our work aimed to evaluate how adiposity and IR affect non-HDLc and ApoB levels in essential hypertensive patients.

Methods: We performed a cross-sectional study on 272 consecutive patients referred to our Hypertension Centre and not taking lipid-lowering drugs. Body mass index (BMI) and waist circumference (WC), measured to the nearest 0.1 cm at the midpoint between the lowest rib and the iliac crest, were used to assess adiposity. IR was evaluated with HOMA-IR index, calculated according to the formula: HOMA-IR = [glucose] (mmol/l) × [insulin] (μU/ml)/22.5.

Results: General characteristics of the study population are summarized in table 1. Overweight/obese patients showed higher prevalence of IR (57.4% of overweight/obese). We found no linear association of both BMI and WC neither with ApoB nor with non-HDLc (all $p>0.05$), while a negative correlation was found with HDLc ($r=-0.295$; $p<0.001$ for BMI and $r=-0.224$; $p=0.009$ for WC) and a positive correlation with triglycerides ($r=0.222$; $p=0.004$ for BMI). A significant correlation emerged between HOMA-IR index and

ApoB100 (r=0.280; p=0.016), independently of BMI.

Table 1. General characteristics of the study population.

Characteristics	Values
Age (years)	50.2 ± 14.5
BMI (Kg/m²)	27.9 ± 4.8
Waist circonference (cm)	99.1 ± 13.0
Colesterolo totale (mg/dl)	209.6 ± 48.3
HDL cholesterol (mg/dl)	52.0 ± 14.8
Triglycerides (mg/dl)	109 (83-155)
LDL cholesterol (mg/dl)	130.2 ± 43.1
Non-HDL cholesterol (mg/dl)	156.2 ± 48.6
ApoB (mg/dl)	113.8 ± 36.4
Glycaemia (mg/dl)	94 mg/dl
Insulin (microUI/ml)	10.2 (7.0-16.5)
HOMA-IR index	2.7 (1.6-3.9)

Figure 1. Prevalence of IR according to BMI.

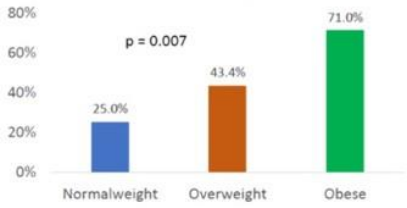


Figure 2. Association between BMI and ApoB.

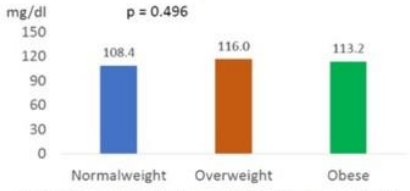
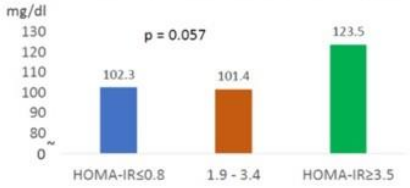


Figure 3. Association between HOMA-IR index and ApoB.



Conclusions: In our study, the excess adiposity is directly linked to HDLc and triglycerides, while IR is directly linked to ApoB levels. Although there is a close association between IR and obesity, not all overweight/obese patients had IR, IR that probably plays a major role in atherogenic lipoprotein levels than just obesity.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

THE ROLE OF METABOLIC SYNDROME, VISCERAL OBESITY AND INSULIN RESISTANCE IN RIGHT AND LEFT VENTRICULAR HYPERTROPHY

POSTER VIEWING SESSION

Ecaterina S. Sedaia, Valeriu Revenco, Viorica Ochisor
Internal Medicine, Cradiology, State University of Medicine and Pharmacy „Nicolae Testemitanu", Chisinau, Moldova

Background and Aims : The impact of metabolic syndrome (MetS) on heart's remodeling was confirmed in many clinical trials. Visceral obesity and insulin resistance represent the hallmark pathophysiological features of MetS and may have an important impact on right (RV) and left (LV) ventricular hypertrophy. The aim of this study was to evaluate the role of visceral adiposity sonographic and anthropometric parameters and insulin resistance (HOMA-IR), in RV and LV hypertrophy in patients with MetS.

Methods: Our study included 70 patients (35 with MetS, 35 controls). For MetS we used ≥3 criteria of IDF, AHA/NHLBI. By echocardiography we assessed epicardial fat thickness (EFT), LVmass/$h^{2.7}$, LVmass/BSA, RV free wall thickness. Anthropometric parameters of visceral obesity included waist-to-hip ratio (WHR) and waist circumference (WC). The status of insulin resistance was determined by HOMA-IR≥2.5.

Results: All the parameters of visceral obesity were significantly higher in MetS group (P<0.01) and positively correlated with LV mass and RV free wall thickness (P<0.001). HOMA-IR positively correlated with LVmass/$h^{2.7}$(r=0.425, P=0.012), LVmass/BSA (r=0.351, P=0.042), RV free wall thickness (r=0.532, P=0.01). In patients with HOMA-IR≥2.5 the risk for RV hypertrophy was approximately 1.8 times higher (P=0.031) and for biventricular hypertrophy 1.4 times higher (P=0.012). Multivariate regression analysis showed that EFT, WC and HOMA-IR were independently associated RV hypertrophy in patients with MetS (P<0.05 for all parameters).

Conclusions: Our findings support that visceral obesity and insulin resistance are associated with RV and LV hypertrophy in patients with MetS. Also, EFT, WC and HOMA-IR are independently associated with RV hypertrophy in pacients with MetS.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-03 Diabetes, insulin sensitivity and resistance*

LIPID SPECTRUM CHANGES AND BLOOD PRESSURE LEVELS IN OBESE PATIENTS WITH TRUE AND PSEUDO-RESISTANT HYPERTENSION

POSTER VIEWING SESSION

Anna Shalimova[1], Anna Isayeva[2], Olena Buriakovska[3], Iryna Komir[3], Maryna M. Vovchenko[3]
[1]Internal Medicine N1, Kharkiv National Medical University, KHARKIV, Ukraine, [2]Complex Risk Reduction Of Chronic Non-communicable Diseases, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine, [3]Complex Risk Reduction Of Chronic Non-communicable Diseases, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Ukraine, Ukraine

Background and Aims : The aim was to conduct a comparative assessment of lipid spectrum changes and blood pressure (BP) levels between true and pseudo-resistant hypertension in obesity.

Methods: The study included 302 patients with uncontrolled hypertension and obesity. Initial treatment efficacy was assessed 3 months after dual therapy was administered. Patients who did not reach target BP in dual therapy were transferred to triple therapy. Among patients in triple therapy, 69 people did not reach target BP. All patients were additionally examined 6 months after the initiation of antihypertensive therapy.

Results: At the initial stage of enrolling patients, there was no significant difference in BP levels between non-resistant and subsequently resistant patients. Despite the achievement of target BP levels after 6 months of therapy, in the presence of resistance, BP levels were significantly higher than in non-resistant patients. At the stage of enrolling patients into the study and 3 months after the start of therapy there was no significant difference in BP levels between true and pseudo-resistance, after 6 months of antihypertensive therapy, patients with true resistance had significantly higher office SBP levels ($p<0.01$) and 24h average SBP according to ABPM data ($p<0.05$) compared with pseudo-resistant patients. Obese patients with true resistance had significantly lower BMI and LDL cholesterol ($p<0.05$).

Conclusions: Even when target BP levels in antihypertensive therapy are achieved, obese resistant patients are characterized by higher BP levels compared with non-resistant patients. Obese patients with true resistance have significantly higher SBP levels, significantly lower LDL-cholesterol and BMI compared with pseudo-resistance.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

MACROPHAGE GLUTAMINOLYSIS SUPPORTS THERMOGENESIS TO CONTROL CARDIOMETABOLIC TRAITS.

POSTER VIEWING SESSION

Coraline Borowczyk, Johanna Merlin, Stoyan Ivanov, Laurent Yvan-Charvet
Umr Inserm U1065/uns, Centre Méditerranéen de Médecine Moléculaire, Nice, France

Background and Aims : Macrophages are important sentinels that control the expandability of visceral adipose tissue and thermogenesis. These factors have emerged as independent risk factors for cardiometabolic diseases. Glutamine metabolism supports macrophage repair and resolving functions but the link between macrophage glutaminolysis and cardiometabolism remains still poorly understood.

Methods: To test the causal relationship between modulation of macrophage glutamine catabolism, adipose tissue homeostasis and cardiometabolic traits, we took advantage of recently generated macrophage cell-specific *Gls1*-deficient ($Lyz2^{cre}$ x $Gls1^{flox}$) mice.

Results: Here, we report that mice with defective macrophage glutaminolysis displayed glucose intolerance independent of excessive visceral fat inflammation and storage. We rather observed that this glucose intolerance was driven by an impaired glucose utilization by thermogenic adipose depots leading to reduced thermogenesis. Mechanistically, we identified that this reduced thermogenic response was the consequence of a lower sympathetic tone as reflected by reduced subcutaneous and brown adipose tissue norepinephrine levels. This phenomenon was associated with upstream perturbation of neuronal activation in the spinal cords of mice deficient in macrophage glutaminolysis. Indeed, altered glutaminolysis reprogrammed spinal cord macrophage metabolism and their neuronal contacts upstream of adrenergic nerves.

Conclusions: Collectively, our study reveals a previously unappreciated homeostatic role for spinal cord macrophage glutaminolysis in the control of sympathetic tone in thermogenic adipose depots. Disruption of these circuits results in metabolic imbalance.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

THE DIET ASSESSMENT CLARIFIES CARDIOVASCULAR RISK

POSTER VIEWING SESSION

Sofya O. Eliashevich[1], Batogab B. Shoibonov[1], Mikhail B. Khudyakov[2], Valida A. Dadaeva[1], Oleg V. Senko[3], Anna V. Kuznetsova[4], Oxana Drapkina[5]
[1]Laboratory Of Eating Behavior Study And Correction, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [2]-, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation, [3]-, Federal Research Center "Computer Science and Control" of the Russian Academy of Sciences, Moscow, Russian Federation, [4]-, Institute of Biochemical Physics named after N.M. Emanuel RAS, Moscow, Russian Federation, [5]Fundamental And Applied Aspects Of Obesity, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation

Background and Aims : To determine the quality characteristics of nutrition in individuals with low cardiovascular risk (SCORE 2 < 2,5%) and to assess the relationship of nutritional characteristics with metabolic disorders and body composition.

Methods: The study included 90 patients: 43.8 ± 3.2 years, 37 men (47%) and 41 women (53%). 62 (69%) participants with central obesity (CO), low cardiovascular risk (SCORE ≤1%, SCORE 2 < 2,5%, CMDS 0-1). All patients were provided with a nutritional questionnaire consisting of 11 questions.

Results: Inappropriate nutrition was registered in all patients with CO. A number of diet factors had a correlation with TG, LDL, TC, WC, body fat mass, hepatic steatosis and epicardial fat. Among them: processed meat (r = 0.3; r = 0.4; r = 0.3; r = 0.4; r = 0.4; r = 0.4; r = 0.48, respectively; p = 0.001), the absence of nuts (r = 0.4; r = 0.4; r = 0.3; r = 0.4; r = 0.4; r = 0.4; r = 0.3, respectively; p = 0.001), insufficient quota of fruits and vegetables (r = 0.7; r = 0.7; r = 0.6; r = 0.7; r = 0.7; r = 0.5; r = 0.7 , respectively; p = 0.001). It is important that according to the nutritional scale the cardiovascular diseases risk became higher in 57% of patients.

Conclusions: The low cardiovascular risk group is very heterogeneous due to the high prevalence of central obesity and unbalanced nutrition. The food scale helps to identify problem areas of the diet within 2 minutes.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

CIRCULATING ADIPOKINE CONCENTRATIONS AND RISK OF NON-ALCOHOLIC FATTY LIVER DISEASE: A MENDELIAN RANDOMIZATION STUDY

POSTER VIEWING SESSION

Nooshin Ghodsian[1], Jérôme Bourgault[1], Benoit J. Arsenault[1,2]
[1]Quebec Heart And Lung Institute, Laval University, Quebec City, Canada, [2]Axe Cardiologie, Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec, Quebec city, Canada

Background and Aims : Non-alcoholic fatty liver disease (NAFLD) is one of the most common diseases of the liver. Elevated adipose tissue (AT) accumulation is an important risk factor for NAFLD. Adipocytes release cytokines called adipokines that stimulate anti and pro-inflammatory pathways which may influence liver steatosis and fibrosis. Adiponectin, leptin, resistin, and plasminogen activator inhibitor-1 [PAI-1] are well-known adipokines that may be involved in the pathogenesis of NAFLD. Epidemiological evidence suggests that these adipokines may be associated with the development of NAFLD, but it is unclear if these associations are causal. The aim of our study is to explore the potential causal associations of adipokines with NAFLD among individuals of European ancestry.

Methods: We performed two-sample Mendelian randomization (MR) analyses using publicly available genome-wide association studies (GWAS) for adiponectin, leptin, soluble leptin receptor, resistin, and PAI-1. We used summary-level data from our recent GWAS on NAFLD (8434 cases and 770,180 controls). To construct the genetic instruments, we included genetic variants with the P-value for association with study exposures $<5\times10^{-6}$ and linkage disequilibrium (R2=0.01).

Results: In the inverse-variance weighted models, out of all adipokines tested, only soluble leptin receptor was significantly associated with NAFLD with beta [95% CI] = -0.075 [-0.173 – -0.133]; and P-value = 0.01.

Conclusions: The plasma level of the soluble leptin receptor, but not leptin levels or other adipokines might be significantly associated with the development of NAFLD. These results suggest that adipokines may not have a key role in the development of NAFLD.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

MONOCARBOXYLATE TRANSPORTER 1 (MCT-1) DEFICIENCY IMPACTS CD8+ T LYMPHOCYTES PROLIFERATION AND RECRUITMENT TO ADIPOSE TISSUE DURING OBESITY

POSTER VIEWING SESSION

Annalisa Moregola[1], Chiara Macchi[1], Maria Francesca Greco[1], Fabrizia Bonacina[1], Massimiliano Ruscica[1], Giuseppe Danilo Norata[2]
[1]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Department Of Pharmacological And Biomolecular Sciences (disfeb), University of Milan, Milan, Italy, Milano, Italy

Background and Aims : T lymphocytes (T cells) accumulate in the adipose tissue during obesity and their activation is paralleled by a switch in their metabolism towards anaerobic glycolysis with elevated amount of lactate production, which should be eliminated properly to limit cytotoxic effects. Aim of this project is to investigate the relevance of a key lactate transporter, namely MCT1 in T cells during obesity.

Methods: MCT1$^{f/f}$CD4-cre mice, which undergo the specific deletion of MCT1 in both CD4 and CD8 T lymphocytes during thymic development, were fed with an high fat diet (HFD) for 20 weeks. Adipose tissue immunophenotyping and gene expression were performed at 20 weeks. Proteomics on T lymphocytes after activation from our animal model was performed.

Results: MCT1 is highly expressed in CD8$^+$T cells after activation. Compared to controls, MCT1 deficient CD8$^+$T cells showed a switch toward oxidative phosphorylation, coupled to increased mithochondria presence. MCT1$^{f/f}$ CD4-cre mice on HFD, despite a similar weight gain and glucose response, presented less CD8$^+$T effector memory cells (Tem) in VAT (Tem CD8$^+$: MCT1$^{f/f}$ 41653cells/g±32894, MCT1$^{f/f}$CD4-cre 10169cells/g±7509, $p<0.001$), independently of cell death. Furthermore, MCT1$^{f/f}$ CD4-cre mice presented a significantly lower expression of visceral adipose tissue (VAT) preadipogenic markers (e.g. PPARγ, PPARδ, cEBPδ; $p<0.001$) associated with decreased VAT accumulation and reduced adipocytes area compared to MCT1$^{f/f}$.

Conclusions: Our data demonstrates that MCT1 transporter deficiency affects metabolic reprogramming of activated CD8$^+$ T cells and their recruitment in adipose tissue during obesity.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

A NOVEL ROLE FOR GALNAC-T2 DEPENDENT GLYCOSYLATION IN ENERGY HOMEOSTASIS

POSTER VIEWING SESSION

Cristy Verzijl[1], Federico Oldoni[2], Natalia Loaiza[1], Justina C. Wolters[1], Antoine Rimbert[3], Dicky Struik[1], Marieke Smit[1], Niels J. Kloosterhuis[1], Amy J. Fernandez[4], Nadine L. Samara[5], Tian E[6], Kelly Ten Hagen[6], Lawrence A. Tabak[7], Johan W. Jonker[1], Jan Kuivenhoven[1]
[1]Pediatrics, University Medical Centre Groningen, Groningen, Netherlands, [2]Department Of Molecular Genetics, University of Texas Southwestern Medical Center, Dallas, United States of America, [3]Inserm U1087 - Cnrs 6291 - Nantes University, Institut du thorax, Nantes, France, [4]Department Of Biophysics And Biophysical Chemistry, Johns Hopkins University School of Medicine, Baltimore, United States of America, [5]Structural Biochemistry Unit, National Institutes of Health, Bethesda, United States of America, [6]Developmental Glycobiology Section, National Institutes of Health, Bethesda, United States of America, [7]Section On Biological Chemistry, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, United States of America

Background and Aims : *GALNT2*, encoding polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2), was initially discovered as a regulator of high-density lipoprotein metabolism. GalNAc-T2 is known to exert these effects through post-translational modification, i.e., O-linked glycosylation of secreted proteins including apolipoprotein C-III, angiopoietin-like 3 and phospholipid transfer protein with established roles in plasma lipid metabolism. More recently it has become clear that loss of GALNT2 in rodents, cattle, nonhuman primates and humans should be regarded as a novel congenital disorder of glycosylation which affects energy metabolism, a topic that has not yet been specifically addressed.

Methods: The UK Biobank was used to study variation in the *GALNT**2*** locus beyond changes HDL metabolism. Experimental data were obtained through studies in *Galnt2*$^{-/-}$ mice and wild-type littermates on both control and high-fat diets.

Results: First, we uncovered associations between *GALNT2* gene variation, adiposity and body mass index in humans. Studies in *Galnt2*$^{-/-}$ mice subsequently reveal decreased adiposity, alterations in insulin signaling and a shift in energy substrate utilization in the inactive phase. Our findings suggest that the insulin receptor is a novel GalNAc-T2 substrate and may be responsible for local rather than systemic effects.

Conclusions: Taken together, our findings identify a novel role for *GALNT2* in energy homeostasis.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

ABDOMINAL ADIPOSE TISSUE ASSOCIATES WITH ADIPONECTIN AND TNF IN MIDDLE-AGED HEALTHY MEN

POSTER VIEWING SESSION

Hani Zaidi
Dept Of Cardiology, Center for clinical Heart Research, Oslo, Norway

Background and Aims : Backgroun: Adipokines, including adiponectin, visfatin and TNF (tumor necrosis factor)-α, are highly active bio-peptides involved in glucose metabolism, insulin regulation and the development and progression of obesity and its associated diseases. It includes, among others **Aim:** In this cross-sectional study, we aimed to investigate whether gene expression levels in subcutaneous adipose tissue (SAT) of selected adipokines and their corresponding circulating levels associate with the amount of AT in superficial (sSAT), deep (dSAT) and visceral (VAT) AT, assessed by computed tomography (CT). Any association with glucometabolic variables were also explored

Methods: Methods: In 103 healthy Caucasian men, fasting venous blood and SAT samples from the gluteal region were collected. Ninety-four of the participants underwent CT assessment of the abdominal AT, which was divided into VAT and superficial - and deep subcutaneous AT (sSAT and dSAT). Circulating levels were measured by ELISA and AT gene-expression by PCR. Insulin sensitivity was determined by glucose clamp, assessing glucose disposal rate (GDR).

Results: Results: Circulating adiponectin and TNF gene expression correlated inversely and positively to sSAT, dSAT and VAT ($r=-0.266$ to -0.276, $p<0.05$ for all) and ($r=0.323$ - 0.368, $p<0.05$ for all), respectively, with strongest correlations to the amount of AT in sSAT and dSAT. Circulating adiponectin correlated inversely to insulin, C-peptide and waist circumference ($r=-456$ to -0.373, $p<0.001$) and positively to GDR ($r=0.356$, $p<0.001$). AT-expressed visfatin correlated inversely to insulin and C-peptide ($r=-0.370$ and $r=-0.404$, $p<0.001$).

Conclusions: Conclusion: Increased amount of AT is associated with low levels of adiponectin and increased levels of TNF.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-04 Adipose tissue homeostasis*

WEIGHT LOSS, VISIT-TO-VISIT BODY WEIGHT VARIABILITY AND COGNITIVE FUNCTION IN A COHORT OF OLDER PEOPLE WITH OR AT RISK OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE.

POSTER VIEWING SESSION

Michelle H. Zonneveld[1], Raymond Noordam[2], Behnam Sabayan[3], David J. Stott[4], Simon P. Mooijaart[2], Gerard J. Blauw[2], Wouter J. Jukema[1], Naveed Sattar[5], Stella Trompet[2]
[1]Cardiology, Leiden University Medical Center, Leiden, Netherlands, [2]Gerontology & Geriatrics, Leiden University Medical Center, Leiden, Netherlands, [3]Neuroscience Center, HealthPartners Institute, Bloomington, United States of America, [4]Institute Of Cardiovascular And Medical Sciences, BHF Glasgow Cardiovascular Research Center, Glasgow, United Kingdom, [5]Bhf Glasgow Cardiovascular Rsearch Centre, University Of Glasgow, Glasgow, United Kingdom

Background and Aims : Unintentional weight loss and higher variability in body weight are associated with increased risk of cardiovascular outcomes. We examined whether this extends to cognitive function in a cohort of older people with or at increased risk of atherosclerotic cardiovascular disease.

Methods: We studied 4,309 participants from the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER) with either existing atherosclerosis or at higher risk thereof. Body weight was measured every three months for 2.5 years. Weight loss was defined as an average slope across all weight measurements and as ≥5% decrease in baseline body weight during follow-up. Visit-to-visit variability was defined as the SD of weight measurements (kg) between visits. Four tests of cognitive function were examined: Stroop test, Letter-Digit Coding test (LDCT), immediate and delayed Picture-Word learning tests. All tests were performed at month 30.

Results: Both larger visit-to-visit body weight variation and loss of ≥5% of baseline weight were independently associated with worse scores on all cognitive tests. Compared to participants who maintained stable weight, participants with significant weight loss scored 5.87 seconds (95%CI 3.78; 7.96) slower on the Stroop test and coded 1.74 digits less (95%CI -2.33; -1.14) on the LDCT. Furthermore, participants with high variability in body weight performed 4.60 seconds (95%CI 2.60; 6.59) slower on the Stroop test and coded 1.97 digits less (95%CI -2.53; -1.41) on the LDCT.

Conclusions: In older people with or at increased risk of atherosclerotic cardiovascular disease, higher variability and loss of body weight are independent risk-factors for worse cognitive function.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

OPTIMIZATION AND VALIDATION OF LIPOPROTEIN(A) KIV2 ISOFORM MEASUREMENT IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Razan Al Zadjali[1], Fahad Zadjali[2]
[1]Biochemistry, Sultan Qaboos University, Al Khoudh, Oman, [2]Clinical Biochemistry, SULTAN QABOOS UNIVERSITY, Khodh, Oman

Background and Aims : Positive correlation is shown between concentration of Lp(a) and severity of coronary artery disease (CAD). Elevated Lp(a) levels are associated with restenosis after percutaneous coronary intervention (PCI). Copenhagen City Heart Study (CCHS) found that extreme Lp(a) levels > 95th percentile predict 3- to 4-fold increase in risk of myocardial infarction. European Atherosclerosis Society (EAS) Consensus Panel recommends screening patients for elevated Lp(a). We evaluated PCR efficiency/ coefficient of variation of Lp(a) KIV-2 repeat genotyping assay, and correlated repeat size in patients with familial hypercholesterolemia with confirmed mutation and mutation negative patients. Further measured apo(a) protein isoform size by SDS-PAGE.

Methods: Optimization: 1- dCtUNKNOWN = CT MEAN ALBUMIN - CT MEAN KIV2 2-ddCt = $\Delta Ct_{UNKNOWN} - Ct_{Cal}$ 3- 2^{ddCt*}KIV2 calibrator size = 48 **Validation:** Multiple runs to obtain coefficient of variation in Ct value of same sample. Inter-assay CV% below 10% is valid. Ran two-fold serial dilution of sample 94.9 ng to 1.48 ng input genomic DNA in duplicates. PCR efficiency/ correlation coefficient of linear equation (r-square) obtained from standard curve of Ct values versus log DNA input. Slope between -3.0 to -3.8 indicates acceptable PCR efficiencies.100% efficient PCR will yield 10-fold increase in PCR products every 3.32 cycle ($2^{3.32} = 10$). Another validation parameter: melting curve assay; information about PCR specificity. **Apo(a) phenotyping:** Western blot measures apo(a) isoforms from plasma samples. Bands detected provides information for each expressed allele, qPCR does not estimate number of KIV2 repeats in allele-specific manner.

Results: See
Attached

Preliminary Results

Optimization and validation of KIV2 and albumin genotyping assays:

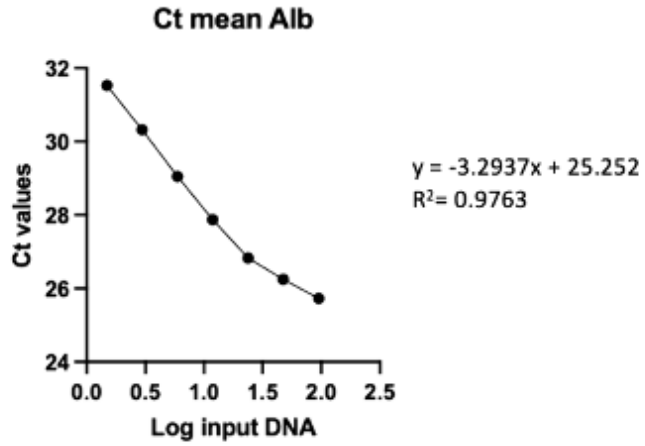

Figure 1. Standard curve of the albumin assay. Slope = -3.2937 (equivalent to 101.9% PCR efficiency) and coefficient of determination R^2= 0.9763

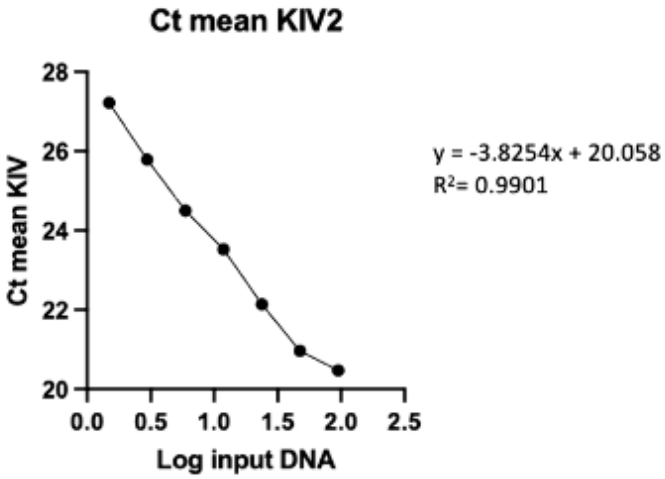

Figure 2. Standard curve of the KIV2 assay. Slope = -3.8254 (equivalent to 82.6% PCR efficiency) and coefficient of determination R^2= 0.9001

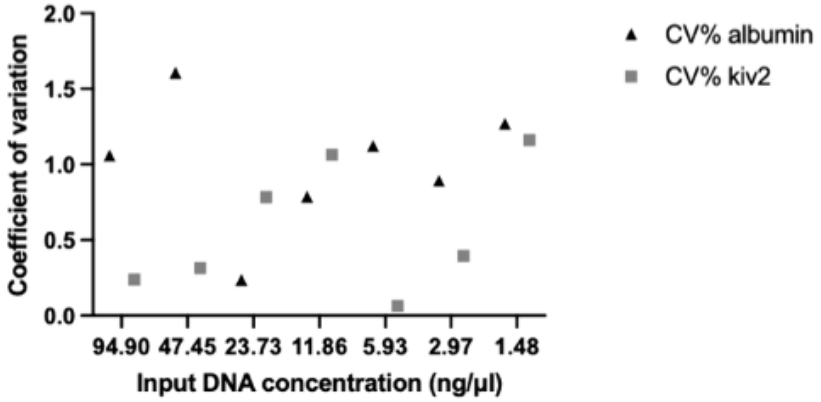

Figure 3. Coefficient of variation in the Ct values of the two-fold serial dilution for both the albumin and KIV2 assays.

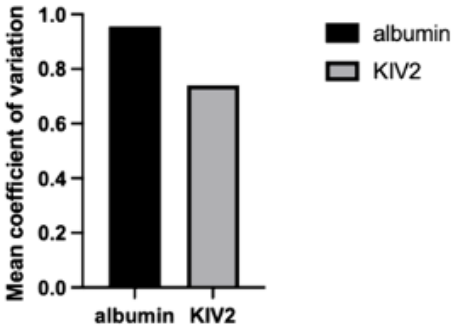

Figure 4. Mean coefficient of variation showing <1% for both albumin and KIV2 assays.

Correlation of KIV2 repeat size in patients with with familial hypercholesterolemia with CVD and non-CVD:

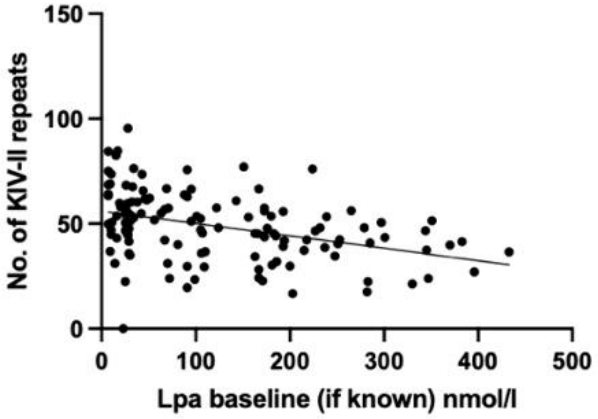

Figure 5. Negative correlation between lipoprotein(a) concentration and KIV2 repeats in the LPA gene with correlation coefficient ($r(s) = -0.425$, $p<0.001$).

Apo(a) phenotyping:

We expect to observe at least one apo(a) isoform band (and a maximum of two) in all plasma samples from the Western blot. Expected molecular weight is ~500kDa.

Conclusions: Assay will be used for patient studies with premature CVD.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

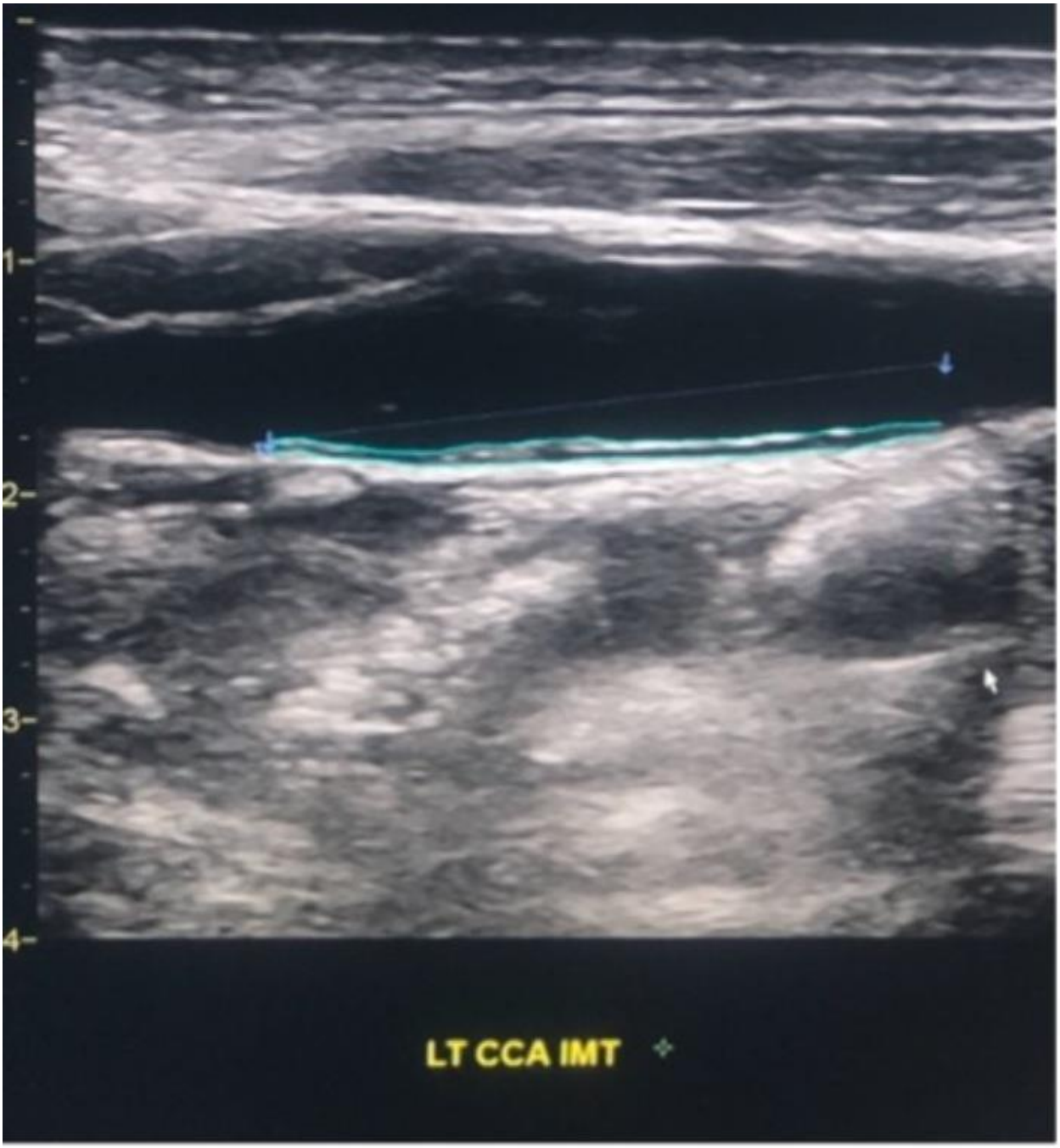
KETOGENIC DIETS EXACERBATING HYPERLIPIDEMIA IN APOE VARIANTS

POSTER VIEWING SESSION

Loba Alam[1], Robert Fishberg[2]
[1]Cardiology, Icahn School of Medicine Mount Sinai Morningside, New York, United States of America, [2]Cardiology, Atlantic Health System, New Jersey, United States of America

Background and Aims : APOE4 variants are one of the known causes of hypercholesterolemia. We present two patients with markedly elevated LDL suspicious for familial hypercholesterolemia who were subsequently diagnosed with APOE3/4 variants while on ketogenic diets.

Methods: Case 1: 58-year-old male with no prior medical history was referred to the hyperlipidemia clinic with cholesterol of 600mg/dL and LDL of 455mg/dL while on a ketogenic diet. Prior to initiating the diet, his cholesterol and LDL were 206mg/dL and 132mg/dL respectively. Genetic testing with GB Health Watch revealed a ApoE3/4 variant. He declined lipid lowering medications and continued his ketogenic diet. Most recent cholesterol increased to 706mg/dL and LDL to >500mg/dL. He had a normal stress test, carotid duplex, zero calcium score, and liver
ultrasound.



Case 2: 53-year-old male with hypertension was referred to the hyperlipidemia clinic for cholesterol of 282mg/dL and LDL of 212mg/dL. Since then he went on a ketogenic diet and lost 100lbs over three years. His most recent lipid panel demonstrated a cholesterol of 400mg/dL and LDL of 317mg/dL. He had a normal stress test and zero calcium score. Genetic testing revealed a APOE3/4 mutation.

Results: We present two patients with APOE3/4 variants who had marked elevation of cholesterol while on ketogenic diets.

Conclusions: We hypothesize patients with APOE variants could have an exaggerated elevation of their LDL levels while on ketogenic diets. Although these two patients do not demonstrate progressive

atherosclerosis, the long-term effect is unknown. We recommend patients with elevated LDL should undergo genetic testing for familial hypercholesterolemia and APOE prior to initiating ketogenic diets.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

PREVALENCE OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION AMONG PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA UNDER PRIMARY PREVENTION

POSTER VIEWING SESSION

Amanda P. Matos[1], Rogério Krakauer[2], Renato J. Alves[2]
[1]Medicine, Santa Casa de Sao Paulo School of Medical Sciences, São Paulo, Brazil, [2]Cardiology, Santa Casa de Misericordia de Sao Paulo Hospital, São Paulo, Brazil

Background and Aims : Familial Hypercholesterolemia (FH) is a disorder characterized by an increased serum LDL-cholesterol level (LDL-c > 190 mg/dL). It leads to complications that can compromise the ventricular myocardium function, especially early coronary artery disease. There are no studies on left ventricular (LV) diastolic function in patients with FH. This study aimed to obtain the prevalence of diastolic dysfunction among patients with FH under primary prevention (PP).

Methods: We performed a cross-sectional study with 42 patients with FH over 18 years old. Patients under PP were included. We excluded those who were under secondary prevention or those who, at the time of the echocardiographic assessment, presented: ejection fraction less than 50%, LV regional wall motion abnormality, significant valve dysfunction, cardiac arrhythmia, pericardial effusion or unavailable information to determine LV diastolic function. Each exam was performed and analyzed by the same physician.

Results: Out of 42 patients, 30 were excluded and 12 were included. Therefore, 28.6% (12/42) underwent the transthoracic echocardiogram exam. After exams' analysis: 75% (9/12) of the patients had normal diastolic function, 8.3% indeterminate function and 16.7% (2/12) presented grade I diastolic dysfunction. Of those with normal function, one had diabetes and one, grade I obesity. Of those with the dysfunction, one had diabetes and one, diabetes and grade III obesity, both elderly.

Conclusions: Patients with FH under PP did not show significant changes in LV diastolic function (low prevalence of grade I dysfunction only). However, new studies must be carried out, with a higher number of patients, for better clarification.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

UPDATE OF THE STUDY OF RARE MONOGENIC FAMILIAL DYSLIPIDAEMIAS IN PORTUGAL

POSTER VIEWING SESSION

Ana Catarina C. Alves[1,2], Mafalda Bourbon[1,2], Beatriz Miranda[1,2]
[1]Btr, BioISI – Biosystems & Integrative Sciences Institute, Faculdade de Ciências, Universidade de Lisboa, Lisboa, Portugal, [2]Departamento De Promoção Da Saúde E Doenças Não Transmissíveis, Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisboa, Portugal

Background and Aims : Dyslipidaemia is a disorder of lipid metabolism, characterized by either an increase or decrease in lipid particles. The majority of the dyslipidaemia and rare and underdiagnosed in most countries. The aim of this study is to review all cases with rare dyslipidaemia studied since 2009 in our lab.

Methods: Molecular analysis was performed by NGS (target panel of 57 genes involved in lipid metabolism: 26 diagnostic and 31 research) (Sure select QXT, Agilent) and samples were run in a NextSEQ Sequencer (Illumina). Analysis was performed with SureCall software (Agilent). Rare variants found in diagnostic genes were confirmed by Sanger sequencing.

Results: This study includes 44 index cases, with different dyslipidaemias. It was possible to find the genetic cause of the disease in 28/44 patients (64%): Familial chylomicronaemia syndrome (8), Familial partial lipodystrophy, Dunningan Type 2 (2), Multifactorial Chylomicronaemia (6), Lysosomal acid lipase deficiency (LALD) (3), hypobetalipoproteinemia (4), HDL deficiency (2), Sitosterolaemia (1) and dysbetalipoproteinemia (2). The remaining are still under study and for some cases an exome sequencing is being discussed. Additionally, cascade screening lead to the identification of another 17 patients (2 sitosterolaemia, 1 LALD and 14 lipodystrophy).

Conclusions: Genetic diagnosis by NGS allowed the correct identification of the disease etiology in several patients, in some changing the clinical diagnosis. Patients with this rare dyslipidaemias have an increased risk of having other serious disorders such as pancreatitis, cardiovascular disease or neurological complications, and should be identified as early as possible in order to minimize or prevent the adverse effects of these conditions.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

EVALUATION OF ARTERIAL STIFFNESS IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA.

POSTER VIEWING SESSION

Allice D.S. Rodrigues[1], Carlos R.D. Oliveira[2], Raphaela P. Pinheiro[3], Maria Julia M. Meneses[4], Renato J. Alves[2]
[1]Cardiology, Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil, [2]Cardiology, Santa Casa de Misericordia de Sao Paulo Hospital, São Paulo, Brazil, [3]Cardiology, Santa Casa de Misericordia de Sao Paulo Hospital, Sao Paulo, Brazil, [4]Cardiology, Santa Casa de Sao Paulo School of Medical Sciences, Sao Paulo, Brazil

Background and Aims : Patients with familial hypercholesterolemia (FH) are at increased risk of early cardiovascular events, and its main characteristic is the increase in LDL-cholesterol (LDL-c), leading to arterial atherosclerosis, which leads to increased risk for acute myocardial infarction and stroke. The main treatment is done with high potency statins. Arterial stiffness (AS) is an important risk marker for cardiovascular disease, which can be assessed by the patient's pulse wave velocity (PWV) and central systolic blood pressure (CSBP). AS has not been evaluated in patients with heterozygous FH. This study aimed to evaluate AS in patients with heterozygous FH using high-potency statins.

Methods: The sample consisted of 15 patients with heterozygous FH, both sexes, over 18 years old, most using high potency statin for primary and secondary prevention, for evaluation of CSBP and PWV.

Results: The sample was 26.66% male, mean age was 59.53 years old, from 40 to 78, and 73.33% female. They were using atorvastatin 80 mg 53.33%, atorvastatin 40 mg 26.66%, rosuvastatin 20 mg 6.66%, simvastatin 40 mg 6.66% and no statin 6.66% (due to statin intolerance). It was observed that the average PWV was 8.66 m/s, the average CSBP was 118.8 mmHg, the average LDL of 130 mg/dL, the average HDL-c was 43.2mg/dL, and the average Triglycerides 137.2 mg/dL.

Conclusions: The data suggest that the use of high-potency statins in heterozygous FH patients contributes to arterial health by keeping AS (assessed by means of PWV and CSBP) within normal limits. The effectiveness of statin treatment needs to be demonstrated in future research.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

LOMITAPIDE IN PAEDIATRIC HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA – REAL-WORLD CLINICAL EXPERIENCE FROM SOUTH AFRICA

POSTER VIEWING SESSION

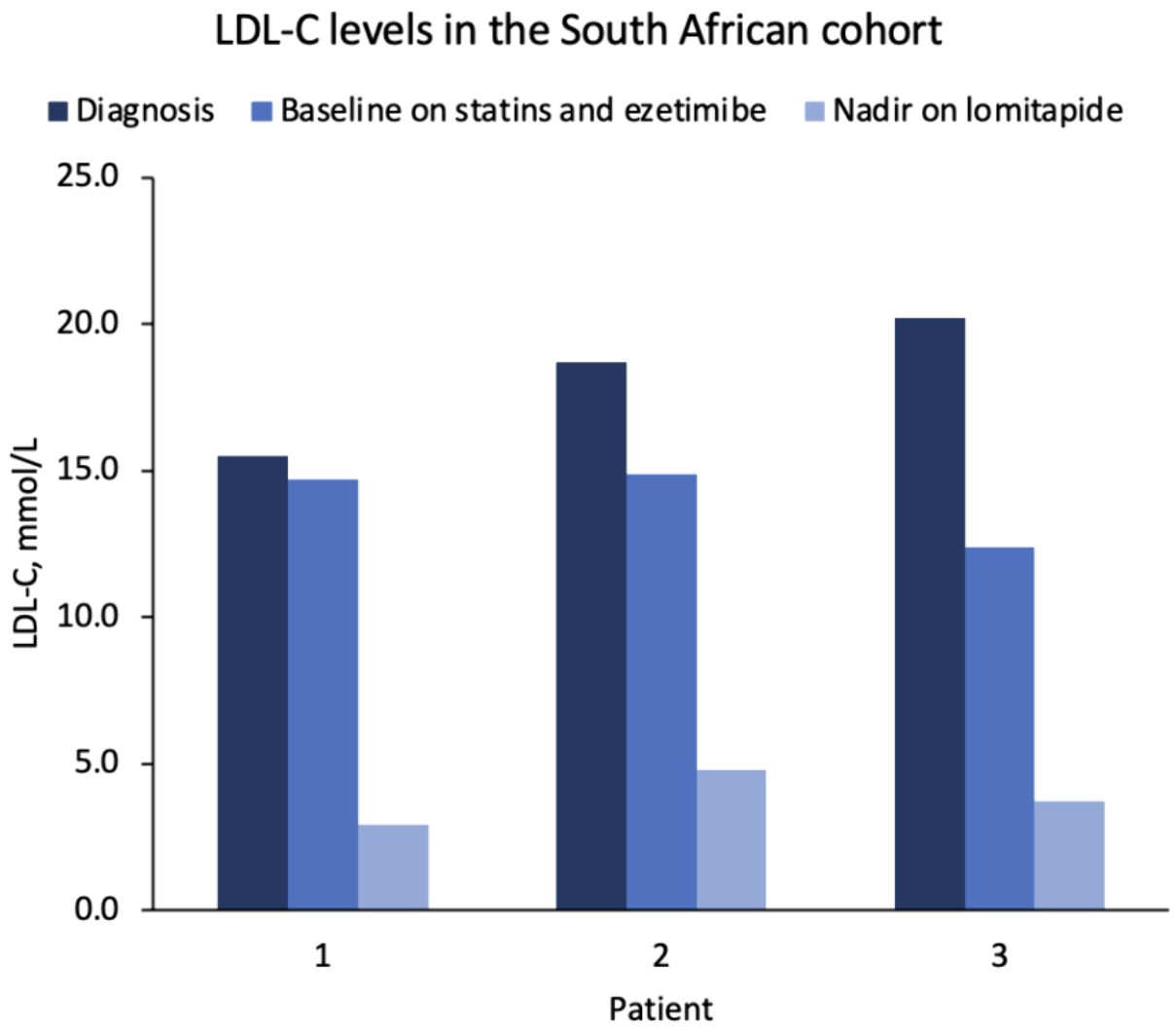
Dirk J. Blom
Department Of Medicine, University of Cape Town, Cape Town, South Africa

Background and Aims : Homozygous familial hypercholesterolemia (HoFH) is a genetic disorder characterized by extremely high levels of circulating low-density lipoprotein cholesterol (LDL-C). Lomitapide is a microsomal transfer protein inhibitor that has demonstrated LDL receptor-independent lipid-lowering efficacy in HoFH patients in long-term clinical trials and real-world studies.

Methods: Three children with HoFH were treated in accordance with local clinical practice in a single clinic in South Africa. LDL-C levels and other laboratory parameters were gathered routinely.

Results: Two patients (1&2) were compound heterozygotes carrying the FH Afrikaner-1 (defective) and -2 (negative) mutations and one (3) was a FH Afrikaner-2 homozygote. All were diagnosed <2 years-old with untreated LDL-C levels 15.5–20.2mmol/L. All patients commenced statins and ezetimibe by age 2.5 years. Patient 1 also commenced plasma exchange (PEX) at age 8 years, and was enrolled on a clinical trial of evolocumab at age 13. At the age of 10 years, Patients 2 and 3 commenced lomitapide at 2.5mg/day and escalated to 40mg/day over 3.8 and 2.9 years respectively. Patient 1 commenced lomitapide (titrated to 20 mg/day) at age 17 years while still receiving evolocumab and PEX, both of which were eventually stopped (follow-up 5.6 years). Compared with baseline LDL-C on statins and ezetimibe, mean LDL-C reduced by up to 10.2±1.6mmol/L, representing a 72.7±6.6 percent reduction at nadir (Figure). Lomitapide was generally well tolerated. No transaminase levels >3x ULN were

observed.



Conclusions: Lomitapide lowered LDL-C effectively in three children with HoFH irrespective of residual receptor function. Further paediatric studies are warranted.

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MAJOR ADVERSE CARDIOVASCULAR EVENTS IN HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

POSTER VIEWING SESSION

Liam Brunham[1], Adam Kramer[2], Leo Akioyamen[3], Jacques Genest[4], Stephen Lee[4]
[1]Centre For Heart Lung Innovation, University of British Columbia, Vancouver, Canada, [2]Medicine, University of British Columbia, Vancouver, Canada, [3]Medicine, University of Toronto, Toronto, Canada, [4]Muhc, McGill University, montreal, Canada

Background and Aims : Homozygous familial hypercholesterolemia (HoFH) is a genetic condition characterized by extremely elevated levels of low-density lipoprotein cholesterol and premature atherosclerotic cardiovascular disease (ASCVD) and death. Due to its rarity, accurate assessment of cardiovascular outcomes associated with HoFH and how they have changed over time has been challenging. The goal of this study was to assess the prevalence and age-of-onset of major adverse cardiovascular events (MACE) among patients with HoFH.

Methods: We searched MEDLINE, EMBASE, Pubmed, Cochrane Central Register of Controlled Trials, Scopus, Africa-Wide, Google Scholar, Open Grey, and various clinical trial registries from inception to February 2020 to identify studies reporting on MACE in HoFH patients. We determined the pooled prevalence and mean age-of-onset of MACE outcomes individually using a random effects inverse variance model.

Results: We identified 94 studies that met our eligibility criteria. Myocardial infarction and coronary revascularization were common with a prevalence of 15.1% (95% CI 10.7% - 20.0%) and 28.3% (95% CI 22.5% - 34.3%), respectively. Mean age-of-onset was 24.5 (95% CI 19.2 - 29.8) years for myocardial infarction, and 32.2 (95% CI 26.6 - 37.8) years for revascularization. Subgroup analyses based on year of publication revealed significant delays in the onset of MACE outcomes post-1990 compared to pre-1990.

Conclusions: ASCVD is common among HoFH patients and occurs at a young age. Age-of-onset of myocardial infarction was delayed by more than a decade pre-1990 post-1990, likely attributable to widespread use of statin therapy and other therapies, reflecting substantial progress in the management of this rare but severe disorder.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

FEATURES OF THE METABOLIC SYNDROME AND SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH CEREBROTENDINOUS XANTHOMATOSIS: AN AUGMENTED RISK FOR PREMATURE CARDIOVASCULAR DISEASE

POSTER VIEWING SESSION

Hofit Cohen[1,2], Sharon Hassin-Baer[1,3]
[1]Sackler Faculty Of Medicine, Tel Aviv University, Tel-Aviv, Israel, [2]Sheba Medical Center, The Bert W. Strassburger Lipid Center, Tel-Hashomer Ramat-Gan, Israel, [3]The Movement Disorders Institute And Department Of Neurology, Sheba Medical Center, Tel-Hashomer, Israel

Background and Aims : Cerebrotendinous xanthomatosis (CTX) is a rare lipid storage disease caused by mutations of the *CYP27A1* gene, resulting in deficiency of sterol-27-hydroxylase, a key enzyme involved in hepatic bile acid synthesis from cholesterol. Xanthomatous lesions in numerous tissues, in conjunction with an elevation of plasma and tissue cholestanol levels. The natural course of CTX is progressive neurologic deterioration from childhood through adulthood, leading to diffuse damage of the central and peripheral nervous systems and eventually to premature death. Chronic treatment with oral chenodeoxycholic acid (CDCA) produces a reduction in cholestanol synthesis and its plasma levels. While neurological presentation is the principal concern in patients with CTX, occurrence of premature vascular involvement has been described, with different clinical manifestations of cardiovascular disease in more than 10% of patients with CTX. The exact mechanism leading to early onset atherosclerosis in this disease is unknown.

Methods: The subjects were diagnosed with CTX, and were of North African Jewish descent, either homozygous or compound heterozygous for either one or two of the mutations described in Jewish families of Moroccan origin. Patients underwent annual evaluations of features the metabolic syndrome, blood samples for glucose, plasma lipid panel and cholestanol levels. Additionally, carotid artery intima-media thickness was performed.

Results: High prevalence of the metabolic syndrome features and preclinical atherosclerotic changes were found in the patients, despite depressed cholestanol levels on appropriate treatment with CDCA.

Conclusions: Cardiovascular disease risk assessment should be implemented in order to conduct preventive measures for risk reduction of atherosclerotic cardiovascular disease in young CTX patients.

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EFFECTIVENESS OF DUTCH LIPID SCORE (MODIFIED FOR ITALY) IN A COHORT OF SUBJECTS AGED > 18 YEARS AND COMPARISON WITH THE SUBPOPULATION BETWEEN 18-45 YEARS

POSTER VIEWING SESSION

Damiano D'Ardes, Ilaria Rossi, Paola Vizzarri, Angelo Floriano Damiani Tripolino, Fabio Troiano, Margherita Caporale, Francesco Cipollone, Marco Bucci
Medicine And Aging Sciences, G. D'Annunzio University of Chieti, Chieti, Italy

Background and Aims : Familial hypercholesterolemia (FH) is the most frequent genetic disorder among dyslipidemias. Our aim is to evaluate the performance of Dutch Lipid Clinic Network Score (DLCNS) modified for Italy (DLCNS-I) in identifying patients with genetically defined FH, particularly in those ones <45 years.

Methods: The DLCNS-I and the result of genetic analysis were assessed retrospectively on a group of 96 subjects aged >18 (mean= 49 years) followed at the Chieti Lipid Clinic and already enrolled in LIPIGEN project.

Results: Within the subcategory with clinically defined FH (score >8), 80.95% of patients presented a positive genetic analysis for FH or variants of uncertain significance (VUS). In the subgroup aged 18-45 (n=34, mean age=34),93.3% presented a positive genetic analysis for FH or VUS among patients with clinically defined FH. Patients aged 18-45 years with missing data to calculate DLCNS-I were less numerous if compared to the total population (respectively 22.9% vs 35.3% had no missing criteria; 30.2% vs 38.2% had 1 missing criterion); whereas patients with 2, 3 or 4 missing criteria were more numerous in 18-45 years subcohort (respectively 24.0% vs 23.5%; 13.5% vs 0%; 9.4% vs 2.9%). DLCNS-I proved to be more effective if we have no more than one missing diagnostic criterion (as between subjects aged 18-45 years), despite lower LDL-C levels and less CV events, probably due to a more comprehensive history collection and more carefully physical examination.

Conclusions: The DLCNS-I confirmed its usefulness in FH diagnosis, even if its effective compilation still represents a difficulty.

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FAMILIAL HYPERCHOLESTEROLEMIA CARE IN ADOLESCENTS-SINGLE CENTRE EXPERIENCE FROM SINGAPORE

POSTER VIEWING SESSION

Sanjaya U. Dissanayake[1], Sharon Li Ting Pek[2], Zit Liang Chan[2], Siti Nur Afiqah Kamaruddin[2], Atiqa Zulkifli[2], Fariha Siraj[2], Wen Yi Wan[2], Tavintharan Subramaniam[1,2,3]
[1]Medicine, Khoo Teck Puat Hospital, Singapore, Singapore, [2]Clinical Research Unit, Khoo Teck Puat Hospital, Singapore, Singapore, [3]Diabetes And Endocrinology, Admiralty Medical Centre, Singapore, Singapore

Background and Aims : Familial Hypercholesterolemia (FH) is an autosomal dominantly inherited disease commonly due to LDL Receptor Mutations. Heterozygous individuals are at risk of developing premature vascular disease due to accumulation of LDL. Early diagnosis and treatment are likely to reduce morbidity and mortality. To study the demographics, diagnostic features and response to therapy in adolescents with suspected FH .

Methods: A prospective study of adolescents with suspected Familial Hypercholesterolemia. Recruitment period was July 2015 to August 2019. Modified Simon Broome criteria was used.

Results: There were 53 adolescents aged 16-21. Most of them were referred with an abnormal lipid profile. Among those 96% (n=51) were males and chinease 73.6% (n=39), According to above criteria, 29 were definite, 13 were possible FH cases. Mean LDL level on 1st visit was 6.05±1.67mmol/. Genetic testing was done in all the cases. Mutation positivity was 58.4% (n=31). Among those, 52.8% (n=28) had LDLR mutations, Lipid lowering treatment was started in 77.4% (N=41). Satisfactory LDL reduction to <3.5 mmol/l was achieved in 75.6 % (N=31/41). Targeted cascade screening of the family members were done in 16 probands. 14 families were positive, and this led to the identification of 18 new cases.

Conclusions: The majority were males; and were clinically silent. A genetic mutation was identified in 58.4% of cases and comparable to other reported FH case series. The commonest defect reported was LDL receptor mutations. LDL treatment target was achieved in more than three quarter of cases started on statin treatment. Cascade screening was successful in identifying new cases.

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REVERSE CASCADE SCREENING IN THE DIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Liliia F. Galimova[1], Dinara I. Sadykova[2], Eugenia S. Slastnikova[1], Chulpan D. Khaliullina[2], Karina R. Salakhova[2]
[1]Pediatric Cardiology, Republican Children's Hospital, Kazan, Russian Federation, [2]Hospital Pediatrics, Kazan State Medical University, Kazan, Russian Federation

Background and Aims : Early diagnosis of familial hypercholesterolemia (FH) and an effective patient monitoring strategy are extremely promising for reducing the risk of atherosclerosis in the future. Aim of the study. Conduct and analyze the results of reverse cascade screening for the diagnosis of FH.

Methods: The study was carried out in the period from December 2018 to August 2021 on the basis of Children's Republican Clinical Hospital, Kazan, City Clinical Hospital No. 7 in Kazan, Kazan State Medical University. Inclusion criteria: age 0-17 years inclusive, diagnosed with "Heterozygous form of familial hypercholesterolemia" in accordance with clinical guidelines according to the criteria of Simon Broome Registry, informed consent for participation in the study of children and / their parents. Exclusion criteria: underlying diseases / conditions, as well as drugs that may cause a secondary increase in LDL cholesterol.

Results: During this period, 34 children were identified with a diagnosis of heterozygous FH (mean age 9.1 ± 2.4 years). After further examination of relatives, FH was diagnosed in 35 parents, 17 siblings, 58 relatives of the 2nd line of relationship. The average age of the parents was 37.8 ± 3.3 years. In 21 (60.6%) of them ischemic heart disease was diagnosed, in 19 (55%) atherosclerosis of the brachiocephalic arteries. In addition, 11 (31%) patients required coronary angiography, 3 (8,5%) - coronary artery bypass grafting, 2 (5,7%) - stenting of coronary vessels.

Conclusions: The diagnostic result of the cascade screening along the "child-parent" path was 3 new cases of FHC per one child-proband.

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CLINICAL AND GENETIC CHARACTERIZATION OF FH CHILDREN AND ADOLESCENTS ENROLLED IN THE ITALIAN LIPIGEN PAEDIATRIC GROUP

POSTER VIEWING SESSION

Marta Gazzotti[1], Stefano Bertolini[2], Cristina Pederiva[3], Maria Elena Capra[4], Alberico L. Catapano[5], Manuela Casula[5]
[1]Fondazione Sisa, Fondazione SISA (Società Italiana per lo Studio dell'Aterosclerosi), Milano, Italy, [2]Department Of Internal Medicine, University of Genova, Genova, Italy, [3]Clinical Service For Dyslipidaemias, Study And Prevention Of Atherosclerosis In Childhood, Paediatrics Unit, ASST Ospedali Santi Paolo e Carlo, Milano, Italy, [4]Centre For Paediatric Dyslipidaemias, Paediatrics And Neonatology Unit, Guglielmo da Saliceto Hospital, Piacenza, Italy, [5]Department Of Pharmacological And Biomolecular Sciences, University of Milan and Multimedica IRCCS, Milan, Italy

Background and Aims : In the last decade, the implementation of familial hypercholesterolemia (FH) pathology registries allowed to investigate specific sub-groups as FH subjects <18 years. Here, we report recent advances from the Italian LIPIGEN Paediatric Group, with a focus on the genotype-phenotype relation.

Methods: From the LIPIGEN study, we identified 1602 clinically and/or genetically confirmed FH-subjects under 18 years, followed up by 31 Italian LIPIGEN sites, with at least one pre-treatment LDL-C measurement and data about genetic testing.

Results: Almost the whole cohort underwent genetic testing. Genetically-confirmed subjects (about 70% of tested individuals) presented higher LDL-C level (mean±SD) compared to subjects with variants of uncertain significance (N=125) or negative diagnosis (N=317) (246.5±102.1 vs 166.4±56.5 vs 159.9±47.7mg/dL; p<0.0001). Among subjects with a genetically-positive diagnosis of FH, 1013 individuals presented one causative mutation (untreated LDL-C =231.6±53.5 mg/dL) in *LDLR* (N=998) or *APOB* (N=15) genes, while in 40 subjects two causative mutations "*in trans*" were detected (untreated LDL-C=623.9±234.7 mg/dL). In heterozygous FH for *LDLR*, more than 200 different causative variants were detected (three the most frequent: p.Gly549Asp (LDL-C=245.0±50.6 mg/dL), p.Gly592Glu (LDL-C=198.7±50.1 mg/dL), and p.Asp221Gly (LDL-C=212.2±41.2 mg/dL)) and a great variability in the LDL-C values was observed even within the same mutation. Stratifying *LDLR* mutations by receptor residual activity, a more severe phenotype was confirmed in children/adolescents HeFH with a null-receptor compared to defective-receptor mutation (245.1±52.0 vs 220.2±51.9 mg/dL; p<0.0001).

Conclusions: The LIPIGEN paediatric database allow for a better clinical and genetic characterization of FH children/adolescents, providing the basis for further longitudinal investigations.

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MANAGEMENT OF A PATIENT WITH DELAYED DIAGNOSIS OF HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLAEMIA

POSTER VIEWING SESSION

Antonina Giammanco[1], Roberto Scicali[2], Chiara Scrimali[1], Antonino Di Pino[2], Federica Brucato[3], Rossella Spina[1], Salvatore Piro[2], Davide Noto[1], Angelo Baldassare Cefalù[1], Francesco Purrello[2], Maurizio Averna[4]
[1]Department Of Health Promotion, Mother And Child Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy, [2]Medicine Department, ARNAS GARIBALDI NESIMA, Catania, Italy, [3]Promise, University of Palermo, Palermo, Italy, [4]Department Of Health Promotion Sciences Maternal And Infantile Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy

Background and Aims : Homozygous familial hypercholesterolaemia (HoFH) is a rare, life-threatening genetic disorder characterized by extremely high low-density lipoprotein-cholesterol (LDL-C) levels and severe and accelerated atherosclerotic cardiovascular disease (ASCVD). We describe the clinical management and molecular characterization of a subject with severe hypercholesterolemia.

Methods: The proband is a 50-year-old man with family history of early cardiovascular disease and hypercholesterolemia (both parents and his two children). Severe hypercholesterolemia (LDL-C 450 mg/dL) was first documented when he was 32 and treatment with statin was begun. When he was 47, over a routine cardiologic workup a coronary angiography revealed diffuse stenotic coronary disease and he underwent to BACG procedure. Genetic analysis of FH candidate genes was carried out by NGS. Additional hypolipidemic therapeutic options were considered for the management of this patients.

Results: The genetic analysis revealed that the patient was compound heterozygous of two already known receptor-defective pathogenic mutations of the LDLR gene (c.1118G>A – p.Gly373Asp - and c.1195G>A – p.Ala399Thr). The patient was treated with alirocumab 150 mg every other week on top of standard care. Once the genetic diagnosis of HoFH was made alirocumab was switched to evolocumab 420 mg once a month. Although an effective reduction of LDL-C levels, the lipid goal was not reached. Therefore we decided to potentiate hypolipidemic treatment by adding a low dose of lomitapide which was well tolerated and very effective (LDL-C:42 mg/dL).

Conclusions: The combination of evolocumab with low-dose lomitapide was an effective and well-tolerated add-on therapeutic option in a HoFH carrier of defective mutations of the LDL-R gene.

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EVALUATION OF LIPID-LOWERING THERAPY IN PATIENTS WITH DEFINITE DIAGNOSIS OF HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA IN LODZ.

POSTER VIEWING SESSION

Paulina Gorzelak-Pabiś[1], Agnieszka Pawlos[2], Zuzanna Staciwa[1], Aleksandra Krulikowska[1], Marlena Broncel[1]
[1]Department Of Internal Diseases And Clinical Pharmacology, Laboratory Of Tissue Immunopharmacology, Medical University in Lodz, Lodz, Poland, [2]Department Of Internal Diseases And Clinical Pharmacology, Laboratory Of Tissue Immunopharmacology, Medical University in Lodz, Lodz, Poland, Łódź, Poland

Background and Aims : The aim of the study was to analyze a type and efficiency of lipid lowering therapy in patients with definite diagnosis of heFH. We also analyzed LDL corrected with Lp(a) and therapeutic LDL achievement in patients with familial hypercholesterolemia on optimal lipid-lowering therapy.

Methods: We conducted retrospective analysis of 20 patients with definite clinical diagnosis of FH (DLCNS>8 score) and very high cardiovascular risk. We analyzed type of lipid lowering therapy (statin, ezetimibe, PCSK9i) baseline and 6 months follow up lipids including total cholesterol, LDL, HDL, non-HDL, Lp(a) and LDL corrected with Lp(a). LDL corrected with Lp(a) was calculated as LDL(corrected) = LDL [mg/dl] – 0,3 x Lp(a)

Results: 20 patients enrolled in the study were 15 women and 5 men in mean age 50,65±15. Average baseline lipid parameters were: Total cholesterol: 321±93mg/dl ; LDL cholesterol 252,58±68mg/dl; HDL cholesterol 54,11±16; non-HDL cholesterol 250,14±116mg/dl; Triglycerides 160,55±112mg/dl; Lp(a) 90,34±111; LDL(corrected) 242,47±72mg/dl. All patients had definite diagnosis of familial hypercholesterolemia and mean DLCNS was 14,25±4. All patients had lipid lowering therapy introduced including high intensity statin (atorwastatin 3/20 patients in mean dose 60mg, rosuwastatin 17/20 in mean dose 27,06mg), ezetimibe 19/20 patients in dose 10mg and 14 patients were on PCSK9 inhibitors (6 on ewolocumab and 8 on alirocumab). After 6 months follow-up, mean lipid parameters were: Total cholesterol: 169,2±65mg/dl ; LDL cholesterol 94±50mg/dl; HDL cholesterol 45,64±8; non-HDL cholesterol 102,97±77mg/dl; Triglycerides 167,8±115mg/dl; Lp(a) 70,25±107; LDL(corrected) 87,33±49mg/dl.

Conclusions: Despite optimal, intensive lipid-lowering therapy, the achievement of therapeutic LDL in patients with FH is not satisfactory.

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CASCADE SCREENING AND REGISTRY FOR PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA IN GERMANY – A FOLLOW-UP SURVEY

POSTER VIEWING SESSION

Ira A. Haack, Alexander Dressel, Winfried Maerz
Geschäftsstelle, D•A•CH-Gesellschaft Prävention von Herz-Kreislauf-Erkrankungen e.V., Hamburg, Germany

Background and Aims : The aim of the registry is to record as many German patients with FH as possible and to raise awareness for FH among patients and physicians in Germany. Will the lipid-lowering therapy (LLT) intensify over the course of 2.5 years? Can the target values according to the EAS guidelines be achieved? Does the patients 'quality of life improve?

Methods: FH-patients are included into the registry after their informed consent. The data is recorded and analyzed using questionnaires for physicians and patients. After 2.5 years and five years follow up questionnaires are collected.

Results: By the end of November, 2.400 FH patients had been entered into the registry. Follow up of 370 patients show that LLT intensified during the previous 2.5 years and average baseline LDL-C values of 132±67 mg/dl decreased to an average of 110±51 mg/dl. The target of the EAS dyslipidemia guideline of an LDL cholesterol below 70 mg/dl in FH is not achieved. FH patients are aware of their condition, which is reflected by a surprisingly healthy lifestyle. The majority (53%) never smoked; 36% have given up smoking and 94% of FH patients are active in sports. They had informed at least two relatives about their FH diagnosis and thus help to raise awareness in the population. One third of FH patients stated that their quality of life had improved, deteriorated, or remained the same, respectively.

Conclusions: The registry can increase awareness of the disease. Despite this, achieving the target values of the EAS guidelines remains difficult.

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A DANISH NATIONWIDE STUDY OF INDIVIDUALS SUSPECTED OF FH REFERRED FROM GENERAL PRACTICE TO LIPID CLINICS: CLINICAL CHARACTERISTICS, PLASMA LIPOPROTEIN(A) AND FINAL DIAGNOSIS

POSTER VIEWING SESSION

Berit Storgaard Hedegaard[1,2], Christian S. Bork[3], Ib Christian Klausen[2], Børge G. Nordestgaard[4], Erik B. Schmidt[5], Albert M. Joensen[3,5]
[1]Department Of Clinical Medicine, Aalborg University, Viborg, Denmark, [2]Department Of Cardiology, Regional Hospital Viborg, Viborg, Denmark, [3]Department Of Cardiology, Aalborg University Hospital, Aalborg, Denmark, [4]Department Of Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen N, Denmark, [5]Department Of Clinical Medicine, Aalborg University, Aalborg, Denmark

Background and Aims : Familial hypercholesterolemia (FH) is an inherited condition characterized by severely elevated plasma levels of low-density lipoprotein (LDL) cholesterol believed to occur in approximately 1:250 subjects. FH is associated with a very high risk of premature atherosclerotic cardiovascular disease. Unfortunately, less than 20% of the affected are currently diagnosed in Denmark, which represents a health challenge here and in most other (Western) countries. The aims of the study were to describe important clinical characteristics and examine the proportion of verified FH diagnoses among adult subjects referred from General Practice to Danish Lipid Clinics on suspicion of FH. Also we aimed to investigate the importance of plasma lipoprotein(a) levels for a diagnosis of FH.

Methods: All subjects referred from General Practice to one of the 15 Danish Lipid Clinics between September 2020 and November 2021 will be included. More than 1.200 individuals are expected to be recruited into the study and informed consent will be obtained from the subjects. Referrals for suspicion of FH were based on pre-specified criteria including LDL cholesterol levels $\geq$ 5.0 mmol/l ($\geq$ 4.0 mmol/l in subjects $\leq$ 40 years) or premature cardiovascular disease. Secondary dyslipidaemias were excluded before admittance. Individuals were interviewed for personal and familial cardiovascular disease, diet, lifestyle, treatment and examined for cholesterol deposits. Individuals were classified according to the Dutch Lipid Clinic Network Score for FH.

Results: Main results will be available in April 2022 and will be presented at the Congress.

Conclusions: Will be presented when the results are available.

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HUNTING FOR HOMOZYGOUS FH - LESSONS LEARNT

POSTER VIEWING SESSION

Shamanna Iyengar, On Behalf Of Lai[1], Raman Puri[2], Preeti Gupta[3], Rashida Melinkeri[4], S Narasingan[5], Akshaya Pradhan[6], Peeyush Jain[7], Ashwani Mehta[8], Milan Chag[9], H Basavanagowda[10], D Prabhakar[11], A Dileep[12]
[1]Cardiology, Manipal Hospital, Bangalore, India, [2]Cardiology, Apollo Hospital, Delhi, India, [3]Cardiology, Safdarjung Hospital, Delhi, India, [4]Cardiology, Clinic, Pune, India, [5]Cardiology, SN Clinic, Chennai, India, [6]Cardiology, KG Medical University, Lucknow, India, [7]Cardiology, Clinic, Delhi, India, [8]Cardiology, GB Pant Hospital, Delhi, India, [9]Cardiology, Clinic, Ahmedabad, India, [10]Medicine, JSS Medical College, Mysore, India, [11]Cardiology, Apollo Hospital, Chennai, India, [12]Cardiology, Vrnchy Hospital, Hyderabad, India

Background and Aims : Familial Hypercholesterolemia (FH) is underdiagnosed and undertreated, leading to prematurely profound adverse cardiovascular events. Lipid Association of India planned to collect cases of homozygous FH (HoFH) and in the process, to identify lacunae that linger in the field.

Methods: Data were collected from the medical records of patients diagnosed as HoFH

Results: Of 49 cases, 20 were females and 23 were 18 years or younger. Youngest was 3 years old and the oldest 50 years. Family history of premature atherosclerotic cardiovascular disease (ASCVD) or dyslipidemia was available in 31 patients. All were nonsmokers, nondiabetics and normotensives. Genetic tests were done in 15, all showing LDL receptor mutation. 12 patients had established ASCVD and 5 calcific aortic valve disease. At baseline, the highest LDL-Cholesterol was 850 mg/dl and the lowest 241 mg/dl. Lp(a) was estimated in 9 patients, 8 having a value of >50 mg/dl. In 8, treatment history was not known, and all others received statin and ezetimibe. 10 received evolocumab as a part of a clinical study for a period of three months.. Three patients underwent lipoprotein apheresis. Follow up was recorded in 19 patients. More than 50% lowering of LDL c was observed in 6 patients. 8 patients showed no change at all with drugs. 3 patients died.

Conclusions: 1 HoFH runs a relentless downhill course unless treated early and effectively. 2 LDL receptor mutation was common 3 Combination therapy is necessary 4 Drugs acting independent of LDL receptors are necessary in some. 5 Treatment modalities have to be more accessible.

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GENETIC ANALYSIS OF A RARE FORM OF DYSLIPIDEMIA: DE NOVO ABCG5/APOB MUTATIONS IN GREECE

POSTER VIEWING SESSION

Eleni Koniari[1], Anastasia Skouma[2], George Chrousos[1,3]
[1]Endocrinology, Research University Institute for the Study of Genetic and Malignant Childhood Diseases, Athens, Greece, [2]Metabolic Division, Institute of Health and Child Care Neonatal Screening Department, Children's Hospital “Aghia Sophia, Athens, Greece, [3]Endocrinology, Research University Institute for the Study of Genetic and Malignant Childhood Diseases, Athens, Endocrinology, Athens, Greece

Background and Aims : Sitosterolemia is a rare autosomal recessive inherited metabolic disorder of lipids, characterized by increased levels of plant sterols in plasma. It is caused by mutations in gABCG5 or ABCG8 genes and recent studies have revealed the fact that heterozygous mutation carriers also exhibit milder manifestations.

Methods: A 11-year-old girl followed up in the Children's Hospital "Aghia Sophia" and admitted with hyperammonemia, hypoglycaemia and serum lipid levels marginally elevated . Proband’s mother and grandmother had cholesterol > 240mg / dl while the second developed atherosclerotic disease at age 57 years. Proband’s father had normal lipid levels. DNA Isolation, PCR, Cardiogena Panel-NGS (Illumina MiSeq) and bioinformatics analysis (Sophia Genetics DDM) were performed.

Results: Patient serum sterol levels were slightly elevated, with sitosterol 6.1 mg / L and cholestanol 5.4mg/L. A novel mutation in the ABCG5 gene c.1273C>T p.Gln425* was identified, which results in a stop codon and premature termination of translation. In addition, two further changes in ABCG5, c.1810C> G, (p.Gln604Glu) and c.148C> T (p.Arg50Cys) were determined in the patient s. Proband’s mother was heterozygous for the null mutation p.Gln425* and APOB rare variants (gnomad<0.01) c.5768A>G, p.(His1923Arg), c.2188G>A, p.(Val730Ile). No rare variants were found in PCSK9 nor ABCG8.

Conclusions: This is the first case of two hyperlipidemic members in the same family exhibit two different genotypes, the one being a carrier of ABCG5 LoF mutation while the second fone was a compound heterozygote for ABCG5 p.Gln425* /APOB His1923Arg. Our case is informative in the perspective of precision medicine, highlighting the importance of the genetic testing.

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COSEGREGATION OF P.H343R ANGPTL3 MISSENSE VARIANT IN A FAMILY WITH HYPOBETALIPOPROTEINEMIA

POSTER VIEWING SESSION

Manon Levy[1,2], Alexandre Janin[3,4], Oriane Marmontel[4,5], Anthony Fourier[4], Séverine Nony[4], Caroline Bouveyron[4], Antoine Rimbert[6], Bertrand Cariou[6], Sylvie Villar-Fimbel[1], Sybil Charriere[1,2,5], Philippe Moulin[1,2,5], Mathilde Di Filippo[4,5]
[1]Service D'endocrinologie, De Diabétologie Et Des Maladies Métaboliques, Hôpital Louis Pradel, Bron cedex, France, [2]Université Lyon 1 Claude Bernard, Faculté de Médecine Lyon Est, Lyon, France, [3]Cnrs Umr5310, Inserm U1217, Institut Neuromyogène, Université Claude Bernard Lyon 1, Université de Lyon, LYON, France, [4]Service De Biochimie Et De Biologie Moléculaire, Laboratoire De Biologie Médicale Multisites, Hospices Civils de Lyon, BRON, France, [5]Inserm U1060, Université Lyon 1, Inrae U1397, Laboratoire CarMen, Oullins, France, [6]Inserm U1087 - Cnrs 6291 - Nantes University, Institut du thorax, Nantes, France

Background and Aims : Angiopoietin-like 3 (ANGPTL3) is a protein involved in lipid metabolism, inhibiting the lipoprotein lipase. If loss of function variants in *ANGPTL3* have been identified in patients with primary hypobetalipoproteinemia, the effect of heterozygous missense variants remains not consensual. The heterozygous p.H343R missense variant in *ANGPTL3* identified in a family referred to our laboratory was found to cosegregate with hypobetalipoproteinemia. The aim of the present study was to assess *in vitro* the functionality of this variant.

Methods: After transfection of an expression plasmid in HEK293T cells, the effect of the variant on ANGPTL3 secretion was investigated using a workflow based on protein detection by ELISA. Total lipase activity assay, using human VLDL-TG as a substrate, was performed with cell medium to determine the effect of the variant on the protein activity.

Results: All family members carrying the p.H343R variant had a concentration of LDL cholesterol below the fifth percentile (7/7). ANGPTL3 concentration in medium of cells transfected with the plasmid carrying the p.H343R variant was 3 times lower than in the wild type cell medium. The inhibitory effect of ANGPTL3 on total lipase activity was reduced in the p.H343R cell medium, representing 88% of wild type activity at equal concentration of ANGPTL3 in the medium.

Conclusions: *In vitro*, the p.H343R variant was responsible for a decrease in ANGPTL3 secretion and activity. Functional characterization of this variant is important to confirm diagnosis in the carriers, and will contribute to a better knowledge of the structure-function relations of *ANGPTL3* heterozygous missense variants.

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ASSOCIATION OF TG/HDL-C AND TYG INDICES WITH THE PREVALENCE OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN ADULT PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Christos Rizos[1], George Liamis[1], Ioannis Skoumas[2], Anastasia Garoufi[3], Loukianos Rallidis[4], Konstantinos Tziomalos[5], Genovefa Kolovou[6], Emmanuel Skalidis[7], Vasileios Kotsis[8], Michalis Doumas[9], Vaia Lambadiari[10], Panagiotis G. Anagnostis[11], George Sfikas[12], Ioanna Dima[2], Estela Kiouri[4], Georgios Polychronopoulos[5], Vana Kolovou[6], Evangelos Zacharis[7], Christina Antza[8], Charalambos Koumaras[12], Evangelos Liberopoulos[13]
[1]Department Of Internal Medicine, University of Ioannina, Ioannina, Greece, [2]Cardiology Clinic, Hippokration General Hospital, Athens, Greece, [3]Department Of Pediatrics, Medical School, National and Kapodistrian University of Athens, B' Pediatrics Clinic, General Children's Hospital "Pan. & Aglaia Kyriakou", Athens, Greece, [4]Department Of Cardiology, Medical School, National and Kapodistrian University of Athens, Attikon University General Hospital, Athens, Greece, [5]1st Propedeutic Department Of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece, [6]Metropolitan Hospital, Cardiometabolic Center, Lipid Clinic, LA apheresis Unit, Athens, Greece, [7]Cardiology Clinic, University General Hospital of Heraklion, Heraklion, Greece, [8]Department Of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Papageorgiou General Hospital Thessaloniki, Thessaloniki, Greece, [9]Department Of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Hippokration General Hospital, Thessaloniki, Thessaloniki, Greece, [10]2nd Propaedeutic Internal Medicine Department And Diabetes Research Unit, National and Kapodistrian University of Athens, Attikon University General Hospital, Athens, Greece, [11]Department Of Endocrinology, Police Medical Centre, Thessaloniki, Thessaloniki, Greece, [12]Department Of Internal Medicine, 424 General Military Training Hospital, Thessaloniki, Greece, [13]1st Propedeutic Department Of Medicine, School of Medicine, National and Kapodistrian University of Athens, Laiko Hospital, Athens, Greece

Background and Aims : Elevated triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) and TyG index (TyG=[Ln[TRG (mg/dL) x Glc (mg/dL)/2]) have been associated with high risk of atherosclerotic cardiovascular disease (ASCVD). We examined the association between these markers and the prevalence of ASCVD in patients with FH.

Methods: A total of 1589 adult non-diabetic patients from the HELLAS-FH registry were evaluated. Patient demographics, lipid profile, and cardiovascular profile were recorded. The TG/HDL-C index was calculated, as well as the TyG index for the subgroup with available fasting Glc.

Results: Patients were 50.3% male and aged 49.9 ± 14.4 years. Pre-treatment lipid profile was: TCHOL 326 ± 90 mg/dL, LDL-C 246 ± 89 mg/dL, HDL-C 52 ± 14 mg/dL and TG 128 (94-174) mg/dL. TG/HDL-C ratio was higher in patients with ASCVD [3.2 (2.1-4.7)] compared with those without [2.4 (1.6-3.6); $p<0.001$]. This difference remained significant ($p<0.001$) after adjustment for major cardiovascular risk factors such as gender, age, hypertension, body mass index, low-density lipoprotein cholesterol, and smoking. In addition, TyG index (8.8 ± 0.5) was higher in individuals with ASCVD compared with those without (8.6 ± 0.5; $p=0.001$). However, this difference did not retain significance after adjustment.

Conclusions: In non-diabetic patients with a clinical diagnosis of FH, the TG/HDL-C ratio is independently associated with prevalent ASCVD.

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ONE YEAR FOLLOW-UP OF PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA: PRELIMINARY DATA FROM THE HELLAS-FH REGISTRY

POSTER VIEWING SESSION

Christos Rizos[1], George Liamis[1], Anastasia Garoufi[2], Ioannis Skoumas[3], Loukianos Rallidis[4], Genovefa Kolovou[5], Konstantinos Tziomalos[6], Emmanuel Skalidis[7], Vasileios Kotsis[8], Vaia Lambadiari[9], Panagiotis G. Anagnostis[10], Ioanna Dima[3], Estela Kiouri[4], Vana Kolovou[5], Georgios Polychronopoulos[6], Evangelos Zacharis[7], Christina Antza[8], Evangelos Liberopoulos[11]
[1]Department Of Internal Medicine, University of Ioannina, Ioannina, Greece, [2]Department Of Pediatrics, Medical School, National and Kapodistrian University of Athens, B' Pediatrics Clinic, General Children's Hospital "Pan. & Aglaia Kyriakou", Athens, Greece, [3]Cardiology Clinic, Hippokration General Hospital, Athens, Greece, [4]Department Of Cardiology, Medical School, National and Kapodistrian University of Athens, Attikon University General Hospital, Athens, Greece, [5]Metropolitan Hospital, Cardiometabolic Center, Lipid Clinic, LA apheresis Unit, Athens, Greece, [6]1st Propedeutic Department Of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece, [7]Cardiology Clinic, University General Hospital of Heraklion, Heraklion, Greece, [8]Department Of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Papageorgiou General Hospital Thessaloniki, Thessaloniki, Greece, [9]2nd Propaedeutic Internal Medicine Department And Diabetes Research Unit, National and Kapodistrian University of Athens, Attikon University General Hospital, Athens, Greece, [10]Department Of Endocrinology, Police Medical Centre, Thessaloniki, Thessaloniki, Greece, [11]1st Propedeutic Department Of Medicine, School of Medicine, National and Kapodistrian University of Athens, Laiko Hospital, Athens, Greece

Background and Aims : To report follow-up findings in patients from the HELLAS-FH registry.

Methods: We evaluated 139 adult patients with a clinical diagnosis of FH with a median follow-up of 12 months. Patient demographics, lipid profile, treatment and atherosclerotic cardiovascular disease (ASCVD) profile were recorded.

Results: Patients were 53.2% male and aged 48.8±13.8 years. A proportion of 67.6% were receiving hypolipidemic treatment at enrollment and lipid profile was: total cholesterol (TCHOL) 215±60 mg/dL, low-density lipoprotein cholesterol (LDL-C) 141±55 mg/dL, high-density lipoprotein cholesterol (HDL-C) 49±13 mg/dL and triglycerides (TGs) 112 (77-156) mg/dL. Only 5.2% of on-treatment patients were on LDL-C target. After a median follow-up of 12 months (IQR 4-31 months), all patients were receiving hypolipidemic treatment. Specifically, 33.3% of patients started statin therapy, 22.7% had their statin therapy uptitrated, in 35.5% ezetimibe was added and in 14.2% a PCSK9i was prescribed. Follow-up lipid profile was: TCHOL 178±51 mg/dL, LDL-C 107±47 mg/dL, HDL-C 53±16 mg/dL and TGs 100 (70-136) mg/dL. At follow-up, 4.2% of patients were on target for LDL-C goal. Regarding ASCVD, 1 non-fatal myocardial infarction and 3 new diagnoses of peripheral arterial disease were recorded.

Conclusions: After a median follow-up of 12 months, intensification of hypolipidemic therapy accompanied by an improvement of lipid profile was observed. Despite that, achievement of LDL-C target remained poor. A new ASCVD event was recorded in 2.8% of patients.

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CARDIOVASCULAR DISEASE IN CHILDREN WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Julia Lischka[1], Margot Baumgartner[1], Charlotte De Gier[1], Andrea Willfort-Ehringer[2], Susanne Greber-Platzer[1]
[1]Department Of Pediatrics And Adolescent Medicine, Medical University of Vienna, Vienna, Austria, [2]Department Of Angiology, Medical University of Vienna, Vienna, Austria

Background and Aims : Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disorder leading to extremely increased LDL-C, resulting in high risk for cardiovascular disease (CVD) in early childhood. Earliest initiation of lipid lowering treatment is required to prevent premature CVD. Therapy consists of fat-reduced diet, lipid-lowering medication (LLM), and additional lipid apheresis (LA) in severe cases. The aim of the study was to evaluate cardiovascular pathology in children with hoFH.

Methods: Retrospective analysis (2012-2021) on five children with hoFH aged 9 to 10 years. Cardiovascular status was evaluated with echocardiography, ECG, carotid ultrasound measuring intima-media thickness (IMT) and coronary CT (cCT).

Results:

Table 1 Lipid levels with max. LLM (without LA) and with max. LLM plus LA, before (Pre-LA) and after LA (Post-LA), respectively.

Patient	LDL-C [mg/dL] on max. LLM	LDL-C [mg/dL] Steady state Pre-LA	LDL-C [mg/dL] Steady state Post-LA
1	688.8[A]	411.2 (288.8-564.6)	153.5[C] (113.8-227.8)
2	535.4 (534.8-536.0)	337.2 (265.0-443.0)	104.7[C] (84.8-151.6)
3	597.1 (521.2-732.0)	244.2[B] (223.0-287.4)	81.0[B] (67.4-99.0)
4	742.0[A]	251.7 (205.0-297.4)	76.4[C] (57.2-94.8)
5	193.0[AD]	no LA	no LA

Values are displayed as means, minimum and maximum over a period of 3 months
[A]only one measurement available, [B]biweekly intervals, [C]weekly intervals, [D]no LA

All children needed LLM, and four children additional LA with weekly or biweekly intervals starting at the age of 3 to 5 years, due to extremely elevated LDL-C levels, which reduced LDL-C by >60% (Table 1). Three children had increased IMT. After initiation of LA, IMT improved or remained stable. Initially, cCT showed regular cardiac results. Despite LA, after five to six years three children developed mild calcification of the aorta ascendens or the aortic valve. Moreover, one ten-year-old girl developed a severe aortic valve calcification with high-grade stenosis (aortic jet velocity 3.8 m/s), now under consideration for cardiac surgery.

Conclusions: We could show that intensive LLM and LA starting at early age seem to prevent rapid coronary atherosclerosis; nevertheless, aortic calcification (including the valve) may occur. Regular screening for CVD in hoFH children is crucial.

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PREVALENCE OF FAMILIAL HYPERCHOLESTEROLEMIA IN EGYPTIAN PATIENTS WITH ACUTE CORONARY SYNDROME

POSTER VIEWING SESSION

Hesham S. El-Din, Essam B. Husein, Dalia El Remisy, Hossam A. Mahrous
Cardiology, Faculty of Medicine, Cairo University, Cairo, Egypt

Background and Aims : Familial hypercholesterolemia (FH) is an autosomal co-dominant monogenic disorder causing premature CVD. We aimed to assess the prevalence of FH, dyslipidemia pattern, and management strategies in ACS patients.

Methods: 2000 ACS patients admitted to Cairo university hospitals were included. Two common algorithms for diagnosis of clinical FH were used: the Dutch Lipid Clinic Network (DLCN) to detect possible (score 3–5 points) or probable/definite FH (>5 points), and the Simon Broome Register (SBR) to detect possible or definite FH. TC, HDL-C, and TG were measured within 24 hours of admission and LDL-C was estimated using Friedewald formula.

Results: 80 patients (4%) had probable/definite FH (PDFH) and 467 (23.4%) had possible FH (PFH) using the DLCN. The SBR identified one patient (0.05%) with definite FH and 238 (11.9%) with PFH. Among 808 (40.4%) patients with premature ACS, the DLCN identified 63 (7.8%) with PDFH and 253 (31.3%) with PFH. For patients with premature ACS, family history of premature CVD, and LDL-C ≥ 160 mg/dl, PDFH prevalence reached 67.8% using the DLCN with high specificity (99.1%) and negative predictive value (97.9%) of the combined three factors for PDFH detection. TC, LDL-C, and TG levels were elevated in 28.5%, 41%, and 39.9% of patients respectively and 62.2% had low HDL-C. Statins were used in 520 patients (26%) at presentation. A high-intensity statin was prescribed for 99.4% of the patients at discharge. Coronary angiography was performed for 74.3% of patients.

Conclusions: A clinical diagnosis of PDFH and PFH is common among Egyptian ACS patients, particularly those with premature ACS.

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INCREASED LP(A) LEVELS IN A CARIBBEAN FAMILY. CASE REPORT AND LITERATURE REVIEW.

POSTER VIEWING SESSION

Demian Arturo Herrera Morban, Maxima Mendez
Lipid Unit, HS Medical Center, Distrito Nacional, Dominican Republic

Background and Aims : Lipoprotein (a) (Lp(a)) is a macromolecule synthesized by the liver, whose serum levels are determined genetically by the LPA gene (1-4). It's associated with increased atherosclerotic risk (1, 2) when levels rise above 50 mg/dl independently of ethnicity (5). The cardiovascular risk (CVR) related to Lp(a) are associated with LDL-C. In patients with familiar hypercholesterolemia, the elevation of Lp(a) increase the risk of cardiovascular event at an early age (6,7). Levels above 180 mg/dl of Lp(a) are considered very high-risk patients (8).

Methods: Patient 0 is a 38-year male seeking a cardiological evaluation without cardiovascular history, no relevant comorbid conditions. As protocol, a lipid profile is indicated, and reports values described in TABLE 1. Screening is indicated for the family. Vascular trace for subclinical atherosclerosis is normal. Father (72y) has arterial hypertension and history of a transient ischemic attack on June 2020, no related morbidities in the family.

Results: Levels above 50 mg/dl have been associated with CVR (5). This family has increased levels but only one has presented a cardiovascular event, because of his age an association between the event with the Lp(a) cannot be established. In a Chinese study isolated increased Lp(a) levels above 300 mg/dl increase CVR (1.37) when compared to a normal population (9). European guidelines suggest Lp(a) screening once in a lifetime (10), American guidelines suggest screening in families with background of cardiovascular event below age 55, familiar hypercholesterolemia

(11).

Table 1: Lipid profile report

	Age (y)	Gender	Lp (a) (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	Apo A (mg/dl)	Apo B (mg/dl)
Patient 0	38	M	233	30	81	132	137	117	94
Offspring (1)	18	M	85	41	83	134	84	103	59
Offspring (2)	4	M	101	40	118	161	41		
Offspring (3)	4	M	102	41	114	157	51	111	82
Offspring (4)	2	F	114	41	117	162	61		
Sibling (2)	33	F							
Offspring (1)	8	F	4	69	61	148	48	168	
Sibling (3)	33	M	69	55	101	159	50	130	71
Parent (1)	72	M	77	44	139	197	103	129	
Parent (2)	66	F	108	54	184	256	93	155	

Conclusions: Statistical data for dyslipidemias in Dominican Republic is lacking.

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MOLECULAR DIAGNOSIS OF GENETIC DYSLIPIDAEMIAS BY NEXT GENERATION SEQUENCING

POSTER VIEWING SESSION

Beatriz Miranda[1], Ana Catarina C. Alves[1,2], Mafalda Bourbon[1,2]
[1]Departamento De Promoção Da Saúde E Doenças Não Transmissíveis, Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisboa, Portugal, [2]Bioisi – Biosystems & Integrative Sciences Institute, Faculdade de Ciências, Universidade de Lisboa, Lisboa, Portugal

Background and Aims : Dyslipidaemia is a group of disorders of lipid metabolism characterized by abnormal lipid concentrations and are associated to serious conditions that can be prevented by early identification of patients. This project aims to characterize 96 Portuguese patients with clinical diagnoses of 3 main familial dyslipidemias.

Methods: Molecular analysis (19 genes of lipid metabolism) was performed by Next Generation Sequencing. NGS Library was run on an Illumina NextSeq.

Results: A final diagnosis was reached in 35/96 cases. Twenty-three index cases (IC) were diagnosed with Familial Hypercholesterolaemia with 21 pathogenic/likely pathogenic different variants being identified in *LDLR*, *APOB*, and *PCSK9* genes. We found one IC carrier of a pathogenic variant in *ABCG8* associated with sitosterolemia. Fifteen detected variants were not described yet in *APOB*, *LDLR*, *ABCG8*, and *ABCG5* genes. Three IC were diagnosed with familial hypocholesterolaemia (FHBL): one true homozygous, one compound heterozygous, and one heterozygous, all for different pathogenic variants in *APOB.* Regarding hypertriglyceridemia, two IC were diagnosed with Familial Chylomicronaemia Syndrome (FCS): both true homozygous for pathogenic variants in *GPIHBP1* and *LPL* genes. Seven IC inherited pathogenic variants in heterozygosity in genes associated with FCS that have been associated with Multifactorial Chylomicronemia Syndrome. Furthermore, we found one true homozygous IC for a pathogenic variant in *GPD1* gene associated with Autosomal Recessive

Hypertriglyceridemia.

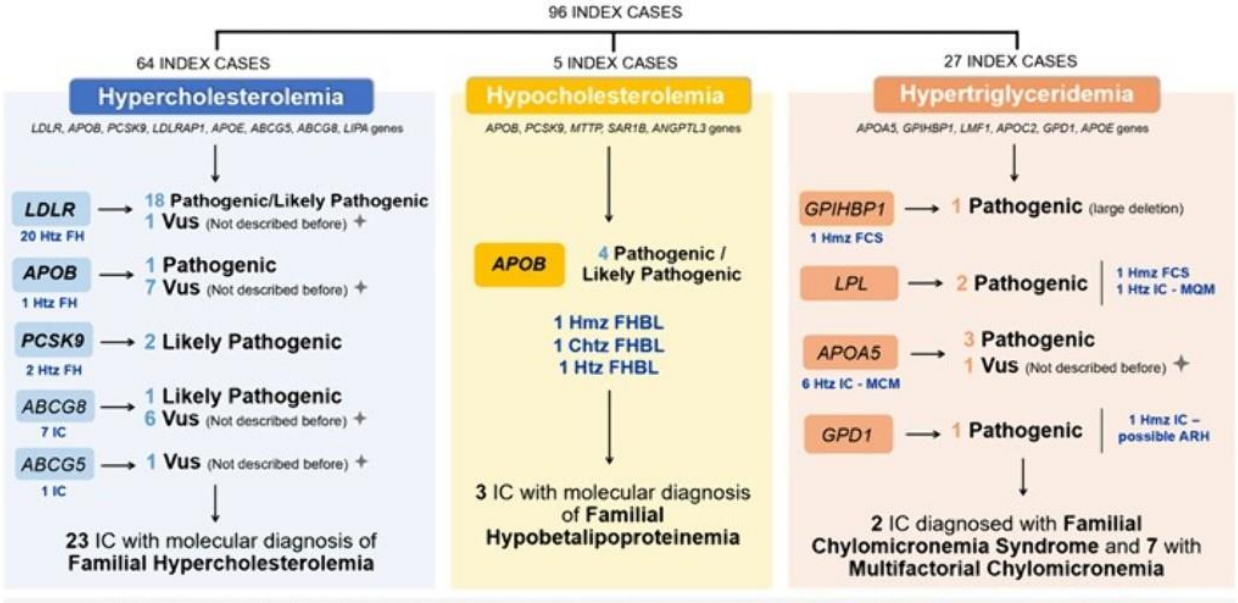

Figure 1 – summary of most relevant molecular results (clinical significance and number of variants detected) for hypercholesterolemia, hypocholesterolemia and hypertriglyceridemia panels, for 96 index individuals. VUS, variant of uncertain significance; FH, Familial Hypercholesterolemia; FHBL, Familial hypobetalipoproteinemia; FCS Familial Chylomicronemia Syndrome; MCM, Multifactorial Chylomicronemia; ARH, autosomic recessive hypertriglyceridemia; Htz, Heterozygous; Chtz, compound heterozygous; Hmz, homozygous; ✦Functional studies will be performed. Genes indicated in bold-type are associated with autosomal dominant or codominant disorders.

Conclusions: This project contributed to a personalized diagnosis and treatment of Portuguese individuals improving patients' prognosis. Since several variants of uncertain significance were found and might constitute a genetic cause of dyslipidemia, functional studies will be essential to investigate their impact.

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CLINICAL SIGNIFICANCE OF LOW-DENSITY LIPOPROTEIN-TRIGLYCERIDES IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Masatsune Ogura[1], Yasuki Ito[2], Mariko Harada-Shiba[3]
[1]Metabolism And Endocrinology, Eastern Chiba Medical Center, Togane, Japan, [2]Vaccine & Diagnostics R&d Department, Denka Co., Ltd, Gosen, Japan, [3]Molecular Pathogenesis, National Cerebral and Cardiovascular Center Research Institute, Suita, Japan

Background and Aims : Association between plasma LDL-triglycerides (LDL-TG) levels and incident atherosclerotic cardiovascular disease (ASCVD) has been reported in a large cohort study. We hypothesized that plasma LDL-TG levels are increased in patients with familial hypercholesterolemia (FH) due to delayed LDL catabolism and it involves the development of atherosclerosis. The aim of this study was to investigate clinical significance of plasma LDL-TG levels in patients with FH.

Methods: Among patients followed up in the outpatient clinic of our hospital, 523 (390 FH and 133 non-FH) consecutive patients were enrolled in this cross-sectional study. LDL-TG were determined by fully automated detergent-based homogeneous methods. Carotid atherosclerosis was evaluated by high-resolution ultrasonography.

Results: Although plasma total TG levels were lower in FH patients than those in non-FH patients, LDL-TG/total TG ratio were significantly higher in FH patients, suggesting LDL receptor pathway is important for determining plasma LDL-TG levels. In statin treated FH patients (N=250), increased LDL-TG levels were associated with presence of corneal arcus (p=0.0015), Achilles tendon thickness (p=0.028), and presence of prior ASCVD events (p=0.0319). LDL-TG was also positively associated with maximum carotid intima-media thickness (p=0.0022). This relationship remained significant after adjustment for cardiovascular risk factors (beta coefficient=0.31; 95% confidence interval, 0.09–0.53; P = 0.0069).

Conclusions: Plasma LDL-TG levels were increased and associated with atherosclerosis in statin treated FH. In view of residual risks after treatment with statins, it remains to be investigated whether therapies targeting LDL-TG could be effective for preventing atherosclerosis in FH.

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POLYGENIC RISK FOR FUTURE CORONARY ARTERY DISEASE EVENTS IN FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

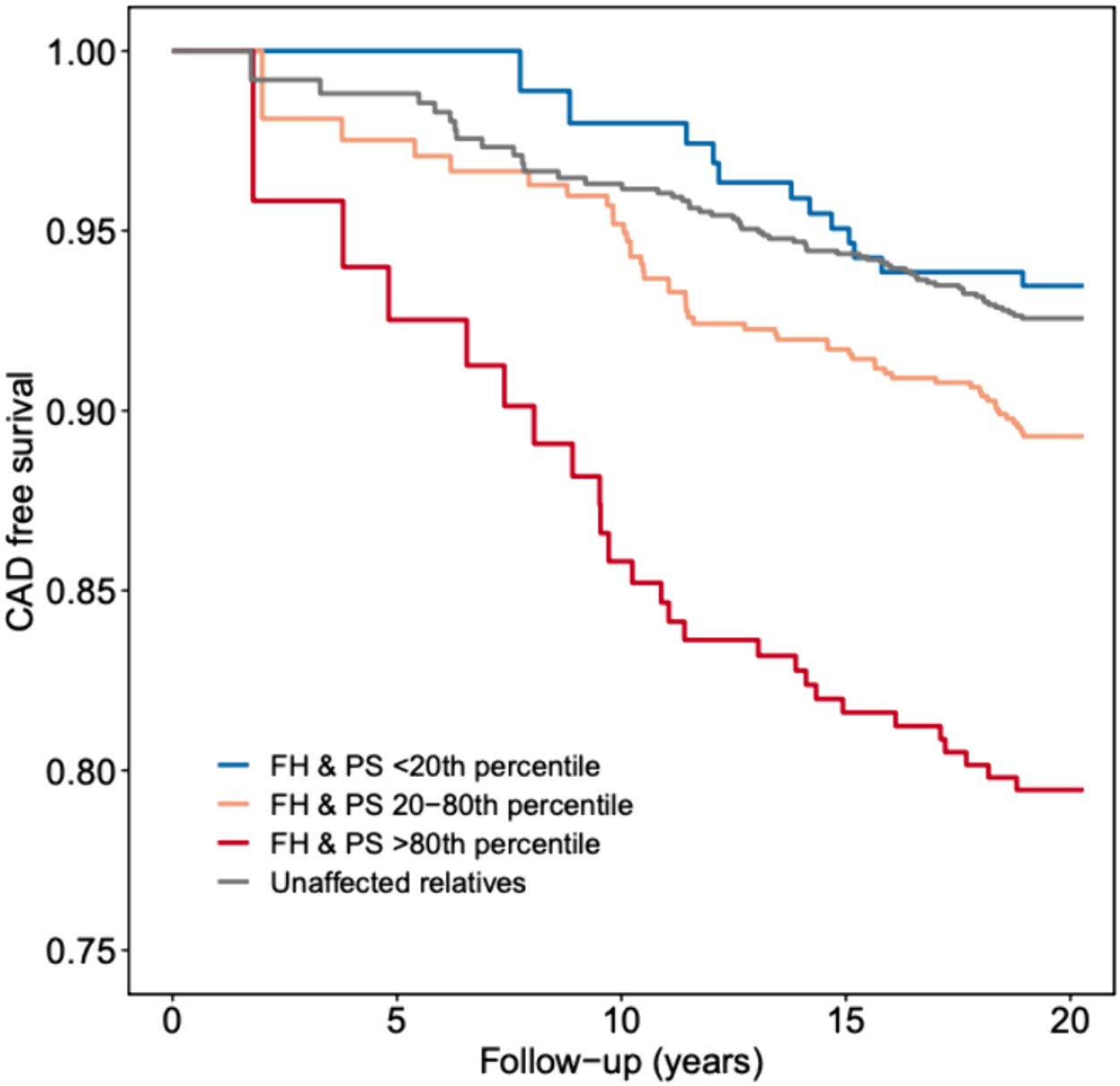
Laurens F. Reeskamp[1,2,3], Injeong Shim[2,3], Jacqueline Dron[2,3], Shirin Ibrahim[1], Tycho R. Tromp[1], Aniruddh P. Patel[2,3], Barbara A. Hutten[4], Erik S. Stroes[1], G. K. Hovingh[1,5], Amit V. Khera[2,3]
[1]Department Of Vascular Medicine, Amsterdam UMC, Amsterdam, Netherlands, [2]Cardiovascular Disease Initiative, Broad Institute of MIT and Harvard, Cambridge, United States of America, [3]Center For Genomic Medicine, Massachusetts General Hospital, Boston, United States of America, [4]Epidemiology And Biostatistics, Amsterdam UMC - Location AMC, Amsterdam, Netherlands, [5]A/s, Novo Nordisk, Bagsværd, Denmark

Background and Aims : A considerable proportion of coronary artery disease (CAD) risk is attributable to an individual's polygenic background. We set out to evaluate whether and to which extent this polygenic risk has an impact on future CAD risk in a large cohort of patients with Familial Hypercholesterolemia (FH).

Methods: We generated a previously developed polygenic score (PS; >1 million SNPs) by means of the Illumina Global Screening Array in heterozygous FH-patients from the Dutch cascade-screening program and used hospital records to ascertain the CAD endpoint (myocardial infarction, PCI, CABG, angina pectoris, or other forms of atherosclerotic CAD). Cox-regression with covariates for sex, age, and five principal components for ancestry was used to assess risk for future CAD events.

Results: Among 1315 FH-patients, mean age 42.1 (SD±14.9), 52.9% female, mean LDL-C 213.7 (±72.7) mg/dL, 84 CAD events occurred during a median follow-up of 10.2 [IQR 7.3-14.6] years. The HR for CAD compared to age and sex-matched unaffected relatives was 1.49 (95%-CI: 1.06-2.10). HR for CAD was 1.35 (1.07-1.70) per SD PS, and 2.62 (1.27-5.39) for FH-patients in the top PS quintile compared to the lowest quintile. The estimated 10-year CAD event rate was 7.0% and 2.2% in the top quintile PS with LDL-C >190 mg/dL and LDL-C <130 mg/dL, respectively. The results were validated in 627 FH-patients in the UK

biobank.



Conclusions: Risk for future CAD events in FH is modified by polygenic risk for CAD and appears to be offset by lower LDL-C levels. Genotyping of FH could include polygenic risk assessment for risk stratification.

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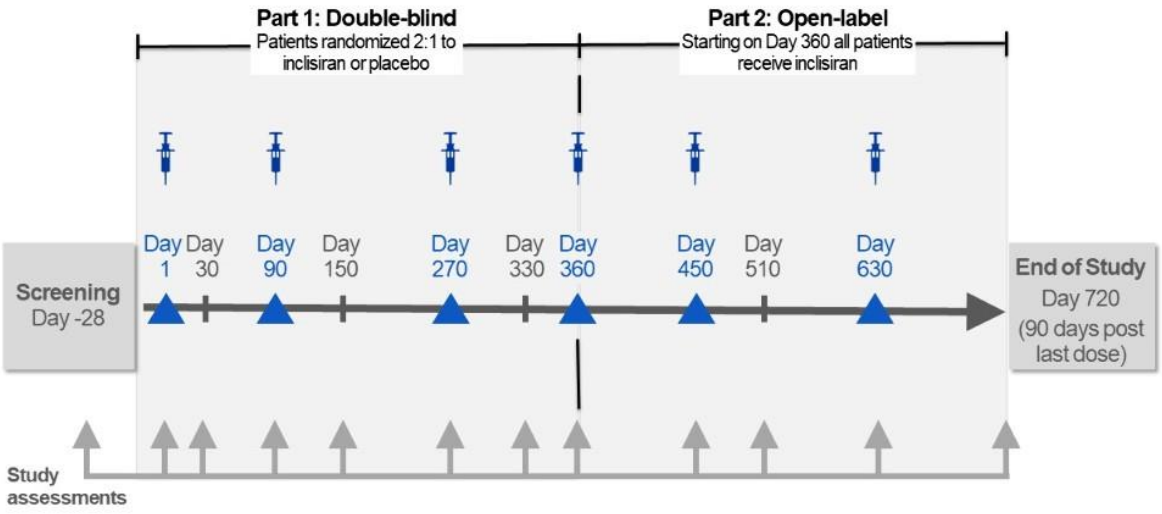
RATIONALE AND DESIGN OF TWO TRIALS ASSESSING EFFICACY, SAFETY AND TOLERABILITY OF INCLISIRAN IN ADOLESCENTS WITH HOMOZYGOUS AND HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLAEMIA

POSTER VIEWING SESSION

M.D. Reijman[1], Anja Schweizer[2], Amy L.H. Peterson[3], Eric Bruckert[4], Christian Stratz[2], Joep C. Defesche[5], Robert A. Hegele[6], Albert Wiegman[1]
[1]Department Of Paediatrics, Amsterdam UMC - Location AMC, Amsterdam, Netherlands, [2]Clinical Development, Novartis Pharma AG, Basel, Switzerland, [3]Department Of Pediatrics, Division Of Pediatric Cardiology, University of Wisconsin School of Medicine and Public Health, Madison, United States of America, [4]Endocrinology And Metabolism, La Pitié-Salpětriére Hospital, Paris, France, [5]Department Of Clinical Genetics, Amsterdam UMC - Location AMC, Amsterdam, Netherlands, [6]Department Of Medicine, Schulich School Of Medicine And Dentistry, Western University, London, Canada

Background and Aims : Inclisiran is a small interfering RNA molecule that reduces low-density lipoprotein cholesterol (LDL-C) by inhibition of proprotein convertase subtilisin/kexin type 9. This subcutaneous, twice-yearly administered agent has been shown to effectively and safely lower LDL-C in adult patients with established atherosclerotic cardiovascular disease, adults with high risk for atherosclerotic cardiovascular disease, as well as in adults with heterozygous familial hypercholesterolaemia. With the current, limited treatment options available to reach treatment goals in children with severe heterozygous familial hypercholesterolaemia, homozygous familial hypercholesterolaemia, or statin intolerance, inclisiran could be a valuable new therapeutic option. The objective of these ongoing studies is to investigate the efficacy, safety, and tolerability of inclisiran in adolescents diagnosed with homozygous familial hypercholesterolaemia (ORION-13) or heterozygous familial hypercholesterolaemia (ORION-16).

Methods:



ORION-13 and ORION-16 are both two-part (1 year double-blind inclisiran versus placebo / 1 year open-label inclisiran, Figure 1) multicentre trials including adolescents aged 12 to <18 years diagnosed with familial hypercholesterolaemia. ORION-13 will include approximately 12 participants diagnosed with homozygous familial hypercholesterolaemia and ORION-16 will include approximately 150 participants diagnosed with heterozygous familial hypercholesterolaemia. The primary endpoint is the percentage change in LDL-C from baseline to day 330. Other efficacy and safety endpoints include: changes in other lipid parameters and adverse events, and also exploratory endpoints, such as individual responsiveness of the participants and change in LDL-C according to the type of underlying causal mutation.

Results: Not applicable yet

Conclusions: Not applicable yet

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

UNUSUAL REACTION TO PCSK9 INHIBITORS AND LIPOPROTEIN APHERESIS: A MIND-BOGGLER CLINICAL CASE

POSTER VIEWING SESSION

Miguel Saraiva[1], Pedro Palma[2], José Alexandre Queirós[1], Isabel Palma[1]
[1]Endocrinology, Centro Hospitalar Universitário do Porto - Hospital de Santo António, Universidade do Porto, Portugal, [2]Cardiology, Centro Hospitalar Universitário de São João, Porto, Portugal

Background and Aims : Heterozygous familial hypercholesterolemia is one of the most common genetic disorders and patients often require PCSK9 inhibitors to reach LDL-c target values. When these medications are not effective enough or not well-tolerated, treatment with LDL apheresis should be implemented.

Methods: Not applicable

Results: A 42-year-old woman was referred to our department because of a poorly controlled hypercholesterolemia despite being on maximal doses of statin+ezetimibe. Her DLCN score was >8points and a pathogenic mutation was identified. Evolocumab was started but after the first dose the patient reported transient headaches, nausea and myalgia. After the second dose, she developed self-limited headaches, dizziness, myalgia and an acute confusional state with spatial disorientation and horizontal binocular diplopia. Evolocumab was then suspended but 6months later her cholesterol levels had risen to alarmingly high levels and the drug was reintroduced. Once again, a worrisome confusional syndrome occurred. Alternatively, she started lipoprotein apheresis with the DALI technique. During the first session, the patient reported abdominal discomfort, airway obstruction and thoracic pain which reverted with intravenous steroids. During the next sessions, the same symptoms occurred despite pretreatment with antihistamines and steroids. As so, we tried changing the apheresis technique to MONET. Since then, no adverse effects were reported.

Conclusions: Although extremely rare, the association between PCSK9 inhibitors and neurocognitive symptoms has been described. They should be monitored in patients taking evolocumab. As happens with hemodialysis, dialyzer reactions may also occur in patients undergoing LDL apheresis and a different technique should be sought when adverse reactions occur with the standard DALI technique.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

FAMILIAL HYPERCHOLESTEROLAEMIA IN THE CARDIOLOGY WARD

POSTER VIEWING SESSION

William G. Simpson[1], Calvin Mackinnon[2], Rita Patel[3], Zofia H. Miedzybrodzka[4]
[1]Clinical Biochemistry, Aberdeen Royal Infirmary & University of Aberdeen, Aberdeen, United Kingdom, [2]General Practice, NHS Grampian, Aberdeen, United Kingdom, [3]Cardiology, Aberdeen Royal Infirmary, Aberdeen, United Kingdom, [4]Medical Genetics, Aberdeen University, Aberdeen, United Kingdom

Background and Aims : To estimate the potential prevalence of Familail Hypercholesterolaemia in patients presenting with Myocardial Infarction.

Methods: A retrospective audit of MI patients in NHS Grampian during the 3-year period 2017-2020. Lipid criteria for consideration of FH diagnosis was cholesterol >7.5 mmol/L and/or LDL-c >4.9 mmol/L. The dataset did not include all elements of the Wales FH genotyping (WFHG) score, but available data (age at MI plus lipids) were also used to help identify possible FH (genetic testing is recommneded if score >=6)

Results: In the period 2017-2020, 2855 patients had MI diagnosed; 757 were aged <60. From epidemiological studies, we estimate that 16 patients have FH. 92/757 had raised lipids without secondary causes, 20 with WFHG >=6. Genetic testing had been performed in 14 patients; 4 (including 1 FH) known prior to the event, and 10 (including 1 variant of unknown clinical significance) performed after the event. Six individuals were previously known to the lipid clinic (including the FH and 3 others FH tested) and 8 had been referred since the event (including 3 FH tested). Genetic testing had not been performed in 11 with WFHG >=6; a further 34 of the 92 dyslipidaemic patients could have WFHG >=6 in the presence of a family history or clincal signs..

Conclusions: It is known that FH is being underdiagnosed in the general population but, surprisingly, the rate of FH diagnosis in people who have experienced premature myocardial infarction is also low.There is an opportunity for improving FH case finding in this group of patients.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-05 Inherited dyslipidemias*

NGS TESTING OF PATIENTS WITH DYSLIPIDEMIA REVEALED TWO PATIENTS WITH A HOMOZYGOUS GPIHBP1 VARIANT

POSTER VIEWING SESSION

Urša Šuštar[1,2], Urh Groselj[1], Barbara Jenko Bizjan[1], Iqbal Khan[3,4], Sabeen Khan[4], Saeed Shafi[4], Jernej Kovač[2], Tadej Battelino[1], Fouzia Sadiq[4]
[1]Department Of Endocrinology, Diabetes, And Metabolic Diseases, University Children's Hospital, UMC Ljubljana, Ljubljana, Slovenia, [2]Clinical Institute For Special Laboratory Diagnostics, University Children's Hospital, UMC Ljubljana, Ljubljana, Slovenia, [3]Department Of Vascular Surgery, Shifa International Hospital, Islamabad, Pakistan, Islamabad, Pakistan, [4]Directorate Of Research, Shifa Tameer-e-Millat University, Islamabad, Pakistan, Islamabad, Pakistan

Background and Aims : Due to unspecific symptoms rare dyslipidemias are frequently diagnosed later in life and hence these are misdiagnosed, overlooked, and undertreated. Better guidelines for the recognition of rare dyslipidemias are urgently required.

Methods: Genomic DNA was isolated from 80 Pakistani patients with hypercholesterolemia and/or triglyceridemia. Next Generation Sequencing (NGS) was employed for genetic screening.

Results: NGS testing revealed the presence of a homozygous missense genetic variant p.Cys77Tyr (c.230G>A, NM_178172) in exon 3 of the *GPIHBP1* (glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1) gene in two of the patients. The patients were 4 and 35 years old. Both patients had elevated total cholesterol (224 and 263 mg/dL) and triglyceride levels (224 and 2883 mg/dL). One of the patients with hypertriglyceridaemia had cholesterol deposits at the hard palate, eruptive xanthomas, lethargy, poor appetite, and mild splenomegaly whilst the other one did not have any clinical symptoms.

Conclusions: Patients with extreme concentrations of plasma low-density lipoprotein cholesterol and triglycerides should be recognized as candidates for genetic testing for rare dyslipidemias. One of the rare dyslipidemias that should not be overlooked is chylomicronemia, a disorder due to variant/s in the *GPIHBP1* gene.

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FAMILIAL HYPERCHOLESTEROLEMIA CAUSING GENETIC MUTATIONS IDENTIFIED IN VILNIUS UNIVERSITY HOSPITAL SANTAROS KLINIKOS IN 2019-2021

POSTER VIEWING SESSION

Viktoras Sutkus[1], Žaneta Petrulionienė[2,3], Odeta Kinčinienė[2,4], Vilija Černiauskienė[2,4], Egle Skiauteryte[2,3], Urtė Aliošaitienė[2,3], Rimantė Čerkauskienė[1,2]
[1]Coordinating Centre For Rare Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [2]Faculty Of Medicine, Vilnius University, Vilnius, Lithuania, [3]Center Of Cardiology And Angiology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, [4]Paediatrics Centre, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Background and Aims : Familial hypercholesterolemia (FH) is one of the main causes of atherosclerotic cardiovascular diseases. Due to lack of research and systematic patient search, exact prevalence of FH and pathogenic genes in Lithuania is unknown. By the end of 2019 families at high risk for FH were invited for genetic screening in Vilnius University Hospital Santaros Klinikos. The aim of this study was to review the prevalence of pathogenic genes in screened patiens with FH.

Methods: Patients with suspected diagnosis of FH who were referred to Vilnius University Hospital Santaros Klinikos were invited to participate in the genetic screening for FH. Those who agreed had their blood sample taken on a dried blood spot card which was then sent to a genetics laboratory. Next generation sequencing was used to identify FH causing mutations (LDLR, APOB, PCSK9, LDLRAP1).

Results: A total of 126 (71 female, 55 male) patients have been screened for FH. 50 (39,7%) have had FH diagnosis confirmed genetically (26 female, 24 male). 31 patient (62%) had a mutation in the LDLR gene and 19 (38%) had a mutation in APOB gene. There were no other pathogenic genes deteceted. 14 patients (28%) had variants of uncertain significance (VUS) identified – 4 patients (8%) with LDLR gene variants and 10 patients (20%) with APOB gene variants.

Conclusions: The two pathogenic genes identified in the screened group were LDLR and APOB, with LDLR causing the majority of mutations. The large number of VUS identified indicates the need to further study this patient group.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-06 Gender and cardiovascular risk*

HIGHER TRIGLYCERIDE TO HDL CHOLESTEROL RATIO IN MEN COMPARED TO PRE-MENOPAUSAL WOMEN IN ARABIC POPULATION.

POSTER VIEWING SESSION

Mustafa Al Hinai[1], Fahad Zadjali[2]
[1]Family Medicine And Public Health, Sultan Qaboos University Hospital, Muscat, Oman, [2]Clinical Biochemistry, SULTAN QABOOS UNIVERSITY, Khodh, Oman

Background and Aims : Triglyceride to HDL (TG:HDL)is a surrogate marker for insulin resistance in elderly population. Cardiovascular disease (CVD)risk is low in young female.However, menopause women and men have similar CVD risk.Both insulin resistance and estrogen actions suggested to contribute in the CVD risk.Previous studies showed that TG:HDL is similar in women and men in pre-menopausal age and different in menopause.In the study, we replicate similar studies in the Arabic population using ad-hoc analysis of previous studies.

Methods: we compared difference between men and women at age below 50 years old (n= 168 and 22-, respectively) and above 65 years old (n= 39 and 35, respectively). We obtained data on their TG:HDL and insulin resistant index (HOMA).

Results: Baseline comparison between men and women showed significant differences. Female had lower systolic blood pressure , fasting serum TG and TG: HDL ratio. Female had higher obesity and HDL cholesterol than men. We observed positive and significant correlation between TG:HDL ratio and HOMA-IR, r= 0.3 , P-value <0.0001. In those with age 20-50 years old, the TG:HDL was significantly lower in females (0.9 mmM TG :mmM HDL) compared to men (1.6 mmM TG :mmM HDL), P-value<0.0001. however in elderly individuals of age 65 years-old and above, the men and women had similar TG:HDL ratio.

Conclusions: The differences in premenopausal age in TG:HDL ratio, a surrogate marker of insulin resistance, suggests its associated role in the risk of cardiovascular resistance. Similar findings were observed in other ethnic groups in which the ratio is positively associated with carotid plaque.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-06 Gender and cardiovascular risk*

REPRESENTATIVENESS OF WOMEN AND RACIAL/ETHNIC MINORITIES IN RANDOMIZED CLINICAL TRIALS ON BEMPEDOIC ACID

POSTER VIEWING SESSION

Federica Fogacci[1], Davide Gori[2], Arrigo F.G. Cicero[1]
[1]Medical And Surgical Sciences Department, University of Bologna, Bologna, Italy, [2]Department Of Biomedical And Neuromotor Sciences, University of Bologna, Bologna, Italy

Background and Aims : Women and racial minorities have continued for a long time to be underrepresented in randomized clinical trials testing lipid-lowering therapies (i.e. statins, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, ezetimibe, bile acid sequestrants, fibrates, niacin, and omega-3 polyunsaturated fatty acids).
We sought to investigate presence of disparities in trials testing the new emergent lipid-lowering drug bempedoic acid (BA).

Methods: Several databases were searched with the use of a purposedly developed search strategy. To minimize the chances of missing data, the identified clinical trials were subsequently searched on http://www.clinicaltrials.gov. Original studies were included in the analysis if they met the following inclusion criteria: (i) being a clinical trial with either multicentre or single-centre design and (ii) having an appropriate controlled design for BA.

Results: Considering together, the overall participation rate and the mean participation rate across the clinical studies, men, whites and non-Hispanic/Latinos were sufficiently represented compared with their proportion in the disease population. Non-whites and Asians were underrepresented. Women, blacks and Hispanic/Latinos were from adequately to over-represented across clinical trials, though in the pooled population their portion was lower than their share of the disease population.

Conclusions: Further efforts are needed to enhance the representativeness of clinical trials according to race and sex and ensure complete information about efficacy and safety of treatment with BA.

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SEX DIFFERENCES IN EFFICACY AND SIDE EFFECTS OF PROPROTEIN CONVERTASE SUBTILISIN / KEXIN 9 (PCSK9) INHIBITORS IN REAL WORLD DATA

POSTER VIEWING SESSION

Annette M.H. Galema-Boers[1], Kim Steward[1,2], Janneke W.C.M. Mulder[1], Jeanine E. Roeters Van Lennep[1]
[1]Internal Medicine, Erasmus MC, Rotterdam, Netherlands, [2]Department Of Internal Medicine, Erasmus Mc, University Medical Centre Rotterdam, Rotterdam, Netherlands

Background and Aims : Proprotein convertase subtilisin/Kexin 9 (PCSK9) effectively reduce low-density lipoprotein (LDLC) and have a favorable safety profile. Previously FOURIER data showed that LDLC reduction was lower in women compared to men. The aim of this study was to assess efficacy and safety in women and men who use PCSK9 inhibitors in real-world setting.

Methods: In this prospective registry of all consecutive patients started with a PCSK9 inhibitor at a lipid clinic of a university hospital. We collected clinical information, including baseline and follow-up mean LDLC levels at 6 months after initiation of PCSK9 inhibitor treatment. Side effects, injection site reactions and drug discontinuation were recorded.

Results: We analyzed 335 patients (154 women), mean age of 58±11 years. Women were older (60 vs 57 yrs P=0.03) and had less often cardiovascular events (58% vs 71% P<0.01). Women had higher baseline LDLC levels compared to men (4.8 vs 4.1 mmol/L, P<0.001) and higher on-treatment LDLC levels after 6 months (2.2 vs 1.6 mmol/L, P<0.001). LDLC reduction was 58%±19%. Women had lower LDLC reduction compared to men (53% vs 61% *P<0.001*). Women more often reported side effects than men (55% vs 45% P=0.03, while injection site reactions (10% vs 6%, P=NS) and drug discontinuation (6%vs 8%, P=NS) were similar.

Conclusions: In line with the FOURIER study, we found that women had lower LDL-C reduction compared to men after initiation of PCSK9 inhibition. Moreover women reported more side effects. Future research is needed to assess reasons for these sex differences.

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SMALL EXTRACELLULAR VESICLES FROM PREGNANT WOMEN WITH MATERNAL SUPRAPHYSIOLOGICAL HYPERCHOLESTEROLEMIA IMPAIR THE FUNCTION OF ENDOTHELIAL CELLS.

POSTER VIEWING SESSION

Susana Contreras-Duarte[1], Claudette Cantin[2], Lorena Carvajal[3], Rodrigo Escalona[1], Paula Gonzalez Mancilla[4], David Zapata[3], Jaime Gutierrez[1], Andrea Leiva[1]
[1]Faculty Of Health Sciences, Universidad San Sebastian, Santiago, Chile, [2]Faculty Of Medicine, Pontificia Universidad Catolica de Chile, santiago, Chile, [3]Faculty Of Biological Sciences, Pontificia Universidad Catolica de Chile, Santiago, Chile, [4]Faculty Of Medicine And Sciences, Universidad San Sebastian, Santiago, Chile

Background and Aims : Maternal total cholesterol (TC) increases during pregnancy (maternal physiological hypercholesterolemia, MPH) assuring fetal development. However, a group of women develop supraphysiological hypercholesterolemia (MSPH), which associates with fetoplacental endothelial dysfunction, among others. Remarkably, MSPH effect on small extracellular vesicles (sEVs), which cold modulate endothelial function, has not been described. Aim: quantify sEVs from plasma of pregnant women with MPH and MSPH characterizing their effect on endothelial cells.

Methods: Serum lipid levels were determined in MPH (n = 15) and MPSH (n = 15, TC>290 mg/dL) women. sEVs were isolated from plasma by ultracentrifugation. Western blots for ApoAI, ApoB100, Alix and Tsg101were performed. sEVS size and concentration were evaluated by nanotracking analysis. Uptake of PKH labeled sEVs was assayed in HMEC-1 cells. Endothelial function was estimated by tube formation assays, endothelial activation and nitric oxide synthesis in the absence or the presence of MPH or MSPH sEVs (7,5 ug/mL, in HMEC-1 cells).

Results: sEVs were not contaminated with lipoproteins. No changes in sEVs proteins were observed between groups. The concentration of sEVs was higher in the MSPH compared to MPH, the size was similar, and both were uptaked by HMEC-1. Number and length of branches was increased with sEVs from MPH and no with vesicles form MSPH. Nitric oxide levels were reduced in cells incubated with sEVs form MSPH.

Conclusions: sEVs of MSPH pregnant women are more concentrated and impair endothelial cell function. Although future studies are required for determine the cargo of these sEVs, we suggest that could modulate maternal or even fetoplacental endothelial function.

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INSULIN RESISTANCE, C-REACTIVE PROTEIN IN MEN WITH CHRONIC CORONARY ARTERY DISEASE AND PROSTATE ADENOCARCINOMA

POSTER VIEWING SESSION

Oksana Sirenko, Olexandr Kuryata
Innere Medicine 2, Dnipro state medical university, Dnipro, Ukraine

Background and Aims : The aim of the study was to evaluate the level of insulin resistance (IR), C-reactive protein in men with coronary heart disease and prostate adenocarcinoma.

Methods: 42 men with prostate adenocarcinoma and chronic coronary heart disease (CAD) were enrolled. The patients were divided into 2 groups: group I patients with CAD and concomitant prostate adenocarcinoma; group II patients with isolated CAD. Standard laboratory blood tests, lipid profile, glucose, renal and liver function tests, serum C-reactive protein (CRP), insulin, testosterone evaluation were performed.

Results: IR was established in 54.8% patients of group I and 40% patients of group II ($p<0.05$). In the group I median level of HOMA index was 3.4 [2.2; 4.9] mg/ml, CRP - 10.8 [5.8; 11.2] mg/ml, in the group II – 2.3 [1.8; 3.9] mg/ml and 6.2 [4.1; 8.3] mg/ml, respectively ($p<0.001$). Correlation relations between IR, CRP level and testosterone level were determined – $r = 0.47$ ($p <0.001$), $r = 0.42$ ($p <0.001$) respectively.

Conclusions: men with CAD and prostate adenocarcinoma are characterized by increased level of IR, CRP correlated with testosterone deficiency

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-06 Gender and cardiovascular risk*

ASSOCIATION BETWEEN CHOLESTEROL SYNTHESIS MARKERS AND BIOLOGICAL SEX IN THE HEALTHY, MIDDLE-AGED POPULATION

POSTER VIEWING SESSION

Sandra Vladimirov, Tamara Gojkovic, Aleksandra Zeljkovic, Natasa Bogavac-Stanojevic, Vesna Spasojevic-Kalimanovska
Department Of Medical Biochemistry, University of Belgrade, Faculty of Pharmacy, Belgrade, Serbia

Background and Aims : Men and women exhibit different epidemiology, manifestation, pathophysiology, and outcomes of atherosclerotic cardiovascular disease (ASCVD). An important pathophysiological feature of ASCVD is increased cholesterol synthesis. However, physiological sex differences in cholesterol synthesis remain understudied. Quantification of cholesterol biosynthesis precursors, desmosterol and lathosterol, in serum can demonstrate the status of endogenous cholesterol synthesis. We aimed to analyze desmosterol and lathosterol serum concentrations in healthy adults and their relationship with biological sex and lipid status.

Methods: The study included 100 middle-aged, healthy subjects (50 women and 50 men). Serum desmosterol (D) and lathosterol (L) concentrations were determined by LC/MS-MS, and cholesterol synthesis index (S) was calculated (D+L). Total cholesterol (TC), triglycerides (TG), LDL-C, HDL-C were quantified using an ILAB300+ analyzer.

Results: Of all lipid status parameters, only HDL-C concentrations differed between men and women ($P<0.001$, 1.2 (0.95-1.34) vs 1.5 (1.17-1.77), mmol/L). Also, a significant differences in D ($P=0.001$; 3.65 (2.92-4.36) vs 2.96 (2.48-3.48), µmol/L) and L ($P<0.001$; 27.12 (17.84-37.74) vs 15.35 (9.77-25.99), µmol/L) concentrations were observed between men and women, respectively. In women, S correlated significantly with HDL ($P=0.023$, $\rho=-0.331$) and LDL ($P=0.031$, $\rho=0.314$) while in men, these correlations were absent. Binary logistic regression analysis showed that male sex is an independent predictor of increased cholesterol synthesis, even when age, BMI, TG, and TC were included ($P<0.001$; OR=5.932, 95%CI (2.218-15.865)).

Conclusions: In a healthy middle-aged population, cholesterol synthesis is sex-dependent, and men have increased cholesterol synthesis compared to women. These findings could offer a new perspective on sex-specific ASVCD prevention.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

IMPACT OF DYSLIPIDEMIA ON THE IGM REPERTOIRE IN ATHEROSCLEROTIC MICE

POSTER VIEWING SESSION

Justine Deroissart[1], Daria Romanovskaia[2], Sophia Derdak[1], Clemens Schulte[3], Diana Pölzl[1], Markus Jeitler[1], Laura Göderle[1], Christoph Bock[2], Martin Bilban[1], Hans M. Maric[3], Christoph J. Binder[1]
[1]Department Of Laboratory Medicine, Medical University Vienna, Vienna, Austria, [2]Cemm, CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria, [3]Center For Integrative And Translational Bioimaging, Rudolf Virchow Center/University of Wuerzburg, Wuerzburg, Germany

Background and Aims : Inflammation together with hypercholesterolemia is a key contributor in atherosclerosis. Importantly, IgM have been shown to play a protective role in atherosclerosis, and data from mice and epidemiological studies in humans demonstrate a negative correlation between IgM levels and atherosclerotic cardiovascular disease. Dyslipidemia has been shown to affect the IgM antibody levels in mouse models of atherosclerosis. Our aim is to investigate the impact of dyslipidemia on the IgM repertoire in the context of atherosclerosis.

Methods: To investigate the impact of dyslipidemia on the IgM repertoire *in vivo,* we combined two complementary approaches. First, we sequenced the variable region (heavy chain) of splenic and bone marrow resident IgM+ plasma cells, which are primarily responsible for the production of IgM in the circulation, in atherosclerosis-prone $LDLR^{-/-}$ mice fed a high-cholesterol (HCD) or chow diet for 13 or 18 weeks. To complement the study, we determined the binding pattern of circulating and plaque-derived IgM in atherosclerotic $LDLR^{-/-}$ mice using customized peptide arrays.

Results: We found that the repertoire of IgM+ plasma-cells exposed to dyslipidemia differs from control mice at different levels (IGVH and IGJH genes usage, occurrence and location of mutations, germline gene usage, abundance of (atheroprotective) T15id+ CDR3 sequence). In addition, circulating IgM of HCD fed $LDLR^{-/-}$ present a different binding pattern compared to chow mice.

Conclusions: We describe for the first time that long term exposure to dyslipidemia affects the quality of the IgM plasma-cells repertoire. These changes are also reflected in the circulation and may reflect different effects on atherosclerosis development.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

COMPARATIVE ANALYSIS BETWEEN THE CALORIC INTAKE AND THE INFLAMMATORY INTAKE OF DIET

POSTER VIEWING SESSION

Elisa Mattavelli[1], Ruben Domenighini[2], Liliana Grigore[2], Laura Redaelli[3], Cristina Tidone[3], Angela Pirillo[3], Fabio Pellegatta[2], Paolo Magni[1,2], Alberico L. Catapano[1,2], Andrea Baragetti[1,2]
[1]Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Polo Scientifico E Tecnologico, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Multimedica Hospital, Milan, Italy, [3]S.i.s.a. Centre For The Study Of Atherosclerosis, Bassini Hospital, Cinisello Balsamo, Milan, Italy

Background and Aims : The increasing access to nutrient-dense foods is believed to impact Cardiovascular Disease (CVD) risk. Whether a pro-or anti-inflammatory effect of the nutrients and foods exists, beyond the caloric intake remains to be addressed.

Methods: We collected dietary information from seven-day-dietary record of 336 subjects from a cohort of free-living individuals. We estimated in each individual: a) dietary energy intake (kcal/day) and b) inflammatory dietary intake (as the sum of the pro-or anti-inflammatory potential of nutrients, normalized by energy intakes). To validate the pro-/anti-inflammatory potential of nutrients, we measured a set of 368 immune-inflammatory proteins (affinity-based multiplexing) that we previously correlated to CVDs risk.

Results: Information of the immune-inflammatory proteins plasma levels on top of the clinical characteristics of the subjects (basal model) improved the ability to identify both subjects with elevated energy intake and those with pro-inflammatory intake. The odds (95% CI) of elevated energy intake for 1 Standard Deviation increase of the first principal component (positively related to all macro-nutrients, including dietary fats) were 2.35 (1.92-2.85); $p<0.001$. Instead, the odds (95% CI) of pro-inflammatory intakes for 1 Standard deviation increase of the second principal component (positively loaded to all micro-nutrients and dietary fiber), were 0.53 (0.47-0.68); $p<0.001$.

Conclusions: We provide for the first time a comparative analysis of the caloric dietary intake versus the inflammatory intake of diet, calling for in depth analyses to discriminate the effect of the amount and the quality of nutrients consumed by foods.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

ASSOCIATION BETWEEN INFLAMMATORY MARKERS LEVELS, INFLAMMATORY INTAKE OF DIET AND ADHERENCE TO THE MEDITERRANEAN DIET.

POSTER VIEWING SESSION

Elisa Mattavelli[1], Ruben Domenighini[2], Laura Redaelli[3], Cristina Tidone[3], Angela Pirillo[3], Liliana Grigore[2], Fabio Pellegatta[2], Paolo Magni[1], Alberico L. Catapano[1,2], Andrea Baragetti[1,2]
[1]Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Polo Scientifico E Tecnologico, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Multimedica Hospital, Milan, Italy, [3]S.i.s.a. Centre For The Study Of Atherosclerosis, Bassini Hospital, Cinisello Balsamo, Milan, Italy

Background and Aims : The beneficial effects of the Mediterranean Diet (Med-Diet) in Cardiovascular Disease (CVD) prevention have been attributed to its anti-inflammatory effects. Recent data aimed to verify a pro-/anti-inflammatory potential of Med-Diet, although suffering from the lack of quantitative evaluation of food groups intake (by commonly used Food Frequency Questionnaires FFQ). We aimed to address this issue by evaluating the anti-inflammatory potential of Med-Diet, analyzing quantitative dietary intakes and relating to circulating immune-inflammatory markers.

Methods: We collected dietary information from the dietary record of 345 subjects from a large survey of the general population in Milan (“PLIC cohort”,N=2,606). By the analysis of seven-day-dietary records, to derive the quantitative intake of food groups, rather than to the commonly used FFQ, we estimated the adherence to the Med-Diet (PREDIMED-score).We then measured a set of immune-inflammatory proteins (that we previously correlated to CVD risk) and we quantitated white cell counts.

Results: The information of immune-inflammatory proteins and white cells did not allow to discriminate with robust significance subjects with lower adherence to Med-Diet (AUC(95%CI):0.538(0.477-0.599)). Principal component analyses including the information of immune-inflammatory markers, performed among subjects with lower/higher adherence to Med-Diet (score 8 as threshold), highlighted differences in correlations and inter-individual-variability of food groups intake (food groups loadings in subjects with highvs.low Med-Diet adherence: vegetables(0.46vs.0.27), whole cereals(0.75vs.0.38) and low-fat cheese(0.08vs.0.30)).

Conclusions: Despite the differences in foods groups intake based on adherence to Med-Diet, its lacking association with plasma inflammatory markers levels built-up the need to develop novel dietary assessment tools to evaluate the relationship between dietary intake and inflammatory markers.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

ASSOCIATION BETWEEN HAIR STEROID HORMONE LEVELS AND CARDIOMETABOLIC RISK FACTORS IN A GROUP OF WOMEN PARTICIPATING IN THE NATIONAL CVD PREVENTION PROGRAM: A CROSS-SECTIONAL STUDY

POSTER VIEWING SESSION

Egle Mazgelyte[1], Agata Vysocka[2], Martynas Narkevičius[2], Neringa Burokienė[2], Tomas Petrėnas[3], Andrius Kaminskas[3], Jurgita Songailienė[3], Algirdas Utkus[3], Dovilė Karčiauskaitė[1]
[1]Department Of Physiology, Biochemistry, Microbiology And Laboratory Medicine, Vilnius university, Faculty of Medicine, Institute of Biomedical Sciences, Vilnius, Lithuania, [2]Clinics Of Internal Diseases, Family Medicine And Oncology, Vilnius university, Faculty of Medicine, Institute of Clinical Medicine, Vilnius, Lithuania, [3]Department Of Human And Medical Genetics, Vilnius university, Faculty of Medicine, Institute of Biomedical Sciences, Vilnius, Lithuania

Background and Aims : Cardiovascular disease (CVD) is the major cause of death worldwide. Although women develop CVD later than men, women's morbidity and mortality from CVD are similar compared with men. Such a high prevalence of CVD cannot be explained completely by conventional risk factors. Recent studies indicate that chronic stress may be an independent CVD risk factor. Thus, we aimed to investigate the relationship between the biomarkers of chronic stress (hair cortisol, cortisone, DHEA levels) and traditional cardiovascular risk factors, as well as Systematic COronary Risk Evaluation (SCORE2) index, in a group of women (50-64 years) participating in the national CVD prevention program.

Methods: Fasting blood samples, anthropometric and lifestyle data were collected from 145 women. Hair steroid hormone concentrations were determined using ultra-high-performance liquid chromatography-tandem mass spectrometry method.

Results: Statistically significant associations between hair cortisol concentration and waist circumference ($r=0.170$, $p=0.042$), systolic ($r=0.246$, $p=0.003$) and diastolic blood pressure ($r=0.227$, $p=0.006$), apoE concentration ($r=0.191$, $p=0.041$) were found. Hair cortisone level correlated significantly with BMI ($r=0.307$, $p=1.85\times10^{-4}$), waist circumference ($r=0.344$, $p=2.38\times10^{-5}$), systolic ($r=0.271$, $p=1.03\times10^{-3}$) and diastolic ($r=0.276$, $p=7.98\times10^{-4}$) blood pressure, glucose ($r=0.177$, $p=0.033$) and HDL-cholesterol concentrations ($r=-0.249$, $p=0.003$). DHEA was associated with systolic ($r=0.194$, $p=0.024$) and diastolic ($r=0.197$, $p=0.022$) blood pressure. Significant associations between SCORE2 index and hair cortisol ($r = 0.181$, $p=0.030$), as well as cortisone ($r=0.253$, $p=0.002$) levels, were found.

Conclusions: Significant association between hair steroid hormones and CVD risk factors supports a link between chronic stress and atherosclerosis in women.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-07 Environmental risk factors*

CARNIVORE DIET – A RARE CAUSE FOR DYSLIPIDEMIA MIMICKING HOMOZYGOUS FH

POSTER VIEWING SESSION

Tycho R. Tromp, Veera A.T. Houttu, Johannes H.M. Levels, Aart J. Nederveen, G.K. Hovingh, Erik S. Stroes
Department Of Vascular Medicine, Amsterdam UMC - Location AMC, Amsterdam, Netherlands

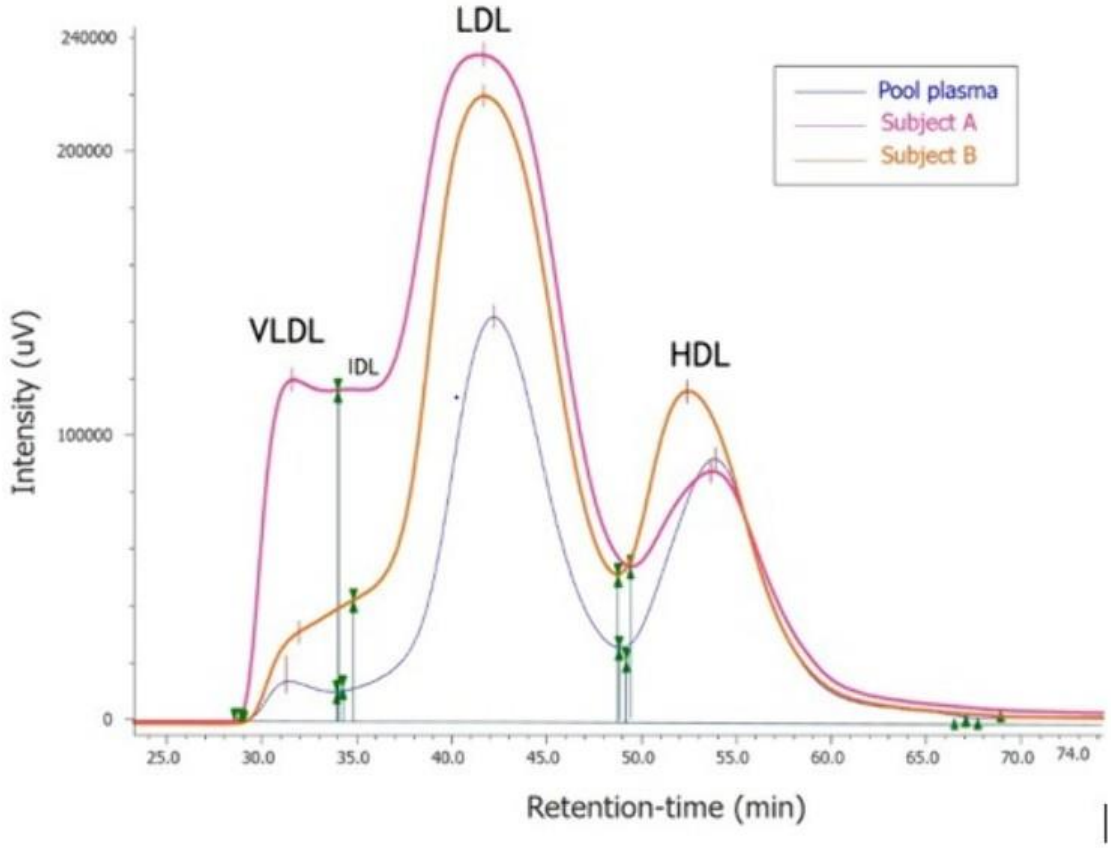
Background and Aims : We aimed to elucidate the cause of hypercholesterolemia in two patients presenting with LDL-C levels >15 mmol/L.

Methods: We performed next-generation sequencing (NGS) on FH genes and performed routine and FPLC analysis on lipoprotein subfractions. We assessed liver fat content using controlled attenuation parameter (CAP) based on vibration-controlled transient elastography (FibroScan) and magnetic resonance spectroscopy (MRS). We screened for early atherosclerosis using carotid ultrasound. Dietary intake was verbally assessed by dietary recall.

Results: Subject A and B are healthy males (aged 33 and 28 years) presenting to our lipid clinic with LDL-C levels of 15 and 17 mmol/L, respectively. Subject used no medications and had no family history of (premature) cardiovascular disease. NGS revealed no pathogenic FH-variants. 1 year prior to presentation, subjects started a carnivorous diet consisting solely of meat, fish and dairy products. Energy intake from carbohydrates was <3 E-% (6-10 g), whereas intake from protein was 37 E-% and fat was 60 E-%. Detailed analysis of lipoprotein subfractions showed disproportionately elevated number of VLDL and IDL particles (Figure 1) suggesting lipoprotein overproduction as possible cause for hypercholesterolemia. Alternatively, we hypothesized downregulated LDL-C uptake due to abundance of cholesterol and fatty acids in hepatocytes, but FibroScan and MRS showed low levels of liver fat (<1%). Carotid ultrasound revealed intima-media thickening (>97th and 90th percentile, respectively) suggesting

early development of atherosclerosis.

Figure 1 – Total cholesterol FPLC profile of Subject A and B, compared to pool plasma as normal control



FPLC, Fast Protein Liquid Chromatography

Conclusions: We present two patients with extremely elevated LDL-C levels due to a carnivorous, ketogenic diet. Subjects agreed to reintroduce carbohydrates to their diets and a repeat cholesterol profile is pending.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

NECK-TO-HEIGHT RATIO, ARTERIAL STIFFNESS AND CARDIOMETABOLIC RISK FACTORS IN HYPERLIPIDEMIC PATIENTS: A PRELIMINARY REPORT.

POSTER VIEWING SESSION

Raphaela P. Pinheiro[1], Carlos R.D. Oliveira[2], Allice D.S. Rodrigues[1], Maria Julia M. Meneses[1], Renato J. Alves[1,2]
[1]Cardiology, Santa Casa de Sao Paulo School of Medical Sciences, Sao Paulo, Brazil, [2]Cardiology, Santa Casa de Misericordia de Sao Paulo Hospital, Sao Paulo, Brazil

Background and Aims : Hyperlipidemia is an important cardiometabolic risk factor. Brachial pulse wave velocity (bPWV) predicts arterial stiffness (AS) and can detect subclinical atherosclerosis with accuracy, however, it's a high-cost tool. Neck-to-height ratio (NHR), inexpensive and easily obtainable anthropometric measurements, may be associated with AS. Aims: To evaluate the relationship between NHR, bPWV, and cardiometabolic parameters in treated hyperlipidemic patients.

Methods: Cross-sectional study with 47 hyperlipidemic patients, over 18 years. Excluded those with cervical anatomical abnormalities. Anthropometric parameters were assessed. The bPWV and pressure parameters were obtained by non-invasive oscillometric method. Laboratory tests results were collected. Data were present as frequency (%) or mean±S.D., using Pearson correlation for analyses, P-value:5%.

Results: •Sample: 53,2% woman, age mean of 63,6±13,2 years, 63,8% Fredrickson's phenotype IIa, 63,8% used high-potency statin, 87,2% hipertensives, 14,9% current smokers. On average, patients were overweight (BMI 28±3,5kg/m²), mean NHR of 23,5±1,8cm/m and bPWV of 9,3±2,2m/s; •There was a significant correlation between NHR and bPWV (r=0.345; p=0.017); •Age (years) was strongly correlated with bPWV (r=0.962, p=0.000) and was also associated with NHR (r=0.386, p=0.007); •NHR, but not bPWV, was correlated with BMI (r=0.457; p=0.001) and creatinine (r=0.408; p=0.004); •bPWV, but not NHR, was correlated with thyroid-stimulating hormone (r=0.390, p=0.007), creatinine clearance (r=-0.664; p=0.000), systolic blood pressure (r=0.411; p=0.004) and central systolic blood pressure (r=0.323; p=0.027); •Was not found association between bPWV, NHR and lipid profile.

Conclusions: NHR and bPWV were correlated with, but mostly not the same, cardiometabolic parameters. Additional analyzes should be performed to better elucidate these correlations.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

RELATIONSHIP BETWEEN NECK CIRCUMFERENCE, NECK-TO-HEIGHT RATIO AND ARTERIAL STIFFNESS IN HYPERLIPIDEMIC PATIENTS: A PRELIMINARY REPORT.

POSTER VIEWING SESSION

Raphaela P. Pinheiro[1], Carlos R.D. Oliveira[2], Allice D.S. Rodrigues[1], Maria Julia M. Meneses[1], Renato J. Alves[1,2]
[1]Cardiology, Santa Casa de Sao Paulo School of Medical Sciences, Sao Paulo, Brazil, [2]Cardiology, Santa Casa de Misericordia de Sao Paulo Hospital, São Paulo, Brazil

Background and Aims : Hyperlipidemia is an important cardiovascular risk factor. Pulse wave velocity (PWV), the gold standard to assess arterial stiffness (AS), can detect subclinical atherosclerosis with accuracy, however, it's a high-cost tool. Neck circumference (NC) and neck-to-height ratio (NHR), inexpensive and easily obtainable anthropometric measurements, may be associated with AS. Aims: To evaluate the relationship between NC, NHR, and AS assessed by PWV in treated hyperlipidemic patients.

Methods: We performed a cross-sectional study with 47 hyperlipidemic patients, over 18 years. Excluded those with cervical anatomical abnormalities. Brachial PWV (bPWV) was obtained by a non-invasive oscillometric method. NC and NHR were assessed. Data were present as frequency (%) or mean±S.D., using Pearson correlation for analyses, P-value:5%.

Results: •Sample: 53,2% woman, mean age of 63,6±13,2 years, 63,8% Fredrickson's phenotype IIa, 63,8% used high-potency statin, 87,2% hipertensives, 14,9% current smokers. On average, patients were overweight (BMI 28±3,5). Mean NHR of 23,5±1,8cm/m, NC of 37,6±3,8cm, bPWV of 9,3±2,2m/s. •bPWV was positively associated with NHR (figure 1), but not with NC (r=0.083; p=0.580); •Age (years), a well-established risk factor for increased AS, was strongly correlated with PWV (r=0.962, p=0.000) and was also associated with NHR (r=0.386,

p=0.007).

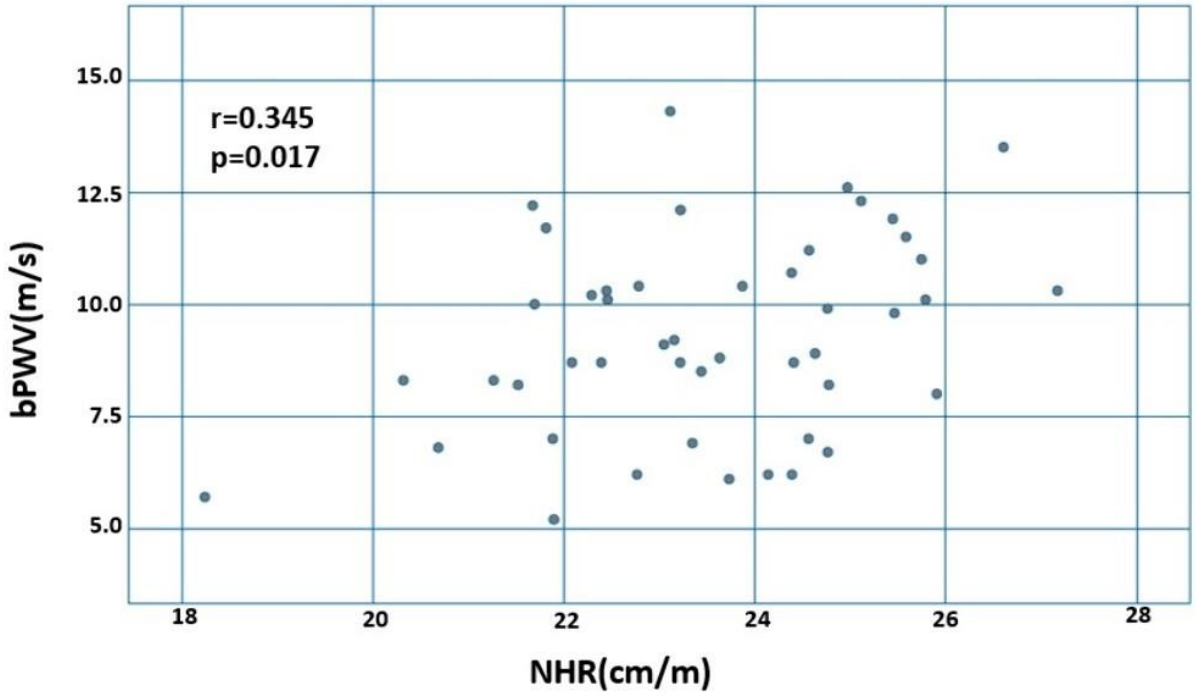

FIGURE 1. Correlation plot between neck-to-height ratio (NHR) and bPWV (brachial pulse wave velocity).

Conclusions: Our findings suggest that NHR, but not NC, was positively associated with bPWV in hyperlipidemic patients and might be an inexpensive potential predictor of arterial stiffness, contributing to the clinical follow-up, and preventing cardiovascular events in this population.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

HUMAN PLASMA GLYCOPROTEIN PROFILE MEASURED BY 1H-NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY IN PATIENTS WITH DIABETES AND/OR ATHEROGENIC DYSLIPIDEMIA, A NEW METHOD TO ASSESS INFLAMMATION

POSTER VIEWING SESSION

Nuria Amigo[1], Rocio Fuertes[1], Ana Malo[2], Nuria Plana[2], Daiana Ibarretxe[2], Josefa Girona[2], Xavier Correig[3], Lluis Masana[2]
[1]R&d, Biosfer Teslab, Reus, Spain, [2]Internal Medicine, Rovira y Virgili University, Reus, Spain, [3]Deeea, Rovira i Virgili University, Tarragona, Spain

Background and Aims : Patients with type 2 diabetes mellitus (T2DM) and atherogenic dyslipidaemia (AD) are at higher risk of developing cardiovascular diseases (CVDs) so interest in discovering inflammation biomarkers as indicators of processes related to CVD progression is increasing. This study aims to characterize the plasma glycoprotein profile of a cohort of 504 participants including patients with and without T2DM and/or AD and controls.

Methods: We characterized plasma glycoprotein profile by using ^{1}H-NMR. We characterized the NMR glycoprotein signals (GlycA and GlycB) which is related to the concentration and aggregation state of the acetyl groups of N-acetylglucosamine, N-acetylgalactosamine and N-acetylneuraminic bond to plasma proteins. The lipoprotein profile was also determined (Liposcale®). Standard clinical and anthropometric measurements were determined. Multivariate classification models were developed to study differences between the study groups.

Results: Reduced HDL-C levels, increased small dense LDL and elevated TG levels were significantly associated with glycoprotein variables. Glycoprotein values in the diagnostic groups were significantly different from those in the CT groups. AD and DM conditions together contribute to a positive and significant synergetic effect on the GlycA area (<0.05) and the H/W ratios of GlycA (<0.01) and GlycB (<0.05). By adding the new glycoprotein variables to the inflammation C-reactive protein marker, the AUC increased sharply for classification models between the CT group and the rest (0.68 to 0.84), patients with and without dyslipidemia (0.54 to 0.86), and between patients with and without diabetes (0.55 to 0.75).

Conclusions: ^{1}H-NMR-derived glycoproteins can be used as possible markers of the degree of inflammation associated with T2DM and AD.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

PROGNOSTIC VALUE OF ECHOCARDIOGRAPHIC DATA IN CHRONIC HEART FAILURE PATIENTS

POSTER VIEWING SESSION

Tea Gamezardashvili, Tamar Avaliani
Cardiology, N(N)LE Remedical, Tbilisi, Georgia

Background and Aims : Heart failure (HF) is one of the most common clinical syndrome worldwide, charasterised with high hospitalization and mortality. Echocardiography plays an important role in the diagnosis of HF. The aim of this study was evaluation of echocardiographic data and determine their prognostic significance in patients with different severity chronic HF.

Methods: The study was performed in 68 patients with chronic HF of II / III / IV functional class, mean age - 64.3 ± 13.4 years. All patients underwent clinical-laboratory evaluation, including echocardiographic examination. Mean EF was 35 ± 10%, LVDD 5.8±0.9 cm, RVDD 3.8±0.5 cm, RA 3.8±0.7 cm, LA 4.4±0.5 cm.

Results:

	II functional class (n=19)	III functional class (n=37)	IV functional class (n=12)
Gender (woman/man)	9/10	12/25	2/10
Ischemic/non-ischemic	9/10	19/18	6/6
Albumin (g/l)	40.9±4.8	39,6±3.9	38.6±5,6
TC (mg/dl)	191,7±50.9	168.9±47.4	149.4±48,3
LDL (mg/dl)	126.3±43.3 *	105.3±35.6	90.4±34.2 *
HDL (mg/dl)	42.8±14.4	40.9±11,3	35.8±12.9
TG (mg/dl)	113.2±32.3	116.6±62.1	116.2±32.5
MPO (ng/ml)	7.8± 4 *	8,9 ± 6,4 *	11,8 ± 7.8 *
hs-CRP (mg/l)	13.6 ± 19.1	9.4 ± 12,0	19.3 ± 24.0
White blood cell x10^9/L	7,3±2.04	7.1±1.98	8.46±2.04
TLC (cell/mm^3)	1363.3 ± 611.5	1445.2± 402.7	1435,7 ±524.3
LVEF (%)	44.9±4,7	33.7±7,7	22,8±5.8
LA (cm)	4.3±0.4	4.4±0.6	4.9±0.5
RA (cm)	3.5±0.5	3.8±0,7	4.7±0,7
LVDD (cm)	5.5±0.8	5.8±0.9	6.6±0.7
RVDD (cm)	3.5±0.3	3.8±0.5	4.4±0.4
IVS (cm)	1.2±0.2	1.3±0.3	1.1±0.1
PW (cm)	1.1±0.2	1.2±0.2	1.1±0.1

The data was analysed among HF functional class, outcome, RVDD and EF quartiles. Statistical analysis was performed using IBM SPSS statistics 16.0. After 6 months follow up we investigated disease

outcome. 10 patients died, from which 8 cases were cardiovascular (CV) mortality. A comparative analysis showed statistically significant increased level of RVDD ($p < 0.005$) and RA ($p < 0.042$) in mortality group, decreased level of total protein ($p < 0.000$), albumin ($p < 0.000$), total ($p < 0.012$), LDL ($p < 0.039$) and HDL ($p < 0.004$) cholesterol, inflammatory markers (MPO, hs-CRP) were statistically elevated. The association of EF with the disease outcome was not found.

Conclusions: In chronic heart failure patients from the echocardiographic data of cardiac functional and structural characteristics, the right ventricular diastolic diameter and right atrium is an indicator of the poor outcome with increased systemic inflammatory parameters and protein-energy malnutrition.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

RELATION AMONG BRAIN-DERIVED NEUROTROPHIC FACTOR, DEPRESSION, AND EXTRACELLULAR VESICLES-DERIVED MIRNA: RESULTS FROM AN ITALIAN COHORT

POSTER VIEWING SESSION

Silvia S Barbieri[1], Patrizia Amadio[1], Chiara Macchi[2], Marta Zarà[1], Chiara Favero[3], Giulia Solazzo[3], Luisella Vigna[4], Maria Francesca Greco[2], Massimiliano Buoli[5,6], Cesare R. Sirtori[2], Alessandro Ieraci[7], Massimiliano Ruscica[2], Valentina Bollati[3]
[1]Unit Of Brain-heart Axis, Centro Cardiologico Monzino IRCCS, Milan, Italy, [2]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [3]Department Of Clinical Sciences And Community Health, University of Milan, Milano, Italy, [4]Occupational Health Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [5]Department Of Neurosciences And Mental Health, Fondazione IRCCS Ca'Granda Ospedale, Maggiore Policlinico, Milan, Italy, [6]Department Of Pathophysiology And Transplantation, University of Milan, Milan, Italy, [7]Department Of Pharmaceutical Sciences, University of Milan, Milan, Italy

Background and Aims : Obesity and depression are intertwined diseases often associated with increased risk of cardiovascular (CAD) complications. Despite modifications in levels of Brain-Derived Neurotrophic Factor (BDNF) in the brain have been observed in subjects with depression and obesity, the relationships among peripheral BDNF, depression and obesity are not well-defined, yet. Changes in extracellular vesicle (EV)-derived miRNAs in blood have been related to obesity, depression and CAD. Here, we investigated the association among BDNF, depression and extracellular vesicles-derived miRNAs related to atherothrombosis.

Methods: 743 overweight/obese individuals (BMI>25 kg/m^2) of the SPHERE cohort were analyzed. A standard biochemical evaluation was assessed. BDNF plasma levels were measured by ELISA, EV-miRNA isolated from plasma and analysed by TaqMan™ OpenArray™. Depression state was evaluated by the Beck Depression Inventory II (BDI-II).

Results: In multivariate analysis, a negative association between BDNF and depression was found (p=0.0004). BDNF levels positively and significantly associated with total cholesterol, low-density lipoprotein-cholesterol, non-high-density lipoprotein cholesterol, triglycerides, and with circulating white and red blood cells and platelets. BDNF levels were associated with a significant increase of 80 miRNAs and a decrement of 59. Several of the genes targeted by these miRNAs were associated with thrombosis, atherosclerosis, atherothrombosis and CAD. miRNA target analysis showed that 15 of these genes fall in all these four datasets. A network between PTGS2, MTHFR, TNF-a, IL6, IL1b, SERPIN1 and BDNF was found.

Conclusions: The link among BDNF, obesity and depression here showed provides one more explanatory variable in the context of overweight and accompanying depression.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

THE CORRELATION OF MYOKINES WITH LIPID METABOLISM AND INFLAMMATION IN YOUTH WITH SEVERE OBESITY

POSTER VIEWING SESSION

Margot Baumgartner, Julia Lischka, Charlotte De Gier, Andrea Schanzer, Nina-Katharina Walleczek, Susanne Greber-Platzer, Maximilian Zeyda
Department Of Pediatrics And Adolescent Medicine, Medical University of Vienna, Vienna, Austria

Background and Aims : Obesity is a global health problem that has been rapidly increasing in the past several decades and is associated with higher cardiovascular risk. As prevention and treatment of obesity are largely insufficient, it is necessary to identify underlying mechanisms with option to reduce obesity-associated cardiometabolic risk. Myokines such as irisin and myostatin have emerged as factors potentially involved in obesity-related disorders. Aim of this study was to investigate whether these myokines are associated with metabolic parameters in pediatric patients with severe obesity.

Methods: Clinical and laboratory data from 108 (68 male) patients with severe obesity between nine and 19 years old was included in this prospective study. Irisin and myostatin concentrations were measured from plasma by ELISA. Pearson- and Spearman-coefficients for normally-distributed and skewed variables were calculated.

Results: Myostatin concentrations correlated with age (p-value < 0.05) and pubertal stage (p-value < 0.05) in males. After adjustment for age and tanner stage, no correlation of myostatin with metabolic markers could be shown, but a negative association of myostatin with CRP remained significant (p-value 0.03). Irisin concentrations correlated positively with HDL cholesterol (p-value 0.01) and negatively with LDL cholesterol values (p-value 0.01), even after adjustment for age and pubertal stage (p-values: HDL-C: 0.02; LDL-C: 0.03).

Conclusions: Irisin concentrations are linked to cholesterol metabolism, as well as myostatin levels with CRP in pediatric patients with severe obesity. Further investigations are necessary to identify causality, but these findings could offer new approaches to prevent inflammation and dyslipidemia, and therefore cardiometabolic risk, in obesity.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

PLASMA CONCENTRATIONS OF APOLIPOPROTEINS AND INCIDENT CARDIOVASCULAR DISEASES IN PATIENTS WITH TYPE 2 DIABETES

POSTER VIEWING SESSION

Mikaël Croyal[1], Pierre-Jean Saulnier[2], Elise Gand[2], Joe De Keizer[2], Chloé Chevalier[1], Valentin Blanchard[3], Bertrand Cariou[1], Samy Hadjadj[1]
[1]Chu Nantes, Cnrs, Inserm, L'institut Du Thorax, Université de Nantes, Nantes, France, [2]Cic 1402, Poitiers University, INSERM, CHU Poitiers, Clinical investigation center CIC 1402, Poitiers, France, [3]Departments Of Medicine, Centre For Heart Lung Innovation, Providence Healthcare Research Institute, St. Paul's Hospital, University of British Columbia, Vancouver, Canada

Background and Aims : Apolipoproteins govern lipoprotein metabolism. Here we evaluated the association of their plasma concentrations with major cardiovascular events (MACE) and coronary artery diseases (CAD) in subjects with type 2 diabetes (T2D).

Methods: MACE (myocardial infarction, stroke, and cardiovascular death) and CAD (myocardial infarction and/or coronary revascularization) were assessed in a single-center cohort of 1382 patients with T2D and without end-stage renal disease (57% males, 65 ± 11 years, eGFR > 15 mL/min/1.73m²). Plasma apolipoprotein concentrations (apoA-I, A-II, A-IV, B100, C-I, C-II, C-III, D, E, F, H, J, L1, M and [a]) were simultaneously determined at baseline by mass spectrometry. Discriminant variables were selected by “Discriminant Factor Analysis”. The associations of plasma apolipoprotein concentrations with incident MACE and CAD were evaluated using Cox proportional-hazard models.

Results: During a median follow-up of 7 years, MACE and CAD developed in 355 (26%) and 214 (15%) individuals, respectively. After adjustments for sex, age, active smoking, SBP, history of myocardial infraction and stroke, estimated GFR and plasma lipids, plasma apoB100-to-apoA-I ratio (per 1 SD naturally log-transformed hazard ratio 1.86 [95% CI: 1.34-2.58]; $p = 0.0002$), apoA-II (0.82 [0.73-0.92]; $p = 0.0005$] and apoF (1.16 [1.04-1.30]; $p = 0.0075$) were associated with the risk of MACE, while only plasma apoB100-to-apoA-I ratio (2.35 (1.58-3.49); $p < 0.0001$) was associated with the CAD risk.

Conclusions: This study illustrates the prognostic value of plasma apolipoproteins in cardiometabolic complications associated with T2D, and confirms that plasma apoB100-to-apoA-I ratio predicts cardiovascular events better than traditional plasma lipids and other apolipoprotein species.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

CHARACTERIZATION OF FETUIN-A LEVELS IN PATIENTS WITH AUTOIMMUNE THYROID DISEASE

POSTER VIEWING SESSION

Inez Lengyel[1], Sándor Halmi[1], Hajnalka Lőrincz[2], Sára Bak-Csiha[1], Mónika Katkó[1], Mariann Harangi[2], Endre V. Nagy[1], Gyorgy Paragh[2], Miklós Bodor[1], Eszter Berta[1]
[1]Department Of Internal Medicine, University of Debrecen, Faculty of Medicine, Debrecen, Hungary, [2]Department Of Internal Medicine, University of Debrecen Faculty of Medicine, Debrecen, Hungary

Background and Aims : Hypothyroidism leads to atherogenic lipid profile and might increase the cardiovascular risk of patients. Fetuin-A is a hepatokine with a regulatory role on mineralization, metabolism and the cardiovascular system. Fetuin-A is increased in obesity-linked diseases

Methods: In our study we investigated the association between thyroid hormone levels, the components of lipid metabolism, anthropometrical parameters and fetuin-A. We enrolled eighty-six patients (7 men, 79 women, mean age 43±13 years, median BMI 25.3 (23.4-30.5) kg/m2) from the Endocrine outpatient clinic of the Department of Medicine, Debrecen. Our patients had autoimmune thyroid disease; their thyroid hormone status varied from hypo- to hyperthyroidism. Serum fetuin-A concentrations were determined with enzyme-linked immunosorbent assay (ELISA). Thyroid hormone levels and lipid parameters were measured by routine laboratory methods.

Results: Median serum fetuin-A level was 929.7 (822.0 – 1038.3) mg/L, LDL-C was 3.2 (2.6-3.8) mmol/l, HDL-C was 1.5 (1.3-1.8), triglyceride was 0.84 (0.49-1.45) mmol/l, while mean total cholesterol level was 5.3±1.1 mmol/l. Mean fT3 and fT4 were 4.67±0.67 and 17.8±3.6 pmol/l, respectively. Significant positive correlation was found between fT3 and fetuin-A levels. There was a significant negative correlation between ApoB100, total cholesterol and fT3. Significant negative correlation was found between TSH and log triglyceride. Among patients receiving levothyroxine substitution, a correlation between CRP and fT3 was present.

Conclusions: The significant correlation between fetuin-A and fT3 levels might indicate a regulatory effect of fT3 on metabolism. However, further clinical investigations are needed to clarify the effect of thyroid status on hepatokine levels.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

PLASMINOGEN ACTIVATOR INHIBITOR-1 LEVEL ASSOCIATED WITH THE COMPONENTS OF METABOLIC SYNDROME IN A 4G/5G POLYMORPHISM DEPENDENT MANNER

POSTER VIEWING SESSION

Hajnalka Lőrincz[1], Erika Galgóczy[1], Mónika Katkó[1], Balázs Ratku[2], Tamás Ötvös[2], Mariann Harangi[1], Gyorgy Paragh[1], Zoltán Szabó[2], Sándor Somodi[1]
[1]Department Of Internal Medicine, University of Debrecen Faculty of Medicine, Debrecen, Hungary, [2]Department Of Emergency Medicine, University of Debrecen Faculty of Medicine, Debrecen, Hungary

Background and Aims : The elevated level of plasminogen activator inhibitor-1 (PAI-1) in obese subjects with metabolic syndrome and in patients with type 2 diabetes is well established. A common 4G/5G single guanine insertion/deletion polymorphism in the promoter region of the PAI-1 gene is of functional importance in regulating PAI-1 expression. We aimed to study the potential different correlations of carbohydrate and lipid parameters and plasma PAI-1 levels in the 4G and 5G carriers in obese and lean subjects.

Methods: Ninety-three morbid obese and thirty-two lean non-diabetic participants were enrolled. PAI-1 4G/5G polymorphism was determined with allele-specific PCR. Plasma PAI-1 levels were measured by ELISA.

Results: The genotype distribution of PAI-1 4G/5G polymorphism was not significantly differed in obese patients (4G/4G 27.9%; 4G/5G 45.2% and 5G/5G 26.9%) compared to controls (4G/4G 31.3%; 4G/5G 46.9% and 5G/5G 21.9%, p=0.8). Slightly higher PAI-1 levels were found in 4G carriers (4G/4G+4G/5G) in obese and control group (p=0.07 and p=0.02, respectively). In all subjects with 4G/5G genotype, plasma PAI-1 correlated negatively with high-density lipoprotein-cholesterol (HDL-C) (p=0.02) and apolipoprotein AI (apoAI) levels (p<0.001). In 5G/5G participants, PAI-1 also correlated negatively with HDL-C (p=0.025) and apoAI (p=0.007) concentrations, moreover positively with triglyceride (p=0.02), fasting glucose (p=0.002) and haemoglobin A1c (p=0.027). These correlations are lacking in 4G/4G participants.

Conclusions: The observed correlations between PAI-1 levels and the components of metabolic syndrome suggest a closer link between PAI-1 and lipid and carbohydrate metabolism in subjects with 5G/5G genotype. This presentation was supported by the Bridging Fund (Faculty of Medicine, University of Debrecen) and PD124126 project.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

SERUM PROGRANULIN LEVEL IN PATIENTS WITH NEWLY DIAGNOSED UNTREATED FAMILIAL HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Bíborka Nádró, Hajnalka Lőrincz, Lilla Juhász, Anita Szentpéteri, Ferenc Sztanek, Ildiko Seres, Dénes Páll, Péter Fülöp, Gyorgy Paragh, Mariann Harangi
Department Of Internal Medicine, University of Debrecen Faculty of Medicine, Debrecen, Hungary

Background and Aims : Familial hypercholesterolemia (FH) is a monogenic form of severe hypercholesterolemia, characterized by elevated total cholesterol and low-density lipoprotein-cholesterol concentrations that, if left untreated, is associated with early onset of atherosclerosis. Progranulin (PGRN) is a recently discovered growth factor with many biological functions. PGRN has anti-inflammatory properties because it inhibits neutrophil degranulation and blocks tumor necrosis factor α transmission, therefore, might be anti-atherogenic. To date, serum level of PGRN in patients with FH has not been studied.

Methods: Eighty-one newly diagnosed, untreated patients with FH and 32 healthy control subjects were involved in our study. Serum PGRN levels were determined by ELISA. We diagnosed FH using the Dutch Lipid Clinic Network criteria.

Results: We could not find significant difference in serum PGRN levels between FH patients and healthy controls (37.66±9.75 vs. 38.43±7.74 ng/mL, ns.). However, we found significant positive correlations between triglyceride, C-reactive protein (CRP), and PGRN levels ($p<0.01$ and $p<0.01$, respectively), while significant negative correlation was found between high-density lipoprotein cholesterol (HDL-C) and PGRN levels ($p<0.05$) both in the whole study population and in FH patients.

Conclusions: Strong correlations between HDL-C, CRP and PGRN levels suggest that PGRN may exerts its anti-atherogenic effect in FH patients by alteration in HDL-C level by amelioration of inflammatory processes. Further studies on larger study populations are needed to clarify the underlying mechanisms. Funding: This presentation was supported by the Bridging Fund (Faculty of Medicine, University of Debrecen) and PD124126 project.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

METABOLIC INDICATORS OF AN ALTERED SPHINGOLIPID METABOLISM ARE BIOMARKERS FOR NON-ALCOHOLIC FATTY LIVER DISEASE

POSTER VIEWING SESSION

Thorsten Hornemann, Florine Wipfli
Clinical Chemistry, University Hospital Zurich, Schlieren, Switzerland

Background and Aims : Non-alcoholic fatty liver disease (NAFLD) is the most frequent cause of chronic liver disease in the western world. Steatosis can be accompanied by inflammation and cell damage (non-alcoholic steatohepatitis, NASH) as well as fibrosis. Sphingolipids and in particular an atypical class of 1-deoxysphingolipids have been associated with NAFLD. Increased 1-deoxySL formation is typically related to an altered amino acid homeostasis. We therefore analyzed the metabolic background that is associated with the increased formation of these lipids in NAFLD.

Methods: The sphingolipid and amino acid profile was analyzed by LC-MS in plasma samples from 350 obese adults who underwent liver biopsy in suspicion of NAFLD.

Results: Clinical variables, sphingolipids and amino acids were compared between No-NASH and NASH, as defined by the Brunt criteria. The most significant differences were seen for ALAT followed by the alanine/serine ratio (p = 6.92E-09) and the waist/hip ratio (p = 3.46E-08). The lipidomics analysis revealed significantly elevated 1-deoxyCeramides (m18:0/22:0, m18:0/24:0, m18:0/24:1, m18:1/20:0, and m18:1/22:0) in NASH. Plasma deoxySL levels showed a significant association with the alanine/serine ratio. A multivariate binary logistic regression model including WHR, ALAT, ala and ser showed a significant association with NASH. The ROC derived from the prediction function of this this model resulted in an ROC AUC of 0.78 (Brunt).

Conclusions: Our results showed that a metabolic signature composed of ALAT, WHR alanine and serine correlates significantly with different stages of NAFLD. It may be used alone or in combination with other markers as a diagnostic criterion and biomarker to diagnose NAFDL and to monitor disease progression.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

THE CERAMIDE- AND PHOSPHATIDYLCHOLINE- BASED CORONARY EVENT RISK TEST2 (CERT2) AND CARDIOVASCULAR MORTALITY IN MEN AND WOMEN WITH TYPE 2 DIABETES

POSTER VIEWING SESSION

Andreas Leiherer[1], Axel Muendlein[1], Christoph H. Saely[2], Barbara Larcher[3], Arthur Mader[3], Maximilian Maechler[3], Lukas Sprenger[3], Valentin Grabher[1], Reijo Laaksonen[4], Mitja Laaperi[4], Antti Jylha[4], Peter Fraunberger[5], Heinz Drexel[6]
[1]Academic Teaching Hospital Feldkirch, Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria, [2]Medical Sciences, Private University of the Principality of Liechtenstein, Triesen, Liechtenstein, [3]Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria, [4]Biosciences, Zora Biosciences, Espoo, Finland, [5]Academic Teaching Hospital Feldkirch, Medical Central Laboratories, Feldkirch, Austria, [6]Internal Medicine, County Hospital Bregenz, Bregenz, Austria

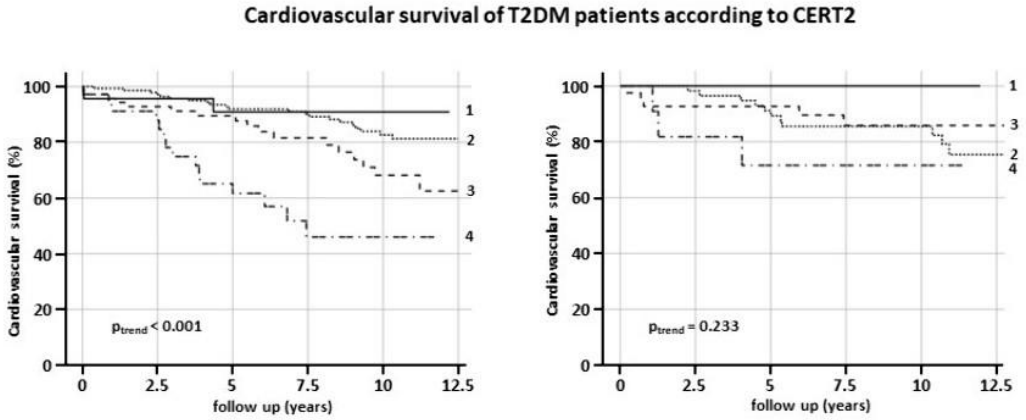
Background and Aims : The recently introduced Coronary Event Risk Test version 2 (CERT2) is a validated cardiovascular risk predictor score that uses circulating ceramide and phosphatidylcholine concentrations. We here aimed at investigating the power of CERT2 to predict cardiovascular mortality in patients with type 2 diabetes (T2DM).

Methods: We investigated mortality in 280 male and 121 female patients with type 2 diabetes.

Results: Prospectively, we recorded 55 cardiovascular deaths in men and 19 in women during a mean follow-up time of 7.6±3.6 and 8.1±3.4 years respectively. Overall, cardiovascular survival decreased with increasing CERT2 risk categories (figure 1). In Cox regression models, CERT2 significantly predicted the incidence of cardiovascular mortality in male patients with T2DM (unadj. HR 1.82 [1.39-2.37] per standard deviation; p<0.001), the unadj. HR in women was 1.36 [0.83-2.22]; p=0.228). After adjustment for age, BMI, current smoking, LDL cholesterol, HDL cholesterol, hypertension, and statin use the HR in men was 1.73 [1.31-2.29]; p<0.001) and in 1.40 [083-2.36]; p=0.210 women. Interaction terms CERT2 x gender were non-significant both in univariate analysis (p=0.354) and after multivariate adjustment (p=0.359).

Conclusions: We conclude that sex does not significantly impact the association of CERT2 with cardiovascular mortality in patients with

T2DM.



The Kaplan Meier plot indicates the cardiovascular survival according to the CERT2 risk categories ranging from low risk (1) to very high risk (4) for men (left) and women (right).

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

REMNANT CHOLESTEROL IN PATIENTS WITH ESTABLISHED CARDIOVASCULAR DISEASE PREDICTS CARDIOVASCULAR EVENTS BOTH AMONG PATIENTS WITH TYPE 2 DIABETES AND AMONG NON-DIABETIC SUBJECTS

POSTER VIEWING SESSION

Arthur Mader[1], Lukas Sprenger[1], Alexander Vonbank[1], Barbara Larcher[1], Maximilian Maechler[1], Valentin Grabher[2], Andreas Leiherer[2], Axel Muendlein[2], Heinz Drexel[3], Christoph H. Saely[4]
[1]Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria, [2]Academic Teaching Hospital Feldkirch, Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria, [3]Internal Medicine, County Hospital Bregenz, Bregenz, Austria, [4]Medical Sciences, Private University of the Principality of Liechtenstein, Triesen, Liechtenstein

Background and Aims : Remnant cholesterol, which is calculated as total cholesterol minus LDL cholesterol minus HDL cholesterol has attracted interest as a marker of cardiovascular event risk. The power of remnant cholesterol to predict cardiovascular events in patients with established cardiovascular disease is unclear and is addressed in the present study.

Methods: We enrolled 1822 consecutive patients with established cardiovascular disease, including 1472 with angiographically proven stable CAD, 350 with sonographically proven peripheral artery disease. Prospectively, cardiovascular events were recorded over a mean follow-up period of 6.2±3.2 years.

Results: At baseline, remnant cholesterol was significantly higher in patients with T2DM (n=608) than in non-diabetic subjects (27±25 vs. 21±21 mg/dl; p<0.001). During follow-up, 584 of our patients suffered cardiovascular events; the event rate was significantly higher in patients with T2DM than in non-diabetic subjects (45.4 vs. 32.2%; p<0.001). Remnant cholesterol in Cox regression models adjusting for age, sex, hypertension, smoking, body mass index and LDL cholesterol independently predicted cardiovascular events in the total study population (standardized adjusted HR 1.15 [1.07-1.23]; p<0.001), and in patients with T2DM as well as in non-diabetic subjects (standardized adjusted HRs 1.17 [1.03-1.34]; p=0.013 and 1.12 [1.01-1.23]; p=0.028, respectively).

Conclusions: From our data we conclude that remnant cholesterol in patients with established cardiovascular disease predicts cardiovascular events both among patients with T2DM and among non-diabetic subjects.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

THE NEW MYOKINE MYONECTIN IS SIGNIFICANTLY ASSOCIATED WITH TYPE 2 DIABETES IN ELDERLY CARDIOVASCULAR DISEASE PATIENTS

POSTER VIEWING SESSION

Andreas Leiherer[1], Axel Muendlein[1], Kathrin Geiger[1], Christoph H. Saely[2], Valentin Grabher[1], Peter Fraunberger[3], Heinz Drexel[4]
[1]Academic Teaching Hospital Feldkirch, Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria, [2]Medical Sciences, Private University of the Principality of Liechtenstein, Triesen, Liechtenstein, [3]Academic Teaching Hospital Feldkirch, Medical Central Laboratories, Feldkirch, Austria, [4]Internal Medicine, County Hospital Bregenz, Bregenz, Austria

Background and Aims : The novel myokine myonectin is predominantly expressed in skeletal muscle and is involved in the regulation of metabolic homeostasis. A putative association between myonectin and type 2 diabetes mellitus (T2DM) has been discussed controversially in current literature. The association between myonectin and T2DM at different ages is still obscure and thus is addressed in the present study.

Methods: We measured myonectin in 410 cardiovascular disease patients with a mean age of 66 years. Myonectin did not correlate with age (r=-0.19; p=0.697). Half of our patients (53%) were elderly (≥66 years; n=219) with a mean age of 74 years. The younger ones (≤65 years; n=191) had a mean age of 57 years. 40.6% (n=89) of elderly patients had T2DM and 42.4% (n=81) of the younger ones.

Results: Myonectin concentrations were significantly decreased in elderly patients with T2DM compared to non-diabetic ones (1.8 vs, 4.2 ng/ml; p=0.002), whereas no significant difference was seen in younger patients (2.6 vs. 2.3 ng/ml; p=0.183). Regression analysis revealed an unadjusted odds ratio (OR) of 0.24 [0.07-0.81] (p=0.021) for the association between myonectin and T2DM in elderly patients but not in younger patients (OR=1.08 [0.80-1.45]; p=0.609). This association remained significant after adjusting for sex, body mass index, LDL-cholesterol, HDL-cholesterol, current smoking, as well as statin intake in elderly but not in younger patients (OR=0.23 [0.07-0.81]; p=0.021 vs. OR=1.05 [0.76-1.46]; p=0.769).

Conclusions: We conclude that plasma myonectin levels are significantly associated with T2DM particularly in elderly cardiovascular disease patients.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

CORRECTION OF LIPID, HEMOSTATIC DISORDERS AND REMODELING OF BRACHIOCEPHAL ARTERIES IN PATIENTS OF VERY HIGH RISK OF CARDIO-VASCULAR DEATH

POSTER VIEWING SESSION

Olesya Rubanenko[1], Anatoly Rubanenko[2], Igor Davydkin[1]
[1]Hospital Therapy, Samara State Medical University, Samara, Russian Federation, [2]Propedeutic Therapy, Samara State Medical University, Samara, Russian Federation

Background and Aims : To study lipid and coagulation indicators and remodeling of brachiocephalic arteries in patients of very high cardiovascular death risk receiving statins.

Methods: Studied were 116 patients with coronary artery disease (mean age – 54.7±3.5 years). We evaluated fibrinogen, D-dimer, von Willebrand factor levels, lipid analysis and performed ultrasound triplex scanning of brachiocephalic arteries.

Results: 24 weeks of atorvastatin and rosuvastatin treatment resulted in reducing of total cholesterol, LDL-cholesterol, triglycerides, von Willebrand factor, D-dimer and fibrinogen levels ($p<0.05$). Atorvastatin also increased HDL-cholesterol level ($p<0.05$). Cross-sectional area of the lumen of the left internal carotid artery due to atorvastatin therapy increased by 25.6% ($p<0.05$), and cross-sectional area of the lumen of the right internal carotid artery due to rosuvastatin treatment increased by an average of 21.6% ($p<0.05$).

Conclusions: Long term statin therapy results in achievement of target levels of lipid indicators and also lowering of D-dimer, von Willebrand factor and fibrinogen levels. Long term statin therapy in some cases decreases atherosclerosis progression in brachiocephalic arteries.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-08 Novel risk factors and biomarkers*

MICRORNAS AS POTENTIAL NOVEL BIOMARKERS FOR VULNERABLE CORONARY PLAQUE CHARACTERISTICS AND EXERCISE EFFECTS.

POSTER VIEWING SESSION

Maria D. Taraldsen[1], Rune Wiseth[1,2], Vibeke Videm[3,4], Erik Madssen[1,2]
[1]Department Of Circulation And Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway, [2]Clinic Of Cardiology, St. Olavs University Hospital, Trondheim, Norway, [3]Department Of Clinical And Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway, [4]Department Of Immunology And Transfusion Medicine, St. Olavs University Hospital, Trondheim, Norway

Background and Aims : MicroRNAs (miRs) are negative regulators of protein synthesis in cells and are involved in the pathophysiology of atherosclerosis. Circulating miRs are therefore proposed as promising novel biomarkers of coronary artery disease (CAD). We hypothesized that circulating levels of miRs were associated with coronary plaque characteristics, plaque burden, and necrotic core volume, before and after aerobic exercise intervention.

Methods: 31 patients with angina pectoris or non-ST elevation acute coronary syndrome treated with percutaneous coronary intervention (PCI) previously included in a randomized controlled trial were included. Patients performed either aerobic interval training or moderate continuous training for 12 weeks following PCI. Predefined CAD-related miRs in plasma and coronary plaque characteristics assessed by grayscale- and radiofrequency intravascular ultrasound were analysed at baseline and follow-up. Linear regression was used to analyze associations between miRs and coronary plaque burden and necrotic core volume, and the possible effects from exercise.

Results: Circulating levels of miR-15a-5p ($p<0.05$), miR-30e-5p ($p=0.01$), miR-92a-3p ($p=0.01$), miR-199a-3p ($p=0.02$), miR-221-3p ($p=0.01$), miR-222-3p ($p=0.04$) were associated with coronary necrotic core volume at baseline. After the exercise intervention, increased levels of miR-146a-5p ($p=0.04$), and decreased levels of miR-15a-5p ($p<0.05$), miR-93-5p ($p=0.03$) and miR-451a ($p=0.01$) were associated with a reduction in coronary plaque burden.

Conclusions: This explorative study demonstrated an association between six miRs and coronary necrotic core volume, a marker of plaque vulnerability. Following exercise, a reduction in coronary plaque burden was associated with changes in four miRs. These findings indicate that miRs may have a potential as novel biomarkers of CAD and vulnerable plaques.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-10 Coagulation*

P-SELECTIN AS A MODULATOR OF FIBRIN CLOT PROPERTIES IN PATIENTS TREATED WITH HIGH-DOSE STATINS

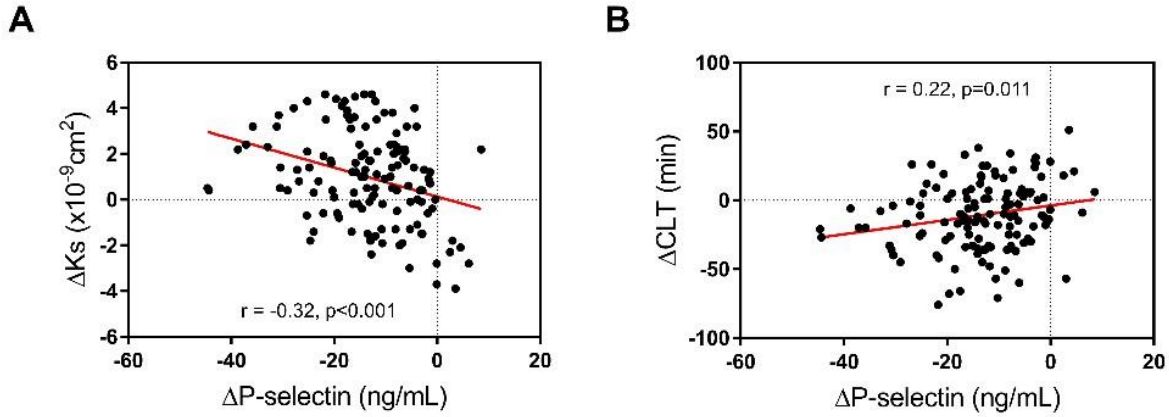
POSTER VIEWING SESSION

Jakub Siudut[1,2], Michal Zabczyk[1,2], Maciej Polak[3], Jacek Jawień[4], Anetta Undas[1,2]
[1]Institute Of Cardiology, Jagiellonian University, Krakow, Poland, [2]Krakow Centre For Research And Medical Technologies, John Paul II Hospital, Krakow, Poland, [3]Department Of Epidemiology And Population Studies, Jagiellonian University, Krakow, Poland, [4]Department Of Pharmacology, Jagiellonian University, Krakow, Poland

Background and Aims : It has been reported that P-selectin, a marker of platelet activation, is associated with denser fibrin networks in coronary artery disease (CAD). It is unclear whether high-intensity statin therapy reduces P-selectin levels and such changes can affect the fibrin clot phenotype in CAD patients.

Methods: We recruited 130 consecutive patients with advanced CAD on statins (aged 50-80 [median, 64 years], median low-density lipoprotein cholesterol [LDL-C] 3.2 mM). At baseline and after 6-12 months of high-dose statin treatment (atorvastatin 80 mg/day or rosuvastatin 40 mg/day), soluble P-selectin, along with plasma fibrin clot permeability (Ks), clot lysis time (CLT), and thrombin generation were determined.

Results: Before high-intensity statin treatment, lower Ks and longer CLT values were associated with increased P-selectin (β -0.29 [95%CI -0.45 to -0.12], p<0.001, and β 0.24 [95% CI 0.04 to 0.44], p=0.018, respectively) after adjustment for potential confounders, including age, sex, body mass index, and smoking. Fibrin clot features, thrombin generation, and P-selectin at baseline showed no association with lipid parameters. After a median high-dose statin therapy of 7 months there was 32% reduction in P-selectin levels (p<0.001). On-treatment change (Δ) in P-selectin correlated with ΔKs and ΔCLT (Figure 1), however, we did not observe any associations between post-treatment P-selectin levels and fibrin clot properties or thrombin
generation.



Conclusions: High-dose statin therapy in CAD patients reduces P-selectin levels in association with improved plasma fibrin clot phenotype, which highlights the impact of platelet-derived proteins on a prothrombotic state in hypercholesterolemia and during its treatment.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-11 Gut microbiome*

IN VITRO STUDIES ON THE MECHANISMS EXERTED BY A MIXTURE OF LACTOBACILLUS PLANTARUM ALONE OR COMBINED WITH BERBERINE AND FERMENTED RED RICE ON CHOLESTEROL HOMEOSTASIS

POSTER VIEWING SESSION

Francesca Bordonaro, Sara Mazza, Elena Frisa, Agnese Granata, Flavia Di Vincenzo, Paola Sperandeo, Alessandra Polissi, Alberto Corsini, Lorenzo Arnaboldi
Dipartimento Di Scienze Farmacologiche E Biomolecolari, Università degli Studi di Milano, milano, Italy

Background and Aims : Nutraceuticals represent a new opportunity in reducing mild-moderate cholesterolemia, even in statin-intolerant patients. *Lactobacillus plantarum* (LP) strains CECT7527-CECT7528-CECT7529 (AB-LIFE), isolated from human intestine, demonstrated cholesterol-lowering properties both in animal and human studies.

Methods: Here we show the *in vitro* effectiveness on cholesterol homeostasis exerted by the AB-LIFE formula (AB-Biotics), alone or associated with berberine (BBR) and fermented red rice (RYR).

Results: Three mechanisms contribute to AB-LIFE's effect on cholesterol homeostasis: **-Removal of cholesterol from LP colture medium** Active- or heat-inactivated LP remove from the medium up to 50-60% of free cholesterol (ethanol-diluted; medium concentrations 20-200ug/ml), after a 20-hour incubation (gas-liquid chromatography analysis). In our experimental conditions, this effect is neither saturable nor specific for cholesterol, since betasitosterol or stigmasterol are equally removed when added. **-Bile Salt Hydrolase (BSH) activity** LP's BSH, by hydrolyzing conjugated intestinal bile salts, prevents free cholesterol reabsoption, thuslowering its plasma concentrations. As shown by thin-layer chromatography and colorimetric analysis, BSH activity is only present in active LP, after incubation with taurocholic- and glycocholic acids for 20 hours (0.3% in colture medium). **-Cholesterol biosynthesis inhibition** 15% conditioned medium from active LP added for 20 hours to the colture medium of human hepatocarcinoma HuH-7 cells reduces cholesterol biosynthesis by 15-20%. The association with BBR (15 ug/ml) and RYR (0,1-1 uM monacoline K; HPLC titration) further reduces cholesterol biosynthesis (up to 70%).

Conclusions: Altogether, these *in vitro* effects corroborate the data on the clinical efficacy of LP strains (AB-LIFE), suggesting their use alone or in combination in the treatment of mild-moderate hypercholesterolemia.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-11 Gut microbiome*

DIETARY CHOLINE INCREASES PLASMA CONCENTRATION OF GUT-DERIVED UREMIC TOXINS AND METABOLITES ASSOCIATED WITH CHRONIC KIDNEY DISEASE PROGRESSION IN APOE-KNOCKOUT MICE WITH ELEVATED HDL

POSTER VIEWING SESSION

Marco Busnelli[1], Elsa Franchi[1], Alice Colombo[1], Stefano Manzini[1], Mariel A. García-Rivera[2], Jennifer Kirwan[2], Giulia Chiesa[1]
[1]Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milano, Italy, [2]Core Facility Metabolomics, Berlin Institute of Health, Berlin, Germany

Background and Aims : Experimental and observational studies have highlighted a positive correlation between increased plasma concentration of choline-derived trimethylamine-N-oxide (TMAO) and adverse cardiovascular events. This study was aimed at investigating how the plasma metabolome of mice prone to atherosclerosis development was modulated by HDL levels and the dietary intake of choline.

Methods: Standard rodent diets with different choline content (0.09% or 1.2%) were administered for 16 weeks to two groups of atherosclerosis-prone female mice: 1) extremely low-HDL mice, deficient for both murine apoA-I and apoE (DKO); 2) high-HDL mice, deficient for both apoA-I/apoE, but overexpressing human apoA-I (DKO/hA-I). At sacrifice, atherosclerosis was evaluated, and a targeted metabolomics of plasma was performed.

Results: Atherosclerosis development evaluated at the aortic sinus, was strongly increased in DKO vs DKO/hA-I mice. Surprisingly, although the high-choline diet resulted into elevated plasma TMAO levels in both genotypes, choline supplementation significantly worsened plaque development only in DKO/hA-I mice. Noteworthy, high-choline diet led to an increased concentration of plasma lipids only in DKO/hA-I mice: mainly total cholesterol, but also ceramides and hexosylceramides. Several markers of increased cardiovascular disease risk and chronic kidney disease progression such as the gut-derived uremic toxins phenyacetylglutamine and indoxyl sulfate and plasma metabolites asymmetric dimethylarginine, symmetric dimethylarginine and acetylcarnitine were increased only in high-choline-fed DKO/hA-I mice.

Conclusions: Dietary choline supplementation worsens atherosclerosis development only in the presence of HDL. Plasma metabolomics clearly indicated that choline supplementation increases the concentration of different lipid classes as well as of different metabolites indicative of augmented cardiovascular risk and impaired kidney function.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

POLYMORPHISM IN THE APOLIPOPROTEIN C3 GENE AND CORONARY LESIONS IN PATIENTS WITH CHD

POSTER VIEWING SESSION

Rano Alieva, Aziz Eshpulatov, Alexander Shek
Cihd,atherosclerosis, RSSMC, Tachkent, Uzbekistan

Background and Aims : The aim of our study was to evaluate the distribution of the APOC3 SstI polymorphism and its impact on the character of dyslipidemia and features of coronary lesions in Uzbek patients with unstable angina.

Methods: The study included 141 patients with unstable angina pectoris (HC) class IIB (Braunwald E. et al., 1989) with LDL cholesterol> 100 mg / dL. The comparison group consisted of 50 healthy, age-matched, randomly selected individuals without clinical and instrumental signs of coronary artery disease according to the results of an exercise test. Coronary angiography was performed on an Allura CV-20 (Philips, Netherlands). Genotyping of SstI APOC3 gene polymorphism by PCR-RFLP. Alleles lacking a restriction site were designated S1, and alleles containing an SstI site were designated S2.

Results: The analysis of the APOC3 SstI polymorphism revealed a significant prevalence of carriers of the S2 allele among patients with UA compared with healthy ethnic Uzbeks. Carriage of the S2 allele was associated with hypertriglyceridemia (> 230 mg / dL) (OR = 2.30, 95% CI: 1.14-4.67; $\chi^2 = 5.485$; P = 0.02) and a higher risk of three- and multivessel lesions. (OR = 2.171, 95% CI: 1.0792-4.3680; P = 0.03).

Conclusions: Our results indicate that the determination of APOC3 SstI polymorphism may be a useful additional marker in assessing cardiovascular risk and indications for coronary angiography.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

GENOME-WIDE ASSOCIATION AND MENDELIAN RANDOMIZATION ANALYSES IDENTIFY NOVEL GENETIC AND METABOLIC DETERMINANTS OF ACUTE PANCREATITIS

POSTER VIEWING SESSION

Jérôme Bourgault[1], Erik Abner[2], Émilie Gobeil[1], Arnaud Girard[1], Eloi Gagnon[1], Christian Couture[3], Patrick Mathieu[1], Tonu Esko[2], Benoit J. Arsenault[1]
[1]Axe Cardiologie, Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec, Quebec city, Canada, [2]Estonian Genome Center, University of Tartu, Tartu, Estonia, [3]Cardiology, Quebec Heart and Lung Institute, Québec, Canada

Background and Aims : Acute pancreatitis (AP) is a complex trait that may be caused by some cardiometabolic risk factors. The genetic architecture of AP is not fully understood. Here, we aimed at identifying novel genetic and metabolic determinants of AP by combining genome-wide association study (GWAS) and Mendelian randomization (MR).

Methods: We performed two new GWAS in the Estonian Biobank (2451 cases and 192521 controls) and the UK Biobank (2359 cases and 405762 controls) and combined these results with FinnGen (3022 cases and 195144 controls) in a genome-wide association meta-analysis totalling 7832 cases and 793427 controls. We then performed a series of inverse variance-weighted MR analyses using 123 metabolites derived from a GWAS of >24,000 Europeans as study exposures. From there, we performed sensitivity analyses using MR-PRESSO and contamination mixture tests to account for horizontal pleiotropy and assess the validity of our instruments, respectively.

Results: Our GWAS meta-analysis identified genome-wide significant variants ($p<5e-8$) at two known AP loci (*ABCG8* and *SPINK1*) as well as at one new locus (*TRPV6*). Out of the 123 metabolites tested, only the amino-acid glycine (beta [95% CI] = -0.11 [-0.16 – -0.06]; $p_{IVW} = 6.21e^{-06}$) was significant and negatively associated with AP. No association between triglycerides and AP were found.

Conclusions: We identified a genetic variant at the *TRPV6* locus as a novel susceptibility locus for AP and as well as a potentially causal negative association between circulating glycine levels and AP. The biological mechanisms underlying these new findings will need to be further investigated.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 Genomics, GWAS and population genetics; Mendelian randomization*

CONTRIBUTION OF APOE GENETIC VARIANTS TO DYSLIPIDEMIA

POSTER VIEWING SESSION

Ana Maria Bea, Fernando Civeira, Victoria Marco-Benedí, Itziar Lamiquiz-Moneo, Rocio Mateo-Gallego, Estibaliz Jarauta, Martin Laclaustra, Ana Cenarro
Unidad Investigación Traslacional, Hospital Universitario Miguel Servet, IIS Aragón, CIBERCV, Zaragoza, Spain

Background and Aims : To identify common and rare genetic variants in *APOE* gene in a cohort of subjects with primary hyperlipidemia and compare them with general population.

Methods: A total of 3180 unrelated consecutive subjects were recruited in the Lipid Unit at Hospital Universitario Miguel Servet, Zaragoza, Spain. Patients were divided according to their lipid phenotype. 1426 patients were diagnosed of isolated hypercholesterolemia if triglycerides (TG) <200 mg/dL + LDL cholesterol (LDLc) ≥160 mg/dL or apo B ≥120 mg/dL; 1515 were diagnosed of mixed hyperlipidemia when TG ≥200 mg/dL + non-HDLc ≥190 mg/dL or apo B ≥120 mg/dL; 239 patients were diagnosed of isolated hypertriglyceridemia when TG≥200 mg/dL + non-HDLc <190 mg/dL + apo B <120 mg/dL; and 376 subjects were considered normolipemic (TG <200 mg/dL + LDLc <160 mg/dL + apo B <120 mg/dL). We also studied 822 random subjects from the Aragon Workers Health Study (AWHS), a longitudinal cohort study of cardiovascular risk factors and subclinical atherosclerosis, as general population. In all subjects, exon 4 of *APOE* gene was sequenced and clinical and analytical variables were registered.

Results: Twelve different APOE gene variants were identified in 59 subjects with different dyslipidaemia phenotype from lipid unit.

Predicted aminoacid change	Nucleotide change	Isolated HC (n=1426)	MH (n=1515)	Isolated HTG (n=239)	Whole dyslipidemia group (n=3180)	Normolipemic (n=376)	AWHS cohort (n=822)	Allele frequency in the general population	
								1000 Genomes Project[a]	GnomAD[b]
None, n(%)	-	1405 (98.5)	1482 (97.8)*	233 (97.5)*	3120 (98.1)**	374 (99.5)	813 (98.9)	-	-
c.237-33C>G, n(%)	-	0	1 (0.07)	0	1 (0.03)	0 (0.0)	0	-	-
p.(Met82Ile), n(%)	c.246G>T rs557845700	0	0	1 (0.42)	1 (0.03)	0 (0.0)	0	<0.001	<0.001
p.(Ala104=), n(%)	c.312G>C	0	0	1 (0.42)	1 (0.03)	0 (0.0)	0	-	-
p.(Arg108Trp)	c.322C>T rs1050106163	0	0	0	0	0	1(0.12)	-	<0.001
p.(Tyr136His)	c.406T>C	0	0	0	0	0	1(0.12)	-	-
p.(Gly145Asp), n(%)	c.434G>A rs267606664	-	2 (0.13)	0	2 (0.06)	0 (0.0)	0	-	<0.001
p.(Arg154Ser), n(%)	c.460C>A rs121918393	2 (0.14)	13 (0.86)	2 (0.84)	17 (0.53)	0 (0.0)	3 (0.36)	-	<0.001
p.(Arg163Cys), n(%)	c.487C>T rs769455	0	5 (0.33)	1 (0.42)	6 (0.19)	0 (0.0)	0	0.007	0.007
p.(Arg165Trp), n(%)	c.493C>T rs1402219759	-	1 (0.07)	0	1 (0.03)	0 (0.0)	0	-	-
p.(Leu167del), n(%)	c.500_502delTCC rs515726148	8 (0.56)	6 (0.40)	1 (0.42)	15 (0.47)	0 (0.0)	0	-	<0.001
p.(Arg168His), n(%)	c.503G>A rs376170967	1 (0.07)	0	0	1 (0.03)	0 (0.0)	0	-	<0.001
p.(Gly191Cys), n(%)	c.571G>T	1 (0.07)	0	0	1 (0.03)	0 (0.0)	0	-	-
p.(Ala217=), n(%)	c.651C>T rs72654468	9 (0.63)	3 (0.20)	0	12 (0.38)	2 (0.53)	4 (0.49)	0.001	0.001
p.(Pro220Leu), n(%)	c.659C>T rs1265743589	0	1 (0.07)	0	1 (0.03)	0 (0.0)	0	-	<0.001

Isolated HC = Isolated hypercholesterolemia; MH = Mixed hyperlipidemia; Isolated HTG= Isolated hypertriglyceridemia
Qualitative variables are expressed as n (%) The * *p* value was calculated by Chi - square comparing every lipid phenotype (Isolated HC, MH and isolated HTG) with normolipemic group (n=376) and **the *p* value was calculated by Chi - square comparing whole dyslipidaemia group (n=3180, all phenotypes included) with normolipemic group (n=376).
a 1000 Genomes Project Consortium, Abecasis GR, Auton A, Books LD et al. An integrated map of genetic variation from 1092 human genomes. Nature 2012;491:56-65.
b GnomAD v.2.1.1. https://gnomad.broadinstitute.org/

Conclusions: Ten different *APOE* gene variants were identified in 30 subjects with different hyperlipidemias, that were not found in controls neither AWHS cohort, suggesting that they could be causally associated with their lipid abnormalities. In summary, our results suggest that the genetic variability in *APOE* gene contributes to the etiology of different dyslipidemias, not only to dysbetalipoproteinemia.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

CHROMATIN CONFIGURATION IS ALTERED IN NASH RESULTING IN DELETERIOUS RNA EXPRESSION RELATED TO NASH ETIOLOGY

POSTER VIEWING SESSION

Fernando Cardona[1], Daniel Castellano-Castillo[2], Bruno Ramos-Molina[3], María Antonia Martínez-Sanchez[3], María Dolores Frutos-Bernal[3], María Isabel Queipo-Ortuño[2]
[1]4. departamento De Especialidades Quirúrgicas, Bioquímica E Inmunología, Facultad De Medicina, Universidad De Málaga, Universidad de Málaga, Málaga, Spain, [2]1. unidad De Gestión Clínica Intercentros De Oncología Médica, Hospitales Universitarios Regional Y Virgen De La Victoria, IBIMA, Malaga, Spain, [3]2. obesity And Metabolism Laboratory, Biomedical Research Institute of Murcia (IMIB), Murcia, Spain

Background and Aims : Metabolic-associated liver disease (MAFLD) is a growing health problem in developed country, being associated to environmental factors such as diet and lifestyle conditions that can influence the epigenetic landscape of the cells. In this study we performed ATAC-seq and RNA-sequencing in liver tissue of subjects with and without NASH to assay the chromatin openness and its effects on transcription during NASH etiology.

Methods: Liver samples (n=12) were processed to purify the cell nuclei, and ATAC reaction was performed. ATAC and RNA libraries were sequenced using Novaseq PE150 (Illumina). Bioinformatic analysis were then performed using R Studio and Python-based software.

Results: Subjects with NASH showed transcriptional downregulation for pathways related to lipid and glucose metabolism such as ABC-transporters, AMPK, FoxO or insulin pathways, compared to non-NASH. We found 229 deregulated genes (ATAC and RNA) in NASH vs non-NASH. Such genes encoded for factors related to lipid transport, nuclear receptor binding, dicarboxylic-acid-transporter, and PPARA-lipid regulation. Such promoters were enriched for motif sequences for TF as ZBTB12, Sox2 or Stat3. Interpolation of ATAC data with known liver enhancer regions showed differential openness at 8 enhancers, some of them linked to genes involved in lipid metabolism, such as FASN, or glucose homeostasis, such as GCGR.

Conclusions: Chromatin is altered in NASH compared to non-NASH. Such alteration might be related to changes in the transcriptional profile which can explain the etiology and pathophysiology of the disease. We demonstrated the importance of the epigenetic landscape in MAFLD, guarantying more studies that could result in the development of new epigenetic-based treatments.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

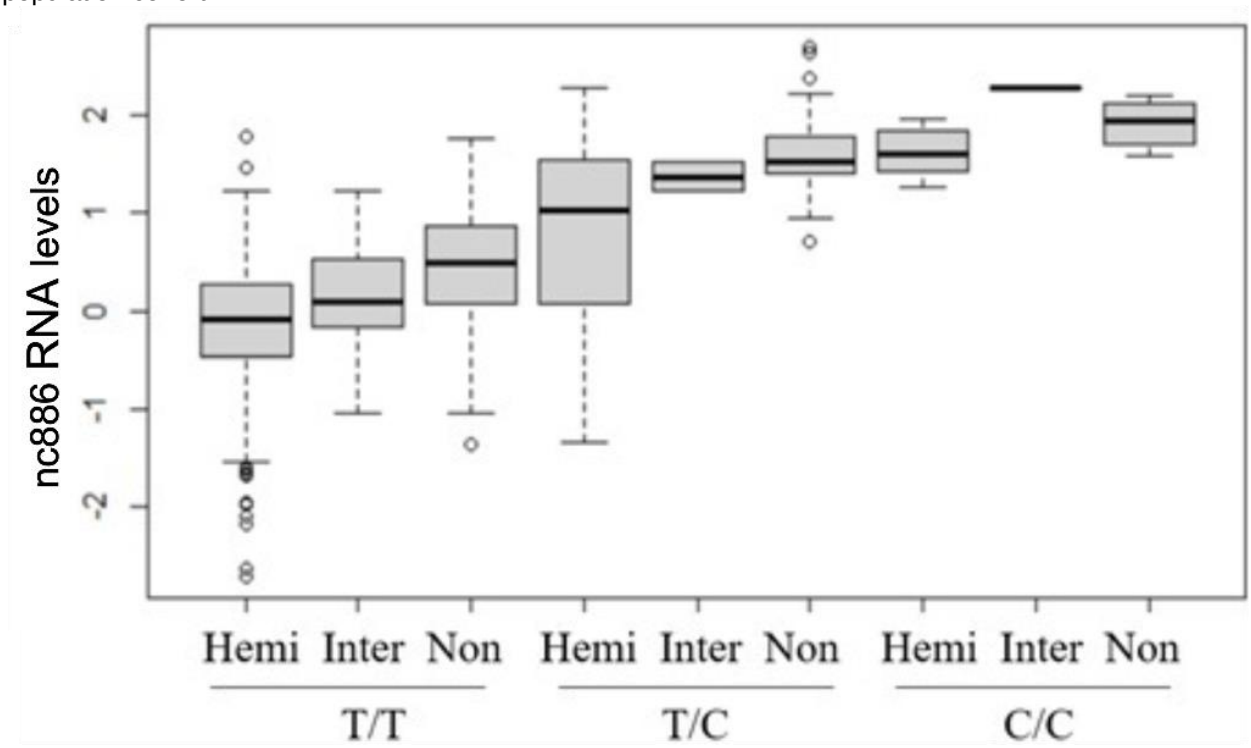
GENETIC AND EPIGENETIC REGULATION OF NC886 RNA LEVELS AND THEIR ASSOCIATION TO CARDIOMETABOLIC PHENOTYPES

POSTER VIEWING SESSION

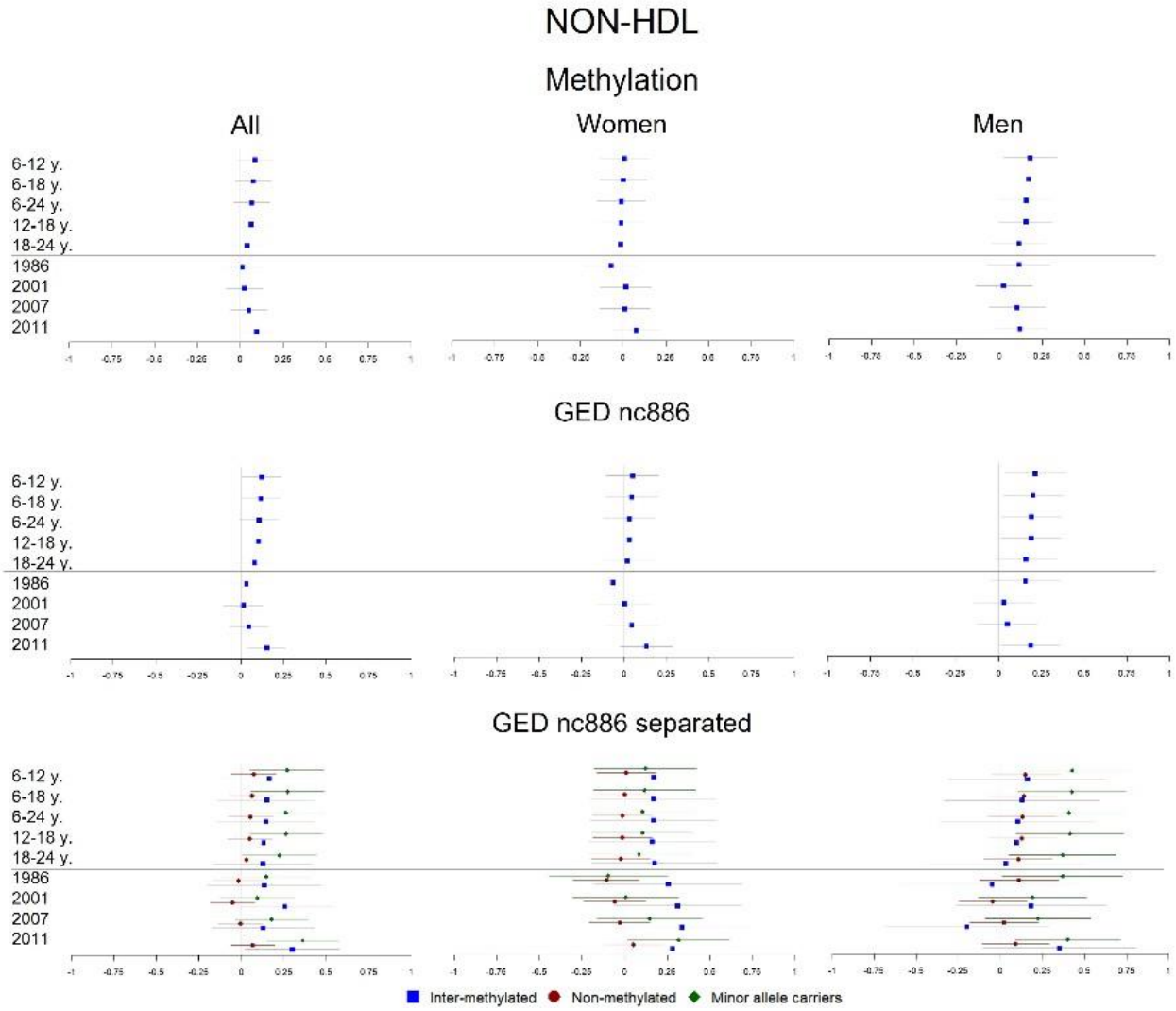
Sonja Rajic[1], Saara Marttila[2], Pashupati Mishra[2], Nina Mononen[2], Olli Raitakari[3], Leo-Pekka Lyytikäinen[2], Mika Kähönen[1], Nina Hutri-Kähönen[2], Melanie Waldenberger[4], Terho Lehtimäki[2], Emma Raitoharju[2]
[1]Faculty Of Medicine And Health Technology, Tampere University, Tampere, Finland, [2]Medicine And Health Technology, Tampere University, Tampere, Finland, [3]Research Centre Of Applied And Preventive Cardiovascular Medicine, University of Turku, Turku, Finland, [4]Research Unit Of Molecular Epidemiology, Helmholtz Zentrum München, Neuherberg, Germany

Background and Aims : A non-coding nc886 RNA is transcribed from a polymorphically imprinted metastable epiallele. Methylation status of this locus is affected by the periconceptional conditions and both the methylation status and the level of nc886 RNAs are shown to be associated with health traits in later life. We have previously shown that, in addition to the methylation status of the nc886 locus, genetics have an independent effect on nc886 RNA levels. As genotypic and methylation data are more commonly available in existing population cohorts than RNA levels, we set out to investigate whether we can leverage this information to further study the cardiometabolic associations of nc886 RNAs.

Methods: We created a variable that acts as an RNA level proxy by combining the effects of a lead SNP and methylation status and performed association analyses of it with the cardiometabolic phenotypes in a population cohort.



Results: Individuals with a genotype/epigenotype combination reflecting higher nc886 RNA levels have elevated insulin throughout their early lives, elevated LDL and non-HDL cholesterols in early and later life, elevated total cholesterol in later life, and decreased glucose in early and later life. Moreover, we found association with this genotype/epigenotype combination and prevalence of type 2 diabetes. We also performed sex-stratified analyses with similar results.



Conclusions: Our hope for the future is to use this variable to study the effect of nc886 RNA levels across different cohorts and further explore the association between nc886 levels and the relevant cardiometabolic phenotypes.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

THE IMPACT OF CHOLESTEROL LOWERING DRUGS ON METABOLISM AND EPIGENETICS

POSTER VIEWING SESSION

Alina Rose[1], Jesus R. Rodriguez-Aguilera[1], Gerda Schicht[2], Andrea Lohrenz[2], Andrey Tvardovskiy[3], Jörg Büscher[4], Anne Hoffmann[1], Georg Damm[2], Ulrich Laufs[5], Daniel Seehofer[2], Matthias Blüher[1], Bilal Sheikh[1]
[1]Vascular Epigenetics, Helmholtz-Institut für Metabolismus-, Adipositas- und Gefäßforschung (HI-MAG), Leipzig, Germany, [2]Hepatobiliary And Transplant Surgery, University of Leipzig, Leipzig, Germany, [3]Institute Of Functional Epigenetics, Helmholtz Zentrum Muenchen, Neuherberg, Germany, [4]Metabolomic, Max-Planck-Institute of Immunology and Epigenetics, Freiburg, Germany, [5]Kardiologie, Klinik und Poliklinik fuer Kardiologie am Universitaetsklinikum Leipzig, Leipzig, Germany

Background and Aims : Cardiovascular diseases (CVDs) are the leading cause of death globally. In patients with CVDs, treatment with cholesterol lowering drugs has been shown to reduce cardiovascular events. Bempedoic acid is a novel drug for lowering low-density lipoprotein cholesterol that has recently been approved for clinical use. Bempedoic acid specifically inhibits ATP citrate lyase (ACLY) in the liver, an enzyme that converts citrate to acetyl-CoA and acts at the interface of carbohydrate and lipid metabolism. ACLY is not only cytoplasmic, but is also found in the nucleus, where it regulates histone acetylation levels. Yet, it is unknown if and how bempedoic acid impacts ACLYs regulatory function in the nucleus.

Methods: By combining chromatin immunoprecipitation sequencing, transcriptomics, tracer metabolomics and mass-spectrometry based histone post-translational modification analysis in primary human hepatocytes, we systematically investigate the impact of bempedoic acid on ACLY at different regulatory levels.

Results: Our data from mouse liver tissue revealed binding of ACLY to promoter regions of metabolic genes. Consistently, gene expression analyses in primary human hepatocytes showed reduced expression of ACLY bound metabolic genes in response to bempedoic acid. Furthermore, histone modification analysis via mass spectrometry and ChIP-seq profiles displayed a highly specific loss of H3K9ac, a promoter-based histone modification known to stimulate gene transcription, upon bempedoic acid treatment. Metabolite profiling revealed reduction in lipid metabolism following bempedoic acid administration.

Conclusions: Taken together, these data suggest that bempedoic acid's mechanism of action involves reprogramming of the epigenetic and transcriptional landscape of ACLY associated genes, together with a reduction in lipid production in hepatocytes.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

CIRCULATING MICRO-RNAS IMPLICATED IN LIPOPROTEIN METABOLISM IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA OF UNKNOWN ORIGIN

POSTER VIEWING SESSION

Tycho R. Tromp, Laurens F. Reeskamp, Aldo Grefhorst, Erik S. Stroes, G.K. Hovingh
Department Of Vascular Medicine, Amsterdam UMC - Location AMC, Amsterdam, Netherlands

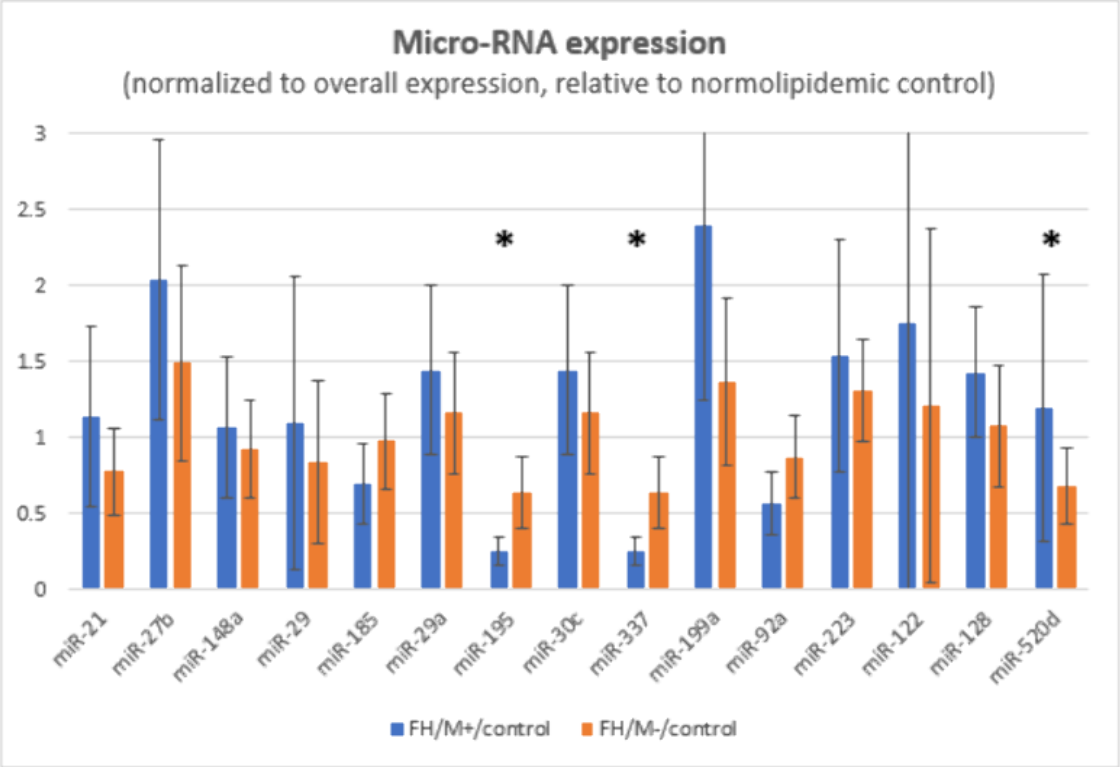
Background and Aims : In many patients with clinical FH, no underlying genetic cause can be identified. MicroRNAs (miRs) are noncoding oligonucleotides involved in the posttranscriptional regulation of gene expression and several miRs have been shown to be associated with regulation of lipoprotein metabolism and plasma LDL-cholesterol levels. We hypothesized that mutation-negative FH is associated with different composition of plasma miRs.

Methods: Patients with FH of unknown were included based on a DLCN score of 'probable FH' or higher in whom no pathogenic FH variant nor secondary causes were found (FH/M-, n=38). These patients were compared to FH patients with a pathogenic *LDLR* variant (FH/M+; n=33). RNA was isolated from plasma, purified for small RNA fragments and 15 pre-selected miRs were quantified by qPCR. Starting concentrations (N_0) were calculated using the LinRegPCR approach. Results were normalized to the overall within-sample miR expression and compared to the mean plasma expression of the selected miRs in normolipidemic controls (n=25).

Results: Plasma concentrations of miR-195 and miR-337 were lower in both FH patient groups compared to controls (both $p<0.001$; Figure 1). Plasma concentration of miR-520d, which is known to be associated with increased LDLR expression through downregulation of PCSK9, was lower in FH/M- patients compared to FH/M+ patients

(p<0.01).

Figure 1 – Relative expression of miRs implicated in lipoprotein metabolism in patients with familial hypercholesterolemia of known and unknown origin



FH, familial hypercholesterolemia; miR, micro-RNA; FH+, FH due to *LDLR* variant; FH-, FH of unknown origin

*Difference between FH/M- group compared with both FH/M+ and control groups, statistically significant after Bonferroni correction for multiple testing. Test: Kruskal-Wallis test.

Conclusions: The plasma concentrations of miRs implicated in lipoprotein metabolism vary between patients with FH of known and unknown origin. The relatively lower plasma expression of miR-520d in FH/M- subjects may suggest a role of this circulating miR in causing FH of unknown origin in some patients.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-14 Epigenetics and microRNA*

THE RECONSTRUCTION OF T CELL-TYPE-SPECIFIC MIRNA-MRNA EXPRESSION IN CAROTID ATHEROSCLEROTIC PLAQUES

POSTER VIEWING SESSION

Aleksei Zarubin[1], Alexei A. Sleptcov[1], Maria Nazarenko[2,3], Anastasiia Diagel[4]
[1]Research Institute Of Medical Genetics, Tomsk National Research Medical Center of Russian Academy of Sciences, Tomsk, Russian Federation, [2]Research Institute Of Medical Genetics,, Tomsk National Research Medical Center of Russian Academy of Sciences, Tomsk, Russian Federation, [3]Department Of Medical Genetics, Siberian State Medical University, Tomsk, Russian Federation, [4]Faculty Of Medicine And Biology, Siberian State Medical University, Tomsk, Russian Federation

Background and Aims : T-cells play an essential role in atherogenesis. Integration of different levels of data such as miRNA and mRNA expression in a cell-type-dependent manner is a relatively new field of study of atherogenesis. This study aimed to reconstruct T cell-type-specific miRNA-mRNA expression in carotid atherosclerotic plaques.

Methods: We performed miRNA sequencing of 5 paired samples of carotid atherosclerotic plaques and intact carotid arteries with NEBNext Multiplex Small RNA Library kit and HiSeq 1500. Data processing, evaluation of miRNA expression, and in-silico cell deconvolution were performed using miARma-Seq package, edgeR, and DeconRNASeq with FANTOM5 miRNA atlas as a reference. The miRNA-mRNA expression changes in T-cells were analyzed by integrating our miRNA-seq data, miRNA-target genes from miRTarBase, and single-cell RNA-seq data (GSE159677).

Results: T-, NK- and macrophage cellular components were found only in the atherosclerotic plaques using deconvolution of artery cell composition by miRNA-seq data. We identified 125 differentially expressed miRNAs (DEmiRNAs) between atherosclerotic plaques and intact carotid arteries ($log2FC>|1|$; $FDR<0.05$) and they have 1371 experimentally validated targets (genes) according to miRTarBase. 119 differentially expressed genes (DEG) were found between T-cells in carotid atherosclerotic plaques and intact carotid arteries. Five genes (PIK3R1, GAS5, VIM, TIMP1, CEBPD) and nine miRNAs (miR-376a-3p, miR-486-5p, miR-155-5p, miR-222-3p, miR-138-5p, miR-134-5p, miR-377-3p, miR-96-5p, miR-95-3p) were detected in the integrated analysis.

Conclusions: We identified 9 DEmiRNAs and 5 DEGs that may contribute to T cell-type-specific miRNA-mRNA expression in carotid atherosclerotic plaques. This research is supported by Grant No. 22-25-00745 from the Russian Scientific Foundation.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

EFFECT OF A HYPOCALORIC MEDITERRANEAN DIET ON BODY COMPOSITION AND METABOLIC PROFILE IN OVERWEIGHT AND OBESITY INDIVIDUALS

POSTER VIEWING SESSION

Fotios Barkas[1], Iliana Prifti[1], Eleni Maggiorou[1], Foteini Apostolou[1], Ad Koutsogianni[1], Petros Adamidis[1], Georgia Anastasiou[1], Sisi-Fotini Sakkou[1], George Liamis[1], Evangelos Liberopoulos[2]
[1]Department Of Internal Medicine, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannnina, Greece, [2]1st Propaideutic Department Of Medicine, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Background and Aims : We aimed to investigate the effect of hypocaloric Mediterranean Diet on the metabolic profile and body composition in individuals with increased body weight.

Methods: A retrospective observational study including adults with body mass index (BMI) ≥25 kg/m^2 followed-up at the outpatient Lipid and Obesity Clinic of Ioannina University General Hospital, Greece. Metabolic parameters and body composition as assessed with bioelectrical impedance were recorded at baseline visit and 3 months after a hypocaloric Mediterranean Diet (-500 Kcal/day).

Results: Among 50 study participants (50±12 years old, 29% men), 90% were obese, 56% fulfilled metabolic syndrome criteria, 40% were diagnosed with hypertension, 10% with type 2 diabetes and 14% with established cardiovascular disease. During follow-up, 45% and 12% of participants lost ≥5% and ≥10% of body weight, respectively. Overall, hypocaloric Mediterranean diet was associated with a reduction of body weight by 5.4%, fat mass by 1.5% and visceral fat by 1.0% ($p<0.05$). A similar improvement was observed in glycemic and lipid profile. **Table** Effect of hypocaloric Mediterranean Diet on the metabolic profile of overweight and obese individuals

Body weight,kg
Body mass index,kg/m ^{2}
Waist circumference,cm
Fat mass,%
Visceral fat,%
Systolic blood pressure,mmHg
Diastolic blood pressure,mmHg
Fasting glucose,mg/dL
HOMA index
Total cholesterol,mg/dL
Triglycerides,mg/dL
High-density lipoprotein cholesterol,mg/dL
Low-density lipoprotein cholesterol,mg/dL

*$p<0.05$

Conclusions: Hypocaloric Mediterranean diet improves metabolic profile and body composition of overweight and obese individuals.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

EFFECT OF STATINS ON ALKALINE PHOSPHATASE IN PATIENTS WITH DYSLIPIDEMIA: A 6-YEAR RETROSPECTIVE STUDY

POSTER VIEWING SESSION

Fotios Barkas[1], Petros Adamidis[1], Sisi-Fotini Sakkou[1], Ad Koutsogianni[1], Georgia Anastasiou[1], Konstantina Kyrili[1], George Liamis[1], Evangelos Liberopoulos[2]
[1]Department Of Internal Medicine, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannnina, Greece, [2]1st Propaideutic Department Of Medicine, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Background and Aims : Alkaline phosphatase (ALP) has been associated with atherosclerotic cardiovascular disease. The effect of statins on ALP is unknown. We aimed to investigate the effect of statin therapy on ALP in patients with dyslipidemia.

Methods: A retrospective observational cohort including consecutive adults with dyslipidemia followed-up for ≥3 years (from 1999 to 2015) was conducted in the outpatient Lipid Clinic of Ioannina University General Hospital, Greece. Clinical and laboratory profile was evaluated at baseline and most recent visit.

Results: Among 1334 patients, 953 (45% men, 56 [48-64 years old]) initiated statin therapy: 31%, 58% and 11% received high-, moderate- and low-intensity statins, respectively. During a median 6-year follow-up (4-10 years), LDL-C levels decreased by 46% (from 175 [149-206] to 95 [78-113] mg/dL, $p < 0.05$) and ALP by 16% (from 69 [55-93] to 58 [48-73] U/L, $p < 0.05$). No significant correlation was observed between the change in ALP and other parameters: $r=0.753$, $p > 0.05$ for the change in eGFR; $r=0.950$, $p > 0.05$ for LDL-C reduction; $r=0.265$, $p > 0.05$ for statin intensity. The change in subjects' ALP was not significantly associated with the risk of incident atherosclerotic cardiovascular disease during their follow-up (OR: 1.001, 95% CI: 0.994-1.009, adjusted for cardiovascular risk factors).

Conclusions: ALP was significantly reduced in statin-treated patients. This reduction seems not to be associated with cardiovascular risk.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

COMPARISON OF HYPOCALORIC MEDITERRANEAN DIET PLUS INTERMITTENT FASTING AGAINST CLASSIC HYPOCALORIC MEDITERRANEAN DIET ON BODY COMPOSITION AND METABOLIC PARAMETERS IN OBESE INDIVIDUALS

POSTER VIEWING SESSION

Fotios Barkas[1], Eleni Maggiorou[1], Alexandros Kokkinos[2], Nikolaos K. Tentolouris[2], Evangelos Liberopoulos[2]
[1]Department Of Internal Medicine, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannnina, Greece, [2]First Department Of Propaedeutic Internal Medicine, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background and Aims : To evaluate the effect of a hypocaloric Mediterranean Diet combined with intermittent fasting (TRFMedDiet) on body composition and metabolic parameters in obese individuals compared with a classic hypocaloric Mediterranean Diet (MedDiet).

Methods: An open label randomized clinical trial comparing TRFMedDiet (14:10) with MedDiet in obese individuals was conducted in the outpatient Lipid Clinic of Ioannina University General Hospital, Greece. Caloric deficit in both groups was 500 Kcal/day. We studied the effect of these diets on subjects' weight, body composition and metabolic profile after a 3-month intervention.

Results: Among study participants (n=20, 42±15 years old, 30% males), 75% were diagnosed with dyslipidemia, 20% with hypertension and 35% fulfilled the criteria of metabolic syndrome. Both diets were effective in improving body weight (MedDiet: -6.9%, TRFMedDiet: -8.4%, $p < 0.05$ for both groups) and composition with no significant differences between them. The rates of body weight reduction by >5% and >10% were 50% and 30%, respectively, in MedDiet group. The corresponding rates were 80% and 30% in TRFMedDiet group. Compared to MedDiet, TRFMedDiet was associated with a significantly higher reduction of TGs by 26.9% ($p < 0.05$), whereas a non-significant trend towards a higher decrease in apolipoprotein B and insulin resistance HOMA index was noticed.

Conclusions: TRFMedDiet and MedDiet are both effective in reducing body weight and related metabolic parameters.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

PATIENT ACTIVATION, HEALTH AWARENESS, AND PATIENT JOURNEY IN PATIENTS WITH CARDIOVASCULAR RISK FACTORS RECEIVING TREATMENT FOR HYPERCHOLESTEROLEMIA

POSTER VIEWING SESSION

Greta Brocculi[1], Agnese Garavaglia[2,3], Liliana Grandi[4], Elisabetta A. Grillo[3]
[1]Communication & Patient Engagement Department, Novartis Farma S.p.A., Origgio, Italy, [2]Medical Department, Novartis Farma, Origgio, Italy, [3]Medical Department, Novartis Farma S.p.A., Origgio, Italy, [4]Marketing Excellence And Strategic Operations, Novartis Pharma S.p.A., Origgio, Italy

Background and Aims : To assess associations between patient activation, disease perception, and patient-physician communication in patients at high cardiovascular risk receiving treatment for hypercholesterolemia.

Methods: A survey of 161 patients (78% men, mean age 61.8±8.6) treated for hypercholesterolemia as primary prevention in CKD/diabetes (n=78), or secondary prevention (n=83). Data collected by Computer-Assisted Web Interview using a questionnaire on awareness of hypercholesterolemia-related cardiovascular risk and the Patient Activation Measure (PAM-13) assessed patient-reported health-related behaviors and outcomes. We compared patients with low-moderate activation (PAM Levels 1+2; n=48) vs. moderate-high activation (PAM Levels 3+4; N=113) regarding disease knowledge and awareness, and patient journey. Descriptive statistics were used.

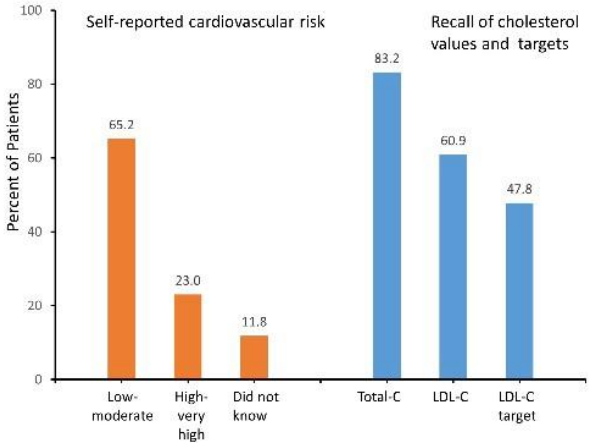
Results: Patient activation (PAM Levels 3+4) was associated with better disease knowledge, seeking of specialist care for hypercholesterolemia, and higher satisfaction with care. It was also associated with more regular physical activity and lower mean LDL-C levels (**Table**).

Table 1. Association between patient activation (PAM-13 level) and attitudes, behavior and outcomes.

	Level 1: Over-whelmed, struggling.	Level 2: More self-aware, still struggling, building confidence	Level 3: Taking action. Able to achieve guideline behaviors.	Level 4: Maintain behaviors and pushing further.
Criteria	**PAM Levels 1+2**		**PAM Levels 3+4**	
Knowledge/perceptions	(n = 48)		(n = 113)	
Disease knowledge (1-7 scale)	4.63		5.27*	
Chose a Specialist* to manage hypercholesterolemia care (%)	40.7		60.4*	
Satisfaction: support and visit frequency with Specialist (%)	69.8		85.3*	
Satisfaction with care (%)	87.5		96.5*	
Behavior				
Physical activity (%)	39.6		57.5*	
Outcomes				
Mean LDL-C levels (mg/mL)	132 ± 10.9		108 ± 6.2*	

PAM, 13-Item Patient Activation Measure; *t-Test, p > 0.05.
*Chose any medical specialist, as opposed to General Practitioner, as the principal reference.

Figure 1. Disease awareness: self-reported cardiovascular risk and serum cholesterol in patients with renal insufficiency and/or diabetes or pervious cardiovascular events.



However, overall knowledge on hypercholesterolemia was poor, with 60.3% reporting low scores (1-5 of 7); 83.2% knew their total cholesterol values; only 60.9% knew their LDL-C values, and only 47.8% knew their LDL-C targets (**Figure**). Cardiovascular risk was underestimated, considering that this population comprises patients in secondary prevention or primary prevention with renal insufficiency and/or diabetes: 65.2% reported low-moderate risk; only 23.0% reported high-very high risk; 11.8% did not know their risk (**Figure**).

Conclusions: Patient activation is associated with more disease knowledge, healthy self-management attitudes/behaviors and better disease control; however, awareness of LDL-C levels/targets and a realistic perception of CV risk are scarce and should be discussed and reinforced by both general practitioners and specialists.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

A BEHAVIOURAL SCIENCE RESEARCH PROGRAMME TO UNDERSTAND THE BARRIERS TO ACHIEVING RECOMMENDED LDL CHOLESTEROL GOALS

POSTER VIEWING SESSION

Amy L. Clarke[1], Silvia Bodini[1], Laura Douglas[1], Alberico L. Catapano[2], Leonardo De Luca[3], Tim Hollstein[4], Jules Payne[5], Matteo Pirro[6], Adie Viljoen[7], Anja Vogt[8], Rob Horne[1,9]
[1]Behavioural Science, Spoonful of Sugar Limited, a University College London (UCL) Business company, Hove, United Kingdom, [2]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [3]Department Of Cardiosciences, AO San Camillo-Forlanini Hospital, Roma, Italy, [4]Division Of Endocrinology, Diabetology And Clinical Nutrition, Department Of Internal Medicine 1, University of Kiel, Arnold-Heller-Straße 3, Kiel, Germany, [5]Chief Executive, HEART UK - The Cholesterol Charity., Maidenhead, United Kingdom, [6]Department Of Medicine And Surgery, University of Perugia, Perugia, Italy, [7]Borthwick Research Unit, Lister Hospital, stevenage, United Kingdom, [8]Medizinische Klinik Und Poliklinik Iv, Klinikum der Universität München, Munich, Germany, [9]Centre For Behavioural Medicine, School Of Pharmacy, University College London, London, United Kingdom

Background and Aims : Evidence suggests a gap between clinical guideline development and successful real-world implementation, with an estimated 4 out of 10 patients receiving non-evidenced-based care.[1] Ensuring research addresses the drivers of this evidence implementation gap is a key health priority. Involving clinicians and patients in research design can help to synthesise existing knowledge and generate key recommendations to guide research. We convened an expert panel, as first step to help guide a 2-year behavioural science research programme - Cardio Connect: which aims to explore barriers to achieving recommended LDL cholesterol goals.

Methods: An expert panel of N=4 behavioural scientists, N=5 clinicians (cardiologists and lipidologists) and a patient organisation representative, from Germany, Italy, and UK, attended a 3-hour virtual meeting. Behavioural scientists proposed a mixed-methods research programme and invited discussion.

Results: Key research guiding principles emerged from the experts discussion and experience: 1) explore experiences of treatment access inequality, accounting for regional differences; 2) explore ways to better empower patients; 3) understand differences in the application of clinical guidelines between clinical specialties; 4) explore perceptual factors (e.g. clinicians concerns) and practical barriers (e.g. financial restraints) to delivering evidence-based care from patients' and clinicians' perspectives. Experts also advised on ways to engage the clinical and patient community: 1) disseminate findings at local and disease specific conferences; 2) engage patient organisations to reach under-served patients.

Conclusions: Research is needed to better understand the evidence-implementation gap in dyslipidaemia. This research programme will apply behavioural science and be co-designed with patient and clinical communities.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

IMPORTANCE OF BASELINE LDL-C IN THE ASSOCIATION BETWEEN LDL-C LOWERING AND CARDIOVASCULAR RISK: A META-REGRESSION ANALYSIS

POSTER VIEWING SESSION

Emma Hawe[1], Sreelatha Meleth[2], Sorrel Wolowacz[1], Aikaterini Bilitou[3]
[1]Health Economics, RTI-HS, Manchester, United Kingdom, [2]Biostatistics, ICON PLC, Dublin, United Kingdom, [3]Health Economics And Outcomes Research, Daiichi Sankyo Europe, Munich, Germany

Background and Aims : Lipid lowering treatments (LLTs) are typically approved based on LDL-C lowering effects observed in randomized controlled trials (RCTs). In economic evaluations, effectiveness in preventing cardiovascular events is typically predicted using the relationship between LDL-C lowering and cardiovascular risk. Several studies have demonstrated that treatments which reduce LDL-C levels also reduce cardiovascular events, and this relationship is robust across diverse biological mechanisms of lipid lowering. We aimed to explore the importance of baseline LDL-C in the relationship between LDL-C reduction and cardiovascular risk.

Methods: Thirty-six RCTs were identified from a systematic literature review supplemented with targeted searches. Random effects meta-regression was performed with and without the inclusion of baseline LDL-C as a covariate. Models were compared using the Akaike and Bayesian Information Criteria (AIC and BIC). Correlation (R-squared) and statistical heterogeneity (Higgins I-squared) were assessed.

Results: For major cardiovascular events, myocardial infarction, cardiovascular mortality, and revascularization endpoints, AIC, BIC, and I-squared were consistently lower, and R-squared was consistently higher, for models including baseline LDL-C as a covariate than those without. P-values for baseline LDL-C were highly significant for these endpoints (P≤0.003).

Table 1. P-values for LDL-C reduction and baseline LDL-C by cardiovascular endpoint (random effects meta-regression for LDL-C reduction with baseline LDL-C as a covariate)

Endpoint	LDL-C reduction *P*-value	Baseline LDL-C *P*-value
Major cardiovascular events	0.0853	0.0007
Myocardial infarction	0.1300	0.0030
Cardiovascular mortality	0.0220	0.0004
Revascularisation	0.0007	0.0030

Conclusions: The results support the well documented association between LDL-C and cardiovascular risk reduction. Furthermore, models accounting for baseline LDL-C as well as the LDL-C reduction on treatment may provide more accurate predictions of cardiovascular risk than models based on LDL-C reduction alone. Limitations of this work include the use of aggregate trial data rather than patient-level data (which were not available to us from source studies).

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

NON-DIPPER PATTERN ON 24 HOURS AMBULATORY BLOOD PRESSURE MONITORING IN NORMOTENSIVE SUBJECTS IS ASSOCIATED WITH LOWER LEVEL OF HIGH-DENSITY CHOLESTEROL

POSTER VIEWING SESSION

Anna S. Isayeva[1], Lolita Matiashova[2]
[1]Department Of Complex Risk Reduction Of Chronic Non-communicable Disease, L.T. Mala National Therapy Institute of NAMSU, Kharkiv, Ukraine, [2]Complex Risk Reduction Of Chronic Non-communicable Diseases, L.T. Mala National Therapy Institute of NAMSU, Kharkiv, Ukraine

Background and Aims : The aim of the work was to study the connection between blood lipids level, inflammation markers, and dipper and non-dipper patterns of blood pressure circadian rhythm.

Methods: Methods. The cross-sectional study included 41 normotensive subjects with age median 52.3 [41.5 ÷ 61.2] years old. Ambulatory blood pressure monitoring was done to all patients with Heaco ABPM50 monitoring. Fasting glucose, blood lipids, creatinine, high sensitive C-reactive protein (hCRP), and interleukin 1 beta were measured. Physical activity was measured using the International Physical Activity Questionnaire. Eating behavior was assessed with standardized soft “Test of Rational Nutrition” (TRP-D02, Ukraine). Data were analyzed with SPSS IBM 19.0.

Results: Results. Parameters of ambulatory blood pressure monitoring are presented in the table1. It was found out that hCRP was significantly higher in a non-dipper subgroup of (2.37[0.97-4.75] *vs* 2.87[1.84-523], p=0,03, Mann-Whitney). Total cholesterol, triglycerides, and low-density cholesterol did not differ significantly between dipper and non-dipper groups. High density cholesterol was low in non-dipper group (1.41 [1.19-1.71] *vs* 1.12 [0.91-1.20] mmol/l, p=0.04, Mann-Whitney). Table 1. Parameters of ambulatory 24 hours blood pressure monitoring, Median, [25%-75%] Quartiles

	Dipper group	Non-dipper group
Daily SBP, mm Hg	122.0 [109.1-125.2]	122.3 [105.5-125.52]
Daily DBP, mm Hg	72.3 [61.7-79.2]	69.1 [62.6-75.5]
Day SBP, mm Hg	125.0 [112.6-129.0]	122.8 [111.1-127.5]
Day DBP, mm Hg	74.2 [65.2-82.7]	72.2 [66.2-79.2]
Night SBP, mm Hg	104.4 [100.3-112.5]	118.6[101.9-121.9]
Night DBP, mm Hg	64.7 [55.9-67.0]	66.9 [61.1-77.8]

Conclusions: Conclusion. The non-dipper pattern of blood pressure circadian rhythm is associated with decreased high-density lipoproteins and elevated hCRP levels in normotensive subjects.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

EFFICACY AND SAFETY OF LONG-TERM ADMINISTRATION OF PEMAFIBRATE, A NOVEL HYPOTRIGLYCERIDEMIC AGENT, IN JAPANESE TYPE 2 DIABETIC PATIENTS RECEIVING A STATIN

POSTER VIEWING SESSION

Masataka Kusunoki[1], Naomi Wakazono[2], Shinichi Matsuda[3], Fumiya Hisano[4], Tetsuro Miyata[5]
[1]Research Center Of Health, Physical Fitness And Sports, Nagoya University, Nagoya, Japan, [2]Research Center Of Health, Physical Fitness And Sports, Nagoya University, nagoya, Japan, [3]Department Of Data Science, Nanzan University, Nagoya, Japan, [4]Graduate School Of Medicine, Nagoya University, nagoya, Japan, [5]Sanno Medical Center, Vascular Center, tokyo, Japan

Background and Aims : Hepatic dysfunction and myopathy are raised as adverse effects on combination therapy of fibrates and statins. In the present study, we evaluated efficacy and safety of long-term administration of pemafibrate in type 2 diabetic patients receiving a statin.

Methods: We recruited type 2 diabetic patients having dyslipidemia and normal or mild renal impairment. The subjects were divided into Statin+PFB (n=12) and PFB (n=10) groups of which the patients were treated with or without a statin (1-4 mg/day pitavastatin or 2.5-5 mg/day rosuvastatin) for 6 months, and then we started additional administration of 0.2 mg/day pemafibrate to both groups. Twelve months after, blood biochemical data of the patients were compared with them measured before the pemafibrate administration.

Results: Pemafibrate significantly reduced serum triglyceride in both groups. Serum total cholesterol and LDL-cholesterol were significantly lowered in the Statin+PFB group whereas no significant change was observed in the PFB group. Also, atherosclerosis index, an indirect parameter of development of atherosclerosis, significantly decreased in the Statin+PFB group. While serum levels of alanine aminotransferase, γ-glutamyl transferase, and creatine kinase was significantly lowered only in the PFB group, we observed no significant elevation of the parameters of hepatic function and myopathy in both the groups.

Conclusions: Pemafibrate kept the triglyceride-lowering effect for 12 months regardless of the presence or absence of the statin treatment in patients with type 2 diabetes. Besides, the combination therapy of statin and pemafibrate could have beneficial effects on development of atherosclerosis via improvement of not only serum cholesterol but also triglyceride without adverse effects.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

ADHERENCE TO MEDITERRANEAN DIET AND THE RELATIONSHIP AMONG WEIGHT STATUS, PHYSICAL ACTIVITY, AND SLEEP BEHAVIOR IN BRAZILIAN UNDERGRADUATE STUDENTS

POSTER VIEWING SESSION

Ana Maria Lottenberg[1], Atila Steigerwald[2], Roberta M. Machado[1]
[1]Faculdade Israelita De Ciências Da Saúde Albert Einstein, Hospital Israelita Albert Einstein, Sao Paulo, Brazil, [2]Faculdade Israelita De Ciências Da Saúde Albert Einstein, Hospital Israelita Albert Einstein, São Paulo, Brazil

Background and Aims : The progressive increase in obesity rates in Brazil has been associated with a sedentary lifestyle, poor sleep quality, and inadequate eating habits. The eating pattern in Brazil is inadequate, with only 34.6% of the adults regularly eating fruits and vegetables. The university environment contributes to inappropriate eating habits. AIM: The present study aims to evaluate the dietary pattern and lifestyle habits and relates it with anthropometric parameters in undergraduate students of Faculdade Israelita de Ciências da Saúde Albert Einstein.

Methods: 132 healthy subjects were engaged (18-24 yr) in a cross-sectional study. The participants self-filled anthropometric data and questionnaires. The Brazilian version of the KIDMED questionnaire (Mediterranean Diet Quality Index in children and adolescents) was applied to assess adherence to the Mediterranean Diet. Sleep pattern was assessed by the Brazilian version of the PSQI-BR (Pittsburgh Sleep Quality Index); the physical activity level was accessed by IPAQ (International Physical Activity Questionnaire).

Results: Subjects age was 21.01 +/- 1.51 yrs and BMI was 23.41 +/- 3.99; 19.30% were overweight, 6.4% were obese grade I, and 1.77% as obese grade

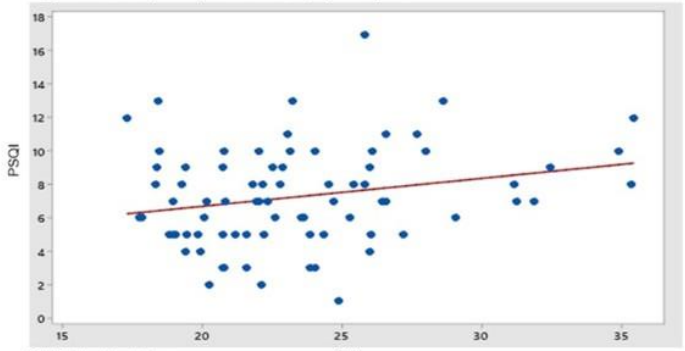
Table. BMI* range in relation to KIDMED score**

KIDMED	n	Mean	CI de 95%
≥ 8 points	31	23.34±3.95	(21.92; 24.75)
4 a 7 points	54	22.79±3.48	(21.72; 23.87)
0 a 3 points	28	24.66±4.82	(23.17; 26.15)

*BMI: Body Mass Index

**KIDMED: Mediterranean Diet Quality Index in children and adolescents

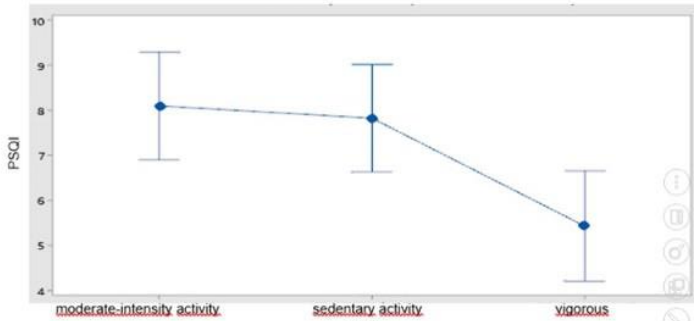
Figure1. BMI* (n=114) *versus* PSQI(n=86)**



*BMI: Body Mass Index

**PSQI: Pittsburgh Sleep Quality Index, BMI x PSQI: Correlation: Pearson: p=0,035

Figure2. PSQI* (n=86) *versus* IPAQ(n=89)**



*PSQI: Pittsburgh Sleep Quality Index

**IPAQ: International Physical Activity Questionnaire

PSQI *versus* IPAQ: p=0,005. Correlation: Tukey

II.

Conclusions: Among the population studied, only 26% presented high adherence to Mediterranean pattern. Inadequate intake of fruits, vegetables and dairy products was observed. Better sleep quality was positively associated with physical activity and inversely associated with BMI. Despite the absence of significant correlation between KIDMED and BMI, overweight individuals were only present in the group with the lower adherence to the Mediterranean diet

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

IMPORTANCE OF URIC ACID THRESHOLD IN ITS CORRELATION WITH METABOLIC SYNDROME

POSTER VIEWING SESSION

Alessandro Maloberti, Ilaria Garofani, Stefano Fumagalli, Claudio Mario Ciampi, Paolo Ossola, Marco Carbonaro, Massimiliano Monticelli, Giovanni Tavecchia, Michele Bombelli, Cristina Giannattasio
Cardiologia 4, ospedale niguarda, milano, Italy

Background and Aims : The relationship between Serum Uric Acid (SUA) and Metabolic Syndrome (MS) is still debate. Whether SUA level is part of MS diagnosis or just a marker of an unfavourable metabolic profile has not been demonstrated. Besides it's unknown whether SUA's addition to MS definition makes a difference in terms of prognosis. In our study we focused on evaluating in a group of hypertensive patients, the correlation between MS diagnosis and SUA defined with classic cut-off (≥6 mg/dL for women and ≥7 for men) and URRAH's threshold (>5.6 mg/dL for both sexes).

Methods: We enrolled 473 Hypertensive patients followed by the Hypertension Unit of San Gerardo Hospital (Monza, Italy), in which SUA was measured. Patients with Hyperuricemia were identified according to the two different thresholds. NCEP-ATP-III criteria were used for diagnosis of MS.

Results: MS was diagnosed in 33.6% while Hyperuricemia was found in 14.8% of subjects according to traditional cut-off and 35.9% according to URRAH study's cut-off. Hyperuricemia and MS coexist in 9.7% (traditional cut-off) and 17.3% (URRAH's threshold) of the population. Hyperuricemia was more frequent in MS than in non-MS subjects (29vs7.6%,p-value<0.0001 for 6/7 mg/dL; 51.6vs28.0%,p-value<0.0001 for 5.6 mg/dL). Linear regression models showed that SUA is related to MS (β=1.597,p-value<0.0001). At logistic analysis Hyperuricemia was strongly related to MS when defined by the HURRAH's cut-off (OR=0.303,p-value<0.0001). The same relation is weak, although significan, when Hyperuricemia was defined by the classic cut-off (OR=0.182,p-value<0.0001).

Conclusions: Hyperuricemia is related with MS diagnosis especially when defined by the recently defined cut-off of 5.6 mg/dL

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

ATRIAL FIBRILLATION INCIDENCE IN SARS-COV-2 INFECTED PATIENTS: PREDICTORS AND RELATIONSHIP WITH IN-HOSPITAL MORTALITY

POSTER VIEWING SESSION

Alessandro Maloberti[1], Cristina Giannattasio[1], Paola Rebora[2], Giuseppe Occhino[1], Nicola Ughi[1], Jacopo Rizzo[1], Saverio Fabbri[1], Filippo Leidi[1], Iside Cartella[1], Michela Algeri[1], Sara Scarpellini[1], Claudio Rossetti[1], Oscar Massimiliano Epis[1], Giulio Molon[1], Paolo Bonfanti[1], Maria Grazia Valsecchi[2], Simonetta Genovesi[3]
[1]Cardiologia 4, ospedale niguarda, milano, Italy, [2]Statistica, University of Milano-Bicocca, Monza, Italy, [3]Neprologhy, University of Milano-Bicocca, Monza, Italy

Background and Aims : Among the different CardioVascular (CV) manifestation of the CoronaVIrus-related Disease (COVID) particular attention has been paid to Atrial fibrillation (AF). The aim of our study was to assess the incidence of AF episodes in patients hospitalized for COVID and to evaluate its predictors and its relationship with in-hospital all-cause mortality.

Methods: We enrolled 3435 cases of SARS-CoV2 infection admitted in four hospitals in Northern Italy. We collected data on clinical history, vital signs, Intensive Care Unit (ICU) admission, laboratory tests and pharmacological treatment. AF incident and all-cause in-hospital mortality were considered as outcomes.

Results: 145 (4.2%) patients develop AF during hospitalization, with a median time of 3 days (IQR:0,11.5) from admission. Incident AF patients were older and had lower eGFR, lower platelet and lymphocytes count and higher C-Reactive Protein (CRP), were admitted more frequently to ICU and more frequently died compared to subjects that didn't present AF. At the Cox regression model significant determinants of incident AF were older age (HR 1.070; 95% CI: 1.048-1.092), history of AF (HR 2.800; 95% CI:1.465-5.351), ischemic heart disease (HR 0.324; 95% CI: 0.130-0.811) and ICU admission (HR 8.030; 95% CI:4.511, 14.292). Incident AF was a predictor of all-cause mortality (HR 1.679; 95% CI:1.170-2.410), together with age (HR 1.053; 95% CI: 1.042-1.065), dementia (HR 1.553; 95% CI:1.151-2.095), platelet count (HR 0.997; 95% CI:0.996-0.999) higher CRP (HR 1.004; 95% CI:1.003-1.005) and eGFR (HR: 0.991; 95% CI:0.986-0.996)

Conclusions: AF present as the main arrhythmia in COVID-19 patients and its development during the hospitalization strongly relates with in-hospital mortality.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

PRESCRIPTIVE APPROPRIATENESS IN PRIMARY CARDIOVASCULAR PREVENTION: DATA FROM NIGUARDA HOSPITAL

POSTER VIEWING SESSION

Alessandro Maloberti, Davide Ceruti, Elena Gualini, Valentina Colombo, Valentina Giani, Martina Milani, Jinwei Sun, Marta Alloni, Cristina Giannattasio
Cardiologia 4, ospedale niguarda, milano, Italy

Background and Aims : The main cause of waste of health resources is represented by overuse of diagnostic and therapeutic procedures. Given its high prevalence and the importance of identifying hypertensive-mediated organ damage, management of patients with arterial hypertension can lead to a lack of appropriateness. The aim of this study was to evaluate the prescriptive appropriateness of non-invasive diagnostic tests (Echocardiography, Carotid ultrasound, ECG exercise testing, 24h Ambulatory blood pressure monitoring) in outpatients referring to an ambulatory of primary cardiovascular prevention.

Methods: 559 specialistic ambulatory visits were retrospectively analysed and appropriateness of every prescription was evaluated. An integration of different Italian and European guidelines was used to define appropriateness. Moreover, we evaluated the correlation between prescriptions, appropriateness and clinical characteristics of the population.

Results: During the 559 ambulatory visits analysed, 449 prescriptions were made, including 198 echocardiographies, 148 carotid ultrasound, 85 24h ABPM and 18 ECG exercise testing. The global percentage of appropriate prescriptions was 40.3%. Focusing on each test, appropriateness rate was 49.4% in 24h ABPM, 43.9% in echocardiography, 38.9% in ECG exercise testing and 30.4% in carotid ultrasound. A significant correlation was identified between the age and cardiovascular risk category of patients and the appropriateness of echocardiography, 24h ABPM and carotid ultrasound, and a correlation between appropriateness of echocardiography and the duration of hypertension and the presence of valvular heart disease.

Conclusions: Our study shows a relevant percentage of inappropriate prescriptions of non-invasive cardiologic exams; moreover, there might be a greater lack of appropriateness in young and low risk patients.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

THE LIPID PROFILE OF POST-CORONARY SYNDROME PATIENTS AND THEIR RESIDUAL CARDIOVASCULAR RISK

POSTER VIEWING SESSION

Fatma Zohra Mebarek, Djamaleddine Nibouche
Cardiology, Hussein Dey university hospital, algiers, Algeria

Background and Aims : - **Dyslipidemia is a major cardiovascular(CV) risk factor, in North Africa, little information is available on the lipidic status of the population, especially of patients with myocardial infarction. - In this study, we evaluated the lipid profile of patients after admission for ACS and their residual risk for CV disease following statin treatment.**

Methods: - **This study was realized at the cardiology department of the Hussein Dey hospital, from September 2020 to January 2021, 146 patients hospitalized for ACS, lipid-lowering treatment(LLT)naîve were included, fasting lipid assessment was performed after admission, mostly after 72 hours, and 08 weeks later. All patients received « Atorvastatin 80mg » as LLT.**

Results: - **Population mean age was 59±10 years, 80.8%were male, the initial mean level of Total cholesterol(TC) was 1.76g/l, LDLc 1,12g/l, HDLc 0,32g/l, Triglyceride 1,58 g/l, and Non-HDLc 1,44g/l. - Dyslipidemia was found in 58.9% of patients.,28,1%had hypercholesterolemia,49,3% hypertriglyceridemia,5,5% high LDLc,82,2% a low HDLc. - After high-intensity statin treatment for secondary prevention, lipidic results showed a remaining high triglyceride level in 25,3% of patients , low HDLc levels in 81,5% ,49,3% of patients had an LDLc levels > 0,55g/l and Non-HDLc levels > 0,85g/l in 40,4%**
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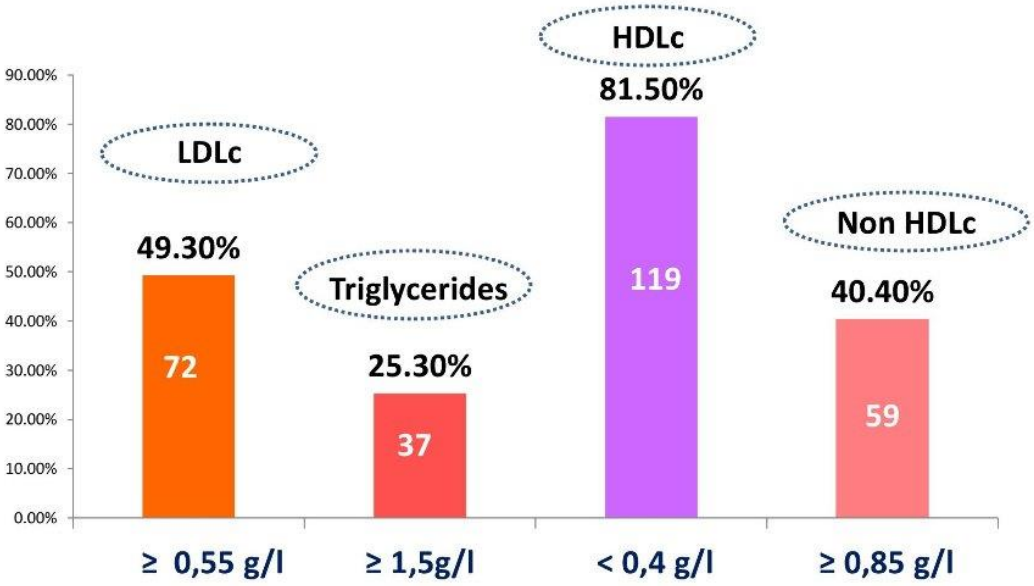
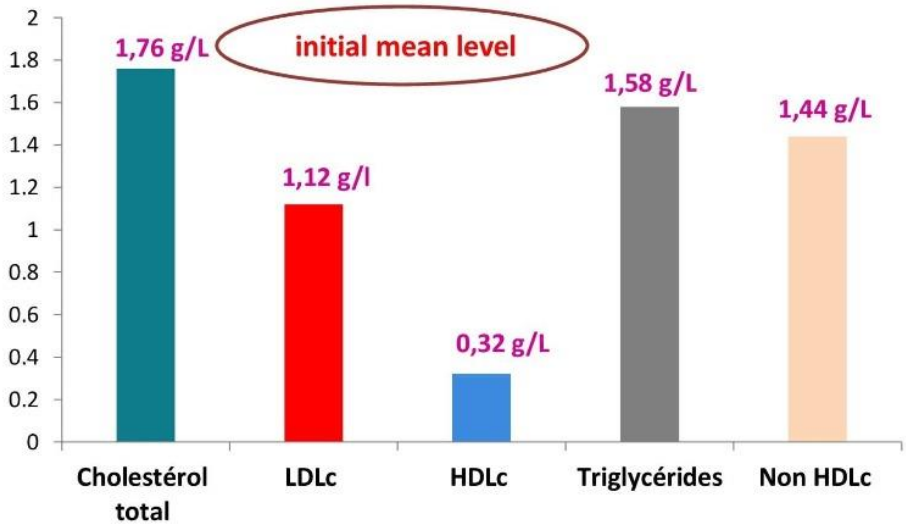
The residual level of lipid parameters according to ESC 2019 after statin treatment



Initial mean total cholesterol, LDLc, triglycerides, HDLc, Non-HDLc levels



Conclusions: - Our population study, had relatively low LDLc levels with high triglyceride levels and very low HDLc levels(atherogenic dyslipidemia) at the admission assessment, contrary to expectations. - More than half of patients remain with low HDLc and high Non-HDLc levels as residual risk after statin treatment, additional therapeutic molecules (fibrates, ezetimibe...) are needed to correct residual lipid abnormalities.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

STATIN INTOLERANCE: WHAT ARE WE OVERLOOKING?

POSTER VIEWING SESSION

Silvia Paredes[1], Liliana Fonseca[2], Miguel Saraiva[2], Helena Ramos[2], Isabel Palma[2]
[1]Endocrinology, Centro Hospitalar do Tâmega e Sousa, Penafiel, Portugal, [2]Endocrinology, Centro Hospitalar Universitário do Porto - Hospital de Santo António, Universidade do Porto, Portugal

Background and Aims : Statin intolerance is defined as any adverse event and/or laboratory abnormality attributed to statin and leading to its discontinuation. Although statins are generally extremely well tolerated, intolerance may occur and requires careful consideration. The authors describe a clinical case where statin intolerance has revealed a more complex diagnosis.

Methods: Description of clinical case

Results: A 56-year-old man was referred to the Endocrinology Department due to metabolic syndrome. He presented obesity, dyslipidemia, prediabetes and fatty liver disease, had no history of tobacco or significant alcohol use or history of cardiovascular disease. Laboratory findings revealed LDL-cholesterol 259.8 mg/dL, AST 47 (0-37) and ALT 76 (0-40) U/L, normal CK. He started on pravastatin 40 mg per day, with a significant reduction of LDL-cholesterol. Two years later, the patient started with complaints of proximal leg weakness and laboratory findings revealed elevated CK (1341 U/L, 6.5X upper limit of normal), aldolase and lactic acid dehydrogenase. Pravastatin was suspended, nevertheless symptoms did not improve and CK remained elevated (717-2484 U/L, reference 24-204), with a normal electromyography. One year later, the patient reported progression of muscle weakness, electromyography was normal, and muscle biopsy evidenced “undetermined myopathy”. Genetic study revealed a RYR1 mutation compatible with the diagnosis of Ryanodine Receptor-1 Related-Myopathy.

Conclusions: In this clinical case, the statin unmasked an underlying pre-symptomatic myopathic condition. When evaluating patients labeled as statin intolerant, the persistence of symptoms after stopping the statin, the severity of the muscle symptoms and the magnitude of CK elevation should call attention for a differential diagnosis.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

SERUM LIPIDS AND IL-6 CONCENTRATION IN RATS FED WITH HIGH PROTEIN DIET AFTER SIBUTRAMINE TREATMENT

POSTER VIEWING SESSION

Maria I. Trapali
Biomedical Sciences, UNIVERSITY OF WEST ATTICA,GREECE, ATHENS, Greece

Background and Aims : Diabetes mellitus is a chronic condition characterized by a disturbance in carbohydrates metabolism,fats and proteins. High Protein Diet is associated with a change in carbohydrate metabolism observed in Diabetes. Sibutramine is a nor adrenaline and serotonin reuptake inhibitor that has beneficial effects on serum lipoproteins. Interleukin 6 (IL-6) is an interleukin that acts as both a pro-inflammatory cytokine and an anti-inflammatory myokine. Studies in experimental animals indicate that IL-6 in the Central Nervous System partly mediates the suppression of food intake and body weight. The aim of the study was to explore the effects of macronutrients and Sibutramine(S) on serum IL-6 and lipoprotein levels in rats fed with standard laboratory diet (SD) and High protein diet (HPD).

Methods: MATERIAL AND METHOD: Two groups of 21 male Wistar rats consumed Standard Diet (SD) or High Protein Diet (HPD) (casein 64%) for 13 weeks. In the last 3 weeks each of them was divided into 3 subgroups received vehicle, Sibutramine 5 or 10mg/kg. Serum lipoproteins and IL-6 were assayed. Serum lipoproteins levels were measured with a photometric method while IL-6 levels were measured by enzyme-linked-immunosorbent assay.

Results: RESULTS: Serum HDL-CHOL was lower in the SDS0 compared to HPDS0 group, in the SDS5 compared to HPDS5, in HPDS10 compared to HPDS5. Sibutramine administration did not affect serum IL - 6, HDL or LDL in any diet group at any dose.

Conclusions: CONCLUSIONS: Further studies are necessary to evaluate the effect of sibutramine on IL -6 levels and demonstrate the long-term effects of sibutramine administration on IL-6 levels.

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Topic: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-16 Other*

CHANGES IN ARTERIAL STIFFNESS AFTER OUTPATIENT AEROBIC TRAINING FOLLOWED BY HOME-BASED TRAINING USING A HEART RATE MONITOR IN PEOPLE WITH METABOLIC SYNDROME

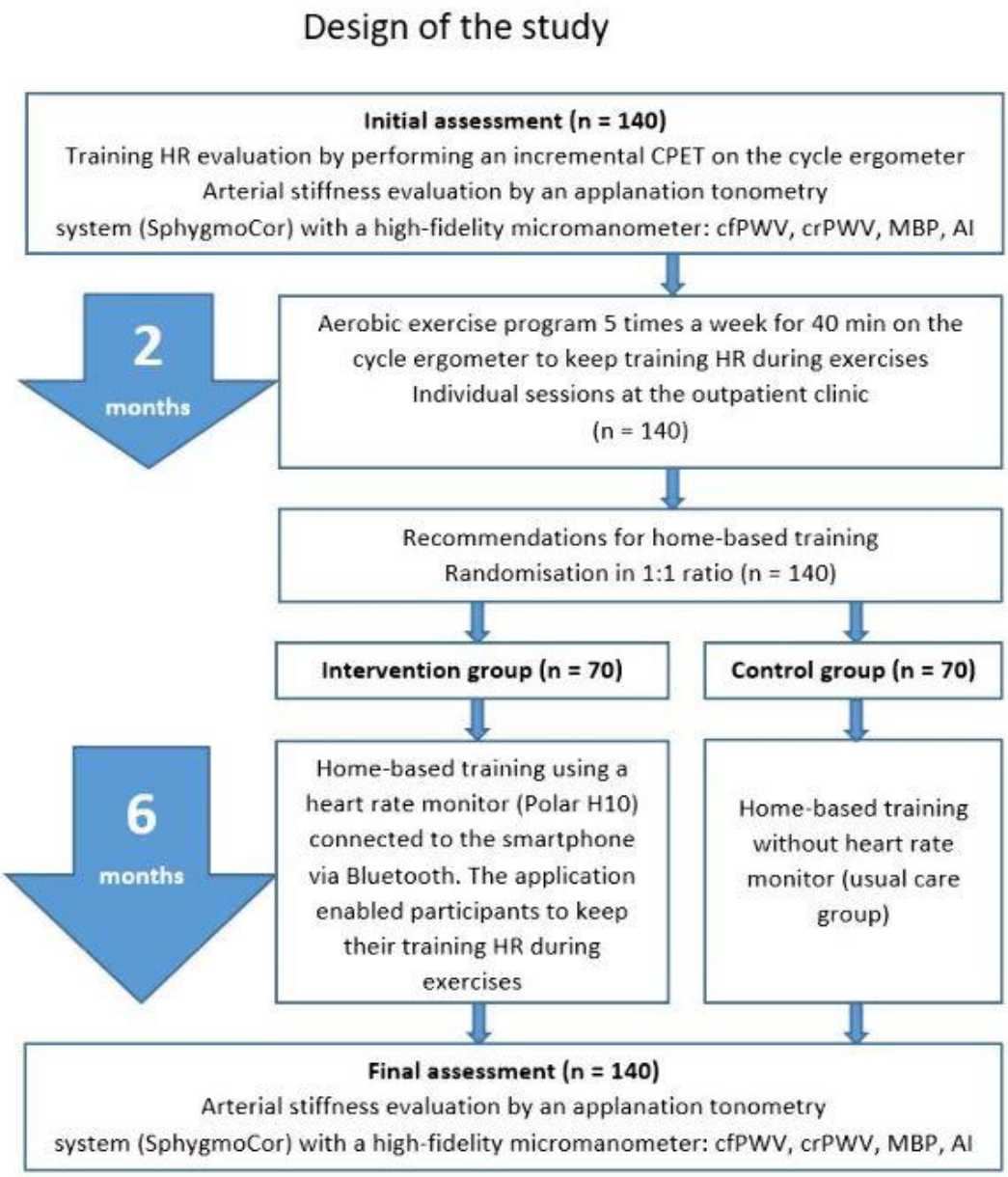
POSTER VIEWING SESSION

Jurate Zupkauskiene, Aleksandras Laucevicius
Clinic Of Cardiac And Vascular Diseases, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Background and Aims : People with metabolic syndrome (MetS) are usually not physically active and are at increased risk for cardiovascular disease. Increased arterial stiffness independently reflects higher cardiovascular risk. The aim was to evaluate the changes in arterial stiffness parameters after the outpatient aerobic exercise program (aEP) followed by the home-based aEP using a heart rate (HR) monitor in people with MetS.

Methods: A total of 140 white caucasians with MetS were included to the prospective study (mean age 52.5±6.18-years, 46.4%-male). Initially, all individuals participated in the 2-month outpatient aEP. Then only the intervention group (n=70) participated in the 6-month home-based aEP using a HR monitor (Polar-H10). Carotid–femoral pulse wave velocity (cfPWV), carotid-radial pulse wave velocity (crPWV), mean blood pressure in the aorta (MBP) and aortic augmentation index (AI) were assessed in all participants at baseline and after 8 months (see

Figure1).



***Abbreviations**: HR, heart rate; CPET, cardiopulmonary exercise test; cfPWV, carotid-femoral pulse wave velocity; crPWV, carotid-radial pulse wave velocity; MBP, mean blood pressure in the aorta; AI, aortic augmentation index.*

Results: After 8 months, cfPWV significantly reduced in both groups (all p<0.001) with better cfPWV improvement in the intervention group (see Figure2). MBP significantly improved only in the control group (p<0.001), but between-group difference was not significant. No statistically significant reduction of AI was observed in any of the groups. After 8 months, crPWV significantly reduced only in the intervention group by 0.51±1.85 m/s (p=0.039).The reduction of crPWV in the intervention group occurred when baseline crPWV was in the 2nd quartile (>7.77 m/s,

p<0.001).

Changes in arterial stiffness parameters after 8 months

	Intervention group					*p* value between	Control group				
Parameter	At baseline	After 8 months	Change		*p* value *	the groups **	*p* value *	Change		After 8 months	At baseline
cfPWV	8.42 ± 1.11	7.56 ± 1.16	-0.9 ± 1.35	-10.69%	**< 0.001**	**0.013**	**< 0.001**	-9.86%	-0.84 ± 1.4	7.78 ± 1.44	8.52 ± 1.28
crPWV	8.8 ± 1.54	8.29 ± 1.27	-0.51 ± 1.85	-5.80%	**0.039**	**0.002**	0.241	-4.03%	-0.37 ± 1.56	8.84 ± 1.17	9.19 ± 1.18
MBP	106 ± 11.5	105 ± 9.54	-1.72 ± 11.96	-1.62%	0.277	0.513	**< 0.001**	-6.97%	-7.32 ± 9.59	98.8 ± 10.5	105 ± 9.28
AI	18.6 ± 9.66	19.8 ± 12.2	1.3 ± 9.12	6.98%	0.287	**0.037**	0.449	-5.29%	-1.2 ± 10.01	22 ± 11	22.7 ± 12.5

Data are presented as mean ± Standard deviation or %. *p* value in bold denotes a statistically significant difference ($p < 0.05$).

*Paired samples T-test. Student's t-test for normally distributed continuous data or the Wilcoxon signed-rank test for non-normally distributed continuous data

**Repeated Measures ANOVA adjusted for group, age, sex, systolic and diastolic blood pressure at baseline.

Abbreviations: cfPWV, carotid-femoral pulse wave velocity; crPWV, carotid-radial pulse wave velocity; MBP, mean blood pressure in the aorta; AI, aortic augmentation index.

Conclusions: People with MetS, who participated not only in the outpatient aEP but also in the home-based aEP using a HR monitor, reached a greater reduction of cfPWV and crPWV.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

FIBRINOLYTIC MARKERS IN CORONARY THROMBI

POSTER VIEWING SESSION

Jostein Nordeng[1,2,3], Ragnhild Helseth[2,3], Sissel Åkra[2], Pavel Hoffman[4], Hossein Schandiz[5], Borghild Roald[1,6], Bjørn Bendz[1,7], Harald Arnesen[1,2], Svein Solheim[2,3], Ingebjørg Seljeflot[1,2,3]
[1]Faculty Of Medicine, University of Oslo, Oslo, Norway, [2]Cardiology, Center for Clinical Heart Research, Oslo University Hospital Ullevål, Norway, Oslo, Norway, [3]Department Of Cardiology, Oslo University hospital, Oslo, Norway, [4]Cardiology, Section for Interventional Cardiology, Oslo University Hospital Ullevål, Oslo, Norway, [5]Pathology, Akershus University Hospital, Nordbyhagen, Norway, [6]Pathology, Oslo University Hospital Ullevål, Oslo, Norway, [7]Cardiology, Oslo University Hospital Rikshospitalet, Oslo, Norway

Background and Aims : The fibrinolytic system plays a role in coronary artery atherosclerosis, and especially circulating PAI-1 associate with increased mortality, infarct size and heart failure in patients with myocardial infarction (MI). We aimed to study whether genes encoding t-PA, u-PA, PAI-1 and PAI-2 are expressed in coronary thrombi from ST-elevation MI (STEMI) patients, and any relations to the degree of myocardial injury measured by peak troponin T, time from symptom to PCI, and to cell types present in the thrombi.

Methods: Intracoronary thrombi were aspirated from 33 STEMI patients treated with primary PCI. The thrombi were snap-frozen for gene expression analyses, relatively quantified by RT PCR. Peripheral blood samples were drawn. Correlations were performed by Spearmans rho.

Results: Investigated genes were present in 74-94% of the thrombi. Median peak troponin T was 3434 m/L and median ischemic time 152 minutes. There were no significant correlations between the measured genes and troponin T, or to ischemic time. Genes encoding t-PA, u-PA, PAI-1 and PAI-2 all correlated significantly to the presence of monocytes/macrophages (CD68) in the thrombi ($p=0.028$, $p<0.001$, $p=0.003$, $p<0.001$). PAI-1 and PAI-2 also correlated to endothelial cells (CD31) ($p=0.002$, $p=0.016$). uPA associated with neutrophil granulocytes (CD 66b) ($p=0.019$).

Conclusions: Genes encoding t-PA, u-PA, PAI-1 and PAI-2 were highly expressed in human coronary thrombi from STEMI patients, indicating fibrinolytic regulators to play active roles in the thrombi, although not related to myocardial injury. All markers related especially to the presence of monocytes/macrophages, indicating these markers to be connected to local inflammatory cells.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

ASSOCIATION OF LIPID INDICATORS WITH BLOOD COAGULATION PARAMETERS IN PATIENTS WITH CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Olesya Rubanenko[1], Anatoly Rubanenko[2], Igor Davydkin[1]
[1]Hospital Therapy, Samara State Medical University, Samara, Russian Federation, [2]Propedeutic Therapy, Samara State Medical University, Samara, Russian Federation

Background and Aims : To evaluate association of lipid indicators with blood coagulation parameters in patients with coronary artery disease (CAD).

Methods: Studied were 132 patients with CAD, mean age - 47.5±6.7 years. All the patients had stable angina pectoris, mean class 1.4±0.3. In all the patients, we studied fibrinogen, D-dimer and von Willebrand factor (vWf) levels. We evaluated total cholesterol, low (LDL) and high-density (HDL) lipoproteins, triglycerides levels.

Results: Mean LDL level was 3.1±0.6 mmol/l, total cholesterol level – 4.64±0.9 mmol/l, triglycerides level – 1.61±0.45 mmol/l, HDL level – 1.26±0.35 mmol/l. Mean fibrinogen level was 3.8±0.7 g/l, vWf level - 134±23.8%, D-dimer – 0.98±0.6 μg/ml. We observed significant correlations between LDL and D-dimer levels ($R=0.42$, $p<0.001$), LDL and fibrinogen levels ($R=0.39$, $p<0.001$), LDL and vWf levels ($R=0.34$, $p<0.001$), total cholesterol and fibrinogen levels ($R=0.47$, $p<0.001$), total cholesterol and D-dimer levels ($R=0.41$, $p<0.001$), total cholesterol and vWf levels ($R=0.4$, $p<0.001$), triglycerides and fibrinogen levels ($R=0.3$, $p<0.001$).

Conclusions: We found that patients with CAD had elevated mean levels of vWf and D-dimer. D-dimer and vWf had significant positive correlations with lipid indicators in patients with CAD.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

CLOPIDOGREL EFFICACY AFTER PERCUTANEOUS CORONARY INTERVENTIONS CONSIDERING WITH CYP2C19 GENETIC POLYMORPHISMS IN PATIENTS WITH CORONARY HEART DISEASE

POSTER VIEWING SESSION

Jamol Uzokov[1], Bakhromkhon Alyavi[2], Akbar Abdullaev[1], Daler Orziev[1], Ibrokhim Madjitov[2]
[1]Cardiology, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan, [2]Cardiology, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

Background and Aims : Aim of the study was to estimate the impact of CYP2C19 genetic polymorphisms on the antiplatelet response with clopidogrel and their possible relationship between mean platelet volume (MPV) in patients with coronary heart disease (CHD) after percutaneous coronary interventions (PCI).

Methods: 110 patients (aged 42-75 years; mean age 55.40±14.2; male n=52) with CHD who were underwent PCI followed by stenting with DES were enrolled. Platelet aggregation (PA) were performed at baseline and after the twelve hours with six hundred mg loading dose of clopidogrel. Genetic polymorphisms of the CYP2C19 were performed using PCR. Platelet count and mean platelet volume (MPV) were assessed.

Results: 48% of patients had CYP2C19*1, 21 % CYP2C19*2, 11% CYP2C19*3 and 20% CYP2C19*17 genetic polymorphisms. 84.0 % of patients had a response to clopidogerel. Most of the non-responders were subjects with CYP2C19*2 and CYP2C19*3 genotypes. Inhibition of PA significantly increased in 12 hours after loading dose in CYP2C19*17 genotype with 5 mmol/L, and 20 mmoll/L ADP ($P<0.05$), and normally increased after 12 hours with loading dose in CYP2C19*1 subjects ($P<0.05$) whilst IPA was not changed significantly in subjects with CYP2C19*2 and CYP2C19*3 genetic polymorphisms with 5 mmol/L and 20 mmoll/L ADP ($P>0.05$). Platelet count did distinguish in all genetic variants. Mean platelet volume was larger in non-responders than responders ($P<0.05$).

Conclusions: Carriers of the CYP2C19*2, CYP2C19*3 single nucleotide polymorphisms are predictor for clopidogrel resistance and CYP2C19*17 polymorphisms are strong responders in our subjects. Platelet count did not differ in all variant while MPV tended to be smaller in responders.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-01 Coagulation and Thrombosis*

GENETIC VARIATION IN ADAMTS13 ARE RELATED TO VWF LEVELS, ATRIAL FIBRILLATION AND CEREBRAL ISCHEMIC EVENTS

POSTER VIEWING SESSION

Ellen Mathea Kirsch Warlo[1,2], Vibeke Bratseth[2], Alf-Åge R. Pettersen[2,3], Harald Arnesen[1,2], Ingebjørg Seljeflot[1,2], Trine B. Opstad[1,2]
[1]Faculty Of Medicine, University of Oslo, Oslo, Norway, [2]Cardiology, Center for Clinical Heart Research, Oslo University Hospital Ullevål, Norway, Oslo, Norway, [3]Medicine, Ringerike sykehus, Hønefoss, Norway

Background and Aims : ADAMTS13 is a metalloprotease cleaving ultra-large von Willebrand Factor (vWF) multimers into less active fragments. ADAMTS13 and vWF have both been related to cardiovascular disease (CVD). Several single nucleotide polymorphisms (SNPs) in the ADAMTS13 gene have been described. We aimed to investigate the influence of ADAMTS13 genetic variants on levels of ADAMTS13 and vWF, the SNPs' frequencies in subgroups of CVD and further any associations with clinical outcome after 2 years follow-up.

Methods: Patients with chronic coronary syndrome (n=1000) were investigated. The 1342 C/G, 284726 G/A and 2699 C/T polymorphisms were determined. ADAMTS13 antigen and activity, as well as vWF antigen, were analysed using chromogenic assays. Endpoints (n=106) were a composite of unstable angina pectoris, myocardial infarction, non-hemorrhagic stroke and death.

Results: None of the investigated ADAMTS13 SNPs were related to ADAMTS13 antigen or activity. The variant 284726 A-allele was significantly associated with higher vWF levels in % compared to the GG genotype [115 (92, 141) vs 102 (78, 129), p<0.001][§]. Patients with the variant 1342G-allele presented with significantly higher frequency of previous atrial fibrillation (n=26) (3.4% vs 0.7%, p=0.016) and cerebral ischemic events (n=47) (5.7% vs 2.4%, p=0.030) than the CC genotype. No relevant associations between the SNPs and clinical outcome were observed.

Conclusions: The association between the ADAMTS13 284726 A-allele and vWF levels indicates that this polymorphism is of importance for vWF regulation. ADAMTS13 has previously been linked to atrial fibrillation and ischemic stroke, and our findings suggest that the 1342G-allele may be of significance. [§]median (25^{th}, 75^{th} percentiles)

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-02 Endothelial dysfunction; Clinical assessment*

VARIABLE ASSOCIATION OF ANGPTL3 AND ANGPTL4 WITH VASODILATOR DYSFUNCTION IN DIFFERENT OBESE PHENOTYPES

POSTER VIEWING SESSION

Francesca Schinzari[1], Giuseppina Vizioli[2], Manfredi Tesauro[3], Carmine Cardillo[2]
[1]Aging, Policlinico A. Gemelli IRCCS, Roma, Italy, [2]Internal Medicine, Catholic University, Roma, Italy, [3]Systems Medicine, University Tor Vergata, Roma, Italy

Background and Aims : Obesity is associated with premature atherosclerosis and increased burden of cardiovascular disease, especially when accompanied by abnormalities of lipid and glucose metabolism. Angiopoietin-like (ANGPTL)3 and ANGPTL4 are metabolic regulators, whose upregulation is associated with dyslipidemia, insulin resistance and atherosclerosis. We analyzed, therefore, changes in circulating ANGPTL3 and ANGPTL4 in obese patients with different metabolic phenotypes and their relation with impaired vasodilator reactivity, an early abnormality in atherosclerosis.

Methods: Circulating ANGPTL3 and ANGPTL4 were compared in 42 lean subjects, 48 obese patients with none of the abnormalities of metabolic syndrome (MHO), 87 obese patients with at least one metabolic abnormality (MUO) and 31 obese patients with type 2 diabetes (T2D).

Results: Compared to lean subjects, ANGPTL3 was elevated in MUO and T2D (both $P>0.001$), but not in MHO ($P>0.05$); ANGPTL4, by contrast, was increased in all obese subgroups (all $P<0.001$ vs. controls), even though it was higher in T2D than in MHO and MUO (both $P<0.05$). Endothelium-dependent and independent vasodilation (plethysmography) to acetylcholine and sodium nitroprusside, respectively, were both lower in the 3 obese subgroups (all $P<0.001$ vs. controls), with greater impairment in T2D than in MHO and MUO (both $P<0.05$). In the whole population, an inverse, linear relationship ($R=0.27$; $P=0.003$) was observed between circulating ANGPTL4, but not ANGPTL3 ($P>0.05$), and endothelium-dependent vasorelaxation.

Conclusions: Circulating concentrations of ANGPTL3 and ANGPTL4 undergo variable changes in obese patients with different metabolic phenotypes. The obesity-related changes in ANGPTL4 relate to the presence of endothelial dysfunction, thereby making this protein a possible target for vascular prevention in these patients.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-03 NASH and other ectopic lipid diseases*

EFFECTS OF AN ISOENERGETIC MULTIFACTORIAL DIET ON PANCREATIC FAT AND INSULIN SECRETION IN PATIENTS WITH TYPE 2 DIABETES: A RANDOMIZED CONTROLLED TRIAL.

POSTER VIEWING SESSION

Giuseppe Della Pepa[1], Giuseppina Costabile[1], Dominic Salamone[1], Valentina Brancato[2], Serena Monti[3], Marco Salvatore[2], Paola Cipriano[1], Marilena Vitale[1], Gabriele Riccardi[1], Angela Albarosa Rivellese[1], Giovanni Annuzzi[1], Lutgarda Bozzetto[1]
[1]Department Of Clinical Medicine And Surgery, University of Naples Federico II, Naples, Italy, [2]Sdn, IRCCS, Naples, Italy, [3]Institute Of Biostructures And Bioimaging, CNR, Naples, Italy

Background and Aims : Pancreatic fat (PF) accumulation may impair beta-cell function. We investigated whether an isocaloric diet able to reduce liver fat in type 2 diabetes (T2D) also affected PF and postprandial insulin secretion.

Methods: Thirty-nine individuals with T2D (64±6 years, 56% male, HbA1c 6.5±0.5%, BMI 31±4 kg/m^2) were randomly assigned to an 8-week isocaloric intervention with 1) a multifactorial-diet rich in fiber, monounsaturated fatty acids (MUFA), n-6 and n-3 polyunsaturated fatty acids, polyphenols, and vitamins C, D, and E (n=18) or 2) a MUFA-diet (n=21). PF content was detected by ^{1}H-MRS, and plasma insulin and glucose concentrations were determined over a 4-h test-meal with a similar composition as the assigned diet. Differences between diets were evaluated by repeated measures analysis.

Results: After 8 weeks, PF significantly decreased after the multifactorial-diet (15.7%±6.5% vs 14.1%±6.3%, p=0.024) and did not change significantly after the MUFA-diet (17.1%±10.1% vs 18.6%±10.6%, p=0.139) (difference between changes, p=0.014). Postprandial glucose $iAUC_{0\text{-}240min}$ was not significantly different between dietary groups. In the first 2-h after the meal, postprandial insulin $iAUC_{0\text{-}120min}$ increased in the multifactorial group (5232±5034 *vs.* 6355±4590 µU/ml·120min, p=0.037), while it did not change significantly in the MUFA group (4354±2603 *vs.* 3884±1766, p=0.190) (difference between changes, p=0.024). In the whole cohort, changes in PF inversely correlated with changes in insulin $iAUC_{0\text{-}120min}$ (r=-0.334, p=0.046).

Conclusions: An isocaloric diet including several healthy components induced a reduction of PF in patients with T2D and increased postprandial insulinaemia, providing first evidence for a role of dietary composition on the pathogenetic link between pancreatic fat and T2D.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-03 NASH and other ectopic lipid diseases*

TITLE: ROLE OF NAFLD-ASSOCIATED GENETIC VARIANTS ON RENAL FUNCTION IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE

POSTER VIEWING SESSION

Alessia Di Costanzo[1], Francesco Baratta[2], Laura D'Erasmo[3], Ilaria Umbro[2], Alessandra Colantoni[4], Nicholas Cocomello[5], Daniele Pastori[2], Marcello Arca[6], Francesco Angelico[4], Maria Del Ben[5]
[1]Department Of Translational And Precision Medicine, Sapienza University of Rome, Roma, Italy, [2]1department Of Clinical Internal, Anesthesiological And Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy, [3]Department Of Translational And Precision Medicine, "Sapienza" University of Rome, Rome, Italy, [4]Department Of Public Health And Infectious Diseases, Sapienza University of Rome, Rome, Italy, [5]Department Of Clinical Internal, Anesthesiological And Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy, [6]Department Of Translational And Precision Medicine, Sapienza University of Rome, Rome, Italy

Background and Aims : NAFLD is associated with an increased risk of chronic kidney disease (CKD). Also, recent observations focused the attention on the role of *PNPLA3* rs738409 variant in the relationship between NAFLD and CKD in non-metabolic patients, but the genetic impact on this association is still matter of debate. We aim to investigate the potential influence of *PNPLA3*, *TM6SF2*, *MBOAT7* and *GCKR* gene variants on renal function in a large population of NAFLD patients.

Methods: All NAFLD susceptibility variants were genotyped by using Real Time PCR. Glomerular filtration rate (GFR) was estimated with CKD-epi formula. The effect of genetic variants was estimated both individually and by calculating a genetic risk score (wGRS). The effect of NAFLD on renal function was assessed by analyzing two endpoints: eGFR<90ml/min (rGFR) or eGFR<60ml/min (moderate-to-severe CKD).

Results: Among 564 NAFLD patients, the 48.0% had an eGFR below 90 ml/min while only 6.6% had moderate-to-severe CKD. The distribution of genotypes was superimposable if considering the entire group of patients with eGFR<90 ml/min or with eGFR<60 ml/min. At multivariate regression analyses (Table 1), we did not observe any correlation between genotypes and renal function. Conversely, MetS associated with rGFR [OR:1.52(1.07-2.18)] and prior ASCVD with moderate-to-severe CKD

[OR:3.54(1.22-10.24)].

Table 1. Multivariate regression analyses

Panel A. Factors Associated with eGFR < 90 ml/min				
	Model A OR (95% C.I.)	**Model B OR (95% C.I.)**	**Model C OR (95% C.I.)**	**Model D OR (95% C.I.)**
Metabolic Syndrome#	1.52* (1.07-2.18)	-	-	1.53* (1.07-2.18)
Arterial Hypertension	-	-	1.45* (1.02-2.06)	-
Panel B. Factors Associated with moderate-to-severe CKD				
	Model A OR (95% C.I.)	**Model B OR (95% C.I.)**	**Model C OR (95% C.I.)**	**Model D OR (95% C.I.)**
Prior ASCVD	3.54* (1.22-10.24)	3.55* (1.19-10.55)	-	3.44* (1.19-9.90)
Arterial Hypertension	-	-	2.85* (1.20-6.79)	-

#According to ATP III modified criteria; *p<0.05

Model A: including BMI, metabolic syndrome, prior ASCVD, PNPLA3 GG/CG and FIB4 -.

Model B: including component of the metabolic syndrome (namely high blood glucose, high waist circumference, high blood pressure, low HDL cholesterol, high triglycerides) instead of the composite score, prior ASCVD, PNPLA3 GG/CG genotype and FIB4 -.

Model C: including arterial hypertension instead of high blood pressure, diabetes instead of high blood glucose, high waist circumference, low HDL cholesterol, triglycerides, prior ASCVD, PNPLA3 GG/CG genotype and FIB4 -.

Model D: including BMI metabolic syndrome, prior ASCVD, weighted GRS and FIB4 -.

Conclusions: In our cohort of adult patients with NAFLD, we found no association between CKD and *PNPLA3, TM6SF2, MBOAT7* and *GCKR* gene variants. Hypertension was the stronger predictor of eGFR impairment. Based on these findings, the association between NAFLD and CKD might be due to the shared metabolic risk factors rather than the genetic NAFLD background.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-03 NASH and other ectopic lipid diseases*

IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE, LIVER STIFFNESS DIRECTLY CORRELATES WITH THE CAROTID PLAQUE BURDEN

POSTER VIEWING SESSION

Alla Kuznetsova[1], Anna Selyanina[1], Gusel Khusainova[1], Anastasiya Dolgushina[1], Igor Shaposhnik[2], Vadim Genkel[2]
[1]Hospital Therapy, South-Ural State Medical University, Chelyabinsk, Russian Federation, [2]Internal Medicine, South-Ural State Medical University, Chelyabinsk, Russian Federation

Background and Aims : It is now well established that non-alcoholic fatty liver disease (NAFLD) is associated with a significant increase in the risk of adverse cardiovascular events. NAFLD-specific cardiovascular risk scores, considering traditional and nontraditional risk factors, are needed to improve patient care. Liver fibrosis may be an integrative indicator of the burden of cardiometabolic risk factors. Liver fibrosis may also represent the burden of subclinical atherosclerosis. The aim of the study was to investigate the relationships between liver stiffness and carotid plaque burden in patients with NAFLD without established atherosclerotic cardiovascular disease.

Methods: A total of 73 NAFLD patients, 42 (57.5%) male and 31 (42.5%) female, with a median age of 48.5 (42.0-55.7) years, were included in the study. Liver steatosis was assessed non-invasively using the ultrasound-based Hamaguchi score. Liver stiffness was investigated by transient elastography using FibroScan®. All patients underwent a carotid duplex scan. Carotid total plaque area (cTPA) was measured as an indicator of carotid plaque burden.

Results: Carotid plaques were identified in 51 (69.8%) patients. Liver stiffness was directly correlated with cTPA (r=0.444; p=0.001). According to linear regression analysis, a change in liver stiffness could explain 26.1% of the variability in cTPA after adjustment for sex and age (see Figure 1). A 1 kPa increase in liver stiffness was associated with a 6.16 (1.78-10.5) mm^2 increase in cTPA.

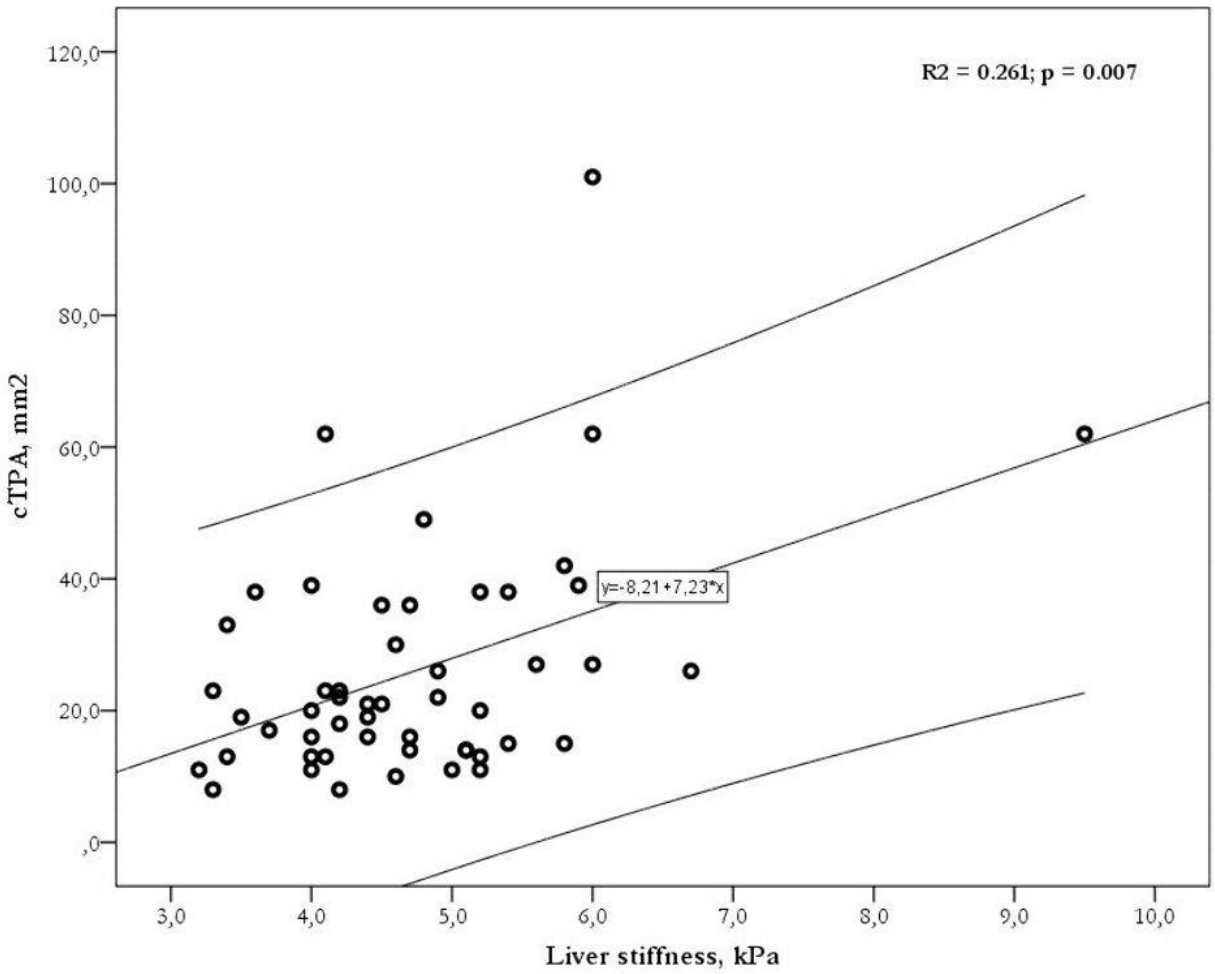

Figure 1. Relationship between liver stiffness and cTPA

Conclusions: In middle-aged patients with NAFLD, increased liver stiffness is associated with an increased carotid plaque burden.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

INTRAVASCULAR LITHOTRIPSY: A NEW WAY TO TREAT CALCIFIED RADIAL ARTERIES IN NON-FUNCTIONING PERIPHERAL FISTULAS FOR DIALYSIS

POSTER VIEWING SESSION

Emiliana Ferramosca[1], Marcello Napoli[1], Vilma Martella[1], Silvia Barbarini[1], Maria Luisa Lefons[1], Paolo Ria[1], Anna Zito[1], Paolo Raggi[2]
[1]Nephrology, Dialysis And Transplantation, Ospedale Vito Fazzi, Lecce, Italy, [2]Medicine-cardiology, University of Alberta, Edmonton, Canada

Background and Aims : Patients with advanced chronic kidney disease receiving hemodialysis (CKD-5D) have extensive arterial calcifications that may prevent the normal function of radio-cephalic fistulas (RCF, Fig 1) utilized as dialysis access. While radial artery angioplasty has given fair results, there is a risk of restenosis. Intravascular shockwave lithotripsy (IVSW) is a new technique to treat heavily calcified peripheral arteries. We describe the first 3 cases of radial artery IVSW (RA-IVSW) therapy in CKD-5D patients.

Methods: Three men, mean age 60 years, average dialysis vintage 4.4 years, two patients with and one without diabetes, were treated with RA-IVSW of failed surgical RCFs. A 5French introducer was inserted above the AV anastomotic site and the IVSW catheter (length 60 mm; diameter 3 mm) was passed through the introducer. Shockwave therapy was applied along the entire length of the radial artery.

Results: All RCFs were functioning at the end of the procedure. At 30 days the fistula blood flow rate measured by Doppler at the brachial artery level was excellent (>800 ml/min, Fig 2) in 2 patients and fair (500 ml/min) in one patient; the latter had a completely obstructed RCF prior to IVSW. All patients are currently undergoing regular dialysis through their RCFs utilizing a double-needle (artery-vein) technique.

Conclusions: IVSW may represent an excellent approach to salvage heavily calcified, non-functioning RCFs in patients receiving chronic hemodialysis. Long-term follow-up is necessary to verify whether IVSW facilitates the long-term patency of rescued
RCFs.

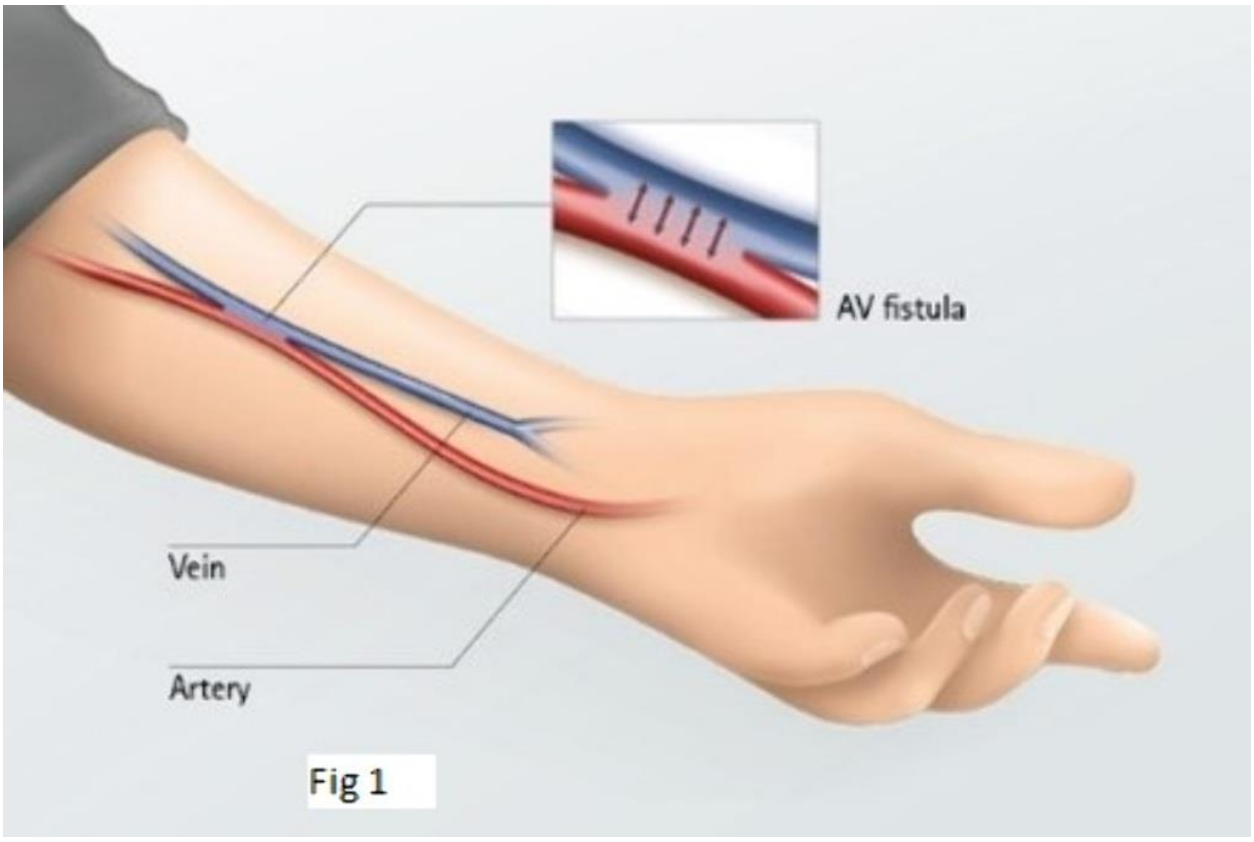

Fig 1

Fig 2a: Before IVSW

Fig 2b: After IVSW

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

BENEFICIAL EFFECTS OF PENTOXIFYLLINE IN THE EVOLUTION OF SUBCLINICAL ATHEROSCLEROSIS IN CHRONIC KIDNEY DISEASE PATIENTS

POSTER VIEWING SESSION

Carla M. Ferri[1,2], Javier Donate-Correa[1], Ernesto Martín-Núñez[1], Nayra Pérez-Delgado[3], Carmen Mora-Fernández[1], Ainhoa González Luis[1,2], Alberto Martín Olivera[1,2], Juan F. Navarro-González[1,4,5,6]
[1]Unidad De Investigación, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain, [2]Escuela De Doctorado Y Estudios De Posgrado, Universidad de La Laguna, San Cristóbal de La Laguna, Spain, [3]Servicio De Análisis Clínicos, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain, [4]Servicio De Nefrología, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain, [5]Instituto De Tecnologías Biomédicas, Universidad de La Laguna, San Cristóbal de La Laguna, Spain, [6]Sociedad Española De Nefrología,, GEENDIAB (Grupo Español para el estudio de la Nefropatía Diabética), Santander, Spain

Background and Aims : Chronic kidney disease (CKD) patients present increased cardiovascular (CV) morbidity and mortality, with atherosclerosis being the underlying phenomenon in most of CV events. Clinical trials and metanalyses have linked administration of pentoxifylline (PTX) with renoprotection secondary to anti-inflammatory and antifibrotic effects in CKD patients, together with increased levels of the anti-aging protein Klotho. However, the effect of PTX on atherosclerosis in CKD patients has not been analysed.

Methods: This single-center prospective study was designed to evaluate the effects of PTX administration on surrogate markers of subclinical atherosclerosis [ankle-brachial index (ABI) and carotid intima-media thickness (CIMT)] in patients with CKD stages 3-4 without a history of clinical CV disease. A total of 34 patients received PTX treatment (1200 mg/day) for 18 months and the evolution was compared with 34 patients without this therapy (control group). All patients have a background of RAS blockade.

Results: At the end of the study, patients treated with PTX presented a lower increment in CIMT values as compared to controls (0,62% pentoxifylline group vs. 1,80% not treated; P<0.000). Likewise, patients receiving PTX presented lower percent decline rates in Klotho levels, both in PBC gene expression (5,15% pentoxifylline group vs. -6,27% not treated; P<0.000) and in serum concentrations (P<0.068). Serum concentrations of inflammatory markers were also lower in the PTX group at the end of the study.

Conclusions: PTX administration to patients with CKD is related with anti-atherosclerotic properties based on lower increases of CIMT. In addition, there was a preservation of Klotho levels and a modulation of inflammatory status.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-04 Chronic kidney disease and nephropathies*

LEFT VENTRICULAR HYPERTROPHY IN CHRONIC KIDNEY DISEASE

POSTER VIEWING SESSION

Antonina Giammanco[1], Giuseppe Mulè[1], Angelo Baldassare Cefalù[1], Davide Noto[1], Alessandro Mattina[2], Giulio Geraci[1], Chiara Nardi[1], Maurizio Averna[3], Emilio Nardi[4]
[1]Department Of Health Promotion, Mother And Child Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy, [2]Diabetes And Islet Transplantation Unit, Department Of Diagnostic And Therapeutic Services, Irccs-ismett, Diabetes and Islet Transplantation Unit, Department of Diagnostic and Therapeutic Services, IRCCS-ISMETT, Palermo, Italy, [3]Department Of Health Promotion Sciences Maternal And Infantile Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy, [4]Department Of Health Promotion, Mother And Child Care, Internal Medicine And Medical Specialties (promise), Azienda ospedaliera universitaria Policlinico Palermo, Palermo, Italy

Background and Aims : CKD patients have a high prevalence of LVH and an increased cardiovascular risk. In this study we have assessed the prevalence of left ventricular hypertrophy (LVH) and left ventricular geometry in a group of 293 patients with high blood pressure and with stage 2–5 chronic kidney disease (CKD), compared with 289 essential hypertensive patients with normal renal function.

Methods: All patients underwent echocardiographic examination. Patients on stage 1 CKD, dialysis treatment, or with cardiovascular diseases were excluded.

Results: LVH was observed in 62.8% of patients with CKD and in 51.9% of essential hypertensive patients ($P<0.0001$). We found increasingly higher left ventricular diameters, thicknesses, and mass from stage 2 to 5 CKD. Distribution of concentric and eccentric LVH was not very different between the two groups. However, after introducing mixed hypertrophy, the difference between the two groups group was disclosed ($P=0.027$). Multiple regression analysis confirmed that the association between renal function and left ventricular mass (β -0.287; $P<0.0001$) was independent by potential confounders. Diastolic function was significantly worse in patients with CKD, especially in more advanced stages.

Conclusions: Our study confirms that LVH is highly prevalent in patients with CKD, especially by using the most recent cut off; in this population, LVH is often characterized by the simultaneous increase of wall thicknesses and diameters with negative effects on diastolic function.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

THE RELATION OF MTOR WITH DIABETIC COMPLICATIONS AND INSULIN RESISTANCE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

POSTER VIEWING SESSION

Ali Abdel Rehim[1], Kamel Rohoma[2], Reham A.Elwafa[3], Hossam Dabees[2], Noha G. Amin[4]
[1]Faculty Of Medicine Alexandria University, Internal Medicine (diabetes, Metabolism& Lipidology Unit), Alexandria, Egypt, University Of Alexandria-Faculty Of Medicine, alexandria, Egypt, [2]Internal Medicine (diabetes, Metabolism& Lipidology Unit), University Of Alexandria-Faculty Of Medicine-Unit Of Diabetes,Lipidology & Metabolic Disease, alexandria, Egypt, [3]Department Of Clinical Pathology, University Of Alexandria-Faculty Of Medicine, alexandria, Egypt, [4]Internal Medicine (diabetes, Metabolism& Lipidology Unit), faculty of medicine alexandria University, alexandria, Egypt

Background and Aims : Background: The aim of the present study was to evaluate the role of the mammalian target of rapamycin (mTOR) in patients with type 2 diabetes, its relation with insulin resistance and relation with diabetic microvascular complications.

Methods: Methods: This cross-section study was conducted on 90 subjects who attended the Outpatient Internal Medicine Clinic in Damanhour Teaching Hospital. Subjects were divided into 3 groups, Group A: 20 healthy subjects as a control group, Group B: 20 subjects with type 2 diabetes without complications, and Group C: 50 subjects with type 2 diabetes with microvascular complications. We measured mTOR, FPG, HbA1c, lipid profile, serum creatinine, fasting insulin, Urine albumin/creatinine ratio (ACR) (twice). Calculation of Estimated glomerular filtration rate (eGFR) using the CKD-EPI formula, HOMA IR2 calculation, and Fundus examination were done. Neuropathy was defined as a positive monofilament test plus an absent ankle reflex or a VPT > 25 V. Diabetic nephropathy was defined as either UACR>30 mg/g or an eGFR< 60 mL/min/1.73 m2.

Results: Results: mTOR was significantly positively correlated to FPS (r=0.508, P<0.001), HbA1C (r=0.530, P<0.001) and HOMA IR2 (r=0.559, P<0.001), and significantly negatively correlated to eGFR (r=-0.370, P=0.002). Multivariate analysis showed that mTOR and HbA1c values were independently associated with microvascular complications. A cutoff value of 8 ng/ml mTOR predicted microvascular complications with a sensitivity of 100% and specificity of 95% with AUC 0.983 and p-value <0.001.

Conclusions: Conclusion: mTOR may act as a predictor of diabetes-related microvascular complications and is associated with insulin resistance in patients with type 2 diabetes.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

IMPACT OF TYPE-2 DIABETES MELLITUS ON EXPRESSION OF ATP-SENSITIVE POTASSIUM CHANNEL SUBUNITS IN HUMAN BYPASS GRAFTS

POSTER VIEWING SESSION

Jovana Rajkovic[1], Milos Gostimirovic[1], Miodrag Peric[2], Jelena Stanisic[3], Radmila Novakovic[1], Vladimir Djokic[1], Snezana Tepavcevic[3], Jelena Rakocevic[4], Milica Labudovic-Borovic[4], Helmut Heinle[5], Ljiljana Gojkovic-Bukarica[1]
[1]Cardiovascular Pharmacology, Institute of Pharmacology, Clinical Pharmacology and Toxicology, Medical Faculty, University of Belgrade, Belgrade, Serbia, [2]Cardiosurgery, Dedinje Cardiovascular Institute, Belgrade, Serbia, [3]Laboratory For Molecular Biology And Endocrinology, Vinca Institute of Nuclear Sciences, Belgrade, Serbia, [4]Histology, Institute of Histology and Embryology, Medical Faculty, University of Belgrade, Belgrade, Serbia, [5]Physiology, Institute of Physiology, University of Tubingen, Tubingen, Germany

Background and Aims : Prevalence of type-2 diabetes mellitus (T2DM) among patients that require coronary artery bypass graft (CABG) surgery increased over the years. It is well knowing that diabetes has impact on endothelial function and that cause impaired vasodilation function of blood vessels. However, vasorelaxation can be, also, achieved through opening of potassium (K) channels on vascular smooth muscle. Thus, the aim of our study was to detect the differences in the expression of ATP-sensitive K (K_{ATP}) channel subunits in bypass grafts (saphenous vein, SV and internal mammary artery, IMA) obtained from patients with and without T2DM. Dominant type of smooth vascular K_{ATP} channel consists of SUR2B and Kir6.1 subunits, while endothelial K_{ATP} channel consists of SUR2B and Kir6.2 subunits.

Methods: Western blot analysis and immunohistochemistry were used for detection of K_{ATP} channel subunits (SUR2B, Kir6.1 and Kir6.2) on segments of bypass grafts obtained from patients who undergoing CABG.

Results: The expression of SUR2B subunit is decreased in diabetic SV compared to non-diabetic SV. In diabetic IMA the expression of the Kir6.1 subunit is lower and the expression of Kir6.2 subunit is higher compared to IMA obtained from patients without T2DM.

Conclusions: K_{ATP} channels are expressed in the vascular smooth muscle of IMA and SV. The presence of T2DM may impact the expression of K_{ATP} channel subunits, and consequently expression of K_{ATP} channels on plasma membrane of vascular smooth muscle of bypass grafts. This may contribute impaired vasodilation of diabetic bypass grafts.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

URSOLIC ACID REDUCES NADPH OXIDASE EXPRESSION AND ENSUING OXIDATIVE STRESS IN DIABETIC KIDNEY

POSTER VIEWING SESSION

Alexandra G. Lazar[1], Mihaela Loredana Vlad[1], Adrian Manea[1], Laura Olariu[2], Simona-Adriana Manea[1]
[1]Functional Genomics Laboratory, Institute of Cellular Biology and Pathology Nicolae Simionescu, Bucharest, Romania, [2]Research, Biotehnos SA, Bucharest, Romania, Bucharest, Romania

Background and Aims : Diabetic kidney disease (DKD) is a major life-threatening complication of diabetes. Triterpenic acids elicit *anti-hyperglycemic effects* and prevent the dysfunction of pancreatic beta cells. The molecular basis of triterpenes action is not completely understood, particularly in DKD. This study aimed at investigating the potential of ursolic acid (UA), a pentacyclic triterpenoid, to modulate NADPH oxidase (Nox) expression, the key source of reactive oxygen species (ROS), in experimental DKD.

Methods: Non-diabetic/streptozotocin-induced diabetic C57BL/6J mice and cultured human endothelial cells (EC) were employed. Non-/diabetic mice were divided into experimental groups to receive (i.p.) 1 mg/kg UA or its vehicle for 4 weeks: (i) non-diabetic+vehicle, (ii) diabetic+vehicle, (iii) diabetic + UA. EC were exposed to normal (5 mM) or high (25 mM) glucose concentrations in the absence/presence of 1-10 µM UA. Real-time PCR, Western blot, microscopy, and in situ detection of ROS (dihydroethidium) were employed.

Results: Up-regulated mRNA and protein levels of Nox1/2/4 subtypes associated with enhanced production of ROS and 4-hydroxynonenal/nitrotyrosine-protein adducts were detected in the kidney of diabetic mice. In UA-treated diabetic mice, the expression of Nox1-4 subtypes, oxidative stress markers, and ROS were significantly reduced. Moreover, UA suppressed the up-regulation of Nox1/2/4/5 isoforms in high glucose-exposed EC.

Conclusions: Ursolic acid promotes anti-oxidative stress effects in the kidney of diabetic mice by reducing the expression of Nox and the ensuing ROS overproduction. Ursolic acid or its biological active derivates could become novel pharmacological tools to reduce renal structural and functional alterations in DKD. **Acknowledgements:** Work supported by PN-III-P2-2.1-PED-2019-2497, PN-III-P2-2.1-PED-2019-2512, PN-III-P4-ID-PCE-2020-1898.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

CYSTATIN C PREDICTS INCIDENT DIABETES IN ANGIOGRAPHIED CORONARY PATIENTS

POSTER VIEWING SESSION

Arthur Mader[1], Lukas Sprenger[1], Alexander Vonbank[1], Barbara Larcher[1], Maximilian Maechler[1], Valentin Grabher[2], Andreas Leiherer[2], Axel Muendlein[2], Heinz Drexel[3], Christoph H. Saely[4]
[1]Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria, [2]Academic Teaching Hospital Feldkirch, Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria, [3]Internal Medicine, County Hospital Bregenz, Bregenz, Austria, [4]Medical Sciences, Private University of the Principality of Liechtenstein, Triesen, Liechtenstein

Background and Aims : Cystatin C is an established marker of renal function, and has also been found to be associated with cardiovascular disease. There is substantial overlap between risk factors for cardiovascular disease and type 2 diabetes; however, it is unclear whether cystatin C predicts new onset diabetes. This issue is addressed in the present study.

Methods: We prospectively followed 481 consecutive non-diabetic patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease over a follow-up period of 5.5 ± 3.5 years.

Results: Overall, 135 patients (28.1%) newly developed diabetes. Cystatin C proved to be a strong predictor of incident diabetes univariately (standardized HR=1.80 [1.14-2.28], p=0.011) and after adjustment for age, gender, hypertension, smoking, LDL cholesterol, HDL cholesterol and fasting glucose (HR=1.86 [1.07-3.21], p=0.027).

Conclusions: We conclude that cystatin C is a strong predictor of incident diabetes in angiographied coronary patients.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

TYPE 2 DIABETES AND RISK OF MAJOR CARDIOVASCULAR EVENTS IN PERIPHERAL ARTERY DISEASE VERSUS CORONARY ARTERY DISEASE PATIENTS

POSTER VIEWING SESSION

Christoph H. Saely[1], Alexander Vonbank[2], Barbara Larcher[2], Arthur Mader[2], Maximilian Maechler[2], Lukas Sprenger[2], Valentin Grabher[3], Andreas Leiherer[3], Axel Muendlein[3], Heinz Drexel[4]
[1]Medical Sciences, Private University of the Principality of Liechtenstein, Triesen, Liechtenstein, [2]Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria, [3]Academic Teaching Hospital Feldkirch, Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria, [4]Internal Medicine, County Hospital Bregenz, Bregenz, Austria

Background and Aims : The prevalence of type 2 diabetes (T2DM) is higher in peripheral artery disease (PAD) than in coronary artery disease (CAD) patients, and PAD overall confers higher cardiovascular risk than CAD. How the incidence of major cardiovascular events (MACE) compares between PAD and CAD patients when analyses are stratified by the presence of T2DM is unclear.

Methods: We prospectively recorded MACE and death over 10.0±4.7 years in 923 patients with stable CAD, of whom 26.7% had T2DM and in 292 patients with PAD, of whom 42.1% had T2DM. Four groups were analyzed: CAD patients without diabetes (CAD/T2DM-;n=677), CAD patients with T2DM (CAD/T2DM+;n=246), PAD patients without diabetes (PAD/T2DM-;n=169) and PAD patients with T2DM (PAD/T2DM+;n=123).

Results: When compared to the incidence of MACE in CAD+/T2DM- patients (25.1%), it was significantly higher in CAD+/T2DM+ patients (35.4%;p<0.001), in PAD+/T2DM- patients (30.2%;p=0.022) and in PAD+/T2DM+ patients (47.2%;p<0.001). Patients with both PAD and T2DM in turn were at a higher risk than CAD+/T2DM+ or PAD+/T2DM- patients (p=0.001 and p<0.001, respectively). The incidence of MACE did not differ significantly between PAD+/T2DM- and CAD+/T2DM+ patients (p=0.413). Compared to patients with CAD, Cox regression analyses after multivariate adjustment showed an adjusted hazard ratio of 1.46 [1.14-1.87],p=0.002 for the presence of PAD. Conversely, T2DM increased the risk of MACE after multivariate adjustment in CAD and PAD patients (adjusted HR 1.58 [1.27-1.98],p<0.001).

Conclusions: In conclusion, our data show that T2DM and the presence of PAD are mutually independent predictors of MACE. Patients with both PAD and T2DM are at an exceedingly high risk of MACE.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-05 Diabetes; macro- and microangiopathies*

DIABETIC CARDIAC AUTONOMIC NEUROPATHY: INSULIN RESISTANCE, N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE, ARTERIAL STIFFNESS AND FUNCTIONAL CHANGES OF THE MYOCARDIUM

POSTER VIEWING SESSION

Victoria Serhiyenko[1], Aleksandr Serhiyenko[1], Volodymyr Segin[2], Ludmila M. Serhiyenko[3]
[1]Endocrinology, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine, [2]Out-patient Department, Lviv Clinical Treatment Diagnostical Endocrinological Dispensary, Lviv, Ukraine, [3]Medical Biology, Parasitology And Medical Genetic, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Background and Aims : To evaluate the changes of insulin resistance (IR), N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, arterial stiffness and echocardiographic parameters in patients with type 2 diabetes mellitus (DM) and cardiac autonomic neuropathy (CAN).

Methods: 44 patients with type 2 DM (19 without CAN and 25 with CAN) and 15 healthy persons were recruited to participate in this study. Arterial stiffness, immunoreactive insulin (IRI), Homeostasis model assessment IR, NT-proBNP parameters and echocardiographic examination were assessed. The glucose concentration in the blood was determined by the glucose oxidase method, NT-proBNP - ELISA; arterial stiffness parameters - using a device TensioMED™ Arteriograph® 24, echocardiography - “Siemens Sonoline Versa Plus”. Statistics: ANOVA.

Results: Development of CAN is associated with increase in IR parameters, NT-proBNP levels and arterial stiffening. Arterial stiffness parameters among patients with CAN exceed physiological values and were considered as high. We found out that among patients of this group the value of brachial augmentation index was normal in 52%, elevated in 40% and pathological in 8%; pulse wave velocity was normal in 16%, elevated in 52% and pathological in 32% of cases. Obtained results showed that development of CAN is accompanied by more pronounced left ventricular diastolic dysfunction and by formation of left ventricular hyperthrophy (LVH), mostly by concentric type. Among patients of this group concentric LVH was diagnosed among 76% and eccentric LVH among 16% of patients.

Conclusions: Development of CAN is associated with increased IR parameters, NT-proBNP levels, arterial stiffening and left ventricular diastolic dysfunction, formation of LVH, mostly by concentric type.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

A CASE OF CERVICAL ARTERY DISSECTION IN A YOUNG WOMAN WITH REPEATED SPONTANEOUS CORONARY ARTERY DISSECTION.

POSTER VIEWING SESSION

Paola Bigolin, Adriana Visonà
Azienda Ulss 2 Marca Trevigiana, Angiology Unit, Castelfranco Veneto, Italy

Background and Aims : Spontaneous coronary artery dissection (SCAD) is an uncommon cause of acute myocardial infarction that mainly occurs in young women with no risk factors and no coronary atherosclerosis. SCAD aetiology is poorly understood. Familial cases have been described and rare cases are reported in association with hereditary connective tissue disorders, but most cases of SCAD are sporadic. SCAD can usually be diagnosed angiographically and there is a growing consensus in favour of conservative management when possible. Fibromuscular dysplasia (FMD) is highly prevalent among patients with SCAD. Besides typical FMD multifocal lesions, other extracoronary vascular abnormalities, such as aneurysms, dissections, have been reported in a substantial proportion of SCAD survivors.

Methods: Duplex ultrasonography and-computed tomography scan (angio-CT scan) from brain to pelvis.

Results: A 42-year old female patient presented with recurrent SCAD. She had no cardiovascular risk factors and she was a former smoker. She had a family history of coronary artery disease. The affected vessel was the posterior interventricular artery. Angio-CT scan demonstrated a dissection at the origin of the left Internal Carotid Artery, the left carotid axis appeared free from calcific or stenotic plaque as the other vessels explored. Laboratory tests were normal. She was treated with conservative medical management.

Conclusions: It appears appropriate to recommend imaging of all vessels, from brain to pelvis, at least once in all patients who have had SCAD in order to assess for FMD and other non-coronary arterial abnormalities.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

ORBITAL ISCHEMIA SYNDROME IN A PATIENT WITH CAROTID ARTERY DISSECTION - CASE REPORT

POSTER VIEWING SESSION

David Cernik
Comprehensive Stroke Center, Department Of Neurology, Masaryk Hospital, KZ a.s., Ústí nad Labem, Czech Republic

Background and Aims : Orbital ischemia syndrome is a very rare presentation of ocular ischemic syndrome. The cause is usually vascular pathology in the carotid artery, most often on the basis of atherosclerosis or, more rarely, dissection of the carotid artery. Our aim is to draw attention in the form of a case report to an unusual clinical manifestation of carotid artery dissection.

Methods: The case report deals with a patient (male, 49 years old) who suffered from intense pain behind the right eye. After a few days of pain, he arrives at the emergency room, where he was sent by a neurologist to the CTA. Preocclusive dissection of the right carotid artery was diagnosed. Neurosonological examination shows a massive reverse flow in the right ophthalmic artery. The pain behind the eye was so intense in the following days that opiate therapy was necessary.

Results: Carotid dissection was treated with anticoagulant therapy and a statin. According to the control CTA, the dissection heals at three-month intervals. Neurosonological control also shows normalization of flow in the right ophthalmic artery. The decrease in residual pain intensity even on analgesic therapy correlated with a decrease in the amplitude of retrograde flow in the ophthalmic artery.

Conclusions: Conclusion: Painful presentation of ocular ischemic syndrome, moreover caused by carotid artery dissection, is very rare.. However, if intense periorbital pain is present, carotid artery CTA should always be performed as part of the diagnostic process.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

TEMPORAL TRENDS IN MEDICAL CARDIOPROTECTIVE TREATMENT IN PATIENTS WITH ABDOMINAL AORTIC ANEURYSMS: A POPULATION-BASED NATIONAL COHORT STUDY

POSTER VIEWING SESSION

Chalotte W. Nicolajsen[1], Mette Søgaard[2], Nikolaj Eldrup[3], Torben B. Larsen[2], Samuel Z. Goldhaber[4], Peter B. Nielsen[2]
[1]Department Of Cardiology, Thrombosis Research Unit, Aalborg University Hospital, Aalborg, Denmark, [2]Thrombosis Research Unit, Aalborg University, Aalborg, Denmark, [3]Department Of Vascular Surgery, Rigshospitalet, Copenhagen, Denmark, [4]Thrombosis Research Group, Division Of Cardiovascular Medicine, Brigham and Womens Hospital, Boston, United States of America

Background and Aims : Patients with abdominal aortic aneurysmal (AAA) disease suffer high morbidity and mortality, driven mainly by cardiovascular comorbidity, and not the aneurysmatic disease itself. Initiation of cardioprotective therapy with statin and antiplatelets is recommended at AAA diagnosis. However, the implementation of recommendations over time is not well described. We aimed to provide up-to-date insights on temporal trends in the use of cardioprotective therapy in patients diagnosed with AAA.

Methods: Through national population-based health registries, we identified patients with an incident diagnosis of AAA from 2000 through 2018. By means of descriptive statistics, we characterized the development in prescription claims of statin and antiplatelet therapy. Analyses were stratified on year of diagnosis in the following intervals: 1999–2003, 2004–2008, 2009-2013, and 2014–2018.

Results: We identified 33,296 individuals with an incident diagnosis of AAA during 2000-2018. Mean age was 74 years. Prevalence of cardiovascular comorbidity (e.g., ischemic heart disease, cerebrovascular disease) ranged between 32.6% and 41.5%. The use of statins increased from 17.9% in 1999-2003 to 66.9% in 2014-2018, use of antiplatelets increased from 45.6% to 63.3%, and combined therapy with both statin and antiplatelets from 11.3% to 44.8%. Developments in medication use plateaued after 2013.

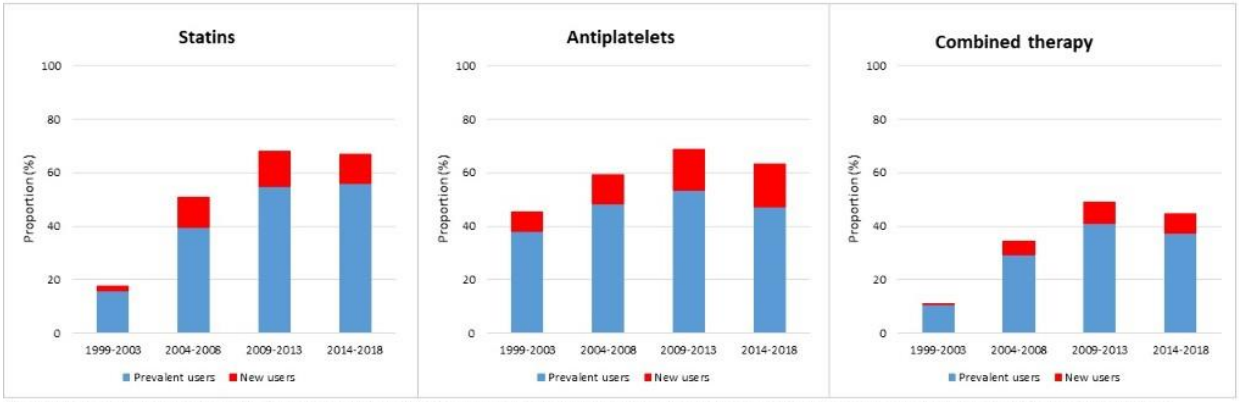
Conclusions: In patients diagnosed with AAA, implementation of cardioprotective therapy with statins and antiplatelets improved over time. However, despite a consensus endorsing intensified medical therapy, no further improvement was observed after 2013, and half of AAA patients were untreated with statin and antiplatelets from 2013 to 2018. Continuous quality improvement could focus on promoting optimal medical cardio
protection.

Table 1. Baseline demographics and comorbidity of study cohort stratified by year of AAA diagnosis

	Period 1 1999-2003	Period 2 2004-2008	Period 3 2009-2013	Period 4 2014-2018
Demographics, % (N)				
N	6009	7784	9602	9998
Age, median (IQR)	73 (67-79)	73 (68-79)	74 (68-79)	74 (69-80)
Female	24.7 (1458)	25.1 (1950)	23.8 (2281)	23.5 (2351)
Any atherosclerotic cardiovascular disease	41.5 (2456)	40.7 (3169)	36.3 (3487)	32.6 (3264)
Cerebrovascular Disease	10.4 (613)	10.7 (832)	9.1 (875)	8.9 (887)
Ischemic Heart Disease	24.3 (1439)	24.5 (1910)	21.7 (2080)	19.2 (1916)
Peripheral Arterial Disease	17.2 (1017)	15.0 (1168)	12.9 (1239)	11.0 (1102)
Comorbidity, other				
Hypertension	17.9 (1059)	26.8 (2084)	30.1 (2889)	30.8 (3084)
Diabetes	5.2 (308)	7.3 (571)	8.5 (819)	8.7 (867)
Heart Failure	9.9 (585)	9.6 (744)	8.1 (773)	7.9 (774)
Chronic Pulmonary Disease	12.5 (740)	13.2 (1025)	13.4 (1288)	14.4 (1440)
Atrial Fibrillation	9.6 (559)	11.5 (892)	11.6 (1112)	12.5 (1251)
Cancer	8.8 (522)	10.8 (844)	12.8 (1233)	13.9 (1394)
Venous Thromboembolism	2.4 (141)	2.6 (201)	3.0 (285)	3.8 (381)

IQR – Inter quartile range, n – number, AAA –abdominal aortic aneurysm

Figure 1. Proportion in medical cardioprotective treatment (statin and antiplatelet therapy) around time of AAA diagnosis.



Prevalent use: prescription claim within 365 to 1 days before AAA diagnosis; New use: prescription claim in treatment naïve patients in the period from 0 to 90 days after AAA diagnosis.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-06 Aneurysms and other non-atherosclerotic arteriopathies*

THE VASA VASORUM DENSITY OF THORACIC AORTA IN THE ANEURISM FORMATION

POSTER VIEWING SESSION

Anton Y. Postnov[1], Maryam Bagheri Ekta[1], Petr V. Chumachenko[2], Vasily N. Sukhorukov[1], Igor A. Sobenin[3,4]
[1]Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation, [2]Laboratory Of Pathomorphology Of Cardiovascular Diseaeses, National Medical Research Center of Cardiology, Moscow, Russian Federation, [3]Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation, [4]Central Pathologoanatomic Laboratory, A.P. Avtsyn Research Institute of Human Morphology, Moscow, Russian Federation

Background and Aims : Damaged connective tissue structures and cystic degeneration of the medial layer can play a primary role in the pathogenesis of the thoracic aorta aneurysm. The underlying mechanisms remain poorly studied. The aim of the study was to examine the vasa vasorum density and endothelium cells abundance in tunica adventitia under the presence/absence of inflammatory infiltrates in the aortic wall.

Methods: Histological samples were obtained from 30 patients of both genders aged 37 to 82 years. Histological analysis is performed by examining a thin slice of thoracic aortic aneurysm tissue with an optical microscope. IHC staining was performed using monoclonal antibodies against coagulation factor VIII, and NO synthase (eNOS), and T-lymphocytes (CD3 and CD4 antigens).

Results: Examination of histological slides of thoracic aorta aneurism allowed to reveal significant infiltration of lymphocytic cells (n = 6) in the arterial wall, and a high density of vasa vasorum adventitia endothelial cells, expressing VIII factor and nitric oxide synthase. The number of vasa vasorum endothelium cells expressing NO synthase and VIII factor was equal.

Conclusions: There may be a direct correlation between the number of vasa vasorum in the tunica adventitia of the thoracic aorta aneurysm and the degree of its infiltration by immunocytes. Secondary angiogenesis may play an important role in the remodeling of the arterial wall during the aortic aneurysm progression. This work was supported by Russian Science Foundation (Grant #20-45-08002).

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-07 Nutrition, nutraceuticals*

MATERNAL FRUCTOSE INTAKE REINFORCES THE EFFECTS OF A WESTERN-TYPE DIET IN PROMOTING SARS-COV-2 CELL ENTRY FACTORS IN MALE OFFSPRING

POSTER VIEWING SESSION

Cristina Donis[1], Elena Fauste[1], Madeín Pérez[1], Lourdes Rodríguez[1], Silvia Rodrigo[1], Juan J. Álvarez-Millán[2], Paola Otero[1], María I. Panadero[1], Carlos Bocos[1]
[1]Facultad De Farmacia, Universidad CEU San Pablo, Madrid, Spain, [2]Cqs Lab, CQS Lab, Madrid, Spain

Background and Aims : Fructose consumption has increased considerably, in a similar way to the prevalence of obesity, cardiovascular disease and diabetes. Further, maternal intake is a key factor involved in the development of diseases in offspring. Severity of COVID-19 has been related to the prevalence of these metabolic diseases. Therefore, fructose-rich processed foods and sugary drinks could place these patients at an increased risk for severe COVID-19. Present work studies whether maternal fructose produces in offspring changes in gene expression of molecules that permit SARS-CoV2 entry to the cell.

Methods: Two experiments were performed in rats to study: 1) the effects of maternal liquid carbohydrate consumption on adult and young male offspring; and 2) the effect of a fructose supplementation alone or being part of a Western-diet along with cholesterol, in this offspring.

Results: Maternal fructose protected older offspring from viral entrance in liver cells since it reduced SARS-CoV2 entry factors gene expression. However, when these descendants were supplemented with liquid fructose, they displayed an elevated protease TMPRSS2 expression. In younger rats, fructose consumption induced ileal gene expression of viral entry molecules in descendants from control mothers, but not in males from fructose-fed mothers. In contrast, maternal fructose intake exacerbated the fructose plus cholesterol-induced rise in viral entry factors expression, suggesting a lower protection against SARS-CoV2 infection.

Conclusions: Maternal fructose intake induces a fetal programming that increases hepatic viral protection and, in contrast, leads to a more pronounced reduction of SARS-CoV2 protection in the small intestine of male progeny when supplemented with a Western-diet.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-07 Nutrition, nutraceuticals*

NON-INVASIVE INSTRUMENTAL EVALUATION OF COENZYME Q10 PHYTOSOME ON ENDOTHELIAL REACTIVITY IN HEALTHY NON-SMOKING YOUNG VOLUNTEERS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED CROSS-OVER CLINICAL TRIAL

POSTER VIEWING SESSION

Federica Fogacci, Antonio Di Micoli, Maddalena Veronesi, Claudio Borghi, Arrigo F.G. Cicero
Medical And Surgical Sciences Department, University of Bologna, Bologna, Italy

Background and Aims : Coenzyme Q10 (CoQ10) is a natural antioxidant compound that prevents the vascular damage induced by free radicals and the activation of inflammatory signaling pathways. Supplementation with CoQ10 is safe though its bioavailability is generally low, as far as variable depending on the pharmaceutical form of preparation. Recently, the development of phytosome technology has improved the bioavailability of CoQ10 and definitely facilitated its effective use in clinical.

Methods: The present double-blind, randomized, placebo-controlled, cross-over clinical study aimed to investigate the effect on endothelial reactivity and total antioxidant capacity (TAC) of either acute and chronic supplementation with CoQ10 phytosome in a sample of 20 healthy young not smoking subjects.

Results: The immediate acute effect of dietary supplementation with CoQ10 phytosome on pulse volume (PV) was sustained in the actively treated group in comparison with placebo and the baseline ($p< 0.05$). Chronic supplementation of the tested pharmaceutical formulation of CoQ10 significantly improved mean arterial pressure and TAC compared to placebo and baseline values ($p< 0.05$ for both comparisons). In the actively treated group, the effect on dietary supplementation with CoQ10 phytosome on PV was also sustained when compared to the baseline ($P<0.05$).

Conclusions: CoQ_{10} phytosome exerts beneficial effects on endothelial reactivity in healthy young subjects. Further studies are needed that confirms our observations in the long term by directly comparing different CoQ_{10} pharmaceutical formulations.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-07 Nutrition, nutraceuticals*

FATTY FISH BUT NOT LEAN FISH CONSUMPTION IS ASSOCIATED WITH REDUCED RISK OF CORONARY HEART DISEASE: A META-ANALYSIS OF PROSPECTIVE COHORT STUDIES

POSTER VIEWING SESSION

Annalisa Giosuè[1], Ilaria Calabrese[1], Gabriele Riccardi[1], Roberta Lupoli[1], Olga Vaccaro[2], Marilena Vitale[1]
[1]Clinical Medicine And Surgery, University of Naples Federico II, Naples, Italy, [2]Pharmacy, University of Naples Federico II, Naples, Italy

Background and Aims : Fish consumption is associated with reduced risk of coronary heart disease (CHD), partly for its high content in long-chain n-3 polyunsaturated fatty acids. However, not all fish species are equally rich in these components, and it is not clear whether the beneficial effects of fish consumption occur with both fatty and lean fish. The aim of this meta-analysis is to evaluate the relation between intake of fatty fish or lean fish and the risk of CHD incidence and mortality.

Methods: The PubMed, Web of Science, and Embase databases were searched all through May 2021 for full-text papers on prospective studies in humans providing multivariate-adjusted relative risks (RRs) and 95% confidence intervals (CIs) for the highest versus the lowest fish consumption categories.

Results: Eligible studies comprised 717,435 participants and 20,531 incident CHD cases for fatty fish, and 904,515 participants and 21,636 incident CHD cases for lean fish. Fatty fish consumption was inversely associated with CHD incidence (RR: 0.92; 95% CI: 0.86, 0.97) and CHD mortality (RR: 0.83; 95% CI: 0.70, 0.98). Conversely, lean fish consumption did not show any relationship with both CHD incidence (RR: 1.02; 95% CI: 0.98, 1.06) and mortality (RR: 1.04; 95% CI: 0.89, 1.22).

Conclusions: The study findings are innovative in highlighting that the cardiovascular benefits so far linked to fish consumption, are, in fact, driven by fatty fish.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-07 Nutrition, nutraceuticals*

AN INNOVATIVE BERBERINE FORMULATION IS ABLE TO IMPROVE BBR BIOAVAILABILITY AND THE LIPID AND GLYCEMIC PROFILE IN HFD-FED MICE.

POSTER VIEWING SESSION

Maria Giovanna Lupo[1], Giovanni Panighel[2], Irene Ferrarese[3], Elisa Brilli[4], Germano Tarantino[4], Stefano Dall'Acqua[3], Nicola Ferri[5]
[1]Dipartimento Di Medicina, Università degli Studi di Padova, Padova, Italy, [2]Dipartimento Di Scienze Del Farmaco, Università di Padova, PADOVA, Italy, [3]Dipartimento Di Scienze Del Farmaco, Università di Padova, Padova, Italy, [4]Department Of Nutrition And Nutraceuticals, PharmaNutra S.p.A., Siena, Italy, [5]Dipartimento Di Medicina, Universitá degli Studi di Padova, Padova, Italy

Background and Aims : Berberine (BBR) is a hyperglycemic and hypocholesterolemic natural alkaloid that is scarcely bioavailable. We aimed to test in HFD-fed mice the efficacy of a new BBR formulation (BBR-U).

Methods: In a pilot study, ten 6-weeks old C57BL/6 wt mice on standard diet (SD) were randomized to receive for 3w oral gavage of BBR or BBR-U 50mg/kg/day, as already published for BBR dosage in mice. Thus, further 28 mice were randomized in 4 groups to receive SD or HFD (60% fat) for 16 weeks and oral gavage of vehicle (v), BBR, or BBR-U for the last 8w according to the following scheme: **G1**, SD+v; **G2**, HFD+v; **G3**, HFD+BBR; **G4**, HFD+BBR-U. BBR was provided at 50mg/kg/day, BBR-U dosage was reduced at 6.25mg/kg/day since the higher C_{max} observed in the pilot study.

Results: We observed 8-fold increase in BBR C_{max} upon BBR-U administration. **G4** showed a higher decrease in TC plasma levels *vs* **G3** (111±22mg/dL *vs* 125±23mg/dL), compared to **G2** (130±11mg/dL). TC of **G1** mice was 80±21mg/dL. BBR-U 6.25mg was as effective as BBR 50mg in improving the HFD-induced insulin resistance according to OGTT AUCs (**G4**: 53430±2127; **G3**: 54165±2990; **G2**: 63338±2990; **G1**: 45765±2334 (mg/dL)*120min). HPLC MS/MS analysis on liver, kidney, brain and VAT samples showed a differential BBR and its metabolites tissue distribution.

Conclusions: The new BBR formulation is an innovative and effective tool to improve BBR bioavailability. Further gene and proteomic expression analyses on tissue samples are ongoing.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-07 Nutrition, nutraceuticals*

DOES LOW GLYCEMIC INDEX DIET SUPERIOR THAN ROUTINE DIET TO CONTROL BLOOD INFLAMMATION STATE AND LIPID PARAMETERS IN PATIENTS WITH CORONARY ARTERY DISEASE?

POSTER VIEWING SESSION

Jamol Uzokov[1], Anis Alyavi[1], Bakhromkhon Alyavi[2], Djamshid Payziev[3], Mirvosit Karimov[4], Dilorom Rakhimova[5], Daler Orziev[1], Ibrokhim Madjitov[2]
[1]Cardiology, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan, [2]Cardiology, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan, [3]Interventional Cardiology, Republican specialized scientific practical medical center of therapy and medical rehabilitation, Tashkent, Uzbekistan, [4]Gastroenterology, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan, [5]Pulmonary Disease, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Background and Aims : Objectives of the study to demonstrate superiority of the low glycemic index diet in patients with CAD in terms of blood inflammation state and lipid parameters.

Methods: One hundred and sixty patients aged 38-76 years established with CAD entered as 12 week dietary intervention either with low glycemic index (n=80) or routine diet (n=80) together with standard therapy from 2016 to 2019 (male=48%; 58.2±12.0 years). Laboratory (including hs-CRP, pro-inflammatory interleukins, IL-1β, IL-6, TNF-α, lipid parameters TC, TG, LDL-Cholesterol, HDL-Cholesterol) and instrumental data were obtained at baseline and in 12 weeks of the intervention.

Results: There were no statistically differences in biochemical data between two groups at their baseline characteristics. Low glycemic index diet positively influenced on hs-CRP (from 252.4±40.6 mg/dL to 161.9±28.5 mg/dL vs. from 237.8±35.6 mg/dL to 202.4±23.8 mg/dL; P<0.05), HbA1c (from 6.95±1.95 % to 4.78±1.18 % vs. 6.80±1.65 % to 6.25±1.45%; P<0.05), TG (from 5.2±2.2 to 3.1±1.8 vs. from 5.8±2.8 to 4.9±2.0, P<0.05), TNF-α (from 1.48±0.91 to 0.88±0.19 vs. from 1.55±1.35 to 1.12±0.35, P<0.05), IL-6 (from 8.2 pg/mL to 4.9 pg/mL vs. from 8.2 pg/mL to 4.9 pg/mL, P<0.005) than routine diet. Although reduction in IL-1β were observed in both groups (from 32.5±17.2 pg/ml to 28.9±16.8 pg/ml, P>0.05; vs. 33.6±21.6 pg/ml to 29.8±20.4, P>0.05;), however there were no statistically significant from baseline and between groups (P>0.05).

Conclusions: Low glycemic index diet demonstrated superiority to routine diet to improve inflammatory state and lipid parameters in patients with CAD.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-08 Bariatric surgery*

EFFECT OF ROUX-EN-Y GASTRIC BYPASS SURGERY ON SUBCLINICAL ATHEROSCLEROSIS, OXIDATIVE STRESS, AND MITOCHONDRIAL DYNAMICS IN LEUKOCYTES OF OBESE PATIENTS: A ONE-YEAR FOLLOW-UP STUDY

POSTER VIEWING SESSION

Sandra López-Domènech[1], Zaida Abad-Jiménez[1], Teresa Vezza[1], Segundo A. Gómez-Abril[2], Celia García-Garballo[1], Meylin Férnandez[1], Celia Bañuls[1], Víctor M. Víctor[1], Milagros Rocha[1]
[1]Department Of Endocrinology And Nutrition, FISABIO-HOSPITAL DR PESET, Valencia, Spain, [2]Department Of General And Digestive System Surgery, University Hospital Dr. Peset, Valencia, Spain

Background and Aims : Little is known about the mechanisms underlying the cardiovascular protective effect of Roux en-Y gastric bypass (RYGB) surgery. The present study aimed to investigate how RYGB influences the oxidative and mitochondrial status of leukocytes and subclinical atherosclerotic markers.

Methods: This interventional study was carried out in 57 obese subjects who underwent RYGB surgery. Leukocytes were isolated at baseline and 12 months after the intervention. We evaluated oxidative stress markers by static cytometry and mitochondrial markers by western blot. Leukocyte-endothelial cell interactions - rolling flux, velocity, and adhesion - were evaluated *in vitro* in a parallel-plate flow chamber.

Results: RYGB induced weight loss and an improvement of anthropometric clinical indicators. At the molecular level, a significant reduction of superoxide production ($p<0.01$) and mitochondrial membrane potential ($p<0.05$) was observed, while GPX1 content increased ($p<0.05$). In terms of mitochondria, RYGB induced upregulation of complexes (I-V) ($p<0.05$ and $p<0.001$), MIEAP ($p<0.05$), and Pink1 ($p<0.05$), and regulated the fusion-fission machinery through an increase in MFN1 ($p<0.05$). Likewise, a significant reduction of sICAM ($p< 0.05$) and sP-Selectin ($p < 0.001$) and of rolling flux ($p< 0.05$) and adhesion of leukocytes ($p< 0.01$) were reported at follow-up.

Conclusions: Our results suggest that patients undergoing RYGB benefit from an amelioration of their prooxidant status and enhanced mitochondrial dynamics in leukocytes, which could be responsible for the reduction of subclinical markers of atherosclerosis after surgery **Acknowledgements:** PI19/00838, PI19/00437, FI17/00144, CD19/00180, CP19/00077 from ISCIII-ERDF (“A way to build Europe”), PROMETEO/2019/027; APOSTD/2020/145, ACIF/2020/371 from the Valencian Regional Government.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-08 Bariatric surgery*

ZINC-ALPHA 2-GLYCOPROTEIN IS ASSOCIATED WITH METABOLIC FEATURES AND BARIATRIC SURGERY OUTCOMES IN PATIENTS WITH MORBID OBESITY

POSTER VIEWING SESSION

José Ignacio Martínez Montoro[1], Rocío Soler Humanes[2], Hanieh Motahari Rad[1], Andrés González Jiménez[3], Alba Subiri[1], Luis Ocaña[2], Eduardo García Fuentes[2], Francisco J Tinahones[1], Lourdes Garrido Sánchez[1], Mora Murri[1]
[1]Endocrinology And Nutrition, Instituto De Investigación Biomédica De Málaga -ibima, Virgen de la Victoria University Hospital, Málaga, Spain, [2]General And Digestive System Surgery, Virgen de la Victoria University Hospital, Málaga, Spain, [3]Ecai Bioinformática, Instituto De Investigación Biomédica De Málaga -ibima, Virgen de la Victoria University Hospital, Málaga, Spain

Background and Aims : Zinc-alpha 2-glycoprotein (ZAG) is an adipokine involved in the regulation of adipose tissue metabolism with potential implications in the pathophysiology of obesity and metabolic syndrome. Our aim was to evaluate the association between ZAG expression and different metabolic parameters in subjects with morbid obesity, as well as its role in bariatric surgery outcomes.

Methods: The study population comprised a total of 41 patients with morbid obesity undergoing bariatric surgery (BS). Baseline visceral (VAT) and subcutaneous adipose tissue (SAT) were obtained at surgery in order to evaluate ZAG expression. Participants were stratified by the 50th percentile of SAT and VAT ZAG expression. Anthropometric and biochemical parameters were determined before and 15 days, 45 days and 1 year after BS.

Results: Subjects in the lower 50th percentile of SAT ZAG presented significantly higher weight and waist circumference compared with the upper percentile, whereas the lower 50th percentile of VAT ZAG presented significantly increased weight, waist circumference, HOMA-IR and triglycerides. In the linear regression analysis, SAT ZAG was inversely associated with weight loss percentage at 45 days after BS. No statistically significant associations were found between VAT ZAG and weight loss percentage after BS.

Conclusions: Lower SAT and VAT ZAG levels were closely related to adverse metabolic characteristics in subjects with morbid obesity. Conversely, SAT ZAG was inversely associated with short-term weight loss after BS. Neither SAT nor VAT ZAG were associated with long-term weight loss after BS.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

ASSESSMENT OF ADHERENCE TO STATIN THERAPY USING URINE ANALYSIS IN PATIENTS ATTENDING SPECIALIZED LIPID OUT PATIENT CLINIC

POSTER VIEWING SESSION

Khamis M. Al Hashmi[1], Abdullah Al Ani[2], Yousif Al Suleimani[2], Khalid Al Rasadi[3], Khalid Al Waili[4], Fahad Zadjali[5], Mohammed Al Zaabi[2]
[1]Physiology, College of Medicine and Health Sciences, Muscat, Oman, [2]Pharmacology, College of Medicine and Health Sciences, Muscat, Oman, [3]Biochemistry, College of Medicine and Health Sciences, Muscat, Oman, [4]Biochemistry, SQUH: Sultan Qaboos University Hospital, Muscat, Oman, [5]Clinical Biochemistry, SULTAN QABOOS UNIVERSITY, Khodh, Oman

Background and Aims : Non-adherence to medications is a common concern across patients with chronic diseases such as dyslipidemia. It has serious consequences in patient's health and in the cost of health services. The aim of the study was to assess adherence to statin therapy using urine analysis in patients attending adult outpatient clinic at a tertiary care hospital.

Methods: This is a cross sectional study conducted in specialized lipid and Hypertension outpatient clinics at Sultan Qaboos University Hospital (SQUH). Adult patients with hyperlipidemia and on statin therapy for three months or more how attended the clinic during the study period were recruited. 119 patients agreed to participate in the study and provided sufficient urine samples for analysis. Urine analysis was performed by HPLC coupled to a tandem mass spectrometer via JetStream electrospray (Agilent Technologies Inc., Santa Clara, California, USA).

Results: The mean (SD) age of participants was 57 (11) year and 58% of participants were females. 49.5% of participants were on rusovastatin and the rest were on atorvastatin or simvastatin. The mean (SD) Low-density lipoprotein cholesterol was 2.6 (1.2) mmol/l. Statin therapy was detected in 109 (91.6%) of the participants indicating a non-adherence prevalence of 8.4%.

Conclusions: Our finding indicates a good adherence to statin therapy in patients attending the outpatient clinics of a university hospital. However, these patients were attending specialized clinic and its finding might not reflect the adherence in general out patient clinics.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EFFECTS OF PATIENT CHARACTERISTICS ON VOLANESORSEN EFFICACY: SUBGROUP ANALYSIS OF APPROACH

POSTER VIEWING SESSION

Joseph L. Witztum[1], Daniel Gaudet[2], Steven Freedman[3], Veronica J. Alexander[4], Marcello Arca[5], Erik S. Stroes[6], Jean Bergeron[7], Handrean Soran[8], Fernando Civeira[9], Sotirios Tsimikas[4], Dirk J. Blom[10], Eric Bruckert[11]
[1]School Of Medicine, University of California San Diego, San Diego, United States of America, [2]Ecogene 21, Université de Montréal, Chicoutimi, Canada, [3]Gastroenterology, Beth Israel Deaconess Medical Center, Boston, United States of America, [4]Clinical Development, Ionis Pharmaceuticals, Inc., Carlsbad, United States of America, [5]Dipartimento Di Medicina Translazionale E Di Precisione, Sapienza Università di Roma, Roma, Italy, [6]Vascular Medicine, Academic Medical Center, Amsterdam, Netherlands, [7]Endocrinology And Nephrology, Centre Hospitalier Universitaire de Québec–Université Laval, Quebec, Canada, [8]Endocrinology, Manchester University Hospital NHS Foundation Trust, Manchester, United Kingdom, [9]Lipid Clinic, Hospital Universitario Miguel Servet, IISA, CIBERCV, Zaragoza, Spain, [10]Division Of Lipidology And Cape Heart Institute, University of Cape Town, Cape Town, South Africa, [11]Endocrinology And Metabolism, La Pitié-Salpětriére Hospital, Paris, France

Background and Aims : To analyze the effect of patient characteristics on efficacy of volanesorsen treatment in patients with familial chylomicronemia syndrome (FCS) from the APPROACH trial (NCT02211209).

Methods: FCS was defined by genotype or by lipoprotein lipase (LPL) activity ≤20% of normal. Patients received volanesorsen 300 mg/week or placebo subcutaneously for 52 weeks. Dose reductions (every other week) for side effects or adverse events were permitted. The primary outcome was percentage change in fasting serum triglycerides (TGs) from baseline to Month 3. Prespecified analyses of the primary endpoint were stratified according to LPL mutation and activity, age, gender, race, and geographic location.

Results: A total of 51 patients (77%) had confirmed mutations in *LPL* or related genes (volanesorsen group, n=25; placebo group, n=26), and 54.5% of patients in each treatment group had LPL activity ≤20% of normal (**Table**). There were significant reductions in serum TGs from baseline to Month 3 in volanesorsen-treated patients with confirmed LPL (−65%), non-LPL (−85.4%), and non-confirmed (−85.2%) pathogenic mutations compared to increases or small decreases in placebo-treated patients (*P*<0.005 all groups vs placebo). Similarly, robust reductions in TGs from baseline to Month 3 were observed in volanesorsen-treated patients regardless of LPL activity (>20%: −83.6%; ≤20%: −72.6%), age (<65 years: −71.2%; ≥65 years: −78.4%), gender (male: −70.3%; female: −73.3%), race (White: −72.6%; Asian: −71.3%; other: −65.1%), or geographic location (North America: −81.2%; Europe: −65.5%; other: −74.5%) compared to placebo-treated patients.

Conclusions: Volanesorsen demonstrated consistent TG reduction irrespective of FCS mutation or LPL activity, and across different patient

subgroups.

Table. Mean Percent Change in Triglyceride Levels from Baseline[a] to Month 3[b] (Full Analysis Set)

	Placebo (n=33)			Volanesorsen (n=33)		
Gender	**Male**		**Female**	**Male**		**Female**
n	14		19	16		17
Mean (95% CI)	35.3 (−26.9, 97.5)		15.9 (−5.9, 37.8)	−70.3 (−83.5, −57.2)		−73.3 (−82.2, −64.3)
Age	**<65 Years**		**≥65 Years**	**<65 Years**		**≥65 Years**
n	31		2	30		3
Mean (95% CI)	24.5 (−4.7, 53.8)		18.6 (−0.8, 37.9)	−71.2 (−79.3, −63.1)		− 78.4 (−103.7, −53.1)
LPL Mutation[c]	**Confirmed**	**Non-LPL**	**Non-confirmed**	**Confirmed**	**Non-LPL**	**Non-confirmed**
n	23	3	7	16	9	8
LS Mean (95% CI)	11.6 (−13.4, 36.6)	139.6 (80.5, 198.6)	−7.7 (−46.2, 30.9)	−65.0 (−93.0, −37.0)	−85.4 (−122.0, −48.8)	−85.2 (−120.2, −50.1)
LPL Activity[c]	**Low (≤20%)**	**Normal (>20%)**	**Missing**	**Low (≤20%)**	**Normal (>20%)**	**Missing**
n	18	11	4	18	10	5
LS Mean (95% CI)	−4.1 (−31.7, 23.5)	66.8 (34.6, 99.0)	−22.3 (−74.8, 30.2)	−72.6 (−98.1, −47.1)	−83.6 (−120.1, −47.2)	−81.3 (−129.4, −33.3)
Race	**White**		**Asian**	**White**	**Asian**	**Other**
N	29		4	24	7	2
Mean (95% CI)	24.0 (−7.1, 55.0)		25.6 (−33.0, 84.1)	−72.6 (−82.3, −62.8)	− 71.3 (−85.2, −57.4)	−65.1 (−199.8, 69.5)
Geographic Location	**North America**	**Europe**	**Other**	**North America**	**Europe**	**Other**
n	14	18	1	11	18	4
Mean (95% CI)	51.7 (−7.8, 111.3)	4.5 (−17.7, 26.7)	−8.6 (NA, NA)	−81.2 (−87.8, −74.7)	−65.5 (−77.3, −53.7)	−74.5 (−113.3, −35.7

[a]The baseline for fasting triglycerides was defined as the average of Day 1 pre-dose assessment and the last measurement prior to Day 1 pre-dose assessment. If 1 of the 2 measurements is missing, then the other measurement is assigned as the baseline value.

[b]The Month 3 endpoint was defined as the average of Week 12 (Day 78) and Week 13 (Day 85) fasting assessments.

[c]Based on analysis of covariance model with percent change from baseline as the dependent variable, treatment, mutation type, history of pancreatitis, presence of concurrent omega-3 fatty acids and/or fibrates and interaction of treatment and mutation type as factors, and baseline in logarithm scale as a covariate.

CI, confidence interval; LPL, lipoprotein lipase; NA, not applicable.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

PREDICTING INDIVIDUAL RISK OF MUSCLE DISORDERS IN PATIENTS ELIGIBLE FOR STATIN TREATMENT: STRATIFY-STATINMD MODEL DERIVATION USING DATA FROM ELECTRONIC HEALTH RECORDS

POSTER VIEWING SESSION

Ting Cai, Constantinos Koshiaris, Jennifer A. Hirst, F.D. Richard Hobbs, Richard J. Mcmanus, James P. Sheppard
Nuffield Department Of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom

Background and Aims : Concerns about muscle-related adverse events have posed a dilemma when considering statin prescription for prevention of cardiovascular disease (CVD). This study aimed to develop a prediction model for an individual's risk of muscle disorders to support clinical decision making in primary care.

Methods: A prospective cohort design was adopted, using electronic health records from the Clinical Practice Research Datalink in the UK. Males aged over 50 and females aged over 60, who were potentially eligible for statin treatment based on their underlying CVD risk, were followed-up for ten years. The primary outcome was hospitalisation or death with a diagnosis of muscle disorders. The Fine-Gray proportional sub-distribution hazards model was fitted to address competing risk of death from other causes. Statin prescriptions within the 12 months before follow up and other predictors were included in the model based on a literature review.

Results: The cohort included 1,785,207 patients, with a mean age of 64 and 44% females. Patients prescribed statins were predicted to have a higher risk of muscle disorders. Female sex, obesity, previous muscle problems, vitamin D deficiency, liver disease, and the use of myotoxic drugs also increased an

individual's risk (Table). An automated risk calculator was developed based on the model

Table. STRATIFY-StatinMD[a] risk prediction model

Predictors	Hazard Ratio (95% Confidence Interval)
Demographics	
Age	
Age_FP1 [illegible]	[illegible]
Age_FP2 [illegible]	[illegible]
Gender	
Male	Reference
Female	[illegible]
Ethnicity	
White	Reference
Black	[illegible]
South Asian	[illegible]
Mixed and Other	1.17 (0.94 - 1.43)
Deprivation	
Level 1 (Least Deprived)	Reference
Level 2	[illegible]
Level 3	[illegible]
Level 4	[illegible]
Level 5 (Most Deprived)	[illegible]
Health Factors	
Alcohol Consumption	
Non drinker	Reference
General drinker	[illegible]
[illegible]	[illegible]
Smoking	
Non smoker	Reference
Ex smoker	[illegible]
Current smoker	[illegible]
BMI (Body Mass Index)	
Normal	Reference
Underweight	[illegible]
Overweight	[illegible]
Obese	[illegible]
Morbidly obese	[illegible]
FI (Frailty index)	[illegible]
Comorbidities	
Cardiovascular disease	[illegible]
Hypertension	[illegible]
Diabetes	[illegible]
Mild liver disease	[illegible]
Kidney disease	[illegible]
Rheumatoid arthritis	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
Hypothyroidism	[illegible]
Vitamin D deficiency	[illegible]
Vitamin B12 deficiency	[illegible]
Concomitant Medications	
Statin interactive drugs	[illegible]
[illegible]	[illegible]
Statin Exposure	
No statin exposure	Reference
Atorvastatin	[illegible]
Rosuvastatin	[illegible]
Simvastatin	[illegible]
Other statins (Fluvastatin/Pravastatin)	[illegible]

[a] [illegible]

[b] [illegible]

Figure. Web-based App of STRATIFY-StatinMD risk calculator (Beta version)

(Figure).

Conclusions: This model uses routinely available patient characteristics to predict an individual's risk of muscle disorders. The calculator may help clinicians and patients communicate the safety concerns and

make shared decisions on statin treatment. External validation of this model is ongoing to support general application in clinical practice.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

PCSK9 ASSOCIATION WITH LDL: EFFECTS OF ANTI-PCSK9 MABS THERAPY.

POSTER VIEWING SESSION

Laura Canclini[1,2], Andrea Baragetti[1,2], Najoua Jabnati[1], Amir M. Malvandi[2], Liliana Grigore[3,4], Alberico L. Catapano[1,2]
[1]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]Irccs, MultiMedica, Milan, Italy, [3]Irccs, MultiMedica, Sesto San Giovanni, Italy, [4]S.i.s.a. Centre For The Study Of Atherosclerosis, Bassini Hospital, Cinisello Balsamo, Milan, Italy

Background and Aims : Proprotein convertase subtilisin-kexin type 9 (PCSK9) increases LDL-C levels in plasma by promoting the degradation of the low-density lipoprotein receptor (LDLR). The use of monoclonal antibodies (mAbs) is an effective approach for the inhibition of PCSK9 activity. PCSK9 associates with LDL in plasma, and this is thought to have biological significance. The aim of our study was to clarify whether anti-PCSK9 mAbs can modify the PCSK9-LDL association.

Methods: Lipoproteins were isolated from plasma of anti-PCSK9 mAbs treated subjects using Iodixanol gradient ultracentrifugation before treatment (T0, n=17) and 1 (T1, n=14), 3 (T3, n=17) and 6 (T6, n=13) months after the first anti-PCSK9 mAb administration. The PCSK9 content of the lipoprotein fractions obtained was quantified with ELISA; cholesterol and triglycerides were measured using clinical grade reactives.

Results: Plasma PCSK9 levels increased after therapy from 417±134 ng/mL (T0) to 3758±1175 ng/mL at T1, 3934±959 ng/mL at T3 and 4004±1078 ng/mL at T6; LDL cholesterol levels decreased from 144±71 mg/dL (T0) to 60±37 mg/dL at T1, 61±50 mg/dL at T3 and 49±24 mg/dL at T6. PCSK9 associated with a specific LDL subfraction before and after anti-PCSK9 mAbs therapy. The absolute amount of LDL-bound PCSK9 increased 17±9 fold after therapy.

Conclusions: Despite the LDL-C reduction due to the mAbs therapy, the PCSK9-LDL association remains and the absolute amount bound is increased. The reason for the increased PCSK9-LDL binding affinity remains to be clarified, as well as the physiological significance of the PCSK9-LDL association.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

STATINS IN SEVERE HYPERCHOLESTEROLEMIC PATIENTS: GENDER AND CARDIOVASCULAR EVENTS GAPS

POSTER VIEWING SESSION

Pablo Corral[1], Laura E. Schreier[2], Facundo Blautzic[1], Benjamin Saenz[1], Agustina Corral[1], María Gabriela Matta[1]
[1]Pharmacology Department,, FASTA University, Mar del Plata, Argentina, [2]Clinical Biochemistry, Lipids and Atherosclerosis Laboratory, Faculty of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, Argentina

Background and Aims : Statins are the first line of treatment in patients with severe hypercholesterolemia (SH) to prevent cardiovascular disease. Even though, it is well known that atherosclerosis is more prevalent in men than in women, there is a lack of information regarding their treatments in this population. Aim: to determine gender differences considering treatment and prognostic in a middle-age population with SH.

Methods: A prospective observational study was conducted to evaluate the use of statins and new-onset cardiovascular events (CVE) after 5 years in 115 patients with SH included in the FH Hypercholesterolemia detection program in Argentina (DA VINCI Study)

Results: Median age was 56 ±10, females 74%. Patients on lipid lowering therapy stratified by sex was 38.8% in women and 26.7% in men. Among these patients, women tend to be better adequately controlled in the last year than men (63% vs 43%, p=0.057) The proportion of patients on lipid lowering therapy at the appointment after 5 years -stratified by sex- was 40.2% in women and 26.67% in men (p=0.187). Moreover 16% of the men population had a new CVE and while only 6.25% of the women ($p<0.05$).

Conclusions: A gap in the use of statins treatment between hypercholesterolemic men and women were observed as well as a remarkably impact in men prognostic and CVE.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

BILE ACID MALABSORPTION – A NOVEL INDICATION FOR PCSK9 INHIBITOR THERAPY: 3 CASES FROM A LIPID CLINIC

POSTER VIEWING SESSION

Eun Ji Kim, Anthony Wierzbicki, Martin Crook, Jamal Williams, Zofia Mcmahon, Oluwayemisi Esan
Chemical Pathology/metabolic Medicine, 5th floor, North Wing, St Thomas hospital, LONDON, United Kingdom

Background and Aims : Introduction: People with bile acid malabsorption/diarrhea and concurrent hypercholesterolaemia struggle to tolerate statins (HMG-CoA reductase inhibitors) and fibrates because these pharmacological agents can worsen their symptoms. Statins increase bile acid production by promoting expression of cholesterol 7α hydroxylase (CYP7A1), the rate-limiting enzyme in synthesis of bile acids from cholesterol. Fibrates increase bile acid transport from hepatocytes by inducing expression of BA efflux transporters and decrease expression of ileal BA transporters reducing uptake. Ezetimibe may increase lithogenic bile acid levels post-cholecystectomy.

Methods: Case reports: 3 patients with a diagnosis of chronic bile acid malabsorption, most confirmed with SEHCAT scans, were referred to a lipid clinic with hyperlipidemia and intolerance to oral lipid-lowering medications. All required lipid lowering therapy taking account their co-morbidities although the calculated CVD risk was not necessarily above the treatment threshold of 10%.

Results:

Patient	Patient history CVD risk (QRISK %)	Drug intolerances	Current Lipid Lowering Medications	TC pre → post (mmol/L) (change %)	LDL-C pre → post (mmol/L) (change %)
1	Mixed hyperlipidemia Bile salt malabsorption HIV Crohn's disease Ex-smoker Prostatic hypertrophy CVD risk 8.1%	- full dose Fenofibrate[a] - moderate intensity statin[b]	Evolocumab (140mg/month) Colesevelam (5 capsules)	5.9 → 7.4 (↑ 25 %)	3.2 → 2.58 (↓19%)
2	Mixed hyperlipidemia Bile salt malabsorption Adenocarcinoma of colon Bowel resection (Colon & terminal ileum) Keratoderma on Acitretin Hypothyroidism CVD risk doesn't apply		Evolocumab (140mg/month) Colesevelam (1.25g TDS) Fenofibrate (160mg OD)	7.2 → 4.2 (↓ 42%)	3.3 → 1.53 (↓ 54%)
3	Hypercholesterolemia Angiographic CAD (CAC score 71; 50% LAD plaque) Bile salt malabsorption Cholecystectomy Hypertension Autonomic failure CVD risk: doesn't apply	- statins - fibrate - anti-hypertensives	Evolocumab (140mg/month) Ezetimibe (10mg OD) Ursodeoxycholic acid (250mg TDS)	6.5 → 4.4 (↓ 32%)	3 → 0.94 (↓ 69 %)
				Average 16%	Average 47%

a: tolerated Fenofibrate 67mg b: tolerated Rosuvastatin 5mg once weekly PCSK9 inhibitor therapy was initiated cautiously using monthly Evolocumab 140mg. Mean LDL-cholesterol was reduced by 47% from 3.2 to 1.7mmol/L and the total cholesterol by 16% from 6.3 to 5.3mmol/L. Previous gastrointestinal symptoms of bile acid malabsorption improved upon treatment with Evolocumab so that the dose of concurrent Colesevelam could be reduced from 8 capsules to 5 capsules daily for one patient.

Conclusions: Conclusions: These cases demonstrate a potential novel indication for PCSK-9 inhibitor treatment for patients who are intolerant of conventional lipid lowering therapy because of bile acid malabsorption.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

META-ANALYSIS ON COMPARISON OF EFFICACY AND TOLERABILITY OF ROSUVASTATIN 5 MG/EZETIMIBE 10 MG VERSUS ROSUVASTATIN 20 MG MONOTHERAPY

POSTER VIEWING SESSION

Sang-Hak Lee
Cardiology, Yonsei University College of Medicine, Seoul, Korea, Republic of

Background and Aims : Data comparing low-dose statins/ezetimibe with higher dose statins have been limited. The aim of this study was to compare the efficacy and tolerability of rosuvastatin 5 mg/ezetimibe 10 mg with rosuvastatin 20 mg by meta-analysis.

Methods: PubMed was searched until September 2021 for randomized controlled trials (RCTs) that compared rosuvastatin 5 mg/ezetimibe 10 mg combination and rosuvastatin 20 mg monotherapy. The primary efficacy and tolerability variables were percentage reduction of LDL-C and percentage of participants experiencing drug-related adverse events. Secondary efficacy variables were percentage reduction of total cholesterol, triglyceride, and percentage elevation of HDL-C. The effect size of treatment groups was assessed by weighted mean difference (MD) using a fixed- or random effect models.

Results: Five RCTs with a total of 495 participants (combination: monotherapy=244:251) were included. Compared to the monotherapy group, combination group did not show difference in percentage reduction in LDL-C (MD 1.2; 95% CI [-1.5, 3.9]); p=0.41). The risk of drug-related adverse events was not different in the combination group either (OR 1.14; 95% CI [0.55, 2.35], p=0.73). However, the percentage reduction in total cholesterol was higher in the combination group (MD 2.1; p=0.004). The percentage reduction in triglyceride (MD -3.7; p=0.37) and percentage elevation in HDL-C (MD 0; p>0.99) were not different in the combination group.

Conclusions: The lipid modifying efficacy and tolerability of rosuvastatin 5 mg/ezetimibe 10 mg were largely comparable to those of rosuvastatin 20 mg. In most cases, these two regimens might be used interchangeably.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

DECIPHERING THE MOLECULAR MECHANISMS UNDERLYING THE INCREASE IN PCSK9 PLASMA LEVELS IN RESPONSE TO ANTI-PCSK9 MABS: IN VITRO STUDY IN HUMAN HEPATOMA-DERIVED HUH7 CELLS

POSTER VIEWING SESSION

Maria Giovanna Lupo[1], Giovanni Panighel[2], Irene Ferrarese[2], Francesca Zimetti[3], Maria Pia Adorni[4], Stefano Dall'Acqua[2], Nicola Ferri[1]
[1]Dipartimento Di Medicina, Universitá degli Studi di Padova, Padova, Italy, [2]Dipartimento Di Scienze Del Farmaco, Università di Padova, Padova, Italy, [3]Department Of Food And Drug, University of Parma, Parma, Italy, [4]Department Of Medicine And Surgery, Unit Of Neuroscience, University of Parma, Parma, Italy

Background and Aims : In response to anti-PCSK9 monoclonal antibodies (mAbs) the circulating levels of total PCSK9 raised by approximately 4/7-fold (Shapiro *et al.* 2018). We aim to study the molecular mechanisms underlying this phenomenon.

Methods: PCSK9 expression in Huh7 cells were evaluated by the means of RT-qPCR, Western Blot, and ELISA assays upon incubation with simvastatin 40μM, and alirocumab or evolocumab 10μg/mL. Untreated cells were used as control. Under the same conditions, PCSK9 transcriptional activity were assessed through *PCSK9*-promoter assay. Intracellular total cholesterol (TC) was measured via HPLC-MS, and cholesterol biosynthesis was analyzed by TLC. Eighteen 3-months-old wt C57BL/6 mice were randomized to receive single IP injections of vehicle or Alirocumab 10mg/kg. Plasma was collected after 72h from IP, and TC and triglycerides (TG) were measured through a colorimetric assay, while plasma Pcsk9 was evaluated by ELISA assay.

Results: In HuH7 cells, simvastatin induced PCSK9 (+10.8) in a time-dependent manner with maximal effect at 48h. On the contrary, mAbs strongly reduced both intracellular and extracellular PCSK9 at 48h. mAbs did not affect *PCSK9* transcriptional activation, conversely to what observed with simvastatin. In mice, a single-dose of alirocumab induced a 5.2-fold increase in Pcsk9 plasma levels, with a -20% decrease both in TC and TG levels.

Conclusions: Our *in vitro* results suggest that alirocumab and evolocumab increase PCSK9 plasma levels not by inducing its liver synthesis but likely by reducing its clearance. The ongoing analyses on livers, and other tissues, from treated mice will further shed light on the effect of mAbs on PCSK9 homeostasis.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

ROLE OF PHYSICIANS' MISPERCEIVED CARDIOVASCULAR RISK AND THERAPEUTIC INERTIA IN LDL-CHOLESTEROL TARGETS ACHIEVEMENT IN DIABETES

POSTER VIEWING SESSION

Mario Luca Morieri[1], Olga Lamacchia[2], Enzo Manzato[1], Andrea Giaccari[3], Angelo Avogaro[1]
[1]Department Of Medicine, University of Padova, Padova, Italy, [2]Department Of Medical And Surgical Sciences, University of Foggia, Foggia, Italy, [3]Deparment Of Surgical And Medical Sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Background and Aims : Greater efforts are needed to overcome the worldwide reported low achievement of LDL-c targets. This survey aimed to dissect whether and how the physician-based evaluation of patients with diabetes is associated with the achievement of LDL-C targets.

Methods: This cross-sectional self-reported survey interviewed physicians working in 67 outpatient services in Italy, collecting records on 2,844 patients with diabetes. Each physician reported a median of 47 records (IQR 42-49) and, for each of them, the physician specified its perceived cardiovascular risk, LDL-c targets, and the suggested refinement in lipid-lowering-treatment (LLT). These physician-based evaluations were then compared to recommendations from EAS/EASD guidelines.

Results: Collected records were mostly from patients with type 2 diabetes (94%), at very-high (72 %) or high-cardiovascular risk (27%). Physician-based assessments of cardiovascular risk and of LDL-c targets, as compared to guidelines recommendation, were misclassified in 34.7% of the records. The misperceived assessment was significantly higher among females and those on primary prevention and was associated with 67% lower odds of achieving guidelines-recommended LDL-c targets (O.R. 0.33, $p<0.0001$). Peripheral artery disease, target organ damage, and LLT-initiated by primary-care physicians were all factors associated with therapeutic-inertia (i.e., lower than expected probability of receiving high-intensity LLT). Physician-suggested LLT refinement was inadequate in 24% of overall records and increased to 38% among subjects on primary prevention and with misclassified cardiovascular risk.

Conclusions: This survey highlights the need to improve the physician assessment of cardiovascular risk and of LLT refinement in patients with diabetes in order to successfully implement guidelines recommendations into everyday clinical practice.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

STATIN USE AND RISK OF DEMENTIA AND ALZHEIMER'S DISEASE: A META-ANALYSIS OF OBSERVATIONAL STUDIES

POSTER VIEWING SESSION

Elena Olmastroni[1], Federica Galimberti[1,2], Marta Gazzotti[1], Alberto Zambon[3,4], Alberico L. Catapano[1,2], Manuela Casula[1,2]
[1]Epidemiology And Preventive Pharmacology Service (sefap) - Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy, [2]., IRCCS MultiMedica, Milan, Italy, [3]Department Of Medicine - Dimed, University of Padova, Padova, Italy, [4]Department Of Medicine-dimed, University of Padua, Padua, Italy

Background and Aims : As the relationship between statins and cognitive impairment remains elusive, we conducted a meta-analysis of observational studies to examine the effect of statin use on the risk of dementia and Alzheimer's disease.

Methods: This meta-analysis was conducted according to the PRISMA reporting guidelines. PubMed, Cochrane and EMBASE were searched since inception to January 2021. Inclusion criteria were: (1) cohort or case-control studies; (2) statin users compared to non-users; (3) Alzheimer's disease and/or dementia risk as outcome. Estimates from original studies were pooled using restricted maximum-likelihood random-effect model. Measure of effects were reported as Odds Ratio (OR) and 95% confidence intervals (CI).

Results: In the pooled analyses, statins were associated with a decreased risk of dementia (36 studies, OR 0.80 [CI, 0.75-0.86]) and of Alzheimer's disease (21 studies, OR 0.68 [CI, 0.56-0.81]). In the stratified analysis by sex, no difference was observed in the risk reduction of dementia between men (OR 0.86 [CI, 0.81-0.92]) and women (OR 0.86 [CI, 0.81-0.92]). Similar risks were observed for lipophilic and hydrophilic statins for both dementia and Alzheimer's disease, while high potency statins showed a 20% reduction of dementia risk compared with a 16% risk reduction associated with low potency statins, although a borderline statistical significance (p-value=0.05) for the heterogeneity between estimates.

Conclusions: These results confirm the absence of a neurocognitive risk associated with statin treatment, and suggest a potential favourable role of statins. Randomized clinical trials are needed to explore the potential neuroprotective effect.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

LPA GENOTYPES AND HAPLOTYPES INFLUENCE LIPOPROTEIN(A) LEVELS BUT NOT ARTERIAL WALL PROPERTIES, IN STABLE POST-CORONARY EVENT PATIENTS WITH VERY HIGH LIPOPROTEIN(A) LEVELS

POSTER VIEWING SESSION

Andreja Rehberger Likozar[1], Ales Blinc[1], Katarina Trebušak Podkrajšek[2], Miran Sebestjen[3]
[1]Of Vascular Disease, UMC Ljubljana, Ljubljana, Slovenia, [2]Chair Of Biochemistry, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, [3]Of Cardioloy, UMC Ljubljana, Ljubljana, Slovenia

Background and Aims : Background and aim: Lipoprotein (a) [Lp(a)] levels are an independent risk factor for coronary artery disease. Two single nucleotide polymorphisms (rs1045587, rs10455872) and KIV-2 repeats in the gene encoding Lp(a) (*LPA*) are strongly associated with increased Lp(a) levels and coronary artery disease. The aim was to initially investigate whether in stable patients following myocardial infarction and with very high Lp(a) levels these genetic variants are associated with increased Lp(a) levels. We then also investigated the functional and morphological characteristics of the arterial wall in these patients.

Methods: Methods: Blood samples from these patients (n = 70; aged ≤55 years) underwent biochemical and genetic analyses. All patients underwent ultrasound measurements for the functional and morphological properties of their arterial walls.

Results: Results: Genotype group rs10455872 and haplotypes AT and GT showed significant association with high Lp(a) levels. Patients with GG genotype showed significantly higher Lp(a) levels compared to those with AG genotype (2180 vs 1391 mg/L, $p = 0.045$). Patients with no AT haplotype had significantly higher Lp(a) levels compared to carriers of one AT haplotype (2158 vs. 1478 mg/L, $p = 0.023$) or two AT haplotypes (2158 vs. 1487 mg/L, $p = 0.044$). There were no significant associations with the properties of the arterial wall. Lp(a) levels significantly correlated with number of KIV-2 repeats ($r = -0.601$; $p < 0.0001$).

Conclusions: Conclusion: In stable patients after acute coronary event and with very high Lp(a) levels, two *LPA* single nucleotide polymorphisms and their haplotypes influence Lp(a) levels, but not arterial wall properties.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EVINACUMAB REDUCES REMNANT CHOLESTEROL IN PATIENTS WITH HYPERCHOLESTEROLEMIA OR HYPERTRIGLYCERIDEMIA

POSTER VIEWING SESSION

Robert S. Rosenson[1], Daniel Rader[2], Shazia Ali[3], Poulabi Banerjee[3], Jennifer Mcginniss[3], Robert Pordy[3]
[1]Metabolism And Lipids Unit, Mount Sinai Heart, Icahn School of Medicine at Mount Sinai, New York, United States of America, [2]Department Of Genetics And Department Of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, United States of America, [3]N/a, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America

Background and Aims : Natural selection (Mendelian randomization) studies support a causal relationship between elevated remnant cholesterol (RC) and atherosclerotic cardiovascular disease (ASCVD). Evinacumab, an angiopoietin-like 3 inhibitor, has previously been shown to reduce LDL-C, non-HDL-C and apolipoprotein B100 – known contributors to ASCVD. This post hoc analysis assessed evinacumab efficacy to reduce RC in patient cohorts from three separate clinical trials with evinacumab, irrespective of treatment arm.

Methods: RC was calculated as total cholesterol – HDL-C – LDL-C. For the 1629 and 1643 trials, LDL-C was calculated using the Friedewald equation unless triglycerides (TGs) were >400 mg/dL, where LDL-C was determined via beta-quantification. For the 1522 trial, LDL-C was determined via beta-quantification. 1629 (NCT03399786): Patients with homozygous familial hypercholesterolemia (HoFH) and LDL-C ≥70 mg/dL were enrolled. 1643 (NCT03175367): Patients diagnosed with refractory hypercholesterolemia, and LDL-C ≥70 mg/dL or ≥100 mg/dL for those with/without ASCVD, were enrolled. 1522 (NCT03175367): Patients with severe hypertriglyceridemia (sHTG; fasting TGs ≥500 mg/dL) were enrolled. Randomization details for all three trials are provided in the **Table**.

Results: Baseline RC was higher for sHTG patients entering 1522 versus other cohorts (**Table**). Reductions in RC were observed across all studies with evinacumab, with more than 50% reduction from baseline observed at the highest doses evaluated in patients with HoFH or refractory hypercholesterolemia. Within all three trials, evinacumab was generally well

tolerated.

Table 1. Lipid values at baseline and percent change from baseline in several study-dictated time points.

	1629		1643							1522	
Trial arm	EVIN, 15 mg/kg IV Q4W (n=43)	PBO IV Q4W (n=22)	EVIN, 450 mg QW SC (n=40)	EVIN, 300 mg QW SC (n=42)	EVIN, 300 mg Q2W SC (n=39)	PBO, QW SC (n=39)	EVIN, 5 mg/kg IV Q4W (n=35)	EVIN, 15 mg/kg IV Q4W (n=38)	PBO, IV Q4W (n=33)	EVIN 15 mg/kg IV Q4W (n=32)	PBO IV Q4W (n=15)
Remnant cholesterol, mg/dL											
Baseline	22.4 (13.7)	23.3 (13.0)	26.7 (13.9)	26.0 (11.4)	29.1 (16.1)	26.0 (12.4)	24.6 (12.6)	26.3 (11.3)	31.7 (14.5)	253.9 (155.2)	207.6 (136.9)
% change	−53.1 (14.6)	+14.4 (54.1)	−54.2 (18.8)	−46.0 (23.1)	−35.9 (33.8)	+9.9 (31.0)	−26.8 (31.3)	−53.7 (21.9)	−5.6 (31.0)	−36.0 (80.3)	+40.4 (80.9)
Fasting triglycerides, mg/dL											
Baseline	91.0 (65.0:145.0)	103.5 (59.0:182.0)	109.5 (82.0:183.5)	118.5 (83.0:177.0)	128.0 (87.0:167.0)	112.0 (85.0:176.0)	102.0 (86.0:156.0)	126.5 (89.0:166.0)	147.0 (104.0:200.0)	2304.0 (1217.0:3464.0)	1616.3 (966.0:3918.3)
% change[a]	−55.0 (3.1)	−4.6 (7.0)	−53.4 (3.9)	−47.7 (4.0)	−38.0 (4.2)	+8.1 (4.5)	−32.1 (4.5)	−52.8 (4.1)	−6.9 (4.7)	−56.6 (−87.1:−12.3)	+1.8 (−16.7:33.0)
LDL-C, mg/dL											
Baseline	259.5 (172.4)	246.5 (153.7)	146.3 (84.6)	159.1 (73.0)	136.2 (70.2)	157.8 (92.4)	146.0 (61.0)	143.1 (54.4)	144.5 (46.6)	44.2 (45.5)	37.9 (21.4)
% change[a]	−47.1 (4.6)	+1.9 (6.5)	−47.2 (6.2)	−44.0 (6.3)	−29.7 (6.4)	+8.8 (6.4)	−23.5 (6.6)	−49.9 (6.1)	+0.6 (6.6)	+42.2 (94.4)	−10.7 (42.1)
Total cholesterol, mg/dL											
Baseline	325.6 (170.8)	315.9 (150.4)	225.5 (86.2)	242.2 (77.3)	217.0 (68.8)	240.1 (91.9)	228.8 (60.2)	220.9 (56.8)	231.6 (50.4)	324.9 (137.7)	266.6 (128.5)
% change[a]	−47.4 (3.0)	+1.0 (4.2)	−45.4 (3.9)	−40.3 (4.0)	−31.0 (4.0)	6.1 (4.0)	−22.6 (4.4)	−46.8 (4.1)	−0.4 (4.5)	−29.3 (44.8)	+15.1 (34.9)
HDL-C, mg/dL											
Baseline[b]	43.6 (14.9)	46.0 (16.1)	52.5 (13.8)	57.0 (22.9)	51.7 (15.5)	56.2 (16.7)	58.2 (16.8)	51.5 (17.4)	55.4 (18.0)	25.8 (24.3)	18.6 (3.5)
% change[b]	−29.6 (13.5)	+0.77 (25.1)	−27.9 (18.5)	−30.3 (15.8)	−19.5 (20.2)	−1.7 (15.6)	−14.9 (16.5)	−31.4 (19.5)	+1.9 (20.4)	−16.6 (30.7)	−1.2 (32.2)

Mean percent change from baseline shown at differing timepoints depending on trial: 1629, Week 24; 1643, Week 16; 1522, Week 12.

Values shown in table are either mean (standard deviation) or median (Q1:Q3).

[a]Mean (standard error) values are provided for 1643 trial.

[b]Baseline data presented for 1643 trial's HDL-C values uses ITT population at baseline and safety analysis set at Week 16.

EVIN, evinacumab; HDL-C, high-density lipoprotein cholesterol; IV, intravenous; LDL-C, low-density lipoprotein cholesterol; PBO, placebo; Q4W, every 4 weeks; QW, every week; SC, subcutaneous.

Conclusions: Despite limitations in comparing the study groups directly, the reductions observed suggest evinacumab treatment lowers RC. RC could be a future target for lipid-lowering therapies.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

THE CHALLENGE OF LIPID-MODIFYING THERAPIES IN THE ACHIEVEMENT OF OPTIMAL LDL-C LEVELS IN HIGH AND VERY HIGH CV RISK PATIENTS: STILL AN OPEN QUESTION

POSTER VIEWING SESSION

Ilaria Rossi[1], Damiano D'Ardes[1], Benedetta Bucciarelli[2], Francesco Bianco[3], Fabio Troiano[1], Paola Vizzarri[1], Margherita Caporale[1], Francesco Cipollone[1], Marco Bucci[1]
[1]Medicine And Aging Sciences, G. D'Annunzio University of Chieti, Chieti, Italy, [2]Pediatrics, Azienda Ospedaliero-Universitaria "Ospedali Riuniti", Ancona, Italy, Ancona, Italy, [3]Cardiology, Azienda Ospedaliero-Universitaria "Ospedali Riuniti", Ancona, Italy, Ancona, Italy

Background and Aims : Hypercholesterolemia is one of the main modifiable atherosclerotic cardiovascular (CV) disease's risk factors. The aim was to evaluate the efficacy of the currently available lipid lowering therapy (LLT) and the achievement of treatment targets (TT) in a cohort of high and very-high CV risk patients treated with maximum tolerated LLT.

Methods: We enrolled 27 consecutive high or very-high CV risk (estimated by ESC-SCORE charts) patients between November-2020 to January-2021 and followed-up them for 8±2months. Four patients were excluded due to missing laboratory data; 23 patients (mean age 60±13 yo, M=74%) represented our final sample of this analysis.

Results: Most patients (n=17/23, 74%) were treated with Ezetimibe; while Rosuvastatin was the most utilized statin (n=10/23, 43%); 9 subjects were treated with both. At the follow-up visit, the entire population experienced a significant reduction in Total- and LDL-Cholesterol (p=0.014 and p=0.011, respectively), with a change from baseline of -28 [-103, 13 (Q1,Q3)] and -34 [-92, 11 (Q1,Q3)] mg/dL. Eleven out of 23 (50%) participants achieved the TT according to the 2019 ESC/EAS recommendations. At the multivariable analysis, PCSK9-i was the most effective LLT to achieve the TT [(OR 2.42, 95% CI: 0.26, 5.12 (p=0.043)].

Conclusions: In our cohort of high and very-high CV risk patients, the addition of PCSK9-i still showed to be the most effective LLT to achieve TT but this is often too expensive. The challenge is that future less expensive therapeutic strategies, currently not available in Italy, could allow the TT to be reached equally.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

NEW DATA OF THE TREATMENT WITH BEMPEDOIC ACID IN CLINICAL ROUTINE

POSTER VIEWING SESSION

Friederike Schumann, Elisabeth Steinhagen-Thiessen, Thomas Bobbert, Ursula Kassner
Lipid Clinic At The Interdisciplinary Metabolism Center, Charité - Universitätsmedizin Berlin, Berlin, Germany

Background and Aims : Bempedoic acid, an inhibitor of ATP citrate lyase, reduces low-density lipoprotein cholesterol (LDL-C) and since 2020 has become an additional treatment option to reach the LDL-C treatment goal. The aim of this analysis is to provide new data of side effects and efficacy of bempedoic acid in a “real-world” cohort.

Methods: We did a retrospectiv analysis of the patients who got bempedoic acid in our outpatients clinic.

Results: 64,8% of our patients were female. The mean age was 64 years and 79,7% had a statin intolerance. Yet 41% of our patients discontinued the treatment due to side effects, insufficient LDL-C lowering or even the additional cost of the small sized drug box. Main side effects were myalgia, arthralgia and gastrointestinal symptoms. Patients who were on single therapy with a PCSK9 inhibitor benefited most from the additional use of bempedoic acid. In this small subgroup the mean percent reduction of LDL-C was 46,5%.

Conclusions: Especially regarding the cohort, which mainly consists of patients with a statin intolerance, bempedoic acid offers, if tolerated, a safe and effective therapeutic option for lipid lowering.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-09 Lipid-lowering therapies*

EFFECTS ON LIPIDS AND PHARMACOKINETICS PARAMETERS OF PCSK9 MABS IN A REAL LIFE SETTING HIGH CV RISK PATIENTS

POSTER VIEWING SESSION

Marco Trevisin[1], Alberto Zambon[2], Sabina Zambon[2], Antonina Giammanco[3], Angelo Baldassare Cefalù[3], Maurizio Averna[4], Maria Giovanna Lupo[5], Nicola Ferri[5]
[1]U.o. Di Medicina Generale, Ospedale di Conegliano - Azienda ULSS 2 Marca Trevigiana, Conegliano, Italy, [2]Department Of Medicine, University of Padua, Padua, Italy, [3]Department Of Health Promotion, Mother And Child Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy, [4]Department Of Health Promotion Sciences Maternal And Infantile Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy, [5]Dipartimento Di Medicina, Universitá degli Studi di Padova, Padova, Italy

Background and Aims : To investigate PCSK9-inhibitor mAbs kinetics and possible correlations between blood levels of total, free and monoclonal antibodies (mAbs)-bound forms of PCSK9 in a group of high CV risk patients.

Methods: Blood samples were obtained from 56 patients (32 men, 24 women) 7 days after administration of PCSK9-i mAbs (Evolocumab or Alirocumab), and again after a wash-out period of 3-4 weeks or before starting therapy. Full lipid profile and total/free-PCSK9 plasma levels were measured by two ELISA assays: a standard ELISA assay for total PCSK9, and in house developed ELISA assay for free-PCSK9. The treatment effects were evaluated as Δ and Δ% of the means. Data were analyzed by paired t-test and the Wilcoxon test.

Results: PCSK9 mAbs decreased TC by 38%; LDL-C by 53%; TG by 17%; non-HDL-C by 50%, and Lp(a) by 15% ($p<0.05$ for all variables); HDL-C increased by 5%. On treatment circulating total PCSK9 values increased by 3.34 fold ($p<0.05$), and free-PCSK9 decreased by 20% ($p<0.05$) with some differences between the two drugs. Four patients were “hypo-responders” with an LDL-C reduction <15%.

Conclusions: In a real-life setting, mAbs effects on LDL-C, non-HDL-C and Lp(a) were comparable to those observed in large clinical trials (FOURIER, ODYSSEY OUTCOMES). Interestingly, PCSK9 plasma values measured 3-4 weeks after last injection show a significant residual effect of PCSK9 mAbs. It is plausible to hypothesize the development of an algorithm using total/free/bound PCSK9 assays to define both adherence to therapy and hypo-responders patients.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-11 Anti-inflammatory therapies*

EX VIVO SERUM TREATMENT WITH MAGNESIUM SULFATE AND EDTA DISODIUM SALT DIHYDRATE ABROGATES CALCIUM- AND PHOSPHATE-INDUCED FORMATION OF CALCIPROTEIN PARTICLES

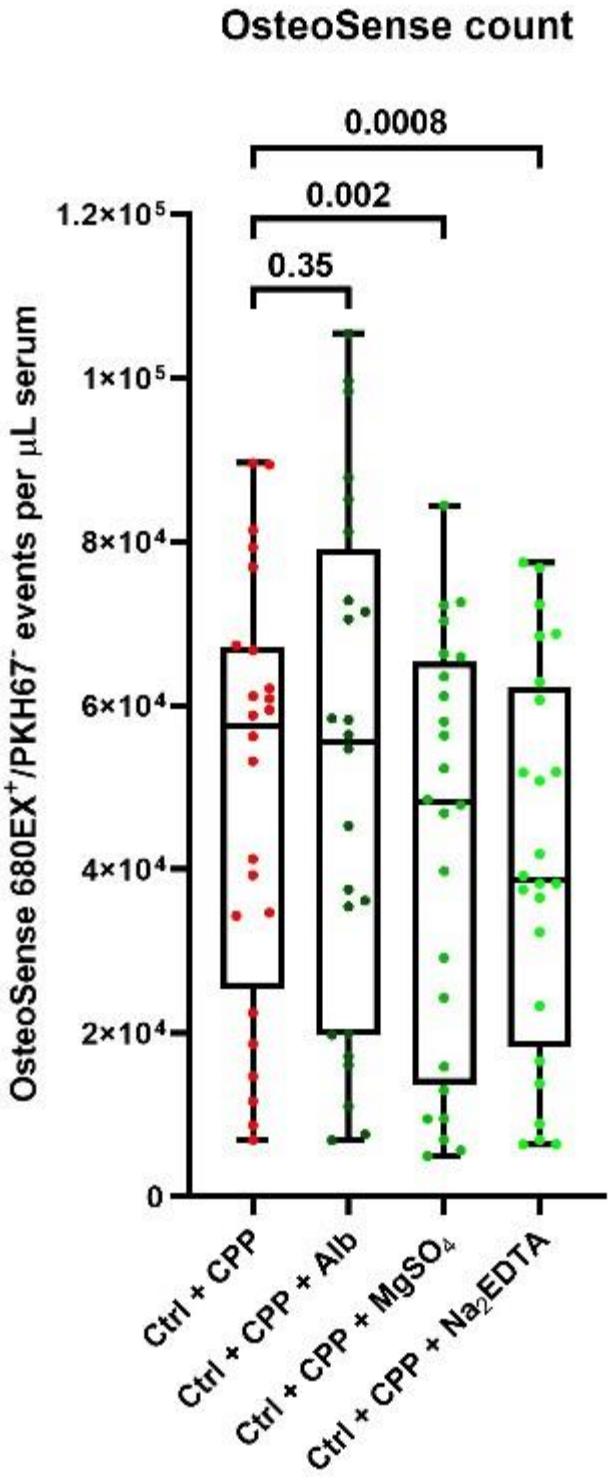
POSTER VIEWING SESSION

Daria K. Shishkova, Victoria E. Markova, Vera G. Matveeva, Olga V. Gruzdeva, Anton G. Kutikhin
Laboratory Of Molecular, Translational, And Clinical Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

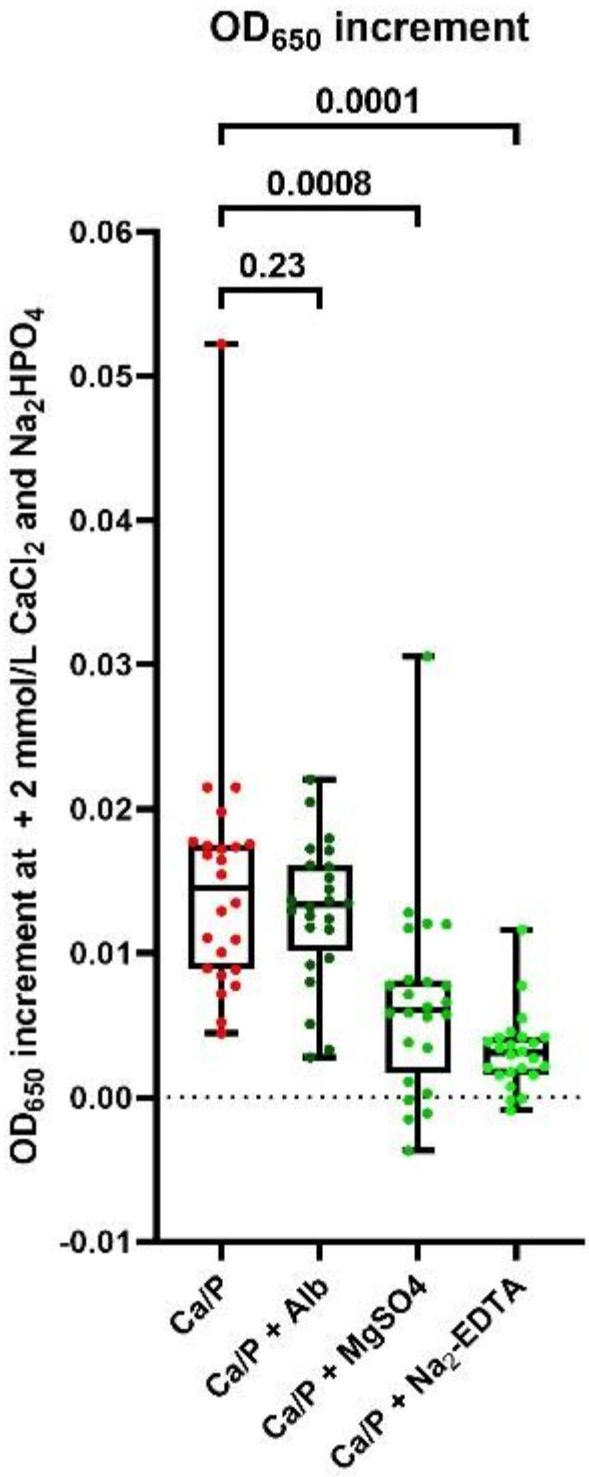
Background and Aims : Calciprotein particles (CPPs), generated in human blood to cope with mineral stress, mediate aggregation and clearance of excessive calcium and phosphate from the circulation. However, increased serum propensity to produce CPPs has been associated with arterial hypertension, cerebrovascular disease, myocardial infarction, and cardiovascular death by causing endothelial dysfunction. As CPPs might represent a link between disturbed mineral homeostasis and cardiovascular disease, we conducted ex vivo testing of potential anti-CPP treatment modalities: albumin (Ca^{2+}-binding protein), Mg^{2+} supplementation and chelation therapy.

Methods: Serum from 24 healthy blood donors was supplemented with either albumin (+10 g/L), $MgSO_4$ (+0.04 g/L), or ethylenediaminetetraacetic acid disodium salt dihydrate (Na_2-EDTA, +1.6 mmol/L) and optionally supersaturated with $CaCl_2$ and Na_2HPO_4 (+2 mmol/L each) with the subsequent incubation at 37°C, 5% CO_2 and high humidity for 24 hours. Serum calcification propensity was evaluated by measurement of the optical density at 650 nm wavelength (OD_{650}) while relative quantification of CPPs was performed by flow cytometry using a fluorescent-labeled bisphosphonate (OsteoSense 680EX).

Results: Both Mg^{2+} supplementation and addition of Na_2-EDTA abrogated $CaCl_2$ and Na_2HPO_4-induced serum calcification propensity and reduced CPP formation, while albumin supplementation had no effect on both of these measures but significantly lowered serum ionised


OsteoSense count
0.0008
0.002
0.35
1.2×10^5
1×10^5
8×10^4
6×10^4
4×10^4
2×10^4
0
OsteoSense 680EX+/PKH67- events per µL serum
Ctrl + CPP
Ctrl + CPP + Alb
Ctrl + CPP + MgSO4
Ctrl + CPP + Na2EDTA

calcium.



Conclusions: Mg2+ supplementation and administration of chelate compounds may be considered as promising anti-CPP therapies, while albumin supplementation might be used as an adjuvant therapy to correct increased ionised calcium. Funding: This study was funded by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities, Research Topic No. 0419-2021-001).

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EARLY CARDIORENAL RISK IS MOLECULARLY EVIDENCED IN HYPERTENSIVE SUBJECTS WITHIN THE NORMOALBUMINURIA CONDITION. NOVEL GLYCOTARGETS FOR CARDIOVASCULAR RISK STRATIFICATION

POSTER VIEWING SESSION

Aranzazu Santiago-Hernandez[1], Marta Martin-Lorenzo[1], Maria Gomez-Serrano[2], Juan A. Lopez[2], Paula J. Martinez[1], Jesus Vazquez[2], Gema Ruiz-Hurtado[3], Maria G. Barderas[4], Julian Segura[3], Luis M. Ruilope[3], Gloria Alvarez-Llamas[1]
[1]Immunology, IIS-Fundacion Jimenez Diaz, Madrid, Spain, [2]Cardiovascular Proteomics, CNIC, Madrid, Spain, [3]Cardiorenal Translational Laboratory, Hospital 12 de Octubre, Madrid, Spain, [4]Vascular Physiopathology, Hospital Nacional de Paraplejicos, Toledo, Spain

Background and Aims : Clinical evidences show early cardiorenal risk in normoalbuminuric subjects within the high-normal range (ACR=10-30). But anticipating who will progress is not possible and subjacent mechanisms are unknown. Thus, normoalbuminuric subjects are out of therapeutic management. We aimed to identify molecular targets of early cardiorenal risk which may aid in individual risk stratification

Methods: Urine samples were collected from hypertensives subjects under RAS suppression classified in control if ACR<10mg/g and high-normal (HN) if ACR=10-30mg/g. The urinary glycoproteome was analyzed by omics (isobaric labeling) (n=16), systems biology analysis was performed and proteins showing differential abundance in HN (Mann-Whitney, p-value <0.05) were confirmed by target-MS (n=37). Pathogenicity score was calculated on glycopeptides and immunohistochemistry was performed on human kidney and aortic tissue to evaluate the renal and vascular components of the observed changes.

Results: 482 N-glycoproteins were identified; 29 show the most significant alteration in HN, mainly A1AT, HPTR, CERU, ATL2, DBF4A and TOM6. Main altered pathways are complement/coagulation cascades (p-value =0.0002), ferroptosis (p-value =0.0015) and platelet degranulation (p-value =0.0009). Increased levels of urinary A1AT reflect significant diminishment in microalbuminuric kidney and in atherosclerotic aorta. A panel of 23 N-glycopeptides reveal the biological significance of N-glycosylation in CVD, showing pathogenicity score ≥0.8 and significant abundance variation in HN even though they protein of origin do not vary.

Conclusions: Urinary protein glycosylation reveal molecular targets for early cardiorenal risk stratification in normoalbuminuric subjects. Those may aid in revising current therapeutic strategies for prevention in hypertensives which may be extended to general population.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

TREATMENT OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONGENITAL HEART DISEASES OF LEFT-RIGHT SHUNT - BOSNIAN AND HERZEGOVINIAN PERSPECTIVE

POSTER VIEWING SESSION

Nedim Begić[1], Zijo Begić[2], Edin Begić[3]
[1]Pediatric Cardiology, Pediatric Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina, [2]Pediatric Cardiology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina, [3]Department Of Cardiology, General Hospital "Prim. dr. Abdulah Nakaš", Sarajevo, Bosnia and Herzegovina

Background and Aims : Pulmonary arterial hypertension (PAH), especially associated with congenital heart disease (CHD) of left-to-right shunt, is a big problem in medicine in terms of diagnostics and treatment. It evolves through increase of vasculare resistance and/or increase of blood flow through lungs, where the mean pulmonary artery pressure is above 25 mmHg and during catheterization above 30 mmHg. Due to volume and pressure load of blood from the left heart cavities in right, hypertrophy and insufficiency with increased production of PAH mediators, necrotizing arteritis of pulmonary capillaries occurs.

Methods: Paper represents retrospective analytical study over a period of 23 years.

Results: In the last 23 year we treated 62 patients with PAH related CHD of left-to-right shunt. In the last 8 years on therapy with endothelin receptor antagonists we have 12 patients who have continuosly received therapy everyday in the doses of 1 – 2.14 mg/kg with evaluation every 1-3 months. In recent period pediatric heart catheterization is done in 48 children due to evaluation of surgical intervention of CHD with L-D shunt. In 30 patients who underwent catheterization with unfixed reversible PAH, 4 children were not surgically treated. During follow-up of patients with PAH and CHD of the L-D shunt so far 11 patients (2-38 years of age) have died.

Conclusions: Continuous administration of endothelin 1 receptor antagonists indicates satisfactory health status of patients with PAH and CHD of the L-D shunt, combined with phosphodiesterase 5 inhibitors and prostanoids as well as other supportive therapy for comorbidities. However, new randomized clinical trials are neccessary.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ENHANCING THE POTENTIAL FOR INCREASED PRIMARY CARE ROLE IN FAMILIAL HYPERCHOLESTEROLAEMIA DETECTION AND MANAGEMENT: COST-EFFECTIVENESS AND RETURN ON INVESTMENT

POSTER VIEWING SESSION

Tom Brett[1], Clara Marquina[2], Jan Radford[3], Clare Heal[4], Charlotte Hespe[5], Gerard Gill[6], David Sullivan[7], Ella Zomer[2], Jedidiah Morton[2], Gerald F. Watts[8], Jing Pang[9], Zanfima Ademi[2]
[1]General Practice And Primary Health Care Research, School Of Medicine, The University of Notre Dame Australia, Fremantle, Australia, [2]School Of Public Health And Preventive Medicine, Monash University, Melbourne, Australia, [3]General Practice, University of Tasmania, Launceston, Australia, [4]General Practice, Mackay Clinical School, James Cook University, Mackay, Australia, [5]General Practice And Primary Health Care Research, The University of Notre Dame Australia Sydney, Sydney, Australia, [6]General Practice, Deakin University, Geelong, Australia, [7]Chemical Pathology, Royal Prince Alfred Hospital, Sydney, Australia, [8]Cardiology And Internal Medicine, University of Western Australia, Perth, Australia, [9]School Of Medicine, University of Western Australia, Perth, Australia

Background and Aims : Aim: We evaluated cost-effectiveness and return on investment (ROI) of detection and management strategy for familial hypercholesterolaemia (FH) in primary care in Australia.

Methods: Methods: We developed multistate Markov model to estimate outcomes (fatal and non-fatal CHD) of implementing detection and management strategy for FH compared to current Australian standard of care (SoC). The population was individuals aged 40 to 80 years, of which 44% had prior coronary heart disease (CHD). Cardiovascular risk, FH prevalence, treatment effect, acute and chronic healthcare costs were derived from published sources. The real-world Australian general practice study involved screening for patients with FH using validated date extraction tool (TARB-Ex) and medical record review, followed-up by consultation to improve the management of phenotypic risk patients. The detection rate was 16%, with 72% of population achieving target LDL-C reductions. The outcomes were quality-adjusted life years (QALYs), healthcare costs, productivity losses, incremental cost-effectiveness ratio (ICER), and ROI. All outcomes were discounted by 5% annually, adopting both healthcare and societal perspectives.

Results: Results: Over the lifetime horizon, the model estimated a gain of 1,508 years of life lived and 1,778 QALYs compared to SoC. The total net cost was AU$22,197,264 with 76% of costs due to FH management. This resulted in an ICER of AU$12,482 per QALY gained (discounted) from healthcare perspective. From societal perspective, this strategy compared to SoC was cost-saving and gave a ROI of AU$8.65 per dollar invested.

Conclusions: Conclusion: Enhancing the additional potential for increased primary care management role in FH patients may be a cost-effective option.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

OPTIMIZATION OF LIPIDS FOR PREVENTION IN PATIENTS WITH DOCUMENTED ATHEROSCLEROTIC CARDIOVASCULAR DISEASES - OUR EXPERIENCES

POSTER VIEWING SESSION

Ivana Burazor[1], Zoran Cosic[2], Rade Babic[1], Petar Otasevic[1], Nebojsa Tasic[1], Snezana Kostic[1], Milovan Bojic[1], Vladmir Kanjuh[3], Vojislav Giga[4]
[1]Cardiology, Institute for Cardiovascular Diseases Dedinje, Belgrade, Serbia, [2]Cardiology, Institute for rehabilitation, Belgrade, Serbia, [3]Cardiology, Serbian Academy of art and sciences, Belgrade, Serbia, [4]Cardiology, University Clinical Center of Serbia, Belgrade, Serbia

Background and Aims : Introduction: Low-density lipoprotein cholesterol (LDL-C) is causal of atherosclerotic cardiovascular disease, the leading cause of morbidity and mortality worldwide. Pharmacologic LDL-C lowering halts the progression of atherosclerosis and improves clinical outcomes in both primary and secondary prevention. Aims: To evaluate attainment of guideline recommended targets for lipid lowering treatment, as well as physical activity level in patients with documented atherosclerotic cardiovascular disease.

Methods: Patients who were included in The SUrvey of CVD Risk Factors in patients with coronary heart diseases (SURF-CHD) in front of our center were analyzed. Data including demographics, CHD, risk factors and use of preventive treatment was collected.

Results: Out of 1098, 102 CHD patients fullfiled the criteria and were included in the study (63.8±8 years, 76.5% males). Previous acute coronary syndrome had 67.6%, previous coronary artery bypass 57.8%. Previous history of dyslipidemia had 87.6% with mean LDL cholesterol 2.46 mmol/l. Mean HDL cholesterol was 1.08mmol/l in males and 1.02mmol/l in females. Tryglicerides were above the recomended levels. Majority of patients were taking statins – 96.1%, and other lipid lowering drugs *such as fibrates and ezetimibe) were added in 3.9% Only 8.8% of patients were at the recommended LDL goal (<1.4 mmol/l). Majority of patients reported low level of previous physical activity (less than 30 minutes - 57,8%). And the rest (42.2%) reported moderate level (moderately vigorous) - 30 min 3-5 times/week.

Conclusions: There is a huge and urgent need to continue to improve risk factor profile, optimize medical therapy to achieve the target LDL cholesterol values.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MESENCHYMAL STEM CELL-DERIVED EXTRACELLULAR VESICLES ATTENUATE CARDIAC HYPERTROPHY IN A CELLULAR MODEL OF HUMAN-INDUCED PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTES

POSTER VIEWING SESSION

Alina Constantin[1], Nicoleta Alexandru[1], Alexandru Filippi[2], Miruna Nemecz[1], Alexandra Vîlcu[1], Leona Chitoiu[3], Mihaela Gherghiceanu[3], Adriana Georgescu[1]
[1]Pathophysiology And Pharmacology, Institute Of Cellular Biology And Pathology Nicolae Simionescu, Bucharest, Romania, [2]Biophysics, Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania, [3]Ultrastructural Pathology And Bioimaging Lab, Victor Babeș National Institute of Pathology, Bucharest, Romania

Background and Aims : Background: Cardiac pathological hypertrophy is a risk factor that usually progresses to heart failure. Novel therapeutic strategies are needed to prevent or reverse pathological hypertrophy. **Aim:** To investigate the effects of mesenchymal stem cell (MSC)-derived EVs of different origin on cardiac hypertrophy.

Methods: Methods: An *in vitro* cellular model of human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs - Ncardia) was used. EVs were isolated from the secretome of human adipose tissue-derived stem cells (EV-ADSCs) or of bone marrow-derived stem cells (EV-BMMSCs). hiPSC-CMs were stimulated for 48h with AngII (200nM) and TGF-β1 (10ng/mL) in the absence or presence of EVs (100µg/ml).

Results: Results showed that exposure of hiPSC-CMs to AngII and TGF-β1 induced a significant increase in cardiac hypertrophic biomarkers ANF, MIF, α-SMA, Cx43, cTnI, COL1A1, ROS production, and of SMAD2/3 and NF-kBp50/p65. Exposure of hiPSC-CMs to EV-ADSCs generated reduction in the expression of ANF, MIF, cTnI and COL1A1. Incubation of hiPSC-CMs with EV-BMMSCs diminished cTnI, ANF, MIF and COL1A1. In addition, both EV-ADSCs and EV-BMMSCs reduced gene expression of SMAD2, SMAD3 and NF-kBp65.The EVs-ADSCs were more effective in reducing the hypertrophic effect of AngII and TGF-β1 than EVs-BMMSCs and this effect could be attributed to their miRNA content (23 miRNAs up-regulated and 22 miRNAs down-regulated).

Conclusions: Conclusion: In human-induced pluripotent stem cell-derived cardiomyocytes the EVs and their cargo reduce the expression of molecules involved in cardiac hypertrophy. The data suggest the potential of EVs to act as therapeutic mediators to reduce cardiac hypertrophy and possible subsequent cardiovascular events. **Acknowledgements:** CNCS-UEFISCDI, P1-1.2-PCCDI-2017–0527; PN-III-P1-1.1-TE-2019–0811 within PNCDI III.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

VALUE OF SPECKLE TRACKING ECHOCARDIOGRAPHY FOR DETECTION OF CLINICALLY SILENT LEFT VENTRICULAR DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

POSTER VIEWING SESSION

Ahmed Elgohari
Cardiology, research institue, cairo, Egypt

Background and Aims : Background: SLE is a chronic autoimmune inflammatory rheumatological disease. Characterized by autoantibodies directed against nuclear antigens. It is a disease of young women, with a peak incidence between the ages of 15 and 40 with a female: male ratio of 9:1. Cardiac involvement in patients with SLE is common. Subclinical involvement is more common than Clinically apparent cardiomyopathy or myocarditis Aim: Assess LV function in asymptomatic SLE patients by conventional, speckle tracking and tissue Doppler echocardiography. Early detect subclinical LV systolic and diastolic dysfunction in this group of patients before developing overt clinical cardiomyopathy

Methods: This is a case control study that included 100 participants who were divided into 2 groups: Control group : 50 non SLE patients. SLE group : 50 patients diagnosed as SLE. INCLUSION ;Patients diagnosed as SLE who fullfilled at least four of the updated revised criteria of the American College of Rheumatology for SLE diagnosis. • Preserved left ventricular ejection fraction. EXCLUSION:Congenital heart disease. • Impaired LV systolic function (LVEF < 50 %). • Ischaemic heart disease. • Prior MI. • Prior PCI or CABG. • Valvular dysfunction. • Any rhythm other than sinus rhythm.

Results: there was significant statistical difference in GLS, E/é ratio in controlled compared to SLE group ($p<0.05$), significant statistical difference in GLS in SLE duration($p<0.05$), there was no significant difference in EF, E/A in controlled compared to SLE group

Conclusions: SLE group had GLS % lower than control group and this was statistically significant denoting early systolic dysfunction. There was a significant positive correlation between (duration of the disease and SLE activity index) and AP4C LS, AP2C LS, AP3C LS and GLS. Longer duration and high SLE activity index significantly affect GLS. GLS is a non invasive good tool for early detection of subclinical left ventricular systolic dysfunction in SLE patients

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

GENETIC POLYMORPHISMS OF HYPERTRIGLYCERIDEMIA AND ASYMPTOMATIC ATHEROSCLEROSIS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

POSTER VIEWING SESSION

Marta Fanlo Maresma[1], Viriginia Esteve Luque[1], M. Ángeles Rodríguez Sánchez[2], Emili Corbella Ingles[1], Ariadna Padró Miquel[3], Beatriz Candás Estébanez[3], Xavier Pintó Sala[4]
[1]Internal Medicine, Hospital Universitari de Bellvitge/IDIBELL, Hospitalet de Llobregat, Spain, [2]Internal Medicine, Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Spain, [3]Biochemistry, Hospital Universitari de Bellvitge/IDIBELL, Hospitalet de Llobregat, Spain, [4]Internal Medicine, Hospital Universitari de Bellvitge/IDIBELL/Universitat de Barcelona, Hospitalet de Llobregat, Spain

Background and Aims : Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease that predominantly affects adult women and is associated with increased cardiovascular risk. The increase in triglyceride-rich lipoproteins and particles containing apolipoprotein B constitute the characteristic dyslipidemia of SLE. The objective of this study was to determine the relationship between the genetic variants of polygenic hypertriglyceridemia, asymptomatic atherosclerosis and lipoprotein disturbances in a population of patients with SLE.

Methods: Seventy-three SLE female patients were recruited and age-sex matched with a control group. Carotid ultrasound, laboratory profiles, and genetic analysis of the *ZPR1, APOA5*, and *GCKR* genes were performed.

Results: The prevalence of carotid plaque, hypertension and dyslipidemia was higher in patients with SLE, compared with the control group (20.5% *vs* 6.9%, p=0.028; 45.2% *vs* 5.5%, p<0.001; 52.1% *vs* 34.2%, p=0.030, respectively). SLE patients had higher triglyceride concentrations (1.0 mmol/L vs 0.8 mmol/L, p=0.008) than control group. The *GCKR* rs1260326 CC genotype (OR=0.111; 95% CI: 0.015 to 0.804, p=0.030) was independently associated with carotid atherosclerosis. In addition, the increase of 1 mmol/L of triglycerides was associated with an increase of 7.5 times in the risk of presenting carotid plaque (OR=7.576; 95% CI: 2.415 to 23.767, p=0.001).

Conclusions: In conclusion, the *GCKR* rs1260326 CC genotype and serum triglyceride concentration were independent predictors of carotid atherosclerosis in women with SLE. These data suggest that adequate control of hypertriglyceridemia and diagnosis of genetic variants related to hypertriglyceridemia may be useful to better stratify and prevent cardiovascular risk in patients with SLE.

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LIPID CORE NANOPARTICLE ASSOCIATED WITH METHOTREXATE IMPROVED LEFT VENTRICULAR CARDIOMYOPATHY IN MICE WITH MARFAN SYNDROME.

POSTER VIEWING SESSION

Maria Carolina Guido[1], Natalia M. Lopes[1], Priscila O. Carvalho[1], Aline O. Silva[1], Leonardo Jensen[2], Lygia V. Pereira[3], Ricardo R. Dias[4], Francisco R.M. Laurindo[5], Raul C. Maranhão[1]
[1]Laboratory Of Metabolism And Lipids, Heart Institute - HCFMUSP, São Paulo, Brazil, [2]Laboratory Of Hypertension, Heart Institute - HCFMUSP, São Paulo, Brazil, [3]Department Of Genetics And Evolutionary Biology, Institute of Biosciences USP, São Paulo, Brazil, [4]Department Of Cardiovascular Surgery, Heart Institute - HCFMUSP, São Paulo, Brazil, [5]Laboratory Of Vascular Biology, Heart Institute - HCFMUSP, São Paulo, Brazil

Background and Aims : Patients with Marfan syndrome (MFS), a disease caused by the mutation of the fibrillin-1 gene, are vulnerable to left ventricular (LV) cardiomyopathy. When MTX is associated to LDE, the cell uptake is increased, which endows MTX with enhanced action mechanisms and the drug toxicity is diminished. The aims of present study was to investigate whether LDE-MTX can prevent the LV cardiomyopathy in MFS mice.

Methods: MFS and wild-type mice were allocated in 3 groups of treatments: LDE only; commercial MTX; LDE-MTX. The treatment occurred weekly at a dose of 1mg/kg ip, between the 3rd and 6th month of life. The animals were submitted to echocardiography, morphometry and protein expression of the LV.

Results: LDE-MTX did not affect the LV diastolic dysfunction and the elastic fibers disruptions in coronary arteries in MFS mice. However, LDE-MTX reduced cardiac hypertrophy by decreasing interventricular septum and the posterior wall thickness and myocytes diameter, and the collagen volume fraction in subendocardial, interstitial and papillary muscle areas. The protein expression of caspase 3, BAX/Bcl-2 and hypoxia-inducible factor 2α were lower, whereas the expression of VEGF and angiopoietin 1/2 was higher in LDE-MTX. The increase in bioavailability of intracellular adenosine in MFS animals treated with LDE-MTX was suggested by the higher protein expression of A1 adenosine receptor.

Conclusions: Despite the lack of effect on LV diastolic function, treatment with LDE-MTX improved the LV hypertrophy, diminished cellular ischemia and LV fibrosis, while increasing angiogenesis. Thus, LDE-MTX had beneficial effects on the cardiac cellular disturbances related with fibrillin-1 mutation in MFS mice.

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CARDIOVASCULAR DISEASE AND HYPERHOMOCYSTEINEMIA: THE ROLE OF EICOSANOIDS

POSTER VIEWING SESSION

Malvina Hoxha[1], Entela Kolovani[2], Bruno Zappacosta[3]
[1]Department Of Chemical-toxicological And Pharmacological Evaluation Of Drugs, Catholic University Our Lady of Good Counsel, Faculty of Pharmacy, Tirana, Albania, [2]Infectious Diseases Department, University of Medicine, Faculty of Medicine, Tirana, Albania, [3]Department For Chemical-toxicological And Pharmacological Evaluation Of Drugs, Catholic University Our Lady of Good Counsel, Faculty of Pharmacy, Tirana, Albania

Background and Aims : Homocysteine (Hcy) has been considered a risk factor for cardiovascular disease (CVD), such as atherosclerosis, stroke, aortic aneurysm. Hyperhomocysteinemia (HHcy) can lead to different pathological conditions, including inflammation, and CVD. Considering the role of arachidonic acid (AA) metabolism in inflammation and vascular homeostasis we aim to investigate the clinical significance of eicosanoids in hyperhomocysteinemia, particularly in Hcy-induced vascular disease through a systematic review of existing studies.

Methods: Pubmed and Scopus databases were used to identify all the studies investigating the role of eicosanoids in HHcy. We extracted and analyzed all the relevant data conformed to the eligibility criteria.

Results: A total of 454 studies were identified, of which 47 were considered eligible. AA is metabolized by different enzymes that are affected by the increase in Hcy levels, such as COX-2 that increases in Hcy-stimulated macrophages, resulting in pro-inflammatory events. HHCy increases the levels of prostaglandin E_2 (PGE_2), thromboxane A_2 (TXA_2), CYP hydroxylase, and 20-HETE, which have vascular inflammatory properties. Interestingly, a reduction in PGI_2 levels, and CYP epoxygenase expression was revealed. Epoxyeicosatrienoic acid (EETs) levels, which have beneficial effects on the cardiovascular system are also reduced.

Conclusions: The data suggest that AA pathway may be involved in Hcy-induced vascular disease. New pharmacological compounds for vascular disease may be obtained by targeting Hcy in AA pathway.

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ASSESSMENT OF DISTAL CORONARY CALCINOSIS BEFORE CORONARY ARTERY BYPASS GRAFTING: THE ROLE OF COMPUTED TOMOGRAPHY

POSTER VIEWING SESSION

Renat Akchurin[1], Andrey A. Shiryaev[1], Vladislav P. Vasiliev[1], Rasul Pashaev[2], Vladimir Zaikovsky[2], Said Kurbanov[1]
[1]Cardiovascular Surgery, NATIONAL MEDICAL CARDIOLOGY RESEARCH CENTER, Moscow, Russian Federation, [2]Cardiovascular Department, FSBI "National Medical Research Center of Cardiology" of the Ministry of Health of Russia, Moscow, Russian Federation

Background and Aims : Coronary artery calcinosis (CAC) limits the possibilities of surgical treatment of coronary artery disease and is associated with worse clinical outcomes. There are no guidelines and algorithms for using the coronary reconstructions (endarterectomies, onlay-flap anastomoses to vessels <1,5% mm in diameter) in severe distal CAC; preoperative assessment of the severity of CAC is not included in clinical practice. Objective: To evaluate the need for preoperative computed tomography (CT) assessment of CAC in candidates for coronary artery bypass grafting (CABG).

Methods: It was a retrospective study in patients operated on in 2017-18 years. A total of 106 patients with distal CAC who underwent CABG were enrolled. All patients in the preoperative underwent CT angiography in doubtful cases. 237 calcified target vessels were identified and distributed into two groups:mild calcification <180 ° (n=124), and severe circular calcification ≥180 ° (n=113). Coronary artery reconstructions were performed by the surgeon. The use of coronary reconstructions was analyzed according to CAC.

Results: A total of 467 distal coronary anastomoses were performed (114 autoarterial, 353 autovenous), the mean number of anastomoses was 4.4±0.7. Some of the distal anastomoses were performed using coronary reconstructions (n=73). The frequency of using the coronary reconstructions was higher in the severe circular calcified arteries (47.8% versus 15.3%, OR = 5.1, 95% CI 2.7-9.3, p <0.001).

Conclusions: Severe circular calcification of the coronary arteries 5-fold increases the need for coronary reconstructions. The using of CT in the preoperative period allows choosing optimal surgical strategy for CABG in patients with CAC.

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THE PLASMA PROTEOME OF RHEUMATIC PATIENTS REVEALS DIFFERENCES IN FINGERPRINT BASED ON THE CARDIOVASCULAR HISTORY

POSTER VIEWING SESSION

Max Van Velzen[1], Romy Hansildaar[2], Eduard Van Der Vossen[1], Mike Nurmohamed[3], Johannes H.M. Levels[4]
[1]Amsterdam Umc - Location Amc, G1-142, Amsterdam, Department of Experimental Vascular Medicine, Amsterdam, Netherlands, [2]Center For Rheumatology And Immunology, READE, Amsterdam, Netherlands, [3]Center For Rheumatology And Immunology, READE, AUMC, Amsterdam, Netherlands, [4]Department Of Experimental Vascular Medicine, Amsterdam UMC - Location AMC, G1-142, Amsterdam, Netherlands

Background and Aims : The risk of cardiovascular diseases in patients with a rheumatic background is much higher compared to the normal population. Still, it's etiology is not fully understood. In this study the plasma proteome of patients with a rheumatic background were compared with a group of patients who on top of their rheumatic background suffered from a cardiovascular event (CVE).

Methods: The cohort consisted of a rheumatic patient control group (n=10) and a patient group (n=10) with a CVE history. Samples were collected 1 year prior to the CVE and 3-6 months after the CVE. Patients were matched with controls based on age, sex and medication use. Depletion of high abundant plasma proteins (TOP-14) was followed by "bottom up" shotgun proteomics using LC-MS/MS. Rstudio was used for normalization assessment and the relative changes in protein/peptide abundance were investigated using Perseus for comparison between the groups.

Results: Principle component analysis (PCA) demonstrated a difference in overall protein and peptide signature between the control group and the CVE group. A total of 282 proteins determined this potential difference. Within the CVE group PCA revealed a more comparable signature before and after the CVE. Nevertheless, still 59 proteins demonstrated significant difference in relative abundancy within the CVE group.

Conclusions: Here we demonstrated the existence of potential differences in the plasma proteome of rheumatic patient's who suffered from a CVE. This signature may already exist prior to a CVE. This gives rise to further investigation of potential risk markers which may predict a relative risk for a CVE in rheumatic diseases.

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L-CITRULLINE AMELIORATES PATHOPHYSIOLOGY IN A RAT MODEL OF SUPERIMPOSED PREECLAMPSIA

POSTER VIEWING SESSION

Wing Chung Man[1], Yawen Zhou[1], Uyen Lam[1], Gisela Reifenberg[1], Anke Werner[1], Alice Habermeier[1], Ellen Closs[1], Andreas Daiber[2], Thomas Münzel[2], Ning Xia[1], Huige Li[1]
[1]Pharmacology, Johannes Gutenberg University Medical Center, Mainz, Germany, [2]Center For Cardiology, Johannes Gutenberg University Medical Center, Mainz, Germany

Background and Aims : Preeclampsia, characterized by hypertension, proteinuria, and fetal growth restriction, is one of the leading causes of maternal and perinatal mortality. By far, there is no effective pharmacological therapy for preeclampsia. The present study was conducted to investigate the effects of L-citrulline supplementation in Dahl salt-sensitive rat, a model of superimposed preeclampsia.

Methods: Parental DSSR were treated with L-citrulline (2.5 g/L in drinking water) from the day of mating to the end of lactation period. Blood pressure of the rats was monitored throughout pregnancy and markers of preeclampsia were assessed. Endothelial function of the pregnant DSSR was assessed by wire myograph.

Results: L-citrulline supplementation significantly reduced gestational hypertension, proteinuria, and levels of circulating soluble fms-like tyrosine kinase 1 in DSSR. L-citrulline improved maternal endothelial function by augmenting the production of nitric oxide in the aorta and improving endothelium-derived hyperpolarizing factor-mediated vasorelaxation in resistance arteries. L-citrulline supplementation improved placental insufficiency and fetal growth, which were associated with an enhancement of angiogenesis and reduction of fibrosis and senescence in the placentas. In addition, L-citrulline downregulated genes involved in the toll-like receptor 4 and nuclear factor-κB signaling pathway.

Conclusions: This study shows that L-citrulline supplementation reduces gestational hypertension, improves placentation and fetal growth in a rat model of superimposed preeclampsia. L-citrulline supplementation may represent an effective and safe therapeutic strategy for preeclampsia that benefit both the mother and the fetus.

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ADAPTATION OF A NEW CARDIAC REHABILITATION PROGRAM IN TIMES OF COVID-19 PANDEMIC

POSTER VIEWING SESSION

Miriam A. Martin Toro, Manuel S. Herruzo Rojas, Eduardo J. Martinez De Morentin Laurenz, Sara Blasco Turrion, Francisco J. Morales Ponce
Cardiologia, HOSPITAL UNIVERSITARIO DE PUERTO REAL, Puerto Real, Spain

Background and Aims : INTRODUCTION: Cardiac rehabilitation(CR) is an IA indication in both ischemic heart disease and heart failure, so its implementation in all centers serving cardiac patients is essential. OBJECTIVES: To describe the characteristics of an CR program in a regional hospital after the first year of its implementation, coinciding with the COVID-19 pandemic.

Methods: Retrospective study, of consecutive cases, in which all patients included in the CR program from July/2020 to July/2021.

Results: N = 130, mean age:57.3 ± 8.6years. 99% ischemic heart disease(4.6% surgical revascularization and 83.8% with complete revascularization) and 1% post-valve replacement surgery. 12.3%women. HBP:40%, DM:28.5%, Dyslipidemia:38%, Smoking:74.6%. Type of program: Low risk:73.1%, moderate:21.5%. On-site program:67.7%, blended:21.5%. Completed:74.6%(10.8% in progress). Program start: mean functional capacity (METS):8.8±2.3, mean BMI:28.1±3.5Kg / m2, abdominal circumference:99.4±8.2cms, LDLc:58.1±19 , 4mg /dL, HbA1c:7.56±1.4%. After one year, both BMI(27.7±5Kg/m2), abdominal circumference (97±3.9cms), LDLc (53.5±54mg/dL) and HbA1c (6.4±0.5%) were reduced, improving functional capacity (10.8± 2.METS), without reaching statistical significance. Average delay time for the first stratification visit: 25.5±39.4days and for the start of the program: 37.05±33.7days.

Conclusions: After launching a new CR program, we have cared for more than 100 patients, mainly with ischemic heart disease and mainly low risk, highlighting a low representation of women (fundamental area of improvement). We have included the blended mode given the current restrictions due to the COVID-19 pandemic, with great acceptance. Positive results have been achieved in relation to control of cardiovascular risk factors and improvement in functional capacity, thus improving its prognosis, without reaching statistical significance in probable relation to the sample size.

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NEW SEMI-PRESENTIAL MODALITY IN CARDIAC REHABILITATION DUE TO COVID-19 PANDEMIC. WHAT RESULTS HAVE WE OBTAINED?

POSTER VIEWING SESSION

Miriam A. Martin Toro[1], Manuel S. Herruzo Rojas[2], Eduardo J. Martinez De Morentin Laurenz[2], Sara Blasco Turrion[2], Francisco J. Morales Ponce[2]
[1]Cardiologia, Hospital Universitario de Puerto Real, Cadiz, Spain, [2]Cardiologia, HOSPITAL UNIVERSITARIO DE PUERTO REAL, Puerto Real, Spain

Background and Aims : INTRODUCTION: COVID-19 has been a challenge for cardiac rehabilitation (CR) units in need of adaptation to the new mobility and capacity restrictions, which is the reason of the new modalities of the programs. OBJECTIVES: To describe the characteristics of the new semi-presential modality as well as the differences in baseline characteristics, compliance and results obtained between the different programs (classics in-person and outpatient), coinciding with the COVID-19 pandemic.

Methods: Retrospective study, of consecutive cases, in which the patients included in the semi-presential modality of the CR program of a regional hospital from July / 2020 to July / 2021 were analyzed.

Results: N=28. Average age:55.21years. 14.3%women HBP:35.7%, DM:35.7%, Dyslipidemia:37.6%, Smoking:78.6%. Type of program: Low risk:75%, moderate rest. Completed:71.4%(10.7% in progress).Program start: mean functional capacity(METS):8.52±2.04, mean BMI:28.8±5.4Kg/m2, abdominal perimeter: 104.2±9.9cms, LDLc:114.38±44 , 32mg/dL, HbA1c: 7.25±0.9%.After one year, both BMI (27.3±1.9Kg/m2), abdominal perimeter (102.5±4.4cms), LDLc (51.25 ± 15.37mg/dL) and HbA1c (7%) were reduced, improving functional capacity (9.75±0.5METS), without reaching statistical significance.Average delay time for the first stratification visit: 14.7±25.8 days and for the start of the program: 28.4±12.6 days.

Conclusions: We have included the semi-presential modality given the current restrictions due to the COVID-19 pandemic to improve the availability and accessibility of our CR program, achieving great acceptance in our sample(>20%), especially among younger patients, mainly from low risk with greater female representation, although it is still insufficient, with a similar compliance rate with respect to the classic modalities.The delay time for the start of the program has been shortened, compared to the face-to-face program.

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CARDIOVASCULAR RISK FACTORS AND CAROTID INTIMA MEDIA THICKNESS: MEDIATION AND INTERACTION BY GRIP STRENGTH

POSTER VIEWING SESSION

Christian Wilfried Mendo[1], Mark Robert Keezer[2], Marie-Pierre Sylvestre[2]
[1]Preventive Medicine, Centre de recherche du Centre Hospitalier de l'Université de Montréal (CrCHUM), Montréal, Canada, [2]Preventive Medicine, Centre de recherche du Centre Hospitalier de l'Université de Montréal (CrCHUM), montreal, Canada

Background and Aims : Reductions in muscle strength, generally assessed by grip strength, are associated with an increased risk for cardiovascular disease. The role of grip strength, however, in the associations between cardiovascular risk factors such as T2D and hypertension and vascular atherosclerosis remain unclear. The purpose of this study is use the four-way decomposition method to simultaneously investigate the mediation and interaction role of grip strength in the association between cardiovascular risk factors and carotid intima-media thickness (cIMT).

Methods: Using the 4-way decomposition method elaborated by Vanderweele, we investigated the role of grip strength, on the effect of cardiovascular risk factors (specifically T2D and hypertension) and the vascular atherosclerotic burden of individuals [measured using carotid intima media thickness (cIMT)]. We present analyses of CLSA, focusing on the 30,097 study participants who underwent serial physical evaluations at one of 11 data collection sites between 2011 and 2018.

Results: Our findings demonstrate that grip strength does not mediate associations between T2D and cIMT, nor between hypertension and cIMT [pure indirect effect (95% CI) ranging from 0.01(-0.03, 0.04) to 0.07(-0.03, 0.08)]. We found evidence of strong synergic interactions between grip strength and T2D as well as hypertension, in their association with cIMT (mediated interaction and interaction only effects ranging from 18.2% to 30.7%).

Conclusions: Grip strength does not mediate the associations between T2D/hypertension and cIMT, but there is evidence of a synergistic interaction between T2D/hypertension and grip strength, when studying their association with increasing cIMT.

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HIGH AND LOW LEVELS OF SERUM SIRTUIN6 IN PATIENTS WITH ACUTE ISCHEMIC STROKE

POSTER VIEWING SESSION

Luca Liberale[1], Markus Arnold[2], Stefano Ministrini[3], Yustina M. Puspitasari[4], Georgia Beer[4], Fabrizio Montecucco[5], Mira Katan[2], Giovanni G. Camici[3]
[1]Dipartimento Di Medicina Interna E Specialità Mediche, Università degli Studi di Genova, Genoa, Italy, [2]Klinik Neurologie, Zurich University Hospital, Zurich, Switzerland, [3]Center For Molecular Cardiology, University of Zurich, Zurigo, Switzerland, [4]Center For Molecular Cardiology, University of Zurich, Schlieren, Switzerland, [5]Department Of Internal Medicine And Centre Of Excellence For Biomedical Research, First Clinic of Internal, Genoa, Italy

Background and Aims : Sirtuin6 (SIRT6) is a ubiquitous isoform of the Sirtuins family, expressed in the cellular nucleus and regulating multiple senescence associated biological processes. SIRT6 knockdown is associated with larger cerebral infarct size, worse neurological outcome, and higher mortality in a murine model of acute brain ischemia.

Methods: We conducted an explorative analysis in a subgroup of subjects from previously published cohort (Copeptinin Osmoregulation and Stress Assessment – COSMOS) to test whether circulating levels of SIRT6 could be predictors of outcome in patients with acute ischemic stroke (AIS). The primary endpoint of the study was survival 90 days after the onset of symptoms. The secondary endpoint was the overall survival (OS). Serum levels of SIRT6 were measured through Enzyme-Linked Immunosorbent Assay (ELISA).

Results: Both lower and higher values of SIRT6 were significantly associated with the primary endpoint ($p=0.007$ for univariate logistic analysis). After correction for potential confounders (age, NIHSS, heart failure, atrial fibrillation, and C reactive protein), both lower and higher values of SIRT6 were significantly associated with both probability of death ($p=0.001$) and OS ($p<0.001$).

Conclusions: Both high and low levels of SIRT6 are associated with increased mortality after AIS. These results confirm the previous observations in animal models. Further studies are needed to test the potential value of SIRT6 as a predictive biomarker in patients with AIS.

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PHARMACOTHERAPY OF INHIBITION OF THE ATHEROSCLEROTIC PROCESS THROUGH THE EFFECT ON NEUROTRANSMITTERS

POSTER VIEWING SESSION

Tetiana Motsak, Viktor Lyzogub, Olena Kupchynska
Internal Medicine No 4, Bogomolets National Medical University, Kyiv, Ukraine

Background and Aims : The problem of generalized atherosclerosis(GAS), a simultaneous damage to the arteries of two or more vascular territories, requires clarification of the pathogenesis and treatment, in particular, the identification of factors and mechanisms underlying the generalization of the process. **The aim** is to determine the levels of serotonin(S) and histamine(H) in patients with coronary, cerebral, mesenteric and femoral atherosclerosis and their changes under the influence of cilostazol(C).

Methods: We examined 58 men with GAS (64.5±7.8 years) who had intermittent claudication syndrome, coronary and cerebral atherosclerosis. The control group (CG) consisted of 18 healthy men aged 61.2±4.7 years. Volumetric blood flow(VF), number of episodes of myocardial ischemia (EMI), painless walking distance(PWD), cognitive function, serum S and H levels (by ELISA) were assessed. Patients with GAS were examined before and after 4 weeks of taking additionally C (100 mg/day).

Results: In patients with GAS baseline levels of S and H exceeded ($p<0.001$) such persons CG, by 4.2 and 2.2 times. Respectively. After treatment, the levels of ultra-high values of S and H decreased ($p<0.05$) by 38.7 and 12.7%, respectively, increased ($p<0.01$) VF in the vessels, which was accompanied by an increase in PWD (by 41.2%; $p<0.001$), reducing the total number of EMI (by 23.4%; $p<0.05$), improving cognitive function due to memory and attention.

Conclusions: Excessively high serum serotonin and histamine levels are observed in patients with generalized atherosclerosis. Additional use of cilostazol (100 mg per day) leads to a significant reduction in their levels in the blood and improve the clinical picture of the disease.

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CAROTID INTIMA-MEDIA THICKNESS (CIMT) AS AN IMPORTANT ULTRASONIC DIAGNOSTIC MARKER OF TRANSIENT ISCHEMIC ATTACKS (TIA)

POSTER VIEWING SESSION

Dusan J. Petrovic
Radiology, Clinical centre of Serbia, Belgrade, Serbia

Background and Aims : The ultrasonic indicators of cerebral atheriosclerosis (TIA and stroke) are CIMT, the degree of lumen stenosis, and the presence of ulceration on the free surface of the carotid artery plaque.The aim of this study was to establish the correlation between CIMT and TIA and between the carotid plaques quantitative and qualitative characteristics and the occurence and type of TIA.

Methods: One hundred and twenty patients with TIA (mean age ± SD, 51 ± 13) were tested by duplex ultrasonography and compared to the control group (n=25 patients) compatible in age and gender (mean age ± SD, 48 ± 8).The examined ultrasonic parameters were: CIMT, the presence and size of the plaque, and the presence of ulceration on the free surface of the plaque. The group of patients with TIA was divided into subgroups based on etiopathological mechanism (emboligenic, hemodynamic and coagulopathy).

Results: Statistically, CIMT was significantly higher ($p<0.05$) among the patients with haemodynamic and emboligenic TIA in comparison with the control group. The frequency of the plaque larger than 70% was statistically significantly higher ($p<0.01$) among the patients with emboligenic and haemodynamic TIA in comparison with the control group. Regarding the frequency of ulceration, the difference between the group of patients with emboligenic TIA and the control group was highly statistically significant ($p<0.01$).

Conclusions: CIMT, the size of the plaque (larger than 70%) correlate with the occurrence of haemodynamic and emboligenic TIA. In addition to that, the presence of ulceration on the free surface of the plaque correlates with the occurrence of emboligenic TIA.

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DIFFERENTIAL PROTEIN EXPRESSION STUDIES IN HYPERCHOLESTEROLEMIC RABBITS USING AQUEOUS TERMINALIA ARJUNA EXTRACT

POSTER VIEWING SESSION

Riyaz Ahmad Rather
Biotechnology, Wachemo University, Hossana, Ethiopia

Background and Aims : Atherosclerosis is the major cause of mortality worldwide. Much attention has been focused on the use of herbal products to cure this disease. Hence the present study was designed to evaluate the cardio-protective effect of aqueous *Terminalia arjuna* extract (TAE) on different proteins in hypercholesterolemic rabbits using proteomic approach.

Methods: Five groups of rabbits were employed and fed normal chow-fed diet (Gp 1), high-fat diet (Gp 2), normal chow-fed diet plus TAE (Gp 3), high fat diet plus TAE (Gp 4) and high-fat diet plus atorvastatin (Gp 5) respectively for 6 months. Aortic lesions were excised and protein lysate was separated by Two-dimensional gel electrophoresis. Differentially expressed proteins were identified by MALDI-TOF in Linear Reflectron Mass Spectrometer.

Results: 850 spots could be detected among which 79 spots ($p<0.05$) matched among all 5 groups and 58 individual proteins were identified from 79 spots. Proteins like Interstitial collagenase, GRB2-related adapter protein 2, Interleukin 2, Myocyte enhancer-factor 2A, Protein S100-A9 and HSP60 with $\geq$10 fold expression were found to be differentially and significantly upregulated in Gp 2. TAE and atorvastatin treatment reduced the expression of these proteins to almost basal level ($\leq$1 fold change). TAE also significantly ($p<0.05$) downregulated expression of 5-lipoxygenase-activating protein, 72 kDa type IV collagenase, HSP90-alpha, and Vimentin proteins. Compared to atorvastatin, TAE was significantly more effective in downregulating all these proteins implicated in atherosclerotic disease.

Conclusions: This study reveals that *Terminalia arjuna* is a potent downregulator of various atherosclerosis-related proteins, hence should be explored in future clinical trials.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CARDIOVASCULAR RISK ASSESSMENT BY PHYSICIANS AND LIPID-LOWERING THERAPY PRESCRIBING IN HIGH- AND VERY HIGH-RISK PATIENTS: RESULTS FROM THE MULTINATIONAL OBSERVATIONAL SANTORINI STUDY

POSTER VIEWING SESSION

Kausik K. Ray[1], Inaam Haq[2], Aikaterini Bilitou[3], Marius C. Manu[2], Annie Burden[4], Alberico L. Catapano[5]
[1]Imperial Centre For Cardiovascular Disease Prevention, Ictu-global, Imperial College London, London, United Kingdom, [2]Medical Affairs, Daiichi Sankyo Europe, Munich, Germany, [3]Health Economics And Outcomes Research, Daiichi Sankyo Europe, Munich, Germany, [4]Biostatistics & Data Management, Daiichi Sankyo Europe, Munich, Germany, [5]Department Of Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy

Background and Aims : Inadequate lipid-lowering therapy (LLT) prescribing may result from an inaccurate assessment of cardiovascular (CV) risk. We investigated physician-assessed versus objectively-assessed CV risk in patients whose risk was claimed to be classified following the 2019 ESC/EAS guidelines and the use of LLT.

Methods: SANTORINI is a European multinational observational study (NCT04271280) including adult patients with high and very high CV risk as assessed by the physician.

Results: At 31st July 2021, data on 9044 patients were available. Overall, 29.2% of patients were classified by the physician as high-risk and 70.8% as very high-risk, with the 2019 ESC/EAS guidelines most commonly cited as the basis for risk assessment (52.0%). However, central re-estimation calculated 6.5% and 91.0% to be high- and very high-risk patients (N=4706), respectively (Table 1). Notably, 41.5% of high-risk patients as classified by the physician had evidence of atherosclerotic cardiovascular disease (ASCVD). Overall, mean (SD) LDL-C was 2.41 (1.211) and 20.1% of patients attained risk-based LDL-C goals. Despite LDL-C levels being above the recommended values, 21.8% of patients had no

documented LLT, 54.2% received monotherapy and 24.0% combination LLT (Table

Table 1. Baseline characteristics and cardiovascular risk factors by risk classification as reported by the physician, and recalculated using ESC/EAS criteria

Characteristic	Overall (N=9044)	Physician-reported risk classification	
		High risk (N=2637 [29.2%])	Very high risk (N=6401 [70.8%])
Female, n (%)	2481 (27.4)	998 (37.8)	1481 (23.1)
Age, years, mean (SD)	65.3 (10.90)	63.5 (11.72)	66.0 (10.45)
ASCVD, n (%)	6954 (76.9)	1094 (41.5)	5856 (91.5)
Diabetes, n (%)	3038 (33.6)	882 (33.5)	2154 (33.6)
Diabetes with target organ damage	610 (6.7)	125 (4.7)	485 (7.6)
Familial hypercholesterolaemia, n (%)	893 (9.9)	413 (15.7)	480 (7.5)
LDL-C, mean (SD), mmol/L	2.41 (1.211)	2.68 (1.290)	2.30 (1.159)
LDL-C at goal, n (%)	1821 (20.1)	632 (24.0)	1189 (18.6)
Basis for risk classification, n (%)			
Missing	6 (0.1)	0	0
Clinical experience	3089 (34.2)	1154 (43.8)	1935 (30.2)
Institutional practice and/or considerations	111 (1.2)	34 (1.3)	77 (1.2)
Institutional guidelines	109 (1.2)	57 (2.2)	52 (0.8)
Regional guidelines	102 (1.1)	73 (2.8)	29 (0.5)
National guidelines	844 (9.3)	361 (13.7)	483 (7.6)
ESC/EAS guidelines	4706 (52.0)	916 (34.7)	3790 (59.2)
Other	77 (0.9)	42 (1.6)	35 (0.6)
Recalculated risk classification by ESC/EAS criteria,[a] n/N (%)			
Missing risk	114/4706 (2.4)	95/916 (10.4)	19/3790 (0.5)
Very high risk	4284/4706 (91.0)	553/916 (60.4)	3731/3790 (98.4)
High risk	308/4706 (6.5)	268/916 (29.3)	40/3790 (1.1)

[a]The risk was recalculated only for those patients the physician classified based on the ESC/EAS guidelines. Missing/not reported risk status, n=6. ASCVD, atherosclerotic cardiovascular disease; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation

Table 2. Use of LTT by risk classification as reported by the physician

LLT	Overall (N=9044)	High risk (N=2637)	Very high risk (N=6401)
No LLT	1972 (21.8)	620 (23.5)	1348 (21.1)
Monotherapy	4902 (54.2)	1538 (58.3)	3362 (52.5)
Statin alone	4537 (50.2)	1436 (54.5)	3099 (48.4)
Ezetimibe alone	158 (1.8)	50 (1.9)	108 (1.7)
PCSK9i alone	150 (1.7)	32 (1.2)	118 (1.8)
Any other oral LLT alone	57 (0.6)	20 (0.8)	37 (0.6)
Combination therapy	2169 (24.0)	478 (18.1)	1691 (26.4)
Statin + Ezetimibe	1446 (16.0)	306 (11.6)	1140 (17.8)
PCSK9i + other oral LLT	411 (4.5)	94 (3.6)	317 (4.9)
Any other oral combination therapy	312 (3.4)	78 (3.0)	234 (3.6)

Missing patients, n=6. LLT, lipid-lowering therapy; PCSK9i, proprotein convertase subtilisin/kexin 9 inhibitor

2).

Conclusions: The SANTORINI study showed that CV risk of patients is often underestimated in clinical practice, which in addition to the underutilisation of combination LLT may result in a substantial proportion of patients remaining at high residual risk of ASCVD events.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EGYPTIAN ATHEROSCLEROSIS AND VASCULAR BIOLOGY ASSOCIATION CONSENSUS ON THE USE OF SODIUM GLUCOSE COTRANSPORTER-2 INHIBITORS IN HEART FAILURE WITH REDUCED EJECTION FRACTION

POSTER VIEWING SESSION

Ashraf Reda[1], Ahmed Shawky[2], Atef Elbahry[3], Ahmed Bendary[4], Ahmed Elkersh[1], Elsayed Farag[5], Mohamed Ashraf[6]
[1]Cardiology, Menoufia University, Shebin Elkom, Egypt, [2]Cardiology, Ain Shams University, Cairo, Egypt, [3]Cardiology, Port Fouad cardiac center, Pot Fouad, Egypt, [4]Cardiology, Benha University, Benha, Egypt, [5]Cardiology, Zagazing University, Zagazig, Egypt, [6]Cardiology, National Heart Institute, Giza, Egypt

Background and Aims : Heart failure (HF) is a common cause of cardiovascular mortality and morbidity. Despite advances in treatment, the prognosis remains poor. Sodium-glucose co-transporter 2 (SGLT-2) inhibitors decrease HF events by 27–39% in high-risk patients with type 2 diabetes mellitus (T2DM)

Methods: DAPA-HF and EMPEROR-Reduced studies randomized patients with HF with reduced ejection fraction (HFrEF) with or without diabetes mellitus to receive guideline-directed medical therapy versus guideline-directed medical therapy plus an SGLT-2 inhibitor. Both studies showed the benefits of SGLT-2 inhibitors. In addition, SGLT-2 inhibitors have shown improvement according to the EMPEROR-Preserved study of HF with preserved ejection fraction (HFpEF). Therefore, a panel of cardiology experts from the Egyptian Atherosclerosis and Vascular Biology Association (EAVA) revised the literature for SGLT-2 inhibitors in HF, along with the recommended indications and contraindications, and this article presents their consensus on the topic

Results: The panel recommended early use of dapagliflozin 10 mg or empagliflozin 10 mg in patients with symptomatic chronic HFrEF, whether diabetic or non-diabetic, to ameliorate HF hospitalization rate, mortality, symptoms, and decline in renal function.

Conclusions: The panel concluded that SGLT-2 inhibitors have significantly benefited patients with chronic HFrEF, as indicated through the DAPA-HF and EMPEROR-Reduced trials

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

INCREASED RISK OF CARDIOVASCULAR DISEASE AND HIGH RISK PROFILES COMPATIBLE WITH METABOLIC SYNDROME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A CROSS-SECTIONAL ANALYSIS OF MATCHED COHORTS

POSTER VIEWING SESSION

Jasmijn A.M. Sleutjes[1], Jeanine E. Roeters Van Lennep[2], Maryam Kavousi[3], Elif Aribas[3], C. J. Van Der Woude[1], Annemarie C. De Vries[1]
[1]Gastroenterology And Hepatology, Erasmus MC, Rotterdam, Netherlands, [2]Internal Medicine, Erasmus MC, Rotterdam, Netherlands, [3]Epidemiology Of Cardiometabolic Diseases, Erasmus MC, Rotterdam, Netherlands

Background and Aims : Patients with inflammatory bowel disease (IBD) have an increased risk of cardiovascular disease (CVD). We assessed CVD risk profiles of IBD patients compared to the general population.

Methods: IBD patients aged ≥45 years were included at the Gastroenterology outpatient clinic. CVD risk profiles were assessed by anthropometrics (blood pressure, height, weight, waist, hip circumference), serum analyses (nonfasting glucose and lipids) and self-administered questionnaires (history of CVD events, traditional risk factors, medication use). 1-4 controls were matched to each IBD case by sex and age (5-year scope). Stratification was applied to assess differences between sex and IBD diagnosis.

Results: 235 IBD patients were included (44% male; median age 59 years (IQR 51-66)) and matched to 829 controls. IBD patients were more frequently diagnosed with CVD (OR 2.01, 95%CI 1.23-3.27) and showed lower odds of overweight (OR 0.48, 95%CI 0.35-0.66) and hypercholesterolemia (OR 0.45, 95%CI 0.31-0.65). Markers of metabolic syndrome were increase in IBD: hypertension (OR 1.67, 95%CI 1.19-2.32), waist circumference and triglyceride level. (**Table 1**) Male patients had higher waist circumference, less favorable lipid profiles and more frequently hypertension (OR 1.72, 95%CI 0.99-2.94). Patients with ulcerative colitis were more frequently smokers (OR 4.34, 95%CI 1.27-16.66) and showed higher odds of hypercholesterolemia (OR 1.85, 95%CI 1.06-3.33) compared Crohn's

disease.

Table 1. Differences in CVD risk profile between IBD patients and age-sex matched controls

		IBD patients (n=217)	Controls (n=829)	P
History of CVD	OR (95%CI)	2.01 (1.23 – 3.27)	1	.005*
Heart failure		2.02 (1.02 – 4.01)	1	.044*
Coronary heart disease[A]		2.01 (1.17 – 3.13)	1	.011*
Stroke		1.08 (0.49 – 2.38)	1	.845
CVD drug use				
Lipid lowering drugs		0.72 (0.49 – 1.07)	1	
Antihypertensive drugs		0.89 (0.62 – 1.27)	1	.511
Glucose regulating drugs		0.94 (0.53 – 1.66)	1	.830
Anticoagulants		1.22 (0.82 – 1.88)	1	.313
Traditional risk factors	OR (95%CI)			
Active smokers		0.66 (0.43 – 1.01)	1	.056
Overweight[B]		0.48 (0.35 – 0.66)	1	<.001*
Hypertension[C]		1.67 (1.19 – 2.32)	1	.003*
Hypercholesterolemia[D]		0.45 (0.31 – 0.65)	1	<.001*
Diabetes mellitus[E]		0.66 (0.40 – 1.10)	1	.109
Metabolic syndrome[F]		1.36 (1.00 – 1.90)	1	.049*
Anthropometrics	Mean (SE)			
SBP, mmHg		148 (18)	142 (17)	<.001*
DBP, mmHg		79 (10)	75 (11)	.001*
BMI, kg/m2		25.9 (3.8)	27.4 (4.8)	<.001*
Waist circ, cm		92 (10)	88 (8)	.006*
WHR		0.91 (0.1)	0.86 (0.1)	<.001*
Serum analysis	Mean (SE)			
Glucose, mg/dL		5.5 (1.1)	5.1 (1.1)	.092
Total cholesterol, mmol/L		4.3 (1.1)	5.4 (1.1)	<.001*
HDL-c, mmol/L		1.2 (0.5)	1.2 (0.4)	.763
LDL-c, mmol/L[G]		2.6 (1.1)	3.8 (1.0)	<.001*
Triglycerides, mmol/L		2.7 (0.8)	2.1 (0.8)	<.001*
10-year CVD risk, %[H]	Mean (SE)	1.0 (0.2)	1.2 (0.2)	.893

**Below significance level 0.05. Generalized linear mixed effect models were applied to assess differences between cohorts, assuming a random intercept for matched pairs, and a fixed effect of IBD diagnosis, age and sex to correct for residual confounding. Reported results apply to a women aged 45 years.*

Abbreviations: CVD: cardiovascular disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; WHR: waist to hip ratio.

A: myocardial infarction, PTCA, CABG; B: BMI >25 kg/m²; C: SBP≥140 mmHg or DBP ≥90 mmHg, diagnosis of hypertension or use of antihypertensive drugs indicated for diagnosis; D: total cholesterol ≥6.2 mmol/L, self-reported diagnosis of hypercholesterolemia or use of lipid lowering drugs; E: fasting glucose >6.9 mg/dL, nonfasting glucose >11.0 mg/dL, self-reported diagnosis of diabetes mellitus or use of glucose regulating drugs; F: according to ATP III criteria; G: calculated by the Friedewald formula; H: using Systematic COronary Risk Evaluation for low-risk countries (i.e. the Netherlands)

Conclusions: IBD patients report higher CVD burden. Risk profiles in IBD patients arecharacterized by components of the metabolic syndrome: hypertension, truncal obesity and hypertriglyceridemia, particularly among males. Prevalence of other risk factors was comparable or lower in IBD. Exploration of targeted preventive management strategies is required.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PATIENT-CENTERED CARDIAC REHABILITATION BY AI-POWERED LIFESTYLE INTERVENTION – THE TIMELY APPROACH

POSTER VIEWING SESSION

Boris Schmitz[1,2], Dimitris Gatsios[3], Carlos Peña-Gil[4], Jose R Gonzalez Juanatey[5], David Cantarero Prieto[6], Vassilis Tsakanikas[7], Hubert Scharnagl[8], Mirela Habibovic[9], Martin Schmidt[10], Marcus E. Kleber[11,12], Gert-Jan De Bruijn[13], Hagen Malberg[10], Frank Mooren[1,2], Jos Widdershoven[14], Winfried Maerz[8,11,12], Dimitris Fotiadis[7], Willem J. Kop[9], Jos Bosch[9]
[1]Lehrstuhl Für Rehabilitationswissenschaften, Klinik Königsfeld der Deutschen Rentenversicherung Westfalen, Ennepetal, Germany, [2]Department Of Rehabilitation Sciences, University of Witten/Herdecke, Ennepetal, Germany, [3]Department Of Material Science And Engineering, University of Ioannina, Ioannina, Greece, Ioannina, Greece, [4]Department Of Cardiology, Hospital Clínico Universitario De Santiago, Instituto de Investigación Sanitaria, CIBER CV, Madrid, Spain., Madrid, Spain, [5]Service Of Cardiology, Spanish Network-center For Cardiovascular Biomedical Research (cibercv), Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, Santiago de Compostela, Spain, [6]Department Of Economics, University of Cantabria, Santander, Spain, Santander, Spain, [7]Foundation Of Research And Technology, Institute of Molecular Biology and Biotechnology, Ioannina, Ioannina, Greece, [8]Clinical Institute Of Medical And Chemical Laboratory Diagnostics, Medical University of Graz, Graz, Austria, [9]Department Of Medical And Clinical Psychology, Center of Research on Psychology in Somatic diseases (CoRPS), Tilburg, the Betherlands, Tilburg, Netherlands, [10]Institute Of Biomedical Engineering, TU Dresden, Dresden, Germany, [11]Vth Department Of Medicine, Medical Faculty Mannheim, Heidelberg University, Heidelberg, Germany, [12]Mvz Humangenetik Mannheim, SYNLAB, Mannheim, Germany, [13]Amsterdam School Of Communication Research, University of Amsterdam, Amsterdam, Netherlands, [14]Department Of Cardiology, Elisabeth-TweeSteden Hospital, Tilburg, Netherlands

Background and Aims : Background: eHealth innovations allow the integration of artificial intelligence (AI) and IoT-devices to optimize personalized care and provide self-care assistance during cardiac rehabilitation (CR). TIMELY is the first AI-driven eHealth approach promoting targeted personalized lifestyle interventions. TIMELY includes continuous risk prediction, decision support tools and assists lifestyle changes based on psychosocial assessment and behavioral change models.

Methods: Methods: TIMELY uses a Living Lab approach for iterative and participatory design. Routes for patient information and communication will be based on an app complemented by adaptive chat bots for the assessment of psychosocial CR-relevant components. Self-applicable ECG devices, activity trackers and hemodynamic monitors will inform about therapy progress and risks. The TIMELY AI will allow continuous risk prediction and AI behavioral change agents will help to optimized program adherence and support long-term lifestyle changes.

Results: Results: Living Lab interviews revealed patients' requirements and good acceptance of the proposed solution. Patients reported high acceptance of the eHealth solution in general and of components informing on current diagnosis, clinical/ laboratory parameters, future risks and support for physical activity (motivational messages, progress documentation, training updates). Assistance with smoking cessation and stress management was considered important, dietary support was not prioritized. Communication by adaptive chat bots was generally accepted, even if personal feedback was highly appreciated.

Conclusions: Conclusions: TIMELY will be the first AI-powered multimodal intervention system supporting CAD patients to achieve long-lasting lifestyle changes. TIMELY may be applied in different European health care settings to coordinate a multidisciplinary care team and improved quality of life and health
outcomes.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

A CLINICAL SCORE INCLUDING PERIPHERAL ATHEROSCLEROSIS FOR PREDICTING UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH STABLE CAD

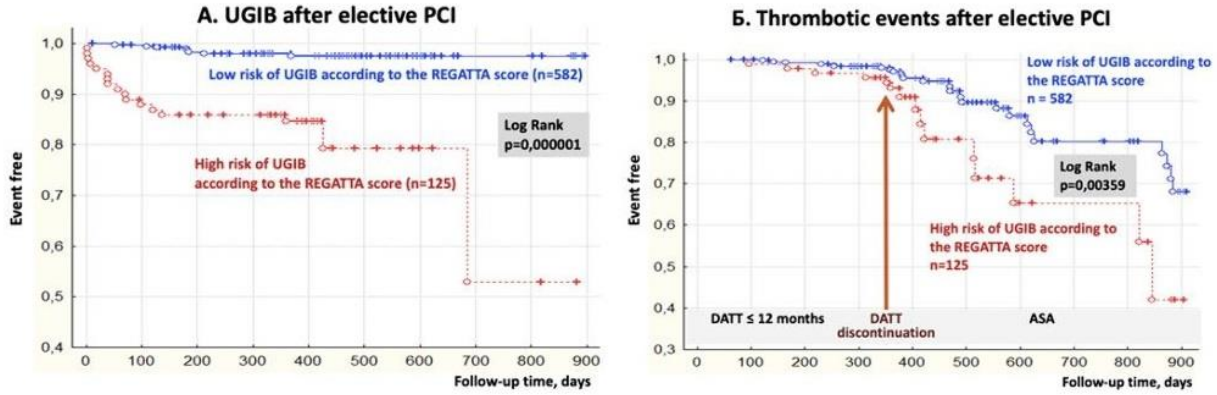
POSTER VIEWING SESSION

Olga Shahmatova[1], Andrey Komarov[2], Valeria Korobkova[2], Elena Yarovaya[3], Alla Shuleshova[4], Elizaveta Panchenko[2]
[1]Clinical Problems Of Atherothrombosis, NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation, [2]Department Of Clinical Problems Of Atherothrombosis, NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation, [3]Department Of Research Organization, NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation, [4]Department Of Endoscopy, NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation

Background and Aims : Identifying CAD patients at high risk of upper gastrointestinal bleeding (UGIB) carries important therapeutic implications. Existing approaches (like algorithm proposed by the European Society of Cardiology (ESC) in 2015) mostly assess local risk factors and ignore comorbidity.

Methods: The UGIB risk scale was developed based on the prospective REGistry of long-term AnTithrombotic TherApy-1 REGATTA-1 (ClinicalTrials.gov Identifier: NCT04347200). The median follow-up was 2,5 [1,1-14,7] years.

Results: Of the 934 patients (median age 61 [53–68] years, 78.6% men) included, 51 patients developed overt UGIB (1.9 per 100 patients per year). Age (≥ 80), abdominal aortic aneurysm and/or peripheral atherosclerosis, heart failure, prior gastric/duodenal erosion, prior gastric/duodenal ulcer, prior gastrointestinal bleeding, NSAIDs/corticosteroids and anticoagulants are independent risk factors of UGIB according to multivariate logistic regression. A risk scoring system REGATTA was constructed using these clinical variables that successfully stratifies patients into 2 risk groups, with good model discrimination (AUC=0.88). Predictive value of REGATTA score was higher than of ESC 2015 score (AUC=0.79), p=0.04. In patients after elective PCI (n=640), the REGATTA score predicts UGIB better than the PRESICE-DAPT score, respective AUCs are 0,87 and 0,70 (p=0,04). Finally, patients with a high UGIB risk according to REGATTA score are also characterized by a high risk of thrombotic events (figure 1) possibly because new scale considers atherosclerosis burden. Picture 1. Survival without upper gastrointestinal bleeding (A) and thrombotic events (B) according to the REGATTA score (Kaplan-Meier curves).



Conclusions: REGATTA score represents simple, non-invasive and highly accurate tool for detecting high risk of UGIB in patients with stable CAD.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY PREDICT ONE-YEAR MORTALITY IN PATIENTS WITH TYPE 2 DIABETES AND PARTIAL FOOT AMPUTATION

POSTER VIEWING SESSION

Evgeniya V. Shalaeva[1,2], Arjola Bano[3], Bakhtiyor Janabaev[4], Markus Laimer[5], Hugo Saner[3]
[1]Cardiology, Tashkent Medical Academy, Uzbekistan, Uzbekistan, [2]Graduate School For Health Sciences, University of Bern, Bern, Switzerland, [3]Institute For Social And Preventive Medicine, University of Bern, Bern, Switzerland, [4]Republican Center Of Purulent Surgery And Complications Of Diabetes, Tashkent Medical Academy, Tashkent, Uzbekistan, [5]Clinic For Diabetology, Endocrinology, Nutrition And Metabolism, University Hospital Bern, Bern, Switzerland

Background and Aims : Type 2 diabetes (T2D) increased the risk for the development of macrovascular complications such as coronary arteries disease (CAD). Partial foot amputations (PFA), generally are not considered high-risk surgeries, and the prevalence of CAD among this category of patients remains unclear. The aim of this study was to evaluate the predictive value of coronary computed tomographic angiography (CCTA) for long-term outcomes in T2D patients after partial foot amputation.

Methods: This is a prospective, single-center, observational cohort study including 199 consecutive patients with T2D and PAD (mean age 60.9±9.1 years; male 64.1%) undergoing PFA with at least 1-year follow-up. CCTA assessment was conducted postoperatively.

Results: 1-year all-cause mortality was 17.6% (n=35), 1-year incidence of major adverse cardiovascular events (MACE) was 30.2% (n=60), After adjusting for age, sex, severity of T2D, cardiovascular diseases, common comorbidities, the higher level of coronary obstruction was associated with increased risk of MACE and 1-year mortality. Compared to no-CAD, having 1-vessel obstructive CAD increased incidence of MACE 5.74-fold (95%CI [1.89, 17.38], p = 0.002), 2-vessels obstructive CAD 7.92-fold (95%CI [2.29, 27.26] p=0.001), and 3-vessels 32.85-fold (95%CI [9.77, 110.4], p<0.001). Compared to no-CAD, having 1-vessel obstructive CAD increased mortality (HR=8.13, 95%CI [0.87 – 75.88], p=0.066), 2-vessels (HR=10.94, 95%CI[1.03–115.8], p=0.047), and 3-vessels (HR=45.73, 95%CI [4.6 – 454.7], p=0.001).

Conclusions: Obstructive coronary artery disease detected on CCTA was associated with 1-year MACE and all-cause mortality in type 2 patients undergoing partial foot amputations, and may be considered for perioperative risk assessment if stress test is not feasible and more sophisticated technical equipment is not available.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

EFFECT OF COLD WATER HARDENING ON THE LIPID PROFILE, SUBCLINICAL ATHEROSCLEROSIS, FAT DISTRIBUTION, INFLAMMATION AND OTHER SELECTED PARAMETERS OF VOLUNTEERS

POSTER VIEWING SESSION

Štefan Tóth[1], Dominik Pella[2], Zdenka Hertelyová[3], Dávid Kaško[4]
[1]Slovacrin, Faculty of medicine, UPJS, Košice, Slovak Republic, [2]1nd Department Of Cardiology, East Slovak Institute Of Cardiovascular Diseases, Faculty of medicine, UPJS, Košice, Slovak Republic, [3]Department Of Experimental Medicine, Faculty of medicine, UPJS, Kosice, Slovak Republic, [4]Institute Of Physical Education And Sport, Facutly of medicine, UPJŠ, Košice, Slovak Republic

Background and Aims : Short time cold water hardening (CWH) is associated with significant acute cardiovascular, metabolic and endocrinological responses. Many mostly observational studies have shown the possitive effect of one-time CWH in sport medicine and rehabilitation. There is however no available study following the long-term effect of repeated CWH on atherogenesis, lipid profile and lipid particles changes, inflammation and fat distribution. This study was aimed to explore the suggested possivite effects.

Methods: 40 healthy patients, without manifested CV diseases and significant CV risk factors, lipid-lowering therapy were exposed to standardized, outdoor CWH procedures 3 times per week,7-10 min for 6months. Volunteers with followed weight or muscle mass changes over 5% were excluded. Equivalent sham control (N=30) was included, without CWH. In the beginning and in the end of the study blood collection and clinical examinations were made for the quantification of lipid profile, liporint, inflammation(hsCRP), LPa,PCSK9,vascular profile(cIMT,echo-tracking), and abdominal ultrasound for the quantification of subcutaneus vs. visceral fat, and ectopic fat deposits. Liver steatosis quantification was based on calculation of hepatorenal index (HRI).

Results: 33 volunteers have successfully completed the given protocol vs. all in the control arm. Significant decrease of cIMT (p=0.0001); AI(p=0.0002); Beta(p=0.0001) and PWV(p=0.0001) was detected CWH. In comparison with the entry values, significant decrease of hsCRP(p=0.01) and PCSK9 (p=0.01) was observed between the entry and end values,resp. control group. Significant decrease of atherogenic particles were detected in lipoprint.Liver fat accumulation decreased by an average of11% in comparison with the entry values (HRIp<0.001).

Conclusions: We suggest possible beneficial effect of repeated-CWH on atherogenesis progression,liver fat accumulation, lipid and non-lipid parameters and inflammatory profile.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE TRIGLYCERIDE/GLUCOSE INDEX IS ASSOCIATED WITH MORE SEVERE ACUTE ISCHEMIC STROKE

POSTER VIEWING SESSION

Christiana Gogou, Anastasia Kontana, Maria Kyziroglou, Maria Kiosi, Danai-Thomais Kostourou, Pavlos Mentizis, Anastasia Gounta, Ioanna Minopoulou, Christina Kourtidou, Athanasios Filippidis, Georgios Chatzopoulos, Konstantinos Tziomalos
1st Propedeutic Department Of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece

Background and Aims : The triglyceride/glucose index (TyG) is a marker of insulin resistance and is associated with increased cardiovascular risk. We aimed to evaluate whether TyG also predicts the severity of acute ischemic stroke.

Methods: We prospectively studied 1,107 consecutive patients who were admitted for acute ischemic stroke (42.1% males, age 79.8±7.2 years). Stroke severity was evaluated at admission with the National Institutes of Health Stroke Scale (NIHSS) and severe stroke was defined as NIHSS≥21. The TyG was measured at the second day after admission in the fasting state.

Results: The TyG correlated with the NIHSS ($r = -0.237$, $p<0.001$) and was lower in patients with severe stroke than in those with non-severe stroke (0.85±0.51 and 1.12±0.54, respectively; $p<0.001$). In binary logistic regression analysis, independent predictors of severe stroke were age (relative risk (RR) 1.079, 95% confidence interval (CI) 1.042-1.117, $p<0.001$), female gender (RR 1.841, 95% CI 1.138-2.980, $p<0.05$), atrial fibrillation (RR 1.678, 95% CI 1.076-2.618, $p<0.05$), diastolic blood pressure at admission (RR 1.020, 95% CI 1.005-1.035, $p<0.01$) and the TyG (RR 0.229, 95% CI 0.124-0.422, $p<0.001$).

Conclusions: The TyG is independently associated with more severe acute ischemic stroke.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE TRIGLYCERIDE/GLUCOSE INDEX PREDICTS IN-HOSPITAL MORTALITY IN PATIENTS ADMITTED WITH ACUTE ISCHEMIC STROKE

POSTER VIEWING SESSION

Anastasios Papadopoulos, Marios Tzavelas, Sarantis Satsoglou, Stavroula Veneti, Eleftheria Ztriva, Alexandra Tsankof, Evripidis Valanikas, Erofili Papathanasiou, Adonis Protopapas, Georgios Polychronopoulos, Georgios Neokosmidis, Konstantinos Tziomalos
1st Propedeutic Department Of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece

Background and Aims : We aimed to evaluate whether the triglyceride/glucose index (TyG), a marker of insulin resistance, is associated with the outcome of acute ischemic stroke.

Methods: We prospectively studied 1,107 consecutive patients who were admitted for acute ischemic stroke (42.1% males, age 79.8±7.2 years). Stroke outcome was evaluated with dependency at discharge (modified Rankin scale (mRS) at discharge 2-5) and with in-hospital mortality. Stroke severity was evaluated at admission with the National Institutes of Health Stroke Scale (NIHSS). The TyG was measured at the second day after admission in the fasting state.

Results: The TyG correlated with the mRS at discharge ($r = -0.227$, $p<0.001$) and was lower in patients who were dependent at discharge than in those who were independent (1.08±0.54 and 1.21±0.52, respectively; $p<0.001$). Independent predictors of dependency were age (relative risk (RR) 1.075, 95% confidence interval (CI) 1.043-1.107, $p<0.001$), history of ischemic stroke (RR 2.201, 95% CI 1.482-3.270, $p<0.001$), family history of cardiovascular disease (RR 1.978, 95% CI 1.166-3.358, $p<0.05$) and NIHSS at admission (RR 1.421, 95% CI 1.334-1.514, $p<0.001$). The TyG was lower in patients who died during hospitalization than in those who were discharged (0.76±0.39 and 1.13±0.55, respectively; $p<0.001$). Independent predictors of in-hospital mortality were atrial fibrillation (RR 2.015, 95% CI 1.083-3.747, $p<0.05$), diastolic blood pressure (RR 1.046, 95% CI 1.024-1.068, $p<0.001$) and NIHSS at admission (RR 1.188, 95% CI 1.148-1.231, $p<0.001$), and TyG (RR 0.372, 95% CI 0.181-0.766, $p<0.01$).

Conclusions: The TyG is an easily measured independent predictor of in-hospital mortality in acute ischemic stroke.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE PROTECTIVE EFFECTS AND MECHANISIM OF ROSUVASTATIN CALCIUM INTERVENTION ON MYOCARDIAL INJURY IN HYPERURICEMIA RAT MODEL

POSTER VIEWING SESSION

Dilidaer Xilifu
Cardiology Unit, The first affiliated hospital of Xinjiang medical university, Urumqi, China

Background and Aims : Back ground and aims: 1) The hyperuricemia rat model induced by yeast extract （YEP）combined with oxonic acid potassium salt (OA), Through rosuvastatin intervene in hyperuricemia rats, we could analyze and evaluate the protective mechanism of rosuvastatin on myocardial cell injury in hyperuricemic rats.

Methods: 1) YEP combined with different doses OA, 60 SD rats were randomly grouped as control group, YEP and OA given for four weeks. UA,BUN,Cr were detected and the changes of cardiac histomorphology and ultrastructure were identified by histopathological method. The effects of the drug on CK,CK-MB,TNI,VCAM-1,1CAMP-1levels, the contents of ATP, ADP, AMP were detedcted.

Results: 1） a hyperuricemia rat model was established which showen an increase of serum levels of UA, CK, CK-MB and TNI while HE staining and ultrastructural observation showed the pathological changes of myocardial cells that were significantly severe thancontrol group. 2）The expression levels of Bax 、p53 and caspcase protein in hyperuricemia group were significantly higher than control group.The high dose of rosuvastatin (10mg / kg. D) was better than allopurinol group. The contents of ATP, ADP and AMP in cardiomyocytes of each treatment group were significantly higher than those of the model group.

Conclusions: 1) Our results suggested that rosuvastatin had a remarkable curative effect on myocardial cell injury and the improvement of myocardial cell pathological changes caused by hyperuricemia; 2) the results showed that rosuvastatin calcium had obvious curative effect on myocardial cell apoptosis and the protein expression, which may be an important mechanism of the pharmacological response of the drug.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-12 Prevention and treatment of cardiovasculardisease; miscellaneous*

STENOTIC AORTIC VALVES HAVE HIGH METAL AND LACK SELENIUM: A NEW TOXIC INFLAMMATION HYPOTHESIS ?

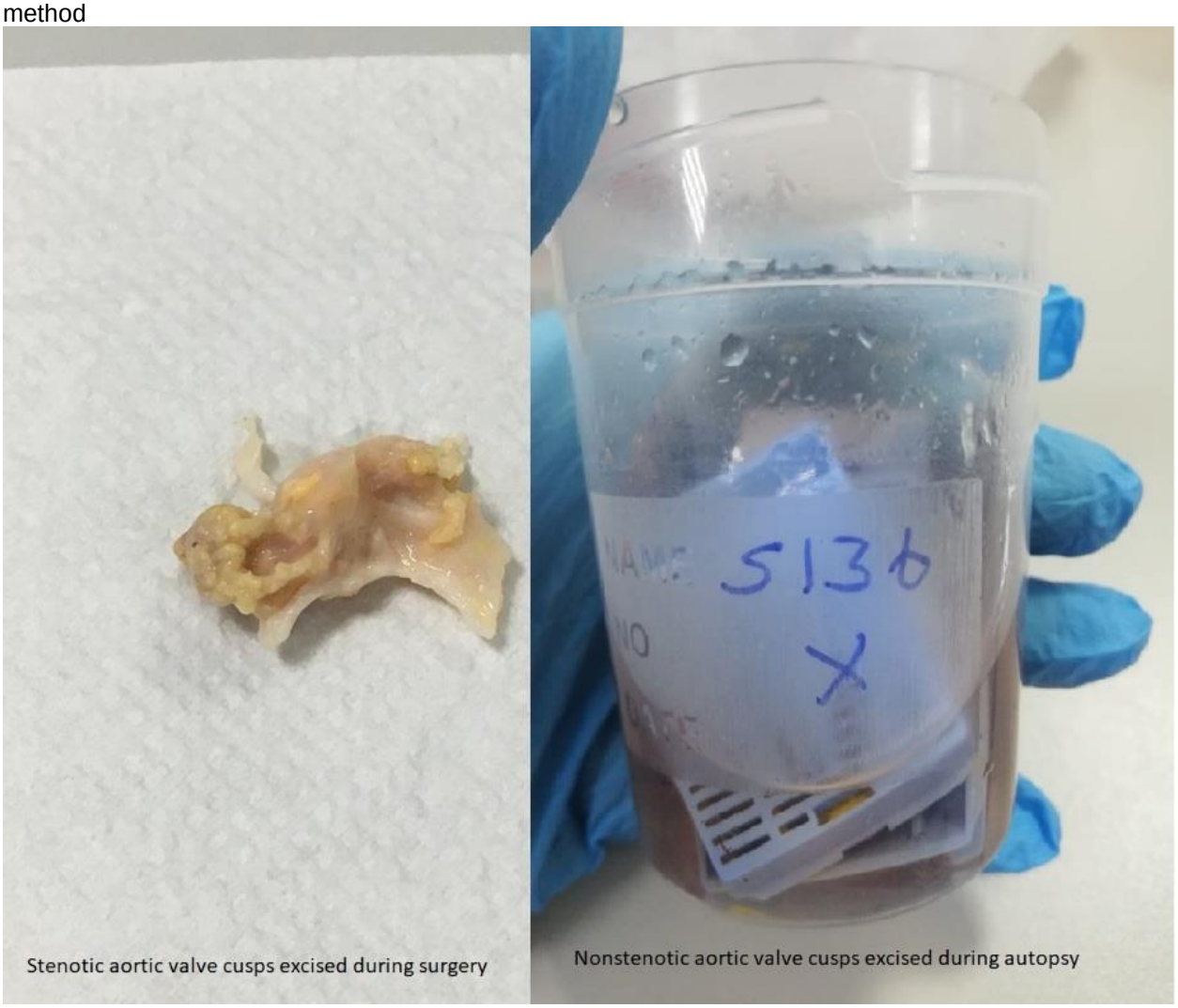
POSTER VIEWING SESSION

Ayhan Olcay[1], Serdar B. Albayrak[2], Onur Yolay[3], Vedat Ozturk[4], Emir Canturk[5], Erdem Tezcan[6], Hasan Karaoglu[7], Ceyhun Kucuk[7], Nail G. Serbest[8], Aydin Umihanic[9]
[1]Cardiology, Bezmialem Vakif University, İstanbul, Turkey, [2]Neurosurgery, Istanbul Aydin University School of Medicine, İstanbul, Turkey, [3]Technology Transfer Office, Bezmialem Foundation University, İstanbul, Turkey, [4]Mechanical Engineering, Istanbul Aydin University School of Medicine, İstanbul, Turkey, [5]Cardiovascular Surgery, Istanbul Aydin University School of Medicine, İstanbul, Turkey, [6]Department Of Nutrition And Dietetics, İstanbul Gedik University, İstanbul, Turkey, [7]Forensic Medicine, The Council of Forensic Medicine, Ministry of Justice, İstanbul, Turkey, [8]Cardiology, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Center, Training and Research Hospital, University of Health Sciences, İstanbul, Turkey, [9]Cardiovascular Surgery, University Medical Center Tuzla, Tuzla, Bosnia and Herzegovina

Background and Aims : Aortic valve stenosis is the most common valvular problem and is generally assumed to be a normal aging process. Trace element alterations and chronic heavy metal exposure are related with inflammation and different atherosclerotic events. We evaluated and compared elemental composition calcific aortic valves and normal valves from autopsies

Methods: Samples of surgical calcific aortic stenosis with no rheumatic or congenital etiologies were taken from 10 consecutive patients (2 men and 8 women, aged >50yr). Samples from 26 autopsy cases (20 men and 6 women, aged >50yr) without aortic stenosis were taken as controls (**Figure 1**). Elemental compositions were determined by ICP-OES

method



Results: K, Ca, Fe, B, Mn, As, Bi, cd, Co, Mo, Ni, Pb, Pt, Sb, Se, Sn, Ti, W levels were not different between two groups. Concentrations of Na, Mg, P, Cu, Zn, Cr, Hg were significantly higher in calcific

aortic stenosis tissue samples. Selenium was significantly lower in calcific aortic stenosis samples (**Table**

Table 1. Elemental composition of normal and calcific aortic valves

Element	Normal Aortic valves (n=26), ppm	Degenerative aortic stenosis (n=10), ppm	P Value
Na	388,17	7361,73	***0,0001***
Mg	213,96	1331,92	***0,0001***
K	140,16	152,36	0,11
Ca	86664,19	94870,65	0,052
P	3977,27	30482,27	***0,0001***
Fe	25,68	23,67	0,016
Cu	0,00	0,35	***0,0001***
B	0,40	0,71	0,39
Mn	0,00	0,00	0,00
Zn	32,83	69,07	***0,0001***
As	0,00	0,00	0,00
Bi	0,00	0,00	0,00
Cd	0,00	0,00	0,00
Co	0,00	0,00	0,00
Cr	0,00	2,67	***0,0001***
Mo	0,00	0,00	0,00
Ni	0,00	0,00	0,00
Pb	0,00	0,00	0,00
Pt	0,00	0,00	0,00
Sb	0,00	0,00	0,00
Se	1,48	1,05	***0,018***
Sn	0,00	0,00	0,00
Hg	0,00	0,35	***0,0001***
Ti	0,00	0,00	0,00
W	0,00	0,00	0,00

1)

Conclusions: We propose a new heavy metal toxic insult and ensuing chronic immune inflammation hypothesis for explaining our study results. High tissue mercury, chromium and low selenium levels are initiator of aortic valve protein structural changes and later low level auto immune inflammatory response

is triggered. High aortic tissue zinc, copper levels are remnants of Cu-Zn superoxide dismutase enzyme which scavenges superoxide ions of chronic autoimmune inflammation in calcific aortic tissues. Toxic inflammation hypothesis should replace passive degeneration concept in aortic stenosis and new preventive and treatment strategies should be developed for aortic stenosis.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-13 New lipid lowering therapies*

EFFECTS OF LIPID-MODIFYING PHARMACOLOGICAL AGENTS ON CIRCULATING PCSK9 IN SEVERE AND FAMILIAL HYPERCHOLESTEROLEMIC (FH) PATIENTS IN ARGENTINA

POSTER VIEWING SESSION

Pablo Corral[1], Gabriela Berg[2], Valeria Zago[2], Michelle Bursztyn[2], Graciela I. López[2], Laura E. Schreier[2]
[1]Pharmacology Department,, FASTA University, Mar del Plata, Argentina, [2]Clinical Biochemistry, Lab Lipids And Atherosclerosis, Universidad de Buenos Aires, Buenos Aires, Argentina

Background and Aims : PCSK9 is a key regulator of cholesterol levels by its action on LDL receptors and would promotes inflammation and atherogenesis. PCSK9 represents a novel pharmacological target for hypercholesterolemia Frequently prescribed lipid-lowering therapy (LLT), particularly statins, has been reported to increase circulating PCSK9, decreasing the effect of statins on lowering LDL-C. Little is known -and with contradictory results- about the effect of statin+ezetimibe (S+E) combination on PCSK9 levels. **Aim**: to evaluate PCSK9 levels in severe hypercholesterolemic (SH) patients receiving LLT.

Methods: 77 SH adults from the Da Vinci FH Detection Study in Argentina were included: 34 on statins (30/34 on atorvastatin -10/20 mg- and rosuvastatin 10 mg), 13 on S+E and 30 without LLT. All patients were genetically tested, 36/77 cases had pathogenic variants in FH genes and 8/77 showed high LDL polygenic risk score, which explains their phenotype. Added to the lipid profile, serum PCSK9 was measured by ELISA

Results: PCSK9 showed an increase through the 3 groups (mean±SD ng/mL) no LLT: 242±107, statins: 323±129 and S+E: 392±100, $p<0.001$. One-way ANOVA contrast analysis showed differences among groups: no treatment vs statins $p<0.001$, vs statin+ezetimibe $p<0.001$ and differences between statins vs S+E showed a trend that did not reach significance ($p=0.07$), probably due to low number of patients in S+E group. PCSK9 maintained significant correlation with apoB $r=0.27$; $p<0.02$.

Conclusions: Given that primary LLT (S+E) increase PCSK9 levels, pharmacologic strategies against PCSK9 might be one of the most effective approaches to achieving very low LDL-C neutralizing the concomitant increase of PCSK9

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-13 New lipid lowering therapies*

EFFICACY AND SAFETY OF SAROGLITAZAR 4 MG COMPARED TO FENOFIBRATE 160 MG IN LATINO ADULTS WITH MODERATE TO SEVERE HYPERTRIGLYCERIDEMIA-A RANDOMIZED CLINICAL TRIAL

POSTER VIEWING SESSION

Deven Parmar[1], René Rodriguez-Gutierrez[2], José Gerardo González-González[3], Farheen Shaikh[4], Jose L Pio Cruz-López[5]
[1]Clinical Research And Development, Zydus Therapeutics Inc., Pennington, United States of America, [2]Endocrinology, UANL, Monterrey, México and Mayo Clinic, Rochester, MN, USA, Monterrey, Mexico, [3]Endocrinology, UANL, Monterrey, México. Facultad de Medicina y Hospital Universitario "Dr. José Eleuterio González", Monterrey, Mexico, [4]Clinical Research And Development, Zydus Worldwide DMCC, Dubai, United Arab Emirates, [5]Clinical Development, Avant Sante Research Center SA de CV., Monterrey, Mexico

Background and Aims : To assess the efficacy and safety of saroglitazar 4 mg in patients with moderate to severe hypertriglyceridemia in comparison with fenofibrate 160 mg.

Methods: This was a multicenter, randomized, double-blinded, double-dummy, active-control non-inferiority trial in patients aged above 18 years with fasting triglycerides level of 500 mg/dL to 1500 mg/dL. Patients were randomized in a 1:1 ratio to receive daily dose of saroglitazar 4 mg or fenofibrate 160 mg for 12 weeks. The primary efficacy endpoint was the percent change in triglyceride (TG) levels at Week 12 relative to baseline. The primary analysis was conducted based on the per-protocol population (PP) using a non-inferiority margin of 4%.

Results: The PP population consisted of 41 patients in the saroglitazar group and 41 patients in the fenofibrate group. The percent reduction from baseline in TG levels at Week 12 was higher in favor of saroglitazar group (LS Mean -55.3%, SE = 4.9) compared with fenofibrate group (LS Mean = -41.1%, SE = 4.9). The LS estimate of the mean difference in percent change in TG levels at Week 12 was 14.1%, with the lower limit of the two-sided 95% confidence interval being 0.14% which is greater than the non-inferiority margin. Overall, 37 treatment-emergent adverse events (AE) were reported in 24 patients (Saroglitazar: 13, Fenofibrate: 11). No serious AEs were reported and no patient discontinued the study due to AEs.

Conclusions: This trial showed saroglitazar 4 mg is non-inferior to fenofibrate 160 mg in reducing TG levels at Week 12. Saroglitazar was safe and well-tolerated.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

FERRITIN AND IRON SIGNIFICANCE IN THE UNFAVORABLE EVOLUTION OF PERIPHERAL ARTERY DISEASE: A PROSPECTIVE STUDY

POSTER VIEWING SESSION

Alexandr Ceasovschih[1], Laurențiu Șorodoc[1], Viviana Onofrei[2], Dan Tesloianu[3], Elesabeta Jaba[4], Antoniu Octavian Petriș[2], Cristian Stătescu[2], Radu A. Sascău[2], Cristina Tuchiluș[5], Cătălina Lionte[1], Elena-Daniela Grigorescu[6], Alexandra Stoica[1], Oana Sîrbu[1], Raluca Ecaterina Haliga[1], Elena Adorata Coman[1], Gabriela Dumitrescu[1], Mihai Constantin[1], Irina M. Jaba[7]
[1]Internal Medicine, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, [2]Cardiology, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, [3]Cardiology, "Sf. Spiridon" County Clinical Emergency Hospital, Iasi, Romania, [4]Statistics, Alexandru Ioan Cuza University, Iasi, Romania, [5]Laboratory Medicine, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, [6]Diabetes, Nutrition And Metabolic Diseases, Grigore T. Popa University of Medicine and Pharmacy Iasi, Iasi, Romania, [7]Statistics, Independent Researcher, Iasi, Romania

Background and Aims : The aim of this study is to evaluate the relationship between ferritin and iron concentrations, and ankle-brachial index values at 6-12 months dynamics for peripheral artery disease (PAD) evolution predictability.

Methods: We examined a group of 216 patients admitted consecutively between January 2017-February 2018. At the initial and dynamic examination at 6 and 12 months, the ankle-brachial index (ABI) was assessed, and blood samples (ferritin, iron) were collected in all patients diagnosed with PAD.

Results: This study included 176 (81.5%) men and 40 (18.5%) women (gender ratio 4:1) with an average age of 68.96±9.26 and range 45-99 years. The correlations between ABI and examined biomarkers values at 0-6-12 months were indirect and highly significant: ferritin – 165.25±70.45 *vs* 193.87±63.48 *vs* 141.91±18.65 (p=0.006) and iron – 77.67±33.95 *vs* 81.98±33.96 *vs* 78.83±30.11 (p=0.028). The ROC curve showed that ferritin seemed to be a good predictor for PAD unfavorable evolution (AUC = 0.603, IC95% 0.488-0.718, cut-off value – 128 mcg/ml).

Conclusions: According to the results, the ferritin evaluation in dynamics has importance in PAD prognostic predictability. However, for greater sensitivity, longer-term studies are needed that include a wider range of PAD-specific biomarkers analysis.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

NEWLY IMAGING BIOMARKER OF HYPERTENSION-RELATED VASCULAR AND KIDNEY DAMAGE: THE OPHTHALMIC ARTERY INDEX

POSTER VIEWING SESSION

Antonina Giammanco[1], Alessandro Mattina[2], Giulio Geraci[1], Marta Zammuto[1], Carlo Maida[3], Emilio Nardi[4], Fabio Tuzzolino[5], Maurizio Averna[1], Santina Cottone[6], Giuseppe Mulè[1]
[1]Department Of Health Promotion, Mother And Child Care, Internal Medicine And Medical Specialties (promise), University of Palermo, Palermo, Italy, [2]Diabetes And Islet Transplantation Unit, Department Of Diagnostic And Therapeutic Services, Irccs-ismett, Diabetes and Islet Transplantation Unit, Department of Diagnostic and Therapeutic Services, IRCCS-ISMETT, Palermo, Italy, [3]Unit Of Internal Medicine, 'g. Longo' Hospital, Mussomeli (cl), 93014, Italy., Unit of InUnit of Internal Medicine, 'G. Longo' hospital, Mussomeli (CL), 93014, Italy.ternal Medicine, 'G. Longo' hospital, Mussomeli (CL), 93014, Italy., Palermo, Italy, [4]Department Of Health Promotion, Mother And Child Care, Internal Medicine And Medical Specialties (promise), Azienda ospedaliera universitaria Policlinico Palermo, Palermo, Italy, [5]Office Of Research, Irccs Ismett (istituto Mediterraneo Per I Trapianti E Terapie Ad Alta Specializzazione), Upmc, Palermo, 90127, Italy., Office of Research, IRCCS ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione), UPMC, Palermo, 90127, Italy.Office of Research, IRCCS ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione), UPMC, Pal, Palermo, Italy, [6]Department Of Health Promotion Sciences, Maternal & Infant Care, Internal Medicine & Medical Specialties (promise), University Of Palermo, Policlinico Universitario Paolo Giaccone, Palermo, 90127, Italy., Unit of Nephrology & Hypertension, European Society of Hypertension Excellence Center,, Palermo, Italy

Background and Aims : Ophthalmic artery resistive index (RI-OA) is associated with atherosclerotic diseases. The aim of this study was to evaluate the association of RI-OA and hypertension-related vascular and kidney damage.

Methods: Two-hundred and eighty hypertensive patients underwent evaluation of RI-OA, carotid atherosclerosis and level of 24 h albuminuria.

Results: Albuminuria and carotid atherosclerosis were positively associated with RI-OA independently of other cardiovascular risk factors. Receiver-operating characteristic curve analysis allowed us to calculate a cut-off value of RI-OA >0.625, which would be suspicious about the existence of atherosclerotic disease.

Conclusions: The ophthalmic vascular circulation allows to study connections between macro- and microcirculation *in vivo*. RI-OA could be a useful marker for a better stratification of the risk of developing kidney and cardiovascular disease.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

TYPES OF POTASSIUM CHANNELS INVOLVED IN THE RESVERATROL'S EFFECTS ON VASCULAR TONE OF DIABETIC PATIENTS

POSTER VIEWING SESSION

Milos Gostimirovic[1], Jovana Rajkovic[1], Igor Zivkovic[2], Dusko Terzic[3], Vladimir Djokic[1], Ljiljana Gojkovic-Bukarica[1]
[1]Cardiovascular Pharmacology, Institute of Pharmacology, Clinical Pharmacology and Toxicology, Medical Faculty, University of Belgrade, Belgrade, Serbia, [2]Cardiosurgery, Dedinje Cardiovascular Institute, Belgrade, Serbia, [3]Cardiosurgery, Clinic for cardiosurgery, Clinical Center of Serbia, Belgrade, Serbia

Background and Aims : Altered vascular tone in prolonged hyperglycemia is mainly due to endothelial impairment and changes in the functionality of smooth muscle potassium channels (SMPC). However, the fact that resveratrol (RSV) is able to cause relaxation of those vessels, poses intriguing lights in the cellular target sites at which it acts in pathological conditions. Our aim was to give an overview at the types of SMPK involved in the mechanism of RSV action in diabetic patients.

Methods: Samples of human saphenous vein (HSV) were taken after coronary arteries bypass grafting (CABG) of patients with DMT2, mounted in an organ bath system and relaxed by increasing concentrations of RSV (1-100 μM).

Results: A highly selective Kv1.2/Kv1.3 and Kv4.2/Kv4.3-channels blockers, margatoxin (MgTx) and phrixotoxin-2 (PhTx) did not significantly modified the vasorelaxant effect of RSV on the HSV from patients with DMT2 ($n = 5$ both, $pD2 = 4.8 \pm 0.3$ in the presence vs. 4.5 ± 0.42 in the absence of PhTx; $pD2 = 4.6 \pm 0.2$ in the presence vs. 4.8 ± 0.3 in the absence of MgTx, $p > 0.05$ both). On contrary, highly selective big Ca^{2+} activated K^+ channel blocker, iberiotoxin (IbTx) significantly modified aforementioned effects of RSV ($n = 5$ both, $pD2 = 4.3 \pm 0.3$ in the presence vs. 4.8 ± 0.3 in the absence of IbTx, $p < 0.05$).

Conclusions: It seems that MgTx and PhTx sensitive SMVC are not involved in the relaxant effects of RSV on HSV from diabetic patients, in contrast with the channels sensitive to IbTx.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

CORONARY ATHEROSCLEROSIS IN COVID-19 SURVIVORS: ASSOCIATION WITH CARDIAC INJURY AND FUNCTION AT 6 WEEKS

POSTER VIEWING SESSION

Roos A. Groen, Michiel A. De Graaf, Wouter J. Jukema, Martin J. Schalij, J L. Stöger, J J.M. Geelhoed, M L. Antoni
Cardiology, LUMC, Leiden, Netherlands

Background and Aims : COVID-19 survivors commonly show cardiac complications, manifesting as elevated troponin or cardiac dysfunction on trans-thoracic echocardiography (TTE). Both have been associated with an impaired prognosis. Possibly, subclinical atherosclerosis could play a major role. The coronary plaque burden can be determined by assessment of coronary artery calcium (CAC). The aim of this study is to determine the relation between coronary calcium and cardiac manifestation in COVID-19 survivors.

Methods: All included patients were admitted to the LUMC upon a PCR confirmed SARS-CoV2 infection and scheduled for TTE at 6 weeks post-discharge. CAC was measured on non-gated computed tomography's of the chest, routinely performed for assessment of pulmonary disease severity. A comparison was made between patients with and without coronary calcium on both elevated troponin levels (i.e. cardiac injury) and myocardial dysfunction assessed through TTE.

Results: A total of 146 patients were included, with a mean age of 62 years and 62% was male. Patients with CAC showed significantly higher levels of troponin than patients without CAC. Overall, patients showed only mild echocardiographic abnormalities. LV dysfunction, assessed through reduced left ventricular ejection fraction (<50%) was present in 12% of patients. RV dysfunction assessed through abnormal TAPSE (≤17mm), was presented in 14% of patients. In multivariate analysis no significant relation was seen between CAC and cardiac dysfunction at 6 weeks follow-up.

Conclusions: This study has shown an association between coronary atherosclerosis and in-hospital cardiac injury in COVID-19 survivors. Simultaneously, no significant relation with cardiac dysfunction at 6 weeks post-discharge was found.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

RISK FACTORS FOR SUBCLINICAL ATHEROSCLEROSIS IN HIV-INFECTED PATIENTS IN BURUNDI: A CROSS SECTIONAL STUDY

POSTER VIEWING SESSION

Deo Harimenshi[1], Théodore Niyongabo[2], Pierre-Marie Preux[1], Victor Aboyans[3], Ileana Desormais[4]
[1]Inserm U1094, Limoges University, Limoges, France, [2]Infectious Diseases, CHU Kamenge, Bujumbura, Burundi, [3]Cardiology, CHU Limoges, Limoges, France, [4]Vascular Surgery, CHU Limoges, Limoges, France

Background and Aims : Several studies have demonstrated higher incidence, prevalence and progression of subclinical atherosclerosis in HIV infected individuals. Chronic disease of people living with human immunodeficiency virus (HIV) infection are now approaching those of the general population. Previous, in vitro studies shown that HIV causes arterial injuries resulting in inflammation and atherosclerosis but direct relationship between HIV infection clinical stages and lower extremity arterial disease (LEAD) remain controversial. No study assessed, with an accurate method, both the prevalence of LEAD and the influence of HIV severity on LEAD in HIV outpatients in Central Africa.

Methods: A cross-sectional study was conducted among 1250 HIV-infected outpatients in Burundi. Inclusion criteria were as follows: age ≥ 20 years, positive HIV status, and currently receiving ART. Clinical data were extracted from Centre records. Personal information and details of PAD-related symptoms were obtained through face-to-face interviews. All patients underwent ankle-brachial index (ABI) measurement and LEAD was diagnosed by ABI≤0.9.

Results: The prevalence of LEAD was 14.72 % (CI 95%: 13.2-22.1). The mean age was 42, 8±7, 4 years. On multivariable analysis, factors associated with LEAD were diabetes (OR= 1.7; 95% CI: 1.09–2.79), obesity (OR=2.5, 95% CI: 1.27–5.02) and stage IV HIV clinical infection (OR=4.7, 95% CI: 2.29–9.85).

Conclusions: This is the first study performed on a large HIV population in Central Africa, reporting high LEAD prevalence. It underlines the influence of HIV infection on peripheral atherosclerosis at latest clinical stage and the need for LEAD screening in HIV-infected patients.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

THE PATIENT WILL SEE YOU NOW: PATIENT PREFERENCES FOR LIPID CLINIC REVIEWS IN A COVID ERA

POSTER VIEWING SESSION

Cormac Kennedy[1,2], Mary Hall[1], Patricia O'Connor[1,2]
[1]Pharmacology And Therapeutics, St James Hospital, Dublin, Ireland, [2]Pharmacology And Therapeutics, Trinity College Dublin, Dublin, Ireland

Background and Aims : The COVID-19 pandemic disturbed health systems across the world. Telephone reviews became the only method of review for most outpatients. For our Lipid Clinic to operate efficiently, staff contacted the patient pre-clinic to organize updated biochemical tests and check availability. We aimed to seek the opinion of our patients to inform our future service model.

Methods: An anonymous survey was created using Google Forms. The survey included sections about preparation for the telephone review, the review itself and the communication afterwards. A distribution list was created using contact details of patients which were requested during patient consultations from March to May 2021.

Results: 97 patients provided contact details. 48% consented to and completed the survey. The majority (89%) reported the pre-clinic call from our nursing staff worked well, however, 23% had difficulty arranging the required blood tests and sending them to us. Over 90% reported the clinical review worked well. Of the patients who received a copy of the communication to their primary care physician, 91% favoured this new practice and 65% reported it improved their self-care. A hybrid clinic, with in person or telephone reviews, was the most popular choice.

Conclusions: Reorganisation of our clinic to facilitate telehealth increased the administrative burden. Including patients in communications to their primary care physician was well received and may improve patient self-care. Patient feedback indicated that a flexible hybrid clinic is required. We now wish to create a patient portal to reduce the administrative burden of telehealth and further improve communication with our patients.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

PREDICTORS OF MAJOR ADVERSE EVENTS OF CARDIOVASCULAR DISEASE IN INDIVIDUALS WITH EARLY ISCHEMIC HEART DISEASE

POSTER VIEWING SESSION

Mikhail Konnov[1], Valery Sergienko[1], Christophe A. Stevens[2]
[1]Laboratory of Clinical Cardiology, Federal Research and Clinical Center of Physical-Chemical Medicine of FMBA, Moscow, Russian Federation, [2]Departement Of Primary Care And Public Health, Imperial college London, London, United Kingdom

Background and Aims : To identify the predictors of the combined endpoint (cardiovascular death, non-fatal myocardial infarction (MI), stroke) in individuals with early onset (≤55 - men; ≤60 - women, years) ischemic heart disease.

Methods: The 393 probands, included in this analysis (males: 65.9%, mean [SD] age: 49.5 [5.84] years, post-MI: 77.1%) were followed for a median ([interquartile range]) 10 [6.33-14.9] years between 1993-2014 in Moscow. Potential predictors included: education level, tobacco smoking, alcohol consumption, BMI, waist circumference, heart rate (HR), SBP, DBP, triglycerides, HDL-cholesterol, LDL-cholesterol, basal glycemia, peripheral arterial disease (PAD), atherogenic dyslipidemia (ATP-III, USA, 2002), arterial hypertension (ESC), diabetes (ADA, 2021), metabolic syndrome (MetS [JIS, 2009 criteria]). All analyses were carried out with adjustment for age, sex and medication taking. To reveal predictors, we used the semi parametric Multivariate Cox proportional hazard test.

Results: We identified 161 fatal (CVD [122]) and 90 non-fatal (MI [n=62], stroke [n=28]) endpoints. CVD-predictors, associated (p<0.1) in the univariate analysis (age ≥50 years, episodic/every day smoking, without statin therapy, heart rate ≥80 bpm, SBP ≥140, DBP ≥90 mm Hg, glycemia ≥5.55 mmol/L, diabetes, PAD and MetS) were included in the stepwise regression procedure (table). Table

Independent predictors	Hazard ratio	95% confidence interval	p-level
Heart rate, bpm	1.03	1.01 – 1.04	<0.001
Ageing, years	1.05	1.02 – 1.07	0.002
Diabetes mellitus	1.68	1.15 – 2.46	0.007
Male gender	1.61	1.10 – 2.34	0.014
Current tobacco smoking	1.48	1.04 – 2.08	0.027

Conclusions: This data primarily encourages us to recommend more active use of rhythm-reducing treatment among persons with early ischemic heart disease.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

CORONARY ARTERY LESIONS WHICH ARE DIFFICULT FOR REVASCULARIZATION. IS THERE ASSOCIATION WITH LP(A) LEVEL?

POSTER VIEWING SESSION

Larisa N. Ilina[1], Elina Vlasova[1], Said Kurbanov[1], Olga I. Afanasieva[2], Marina I. Afanasieva[1], Andrey A. Shiryaev[1], Vladislav P. Vasiliev[1], Damir M. Galyautdinov[1], Sergey N. Pokrovsky[1], Renat Akchurin[1]
[1]Cardiovascular Surgery, NATIONAL MEDICAL CARDIOLOGY RESEARCH CENTER, Moscow, Russian Federation, [2]Laboratory Of Problems Of Atherosclerosis, FSBO National Medical Research Center of Cardiology of Russian Ministry of Health, Moscow, Moscow, Russian Federation

Background and Aims : Background. Diffuse atherosclerosis and calcinosis of coronary arteries limit surgery and increase the risks of coronary bypass grafting. It is still actual to determine risk factors, associated with heavy lesions of coronary arteries. **Aim**. To compare Lp(a) and lipids levels in CAD patients with different types of coronary artery lesions (local, diffuse, with and without calcinosis), including combinations of these phenotypes.

Methods: A total of 357 patients scheduled for coronary artery bypass grafting (CABG) were enrolled in one-center study. Patients were divided into four groups according to the phenotype of coronary atherosclerosis: 1 (n=122) – local lesions without calcinosis, 2 (n=172) – with diffuse lesion without calcinosis, 3 (n=20) – with local lesion and calcinosis, 4 (n=43) – with diffuse lesion and calcinosis. Lesion was considered calcified or diffuse when at least 2 target coronary arteries distal to the lesion were involved in calcinosis or atherosclerosis and had a diameter less than 1.5 mm.

Results: There was no significant difference between groups of patients with different types of coronary artery lesions in levels of total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides. At the same time the median Lp(a) concentration in groups from 1 to 4 rose gradually and had a significant difference: 14.9 mg/dl (6.0-47.0), 24.3 mg/dl (8.3-63.4), 29.9 mg/dl (12.5-76.1), 43.6 mg/dl (10.1-83.1), p=0.033.

Conclusions: The most difficult phenotype of coronary artery lesions (diffuse with calcinosis) for surgical revascularization is associated with the highest level of Lp(a). We suppose that CAD patients have a better prognosis if their Lp(a) level declines.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

RADIATION-INDUCED CAROTID STENOSIS

POSTER VIEWING SESSION

Sunil Lee
Department Of Neurosurgery, Inje University Haeundae Paik Hospital, Busan, Korea, Republic of

Background and Aims : With the expanded use of radiation in the treatment of neck and mediastinal malignancies, reports of radiation-induced extracranial carotid stenosis became more prevalent. Radiation is commonly used to treat many vascular pathologies, including arteriovenous malformations, arteriovenous fistulas, cavernous malformations, and vascular tumors. In some cases, however, radiation to the normal artery can induce pathology. Histologic studies have demonstrated that radiation has variable effects, depending on the arterial size and radiation dose.

Methods: A carotid duplex scan should give sufficient information about most of the cervical carotid artery, but it is a poor choice for the evaluation of the proximal CCA and the distal cervical ICA. MRA of the arteries can give a more complete view of the arterial origins in high cervical segments but may not be obtainable in some patients. Cervical and cerebral angiography remains the “gold standard” for evaluating potential radiation stenosis.

Results: We reported their outcomes of carotid artery stenting for radiation-induced stenosis. Their periprocedural TIA rate was 8%, and the periprocedural stroke (nondisabling) rate was 4%. The restenosis rates were 17%, 33%, and 42% at 3, 12, and 24 months, respectively, but none of these patients developed symptoms. The authors finally concluded that the length of the interval between irradiation and CAS was the only significant risk factor for restenosis.

Conclusions: Radiation-induced extracranial carotid stenosis is usually more challenging mainly because it involves extensive segments of the carotid artery and is associated with fibrosis of the arterial wall and the normal tissue, which makes endarterectomy more difficult.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

LOW-DENSITY LIPOPROTEIN CHOLESTEROL TARGET ATTAINMENT IN POST-ACUTE CORONARY SYNDROME PATIENTS: ABOUT A PROSPECTIVE STUDY

POSTER VIEWING SESSION

Fatma Zohra Mebarek, Djamaleddine Nibouche
Cardiology, Hussein Dey university hospital, algiers, Algeria

Background and Aims : - During acute coronary syndrome(ACS), lowering LDLc with high-dose statins reduces the risk of recurrent cardiovascular events, which is why the 2019 ESC recommendations advocate lowering LDLc to less than <0.55g/l and reducing the initial level by 50%. - In our country, little data is available on LDLc levels. through this study, never realized in Algeria before, We aimed to assess LDLc target attainment in post-ACS patients according to the latest recommendations.

Methods: - This observational study was realized at the cardiology department of Hussein Dey hospital, from September 2020 to January 2021, 146 patients hospitalized for ACS were included, 80,8% were male. - lipid assessment was performed after admission and 08 weeks after the start of statin. All patients received « Atorvastatin 80mg » as a lipid-lowering treatment(LLT). - **Statistical analyses were conducted using SPSS, factors associated with failure to achieve LDLc target were identified using multivariate logistic regression.**

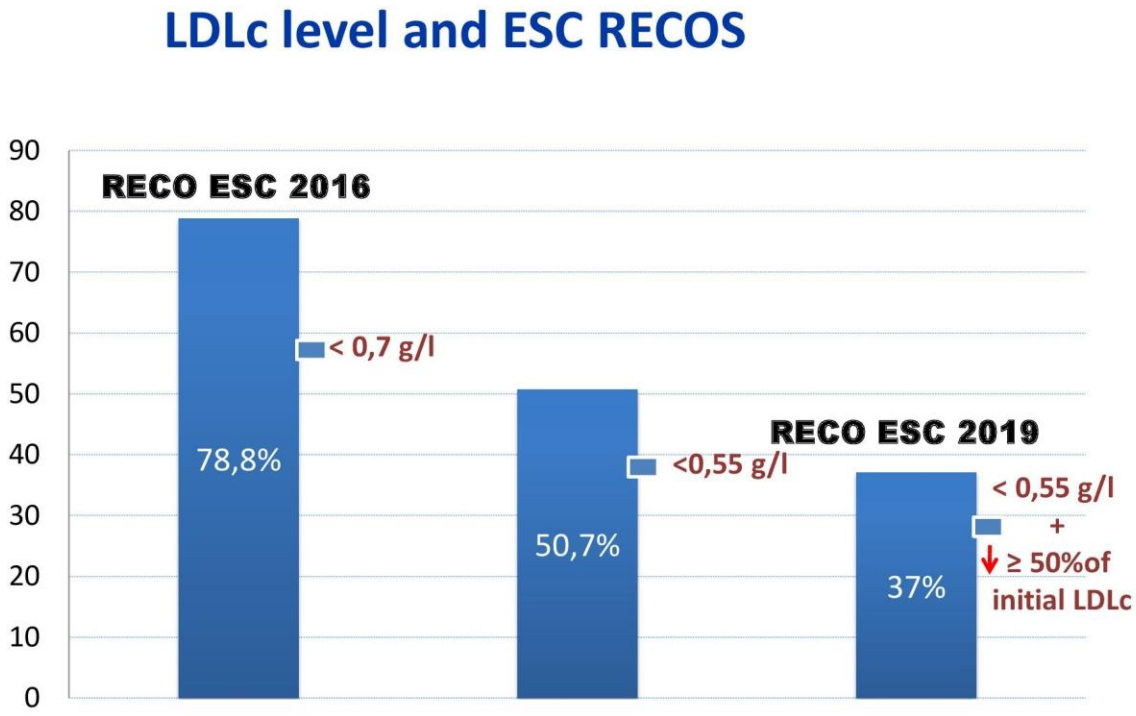
Results: - Population mean age was 59±10 years, 83,6%of patients were adherent to treatment, with a mean LDLc reduction of 47,39%. - Only 37% of the population study achieved the LDLc target at 08 weeks. - High cholesterol levels at admission, an initial LDLc level ≥1,3g/l,non-adherence to treatment, were independently associated with failure to achieve the LDLc target.

		LDLc target achieved N=54 (37 %)	LDLc target not achieved N=92 (63 %)	P value
Age (mean ±ES)		59,48 ± 12	59,15 ± 10	0,11
Male sex (%)		46(85,20%)	73(76%)	0,18
Female sex (%)		08(14,80%)	20(21,7 %)	0,20
BMI (Kg/m2)		27,5±4,97	27,16±4,82	0,90
Overweight		23(42,6 %)	40(43,5 %)	0,60
Obesity		15(27,8 %)	20(21,7 %)	0,60
Diabetes		21(38,9%)	47 (51,1 %)	0,10
HTA		20(37 %)	44(47,8 %)	0,13
smoking		21(38,9%)	37(40,2%)	0,50
Dyslipidemia		29(53,7%)	61(66,3 %)	0,16
Hypercholesterolemia		08(14,8%)	39(42,4%)	0,001
Initial cholesterol				
	< 02 g/l	58(63%)	47(87%)	0,004
	≥ 02 g/l	34(37%)	07(13%)	0,004
Initial LDLc	< 1,3 g/l	46(85,2%)	59(64,1%)	0,01
	≥ 1,3g/l	08(14,8%)	33(35,9%)	0,01
Adherence		53 (98,1%)	69(75%)	<0,01
Dietary rules		21(38,9%)	11(12%)	<0,01

Achievement of the LDLc therapeutic target

General population
N= 146

LDLc < 0,55g/l
And
50% reduction in baseline LDLc



Conclusions: - Despite the patient's adherence to treatment and the use of high-intensity statin, achieving an LDL-C target lower than 0.55 g/L is difficult. - The implementation of ezetimibe and PCSK9 inhibitors now seems unavoidable to help increase the achievement of the LDL-C target recommended.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

INVESTIGATING THE OXIDATIVE STRESS EPITOPE MALONDIALDEHYDE IN MYOCARDIAL ISCHEMIA REPERFUSION INJURY IN A 2D AND 3D HEART-ON-CHIP SETTING.

POSTER VIEWING SESSION

Merel C. Peletier[1], Kim E. Dzobo[2], Jeffrey Kroon[3]
[1]Department Of Experimental Vascular Medicine, Vascular Metabolism and Inflammation Lab, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands, [2]Experimental Vascular Medicine, Amsterdam UMC, location AMC, Amsterdam, Netherlands, [3]Experimental Vascular Medicine, Amsterdam UMC - Location AMC, Amsterdam, Netherlands

Background and Aims : Myocardial ischemia reperfusion injury (MI-R) is the cellular damage or dysfunction of cardiac tissue caused by reperfusion induced oxidative stress and inflammation following ischemia. Malondialdehyde epitopes (MDA/MAA) are end-products of lipid peroxidation. MDA/MAA are enriched in the lesion site of patients that suffered a myocardial infarction and have the ability to increase apoptosis, inflammation and induce new ROS formation. Our aim is to further investigate and develop a 3D heart-on chip model to study the molecular mechanisms of MI-R and the role/formation of MDA/MAA in a physiological context.

Methods: Inflammatory cytokines secretion/expression after MDA/MAA stimulation on HAECs, iPSC-CMs and THP-1s were measured using ELISA and qPCR. Apoptosis was quantified utilizing a live/dead staining and subsequent LDH assay. Phagocytosis of MDA-expressing apoptotic thymocytes by THP-1s is investigated by FACS. The 3D *in-vitro* perfusion model is based on Emulate organ-on-chip technology.

Results: MDA/MAA stimulation led to a dose dependent increase in cellular apoptosis as well as increased IL-8 gene expression and secretion in HAECs. The 3D *in-vitro* heart-on-chip perfusion model was designed by co-culturing an confluent ECs vessel with iPSC-CM in the second channel, the IPSC-CM layer demonstrated spontaneous beating after 24 hours and the chip remained stable for 8 consecutive days.

Conclusions: MDA/MAA stimulates inflammation and apoptosis in HAECs. Furthermore, the heart-on-chip will be further optimized that reperfusion induced MDA/MAA formation and its effect on inflammation and apoptosis and the interplay between ECs and CMs in a MI-R context can be studied. Data on this novel 3D system will be presented at EAS 2022.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

PROGNOSTICATION OF LEFT VENTRICULAR REMODELING IN OBESE PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

POSTER VIEWING SESSION

Olga Petyunina[1], Mykola Kopytsya[1], Alla Kobets[1], Anna Isayeva[2]
[1]Department Of Prevention And Treatment Of Emergency Conditions, The Government Institution "National Institute of Therapy named by L.T. Malaya of National Ukrainian Academy of Medical Science",, Kharkov, Ukraine, [2]Complex Risk Reduction Of Chronic Non-communicable Diseases, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine

Background and Aims : The high level of adipose tissue promotes inadequate myocardial perfusion and following this pathologic cardiac remodeling and heart failure in future. Thus, to determine predictors of pathological remodeling in patients with ST-segment elevation myocardial infarction (STEMI) with obesity is very significant.

Methods: 111 patients that were hospitalized from January 2018 to February 2021 were included to the retrospective cohort study. TIMI-3 flow was restored in all patients. Early cardiac postinfarction pathological remodeling was defined as left ventricular ejection fraction (LF EF) <50% and/or E/e`≥13; LV diastolic dysfunction was defined as LV EF ≥ 50% and/or E/e` <13 units. Echocardiography was performed using Toshiba Aplio 500, model TUS-A500. OMRON BF511 floor scales were used to determine key body parameters. The program Statistica 6.0 (StatSoft Inc., № AXXR712D833214FAN5) was used for statistical analysis. MANCOVA test was used to compare three or more variants.

Results: Patients were divided into two subgroups - with obesity (BMI≥30 kg/m2), n=49, and without (BMI <30 kg/m2), n=62. The prognostic value of various factors for pathological remodeling of left ventricle was studied in patients with acute myocardial infarction with and without obesity. Pathological remodeling was assessed as systolic - with reduced LF EF <50%, and diastolic - with E/e '<13. It was found that multivascular injury is more important for the development of LV remodeling in patients with LVEF<50% regardless of diastolic function. Visceral fat leads to LV remodeling due to diastolic dysfunction.

Conclusions: The obesity is the predicor of early myocardial remodeling regardless the localisation of STEMI and multivessel injury.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

ASSOCIATION G634C POLYMORPHISM OF THE VEGF-A GENE WITH CLINICAL OUTCOMES IN PATIENTS WITH MYOCARDIAL INFARCTION WITHIN 12 MONTHS

POSTER VIEWING SESSION

Iulia Rodionova[1], Inna Kutya[1], Mykola Kopytsya[2], Yaroslava Hilova[1], Olga Godlevska[3], Yana Samburg[3], Alla Kobets[1]
[1]Department Of Prevention And Treatment Of Emergency Conditions, Government Institution “l.t.malaya Therapy National Institdepartment Of Prevention And Treatment Of Emergency Conditions, Kharkiv, Ukraine, [2]Department Of Prevention And Treatment Of Emergency Conditions, GI "LT Malaya National Therapy Institute of the NAMSU", Kharkiv, Ukraine, [3]Cardiology, Internal Medicine And Nephrology, Kharkiv Medical Academy Of Postgraduate Education, Kharkiv, Ukraine

Background and Aims : Objective: to investigate the associations between the single nucleotide polymorphism of the G634C VEGF-A gene (rs 2010963) with the development of adverse events in 12-month follow-up period in patients with myocardial infarction with ST-segment elevation (STEMI).

Methods: The study included 135 patients with STEMI, average age 59.21 years. Control group of 30 healthy volunteers included.VEGF-A was determined by enzyme immunoassay. The allelic polymorphism of the G634C gene were performed by real-time polymerase chain reaction. The combined endpoint included cardiovascular death, recurrent myocardial infarction, and the occurrence/progression of heart failure that required hospitalization

Results: GG, GC and CC genotypes was 51.9%, 47.4%, and 0.7%, respectively in patients with STEMI. Significantly increased VEGF-A level was in carriers of the GG genotype 314.01 [159,94-627,66] pg / ml compared with the GC genotype 221,28 [77,58-440,82] pg / ml, (p = 0.045) in the acute period of the disease. Kaplan-Meier analyses showed the GG genotype had a lower accumulation of the combined endpoint compared to GC + CC genotypes after 12 months of follow-up (F-Crit. Cox p = 0.039). The ROC analysis showed that the level of VEGF-A less 247.51 pg / ml (area under the ROC curve 0.680; 95% confidence interval 0.588-0.739; p = 0.044) with a sensitivity of 76% and a specificity of 61% has prognostic value in 12 months of follow-up.

Conclusions: Significantly higher levels of VEGF-A and the GG genotype in contrast to GC + CC genotype are significant predictors of adverse events during 12 months of follow-up after STEMI.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

THE INFLUENCE OF CORONARY ARTERY BYPASS GRAFT ON INFLAMMATION AND MIOCARDIAL INJURY IN PATIETNS WITH CORONARY ARTERY DISEASE

POSTER VIEWING SESSION

Olesya Rubanenko[1], Anatoly Rubanenko[2], Igor Davydkin[1], Larisa Limareva[3]
[1]Hospital Therapy, Samara State Medical University, Samara, Russian Federation, [2]Propedeutic Therapy, Samara State Medical University, Samara, Russian Federation, [3]Institute Of Experimental Medicine And Biotexnology, Samara State Medical University, Samara, Russian Federation

Background and Aims : To estimate the influence of coronary artery bypass graft on imflammation and miocardial injury markers in patients with coronary artery disease.

Methods: We enrolled 96 patients in who interleukin - 6 (IL-6), interleukin - 8 (IL-8), interleukin - 10 (IL-10), C-reactive protein (CRP), fibrinogen and troponin levels were studied.

Results: Determination of white blood cells and leukocyte counts showed a significant increase of these indicators after reconstructive surgery. We found significantly higher mean concentration of IL-6 and fibrinogen in postoperative period (21.4±30.7 pg/ml versus 47.2±57.1 pg/ml, $p<0.0001$ and 3.3±0.9 g/l versus 4.3±1.1 g/l, $p<0.0001$ respectively). IL-8, IL-10 and CRP also raised in postoperative period, but remained within normal range. Mean troponin level was significantly higher in postoperative period (0 versus 2.8±2.2 mcg/l, $p<0.0001$).

Conclusions: An increasing of white blood cells, fibrinogen and interleukin-6 in postoperative period is accompanied with an increasing of systemic inflammation. Conorary artery bypass graft leads to miocardial ischemia, which is accompanied with an increasing of troponin levels.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

ASSESMENT OF RELATIONSHIP BETWEEN SARCOPENIA AND VASCULAR CALCIFICATION IN PATIENTS WITH SEVERE AORTIC STENOSIS

POSTER VIEWING SESSION

Yusuf Ziya Şener[1], Selin Ardali[2], Uğur Nadir Karakulak[3], Ahmet Hakan Ateş[3], Mehmet Levent Şahiner[3], Ergün Barış Kaya[3], Tuncay Hazirolan[2], Enver Atalar[3], Necla Özer[3], Kudret Aytemir[3], Lale Tokgözoğlu[3]
[1]Cardiology Department, Beypazarı State Hospital, Ankara, Turkey, [2]Radiology, Hacettepe University Hospital, Ankara, Turkey, [3]Cardiology, Hacettepe University Hospital, Ankara, Turkey

Background and Aims : Sarcopenia is a progressive disorder involving the accelerated loss of muscle mass and function. Sarcopenia becomes more frequent by ageing. Sarcopenia is associated with inflammation and increased risk for coronary artery disease. Sarcopenia may be diagnosed by several techniques including measurement of spinal muscle area in computed tomography (CT) images. We aimed to evaluate relationship between sarcopenia and vascular calcification in patients scheduled for TAVR.

Methods: All of the patients who underwent CT for TAVR planning between 2013 and 2020 were screened and skeletal muscle area at L3 vertebrae level was measured. Parameters regarding vascular calcification were also measured from CT images.

Results: A total of 291 patients were enrolled. Mean age was 76.2±10.2 years and 37.4% of the patients (n=109) were male. Sarcopenia was detected in 120 (41.2%) patients and median follow-up was 26.2 (0-89.1) months. Baseline characteristics were listed in Table-1. Aortic valve area was similar between sarcopenic patients and counterparts, however aortic valve calcification volume was significantly higher in sarcopenic cases (1.43 cm^3 vs 1.16 cm^3, p=0.049). Both frequency and calcification volume of MAC was distinctly higher in sarcopenic arm (Table-2). Although, follow-up duration was significantly higher in patients with normal SMI values, all-cause mortality rate was higher in patients with sarcopenia; however it was not statistically significant (39.2% vs 29.2%, p=0.077).

Table-1. Baseline characteristics of the patients			
	Sarcopenia (+)	**Sarcopenia (-)**	**p value**
Age, years	76.7 ± 11.8	75.8 ± 9.1	0.448
Gender, female, n (%)	59 (49.2 %)	123 (71.9 %)	<0.001**
Comorbidities, n (%);			
***Hypertension**	87 (72.5 %)	132 (77.2 %)	0.361
***Diabetes mellitus**	43 (35.8 %)	52 (30.4 %)	0.331
***Coronary artery disease**	53 (44.2 %)	72 (42.1 %)	0.727
***Chronic kidney disease**	16 (13.3 %)	11 (6.4 %)	0.073
***COPD**	24 (20.0 %)	38 (22.2 %)	0.649
***Atrial fibrillation**	24 (20.0 %)	33 (19.3 %)	0.933
Medications;			
***RAS blocker**	68 (56.7 %)	89 (52 %)	0.436
***Statin**	41 (34.2 %)	76 (44.4 %)	0.078
***Beta-blocker**	74 (61.7 %)	116 (67.8 %)	0.276
***Diuretics**	62 (51.7 %)	84 (49.1 %)	0.669
***OAC**	28 (23.3 %)	38 (22.2 %)	0.824
Echocardiography;			
***LV EDD, mm**	48.8 ± 6.0	49.3 ± 6.5	0.559
***LV EF, %**	53.8 ± 11.8	54.9 ± 11.4	0.439
***IVS, mm**	12.0 ± 1.9	12.8 ± 1.9	0.001**
***Aortic gradient, mean**	44.1 ± 15.5	47.2 ± 14.5	0.081
***AVA, cm^2**	0.78 ± 0.24	0.76 ± 0.21	0.287
L3 SMA,cm^2	77.5 (16-143)	133 (94-235)	<0.001**
L3 SMI, cm^2/m^2	42.5 (8.7-85.5)	73.0 (43.7-117.0)	<0.001**
BSA, m^2	1.83 ± 0.42	1.82 ± 0.18	0.845
Abbreviations: COPD: Chronic obstructive pulmonary disease, RAS: Renin angiotensin system, OAC: Oral anticoagulant, LV EDD: Left ventricular end-diastolic diameter, LV EF: Left ventricular ejection fraction, IVS: Interventricular septum, SMA: Skeletal muscle area, SMI: Skeletal muscle index, BSA: Body surface are			

Table-2. Outcomes			
	Sarcopenia (+)	**Sarcopenia (-)**	**p value**
MAC, n (%)	79 (69.9 %)	89 (56.0%)	0.020**
MAC volume, cm^3	0.33 (0-7.97)	0.04 (0-10.2)	0.044**
AVA, cm^2	0.59 ± 0.25	0.51 ± 0.21	0.434
Aortic valve calcification,volume, cm^3	1.43 (0.10-7.60)	1.16 (0.04-4.00)	0.049**
Renal artery stenosis, n (%)	28 (23.3 %)	45 (26.5 %)	0.544
In-hospital mortality	9 (7.5%)	6 (3.5%)	0.178
All-cause mortality	47 (39.2 %)	50 (29.2 %)	0.077
Follow-up, months	16.0 (0-76.3)	42.0 (0-89.1)	<0.001**
Abbreviations: AVA: Aortic valve area, AV: Aortic valve, MAC: Mitral annular calcification			

Conclusions: Sarcopenia is an important marker of vascular calcification and it may be measured easily from CT images performed for any indication. MAC and all-cause mortality rate during follow-uo are more frequent in patients with sarcopenia.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

ASSOCIATION BETWEEN OSTEOPOROSIS AND VASCULAR CALCIFICATION IN PATIENTS WITH SEVERE AORTIC STENOSIS

POSTER VIEWING SESSION

Yusuf Ziya Şener[1], Selin Ardali[2], Ahmet Hakan Ateş[3], Mehmet Levent Şahiner[3], Ergün Barış Kaya[3], Tuncay Hazirolan[2], Enver Atalar[3], Necla Özer[3], Kudret Aytemir[3], Lale Tokgözoğlu[3]
[1]Cardiology Department, Beypazarı State Hospital, Ankara, Turkey, [2]Radiology, Hacettepe University Hospital, Ankara, Turkey, [3]Cardiology, Hacettepe University Hospital, Ankara, Turkey

Background and Aims : Frequency of atherosclerosis and osteoporosis increases by ageing and vascular calcification is associated with osteoporosis. Despite diagnosis of osteoporosis is confirmed by bone mineral density (BMD); measure of L1 vertebrae computed tomography (CT) attenuation value is correlated with BMD measurements. In this study, we aimed to evaluate relationship between vascular calcification and CT diagnosed osteoporosis.

Methods: Patients who underwent CT for TAVR planning between 2013 and 2020 were screened and L1 vertebrae CT attenuation values (HU) were measured for the assessment for osteoporosis. Cut-off value for osteoporosis diagnosis was determined as 135 HU. Parameters regarding vascular calcification were also measured from CT images.

Results: A total of 286 patients were included. Mean age of the population was 76.5±9.9 years and 61.9% of the patients were female. Median follow-up was 26(0-89) months. Osteoporosis was detected in 202 (70.6%) patients. Baseline characteristics were presented in Table-1.Renal artery stenosis (29.2% vs 15.5%,p=0.022) and mitral annular calcification (66.3% vs 51.2%,p=0.016) was significantly more frequent in patients with osteoprosis than patients without osteoporosis. Additionally, MAC volume was higher in cases with osteoporosis. Aortic valve area measured by CT was significantly lower in osteoporotic patients; however there was not significant difference in aortic valve calcification volumes between the groups. In-hospital mortality and all-cause mortality rates during follow-up were similar between the two groups (Table-

2).

Table-1. Baseline characteristics of the patients			
	Osteoporosis (+)	Osteoporosis (-)	p value
Age, years	78.1 ± 7.6	72.7 ± 13.3	<0.001**
Gender, female, n (%)	146 (72.3 %)	31 (36.9 %)	<0.001**
Comorbidities, n (%);			
*Hypertension	161 (79.7 %)	55 (65.5 %)	0.016**
*Diabetes mellitus	63 (31.2 %)	31 (36.9 %)	0.349
*Coronary artery disease	82 (40.6 %)	40 (47.6 %)	0.274
*Chronic kidney disease	16 (7.9 %)	11 (13.1 %)	0.254
*COPD	44 (21.8 %)	18 (21.4 %)	0.947
*Atrial fibrillation	42 (20.8 %)	14 (16.7 %)	0.694
Medications;			
*RAS blocker	113 (55.9 %)	40 (47.6 %)	0.119
*Statin	78 (38.6 %)	36 (42.9 %)	0.504
*Beta-blocker	131 (64.9 %)	54 (64.3 %)	0.927
*Diuretics	102 (50.5 %)	42 (50 %)	0.939
*OAC	44 (21.8 %)	18 (21.4 %)	0.947
-Warfarin	18 (8.9 %)	10 (11.9 %)	0.577
Echocardiography;			
*LV EDD, mm	48.5 ± 6.1	50.0 ± 6.4	0.067
*LV EF, %	55.3 ± 10.9	52.5 ± 12.9	0.084
*IVS, mm	12.6 ± 2.0	12.4 ± 1.8	0.457
*Aortic gradient, mean	46.8 ± 14.2	45.4 ± 15.3	0.436
*AVA, cm^2	0.75 ± 0.15	0.73 ± 0.15	0.345
Abbreviations: COPD: Chronic obstructive pulmonary disease, RAS: Renin angiotensin system, OAC: Oral anticoagulant, LV EDD: Left ventricular end-diastolic diameter, LV EF: Left ventricular ejection fraction, IVS: Interventricular septum			

Table-2. Outcomes			
	Osteoporosis (+)	Osteoporosis (-)	p value
CT findings;			
*AVA, cm^2	0.51 ± 0.22	0.62 ± 0.24	<0.001**
*AV calcification, volume, cm^3	1.3 (0.04-7.60)	1.28 (0.11-4.60)	0.986
*MAC, n (%)	134 (66.3 %)	43 (51.2 %)	0.016**
*MAC volume, cm^3	0.31 (0-10.2)	0.05 (0-5.3)	0.018**
*Renal artery stenosis	59 (29.2 %)	13 (15.5 %)	0.022**
In-hospital mortality	11 (5.4 %)	4 (4.8 %)	1.000
All-cause mortality	71 (35.1 %)	25 (29.8 %)	0.380
Follow-up	30.0 (0.89.1)	20.6 (0-86.7)	0.033**
Abbreviations: AVA: Aortic valve area, AV: Aortic valve, MAC: Mitral annular calcification			

Conclusions: Osteoporosis is associated with vascular calcification with several underlying mechanisms. This study shows that presence of renal artery stenosis and both presence and severity of MAC are more frequent in patients with osteoporosis.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

EVALUATION OF RELATIONSHIP BETWEEN EPICARDIAL ADIPOSE TISSUE AND VASCULAR CALCIFICATION IN PATIENTS WITH SEVERE AORTIC STENOSIS

POSTER VIEWING SESSION

Yusuf Ziya Şener[1], Selin Ardali[2], Uğur Nadir Karakulak[3], Ahmet Hakan Ateş[3], Mehmet Levent Şahiner[3], Ergün Barış Kaya[3], Tuncay Hazirolan[2], Enver Atalar[3], Necla Özer[3], Kudret Aytemir[3], Lale Tokgözoğlu[3]
[1]Cardiology Department, Beypazarı State Hospital, Ankara, Turkey, [2]Radiology, Hacettepe University Hospital, Ankara, Turkey, [3]Cardiology, Hacettepe University Hospital, Ankara, Turkey

Background and Aims : Epicardial adipose tissue (EAT) is the true visceral fat depot of the heart that covers 80% of the cardiac surfaces and accounts for approximately 20% of total heart weight. EAT produces atherogenic adipokines and accelerates atherogenic process. We aimed to evaluate relationship between EAT and vascular calcification in patients who underwent TAVR.

Methods: All of the patients who underwent CT for TAVR planning between 2013 and 2020 were screened. EAT volume and parameters regarding vascular calcification were measured from CT images. Patients were divided into 3 groups according to EAT volumes.

Results: A total of 292 patients were included. Mean age of the population was 76.2±10.3 years and 62.3% of the patients (n=182) were female. Median follow-up was 26 (0-89) months. Frequency of hypertension was significantly in tertile 1 while diabetes was significantly more frequent in tertile 3. Coronary artery disease prevalence and used medications were similar between the groups. Baseline characteristics were presented in Table-1. Renal artery stenosis was significantly more frequent in tertile 3 than other two groups (p=0.036). There was not difference between the groups about both frequency and volume of mitral annular calcification. Both all-cause mortality and in-hospital mortality rates were similar between the three groups. Outcomes were listed in Table-
2.

Table-1. Baseline characteristics of the patients				
	Tertile 1 (n=97)	Tertile 2 (n=98)	Tertile 3 (n=97)	p value
Age, years	75.3 ± 13.0	77.4 ± 8.9	75.8 ± 8.4	0.326
Gender, female, n (%)	64 (66.0 %)	62 (63.3 %)	56 (57.7 %)	0.482
Comorbidities, n (%);				
*Hypertension	65 (67.0 %)	81 (82.7 %)	74 (76.3 %)	0.039**
*Diabetes mellitus	21 (21.6 %)	36 (36.7 %)	39 (40.2 %)	0.014**
*Coronary artery disease	37 (38.1 %)	47 (48.0 %)	41 (42.3 %)	0.380
*Chronic kidney disease	11 (11.3 %)	10 (10.2 %)	6 (6.2 %)	0.408
*COPD	17 (17.5 %)	22 (22.4 %)	23 (23.7 %)	0.538
*Atrial fibrillation	12 (12.4 %)	27 (27.6 %)	18 (18.6 %)	0.027**
Medications;				
*RAS blocker	47 (48.5 %)	57 (58.2 %)	54 (55.7 %)	0.369
*Statin	34 (35.1 %)	47 (48.0 %)	43 (44.3 %)	0.171
*Beta-blocker	63 (64.9 %)	58 (59.2 %)	69 (71.1 %)	0.216
*Diuretics	52 (53.6 %)	42 (42.9 %)	53 (54.6 %)	0.190
*OAC	18 (18.6 %)	24 (24.5 %)	24 (24.7 %)	0.498
Echocardiography;				
*LV EDD, mm	48.8 ± 6.8	48.1 ± 5.2	50.3 ± 6.6	0.049**
*LV EF, %	53.3 ± 13.6	56.6 ± 9.3	53.4 ± 11.2	0.074
*IVS, mm	12.6 ± 2.1	12.4 ± 2.0	12.5 ± 1.8	0.853
*Aortic gradient, mean	47.4 ± 17.1	46.0 ± 15.9	44.4 ± 11.0	0.380
*AVA, cm^2	0.74 ± 0.28	0.78 ± 0.20	0.78 ± 0.18	0.423
Abbreviations: COPD: Chronic obstructive pulmonary disease, RAS: Renin angiotensin system, OAC: Oral anticoagulant, LV EDD: Left ventricular end-diastolic diameter, LV EF: Left ventricular ejection fraction, IVS: Interventricular septum				

Table-2. Outcomes				
	Tertile 1 (n=97)	Tertile 2 (n=98)	Tertile 3 (n=97)	p value
CT findings;				
*EAT volume	70 (15-93)	112.5 (94-132)	161 (132-290)	<0.001**
*AVA, cm^2	0.55 ± 0.22	0.54 ± 0.24	0.54 ± 0.24	0.945
*AV calcification, volume, cm^3	1.34 (0.04-7.60)	1.38 (0.11-5.70)	1.20 (0.10-5.00)	0.881
*MAC, n (%)	57 (62.0 %)	59 (63.4 %)	53 (60.2 %)	0.906
*MAC volume, cm^3	0.14 (0.0-5.60)	0.21 (0.0-7.42)	0.4 (0.0-10.20)	0.985
*Renal artery stenosis	19 (19.6 %)	21 (21.4 %)	33 (34.4 %)	0.036**
In-hospital mortality	9 (9.3 %)	3 (3.1 %)	3 (3.1 %)	0.093
All-cause mortality	35 (36.1 %)	39 (39.8 %)	24 (24.7 %)	0.068
Follow-up	30.0 (0-89.1)	20.7 (0-79.8)	29.6 (0-82.3)	0.121
Abbreviations: EAT: Epicardial adipose tissue, AVA: Aortic valve area, AV: Aortic valve, MAC: Mitral annular calcification				

Conclusions: EAT is an important opportunistic cardiovascular risk factor that can be easily detected via echocardiography or cardiac CT. Despite coronary artery disease frequency did not increase in

conjunction with EAT volume in our study, renal artery stenosis is more frequent in patients with higher EAT volumes.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

PREDICTORS OF CARDIOVASCULAR OUTCOMES IN PATIENTS WITH LOW EXTREMITY PERIPHERAL ARTERY DISEASE

POSTER VIEWING SESSION

Ahmet Yetkin[1], Yusuf Ziya Şener[2], Ahmet Hakan Ateş[1], Mehmet Levent Şahiner[1], Ergün Barış Kaya[1], Enver Atalar[1], Kudret Aytemir[1], Lale Tokgözoğlu[1]
[1]Cardiology, Hacettepe University Hospital, Ankara, Turkey, [2]Cardiology Department, Beypazarı State Hospital, Ankara, Turkey

Background and Aims : Lower extremity peripheral artery disease (LE-PAD) is an important cause of morbidity and it is related to increased cardiovascular outcomes. We aimed to assess both the related factors and frequency of long term cardiovascular outcomes in patients with LE-PAD.

Methods: All of the patients who were diagnosed LE-PAD between January 2016- January 2017 in our hospital were included. Outcomes were determined as development of acute coronary syndrome (ACS), stroke, atrial fibrillation (AF), major adverse limb events (MALE) and all-cause mortality. MALE was defined as presence of acute limb ischemia or requirement of either revascularization or amputation due to progression of PAD.

Results: A total of 144 patients were enrolled. Mean age of the population was 65.5±15.9 years and 36.1% of the patients (n=52) were female. Median follow-up was 63.3 (0.07-71.20) months. The most common comorbidity was hypertension and it was present in 98 (68.1%) cases. Baseline characteristics were listed in Table-1. Acute coronary syndrome developed in 10(6.9%) paitents and ischemic stroke was occured in 6 (4.2%) cases. Outcomes were presented in Table-2. Multivariate Cox regresssion analysis revealed that age [HR:1.07 (1.02-1.12) ; p=0.002] and glomerular filtration rate [HR:0.97(0.95-0.98; p=0.001)] were ther predictors of all cause mortality. Multivariate logistic regression analysis showed that coronary artery disease [HR:7.64 (1.58-36.84);p=0.011] and Rutherford class [HR:4.29 (2.23-

8.22);p<0.001] were associated with MALE development.

Table-1. Baseline characteristics	
Age, years	65.5 ± 15.9
Gender, female, n (%)	52 (36.1 %)
Comorbidities, n (%);	
*Hypertension	98 (68.1 %)
*Diabetes mellitus	71 (49.3 %)
*Coronary artery disease	69 (47.9 %)
*Stroke	19 (13.2 %)
*Carotid artery disease	23 (16.0 %)
Smoking	66 (45.6 %)
NYHA Class	2 (0-4)
Fontaine class	2 (0-4)
Rutherford class	3 (0-6)
Laboratory parameters;	
-Total cholesterol, mg/dL	195.5 (0-368)
- LDL-C, mg/dL	131.5 (0-244)
-Triglyceride , mg/dL	140 (0-1056)
- HDL-C, mg/dL	42 (0-74)
- GFR, mL/min/m²	84 (8-146)
Follow-up, months	63.3 (0.07-71.20)
Abbreviations: NYHA: New York Heart Association, LDL-C: Low density lipoprotein cholesterol, HDL: High density lipoprotein cholesterol, GFR: Glomerular filtration rate	

Table-2. Outcomes	
Acute coronary syndrome, n (%)	10 (6.9 %)
Stroke	6 (4.2 %)
Atrial fibrillation	8 (5.6 %)
MALE	34 (23.6 %)
All-cause mortality	40 (27.8 %)
Abbreviations: MALE: Major adverse limb event	

Conclusions: Age and GFR is associated with all cause mortality in patients with LE-PAD, while Rutherford class and coronary artery disease are the predictors of future MALEs.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

CORONARY ARTERY DISEASE IS AN INDEPENDENT RISK FACTOR FOR IN-HOSPITAL COVID-19 ALL-CAUSE MORTALITY

POSTER VIEWING SESSION

Aleksandra V. Shalaeva[1], Khilola T. Mirakhmedova[1], Nailya A. Dadabaeva[2], Sayyora S. Egamova[1], Ulugbek S. Abdullaev[1], Alisher K. Shadmanov[3]
[1]Internal Medicine, Tashkent Medical Academy, Tashkent, Uzbekistan, [2]Internal Medicine, Cardiology, Tashkent Medical Academy, Tashkent, Uzbekistan, [3]Urology, Tashkent Medical Academy, Tashkent, Uzbekistan

Background and Aims : Coronary artery disease (CAD) is an independent risk factor for all-cause mortality. The goal of the study was to examine whether there is an association between CAD and the more severe course of COVID-19 disease and in-hospital outcomes among those who require COVID-19 hospitalization due to pneumonia.

Methods: This is a prospective cohort study of patients 1205 consecutive patients (mean age 52.2±8.4 years old who received in-hospital COVID-19 treatment at the multidisciplinary clinic 2020-2021. Baseline characteristics, e.g. age, gender, cardiovascular and other comorbidities were retrieved on the day of admission. Of them, 417 patients had a diagnosis of CAD.

Results: Of 1205 consecutive patients, 49 died in-hospital (4.06%). Unadjusted univariate logistic regression showed that CAD increased in-hospital mortality 6.27-fold (95%CI [2.96–12.78]), p<0.001. Multiple logistic regression analysis was conducted to analyze whether the presence of CAD was associated with an increased risk of in-hospital mortality. After adjusting for confounders (age, gender, smoking, obesity, diabetes and its complications, kidney diseases, hypertension, patients who were diagnosed with CAD had increased the odds of in-hospital mortality 1.82-fold (95%CI [1.39–2.35]), p=0.004. Our findings suggest that those who were on dual antiplatelet therapy prior to COVID-19 hospitalization had a lesser risk for in-hospital mortality.

Conclusions: Our findings may suggest that diagnosed CAD increased the risk of in-hospital mortality after COVID-19. Secondary and tertiary preventive measures are of utmost importance to prevent complications. More studies are needed to decrease risk in such a group of patients.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

ESSENTIAL ROLE OF CCN2 IN THE TGF-B PATHWAY REGULATION IN VASCULAR SMOOTH MUSCLE CELLS BY ENHANCING TGF-B RECEPTOR TYPE II EXPRESSION.

POSTER VIEWING SESSION

Antonio Tejera-Muñoz[1], Laura Marquez-Expósito[2], Lucía Tejedor-Santamaría[1], Sandra Rayego-Mateos[1], Macarena Orejudo[1], Beatriz Suárez-Álvarez[3], Carlos López-Larrea[3], Marta Ruiz-Ortega[1], Raul Rodrigues-Diez[3]
[1]Investigación - Nefrología Y Patología Vascular, Instituto de Investigación Sanitaria Hospital Fundación Jiménez Díaz, Madrid, Spain, [2]Molecular And Cellular Biology In Renal And Vascular Pathology, IIS-Fundación Jiménez Díaz-Universidad Autónoma Madrid, Madrid, Spain, [3]Translational Immunology, Health research institute of Asturias, Oviedo, Spain

Background and Aims : Background: Besides the traditional role attributed to the cellular communication network factor 2 (CCN2/CTGF) as a main mediator of transforming growth factor β (TGF-β) induced fibrotic responses, recent evidences have demonstrated a direct role of CCN2 acting as a growth factor in vascular smooth muscle cells (VSMCs) inducing oxidative and proinflammatory responses. However, presence of both, CCN2 and TGF-β, are needed to induce a persistent fibrotic response in some tissues. **Aims:** Considering the main role of TGF-β receptors (TβR) in the TGF-β pathway activation, our aim was to explore the effects of CCN2 in the regulation of TβRI and TβRII levels in VSMCs.

Methods: Methods: Studies were performed in a murine VSMC cell line.

Results: Results: No differences were obtained in TβRI levels, but a significant increase in TβRII expression at both gene and protein levels were found 48 hours after stimulation with the C-terminal fragment of CCN2 (CCN2(IV)). Interestingly, pretreatment with a TβRI inhibitor did not alter TβRII increment induced by CCN2(VI), proving the independence from TGF-β in this CCN2-induced response. On the other hand, CCN2(IV) rapidly activated the SMAD pathway in VSMCs, which resulted essential in the TβRII upregulation, since the preincubation with a SMAD3 inhibitor prevented it. Similar results were observed with erlotinib, an epidermal growth factor receptor (EGFR) kinase inhibitor, which abolished TβRII upregulation, suggesting an important role of this receptor in the observed TβRII expression triggering.

Conclusions: Conclusions: Our findings propose the direct role of CCN2 in maintaining TGF-β pathway activation by increasing TβRII expression in an EGFR-SMAD dependent manner activation.

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Topic: *ASA04 - CLINICAL VASCULAR DISEASE / ASA04-14 Other*

MONOCYTE-DERIVED MACROPHAGES MEDIATE S100A8/A9-INDUCED OXIDATIVE STRESS AND INFLAMMATION IN THE ISCHEMIC MYOCARDIUM

POSTER VIEWING SESSION

Mihaela Loredana Vlad[1], Ravan G. Mares[2], Alexandra G. Lazar[1], Simona-Adriana Manea[1], Bogdan M. Preda[1], Maya Simionescu[1], Alexandru Schiopu[2], Adrian Manea[1]
[1]Functional Genomics Laboratory, Institute of Cellular Biology and Pathology Nicolae Simionescu, Bucharest, Romania, [2]Department Of Functional And Complementary Sciences M2 M.d. Phd Student, University of Medicine and Pharmacy of Târgu Mures, Targu-Mures, Romania

Background and Aims : Neutrophil-derived S100A8/A9 plays an important role as inflammatory mediator in the initial inflammatory phase of the immune response to myocardial infarction (MI)**.** Monocytes (Mon) are recruited into the injured myocardium following the ischemic insult. We aimed at investigating the role of Mon-derived macrophages (Mac) as potential cellular effectors of S100A8/A9 in MI.

Methods: MI was induced in C57BL/6J mice by permanent ligation of the left descending coronary artery. Following MI/sham operation, the animals were randomized to receive (i.p.) **30mg/kg** S100A9 inhibitor ABR-238901/PBS, **for 3 days. Cultured mouse Mon-derived Mac were** exposed to 0.3 μg/ml S100A9 in the absence/presence of 10μM ABR-238901. Real-time PCR, Western blot, and microscopy were employed to assess the expression/localization of oxidative stress-related enzymes (Nox) and pro-inflammatory mediators.

Results: Significant increases in mRNA and protein levels of Nox1/2/4, TLR2/4, NOS2, MCP-1, TNFα, NLRP3, caspase-1, IL1β, and IL18 were found in the left ventricle **of MI mice as compared to sham-operated animals. Treatment of MI mice with** ABR-238901 prevented the up-regulation of the **pro-oxidant enzymes and inflammatory mediators**. **Nox isoforms were localized in the Mac-rich area in the infarcted myocardium. In-vitro,** S100A9 induced upregulation of the same molecules in cultured Mac. This effect was suppressed by ABR-238901.

Conclusions: Inhibition of S100A9 reduces the expression of markers defining the pro-inflammatory macrophage phenotype in the ischemic myocardium of mice and in S100A9-challenged Mac. S100A9 could become a novel therapeutic target to alleviate Mac-dependent inflammation and oxidative stress in MI. **Acknowledgements:** Work supported by **PN-III-P4-ID-PCCF-2016-0172,** PN-III-P4-ID-PCE-2020-1898, PN-III-P2-2.1-PED-2019-2497, **PN-III-P2-2.1-PED-2019-2512**.