91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

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 Mannheim 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.

001 / #591

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

MICRORNA 127-3P, 367-3P AND 148A-3P AND THEIR EFFECT ON NEOVASCULARIZATION AFTER MYOCARDIAL INFARCTION

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

Laura Hehl, Katrin Kalies, Fiene Daniel, Jan Michael Köster, Simon Gürlach, Kai Knöpp, Jochen Dutzmann, Daniel Sedding
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Background and Aims: To improve the healing after myocardial infarction (MI), a well-coordinated angiogenic response is necessary. MicroRNAs (miRNAs) were identified as regulators of angiogenesis, however, strategies to improve angiogenesis by targeting miRNAs are challenging. Here, we evaluate novel miRNA candidates concerning their therapeutic potential toward neovascularization after MI.

Methods: The respective microRNAs (miRNA 127-3p, 148a-3p, miRNA 367-3p) were characterized regarding gene/protein expression for their contribution to EC function, i.e. proliferation, migration, and metabolism after either pre- or anti-miR transfection. In consecutive experiments, tube and sprouting formation ability *in vitro* and the angiogenic capacity of ECs *in vivo* were determined.

Results: Under hypoxic conditions, as observed in the MI zones, all three miRNAs were upregulated in ECs. For miRNA-127-3p and 148a-3p, this upregulation under hypoxia is independent of senescence, whereas miRNA 367-3p is upregulated especially in senescent ECs under hypoxia. After transfection of pre-miR 367-3p, an improvement in migration capacity, as assessed per scratch wound assay, was observed. Pre-miR 367-3p and pre-miR-148a-3p promoted migration whereas anti-miRs of the same microRNAs reduced the migration. Pre and anti-miR 127-3p showed no effect on migration. Overexpression of pre-miRs of all miRNAS increased the metabolic activity of ECs.

Conclusions: Summarizing different expression levels of miRNA 127-3p, 148a-3p and miRNA 367-3p exerted distinct effects on EC function, especially under hypoxic conditions. Our experimental data regarding cellular function show that these miRNAs are involved in the angiogenetic response and hold

the potential to serve as therapeutic targets. In future experiments, we will evaluate the microRNA potential on MI healing *in vivo*.

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002 / #774

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

TRANSCRIPTIONAL ELONGATION CONTROLS ENDOTHELIAL-TO-MESENCHYMAL TRANSITION

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Endothelial-to-mesenchymal transition (EndMT) is a process, in which endothelial cells (EC) lose endothelial characteristics and trans-differentiate into mesenchymal-like cells. EndMT has been associated with the progression of atherosclerosis. Stress stimuli like hypoxia require immediate adaptive gene expression to ensure cell survival. The super elongation complex (SEC) controls this rapid response mechanism through controlled transcriptional elongation. The SEC is built around the scaffold proteins AFF1 and AFF4 and mediates immediate gene induction by pausing and release of RNA Polymerase II (RNAPII). We hypothesized that transcriptional elongation regulates EndMT and analyzed the contribution of the SEC during EndMT.

Methods: AFF regulation was analyzed in carotid plaques and EndMT single cell sequencing data. RNA elongation rates were determined using 4-thiouridine-DRB-sequencing. Promoter states of paused genes were analyzed using chromatin immunoprecipitation-sequencing.

Results: AFF1 and AFF4 expression was increased in EndMT. Treatment of EC with chemical SEC inhibitors led to degradation of AFF1 and AFF4 on protein level and reduced the induction of mesenchymal markers during EndMT. Sequencing of newly transcribed RNA revealed increased RNA elongation rates after EndMT treatment, which were reduced by SEC inhibition. Chromatin immunoprecipitation-sequencing revealed less RNAPII occupancy at gene promoters after EndMT induction, indicating less promoter-proximal pausing of RNAPII during EndMT. SEC inhibition increased promoter-proximal pausing during EndMT. The regulation of immediately regulated target genes was validated using qPCR.

Conclusions: In summary, we identified increased RNA elongation rates during EndMT, which were decreased by SEC inhibition. We propose transcriptional elongation as a new regulatory mechanism during the process of EndMT.

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003 / #640

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

EICOSAPENTAENOIC ACID (EPA) MODULATED EXPRESSION OF ENDOTHELIAL PROTEINS LINKED TO DETOXIFICATION AND INHIBITION OF OXIDATIVE STRESS DURING INFLAMMATION

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

Samuel Sherratt[1,2], Peter Libby[3], Deepak Bhatt[4], Preston Mason[2,3]
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Background and Aims: Reactive oxygen species (ROS) and related toxins generated during endothelial cell (EC) dysfunction contributes to atherosclerosis. Cellular detoxification enzymes including peroxiredoxins (PRDX) inactivate ROS. The omega-3 fatty acid EPA reduced a broad range of cardiovascular (CV) events in high-risk patients (REDUCE-IT). We measured the effects of EPA on expression of proteins involved in detoxification and ROS in vascular ECs under conditions of inflammation caused by the cytokine IL-6 and the effector of the renin angiotensin system, angiotensin II (AngII).

Methods: Human umbilical vein endothelial cells (HUVECs) were challenged with either IL-6 (12 ng/mL) or Ang II (100 nM) for 2 h, then treated with EPA (40 µM) for 24 h. Global proteomic analysis was performed using LC/MS to measure relative expression levels simultaneously. Significant ($p<0.05$) changes in expression between treatment groups >1-fold were analyzed by differential enrichment analysis of proteomics data (DEP) and included in gene set enrichment analyses (GSEA).

Results: Compared with AngII and IL-6 alone, EPA significantly modulated expression of 1,012 and 1,016 proteins, respectively. Many of these proteins and related pathways regulate ROS and detoxification. Specifically, compared to AngII and IL-6, EPA significantly increased expression of PRDX2 by 1.1-fold and catalase by 1.2 and 1.1-fold, respectively. EPA significantly modulated the “cellular response to oxidative stress” pathway (GO:0034599) compared to either stimulus.

Conclusions: EPA modulated the expression of ROS detoxification proteins, including peroxiredoxin isoforms. The potential effects of EPA on ROS and detoxification proteins during inflammation could contribute to reduced atherothrombotic risk.

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004 / #665

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

EICOSAPENTAENOIC ACID (EPA) INCREASES ENDOTHELIAL EXPRESSION OF HEME OXYGENASE-1 AND RELATED IRON STORAGE PROTEINS DURING CHALLENGE WITH ANGIOTENSIN II

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

Samuel Sherratt[1,2], Peter Libby[3], Deepak Bhatt[4], Preston Mason[2,3]
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Background and Aims: Heme oxygenase-1 (HO-1) is a cytoprotective protein which catalyzes degradation of heme into carbon monoxide, biliverdin and free iron. The elevated free iron leads to increased ferritin and frataxin levels. Angiotensin II (AngII) promotes oxidative stress and cardiovascular (CV) risk. The omega-3 fatty acid, eicosapentaenoic acid (EPA), administered as icosapent ethyl (IPE) was associated with reduced CV events in REDUCE-IT. We measured the effects of EPA on HO-1 expression and related iron storage proteins in vascular endothelial cells (ECs) during inflammation.

Methods: Human umbilical vein ECs (HUVECs) were challenged with AngII (100 nM) for 2 h and then treated with vehicle or EPA (40 μM) for 24 h. Global proteomic analysis was performed using LC/MS to measure relative expression levels simultaneously. Significant ($p<0.05$) changes in expression between treatment groups >100% were analyzed by differential enrichment analysis of proteomics data (DEP) and included in gene set enrichment analyses (GSEA).

Results: EPA significantly decreased/increased expression of 507/505 proteins compared with AngII alone. With EPA, HO-1 increased 170% ($p=2.24\times10^{-5}$) compared to AngII, along with ferritin (130%, $p=0.0006$) and frataxin by 120% ($p=0.005$). GSEA revealed the changes in frataxin were implicated in pathways related to apoptosis.

Conclusions: EPA increased expression of HO-1 in vascular ECs along with related iron storage and transport proteins following AngII challenge. The ability of EPA to increase expression of atheroprotective proteins during inflammation may reduce CV risk as demonstrated in outcome trials.

91ST EAS CONGRESS
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005 / #668

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

EICOSAPENTAENOIC ACID MODULATED EXPRESSION OF ENDOTHELIAL NITRIC OXIDE SYNTHASE (ENOS) AND ITS MODULATORS DURING INFLAMMATION

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: The omega-3 fatty acid EPA exerts endothelial effects that may contribute to reduced events in patients with cardiovascular (CV) risk (REDUCE-IT) including increased nitric oxide (NO) bioavailability. Activation of the renin-angiotensin system and its effector, AngII, promote generation of superoxide anion that leads to eNOS uncoupling. We measured the effects of EPA treatment on expression of eNOS and its regulators in vascular ECs during challenge with AngII.

Methods: Human umbilical vein ECs (HUVECs) were challenged with AngII (100 nM) or for 2 h and then treated with vehicle or EPA (40 µM) for 24 h. Global proteomic analysis was performed using LC/MS to measure relative expression levels simultaneously. Only significant ($p<0.05$) changes in expression between treatment groups >1-fold were analyzed by differential enrichment analysis of proteomics data (DEP) and included in gene set enrichment analyses (GSEA).

Results: EPA significantly modulated expression of 1,012 proteins compared with AngII alone. AngII alone increased eNOS expression 1.1-fold ($p=0.002$) relative to control, while EPA decreased the expression 1.1-fold ($p=0.044$) compared to AngII. EPA also significantly increased expression of progranulin (1.3-fold) and dimethylargininase-2 (1.3-fold), both of which increase NO bioavailability. GSEA revealed that 7 proteins within the “regulation of nitric oxide synthase” pathway (GO:0050999) were significantly modulated with EPA (adjusted p-value for pathway = 0.002).

Conclusions: EPA modulated expression of eNOS and related proteins that improve NO bioavailability and vasodilation following challenge with AngII. The effects of EPA on EC function may contribute to reduced risk for patients with CV disease as evidenced in REDUCE-IT.

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006 / #803

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

REGULATION OF INTERLEUKIN 1B DRIVES ENDOTHELIAL-TO-MESENCHYMAL TRANSITION OF VALVE ENDOTHELIAL CELLS IN PATIENTS WITH AORTIC VALVE SCLEROSIS

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Aortic valve sclerosis (AVSc) is the first stage of calcific aortic valve stenosis (CAVS), with a prevalence of 25-30% in subjects older than 65 years. It is a clinically silent phase characterized by non-uniform leaflet thickening and no obstruction of the blood flow. At molecular level, AVSc is characterized by local oxidative stress, inflammation, endothelial-to-mesenchymal transition (EndMT), fibrosis, and microcalcification. Our aim is to investigate which systemic process(es) is(are) involved in AVSc onset.

Methods: We enrolled 80 healthy subjects and 77 AVSc patients. Echocardiography was used to detect AVSc presence. Plasma and serum were collected to evaluate circulating microRNA (RNA-sequencing) and interleukin 1 (IL1β, ELISA), respectively. Functional analysis was performed to reveal systemic pathway regulation. Healthy human valve endothelial cells were treated with IL1β to evaluate EndMT (morphological analysis and quantitative PCR).

Results: Fifty-nine microRNA resulted down-regulated, while 93 were up-regulated in AVSc patients compared to healthy subjects (adjusted-$p<0.05$). The functional analysis revealed that inflammatory pathways were enriched in AVSc, indeed serum IL1β levels were higher in AVSc vs. healthy (5.74±3.93 vs. 4.62±2.64pg/ml; $p=0.037$). In vitro chronic IL1β treatment induced a decrease in cell roundness and an increase in total area (0.40±0.18 *vs* 0.47±0.19AU, $p<0.0001$; and 0.75±0.73 vs 0.45±0.48AU, $p<0.0001$; respectively). Quantitative PCR revealed EndMT activation: SNAI1 (1.87±0.57 $\log_2$(foldchange), $p<0.0001$) and SNAI2 (2.19±0.46 $\log_2$(foldchange), $p<0.0001$).

Conclusions: AVSc patients are characterized by an activated systemic inflammatory status and its master regulator, IL1β, seems involved in the EndMT progression of valve endothelial cells, eventually leading to fibrosis of aortic leaflets.

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007 / #99

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

SINGLE BOUT HIKING IMPROVES ENDOTHELIAL FUNCTION, ARTERIAL STIFFNESS AND ENDOTHELIAL PROGENITOR CELLS IN YOUNG HEALTHY VOLUNTEERS.

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: A disrupted balance between endothelial injury and repair induces endothelial dysfunction and endothelial progenitor cells (EPC) augment vascular repair. So, exercise improves endothelial function through increased numbers of circulation EPC. We investigated even single bout hiking can improve endothelial function, arterial stiffness and EPC or not. So, we measured the number of circulating EPC, and tested vascular health by flow-mediated dilation (FMD), brachial-ankle pulse wave velocity (baPWV), Augmentation Index (AIx) before and after hiking in young healthy volunteers.

Methods: 24 young healthy volunteers were enrolled. They hiked the Seorak mountain (1708m height, 16km long, 11 hours 20 minutes distance by walk) together once this summer. We tested FMD, baPWV, AIx and measured EPCs (CD34/KDR, CD34/CD117, CD34/CD133) at baselines and immediate after hiking. FMD is a marker of endothelial function, AIx and baPWV can show arterial stiffness. We checked exercise intensity by Polar monitoring. All volunteers completed hiking within 13 hours.

Results: 16 volunteers were male (67%) and mean age was 27.3(±5.7). mean BMI(body mass index) was 21.4(±3.4) and they did not have medical history including hypertension and diabetes mellitus. After moderate degree hiking, FMD and AIx improved significantly compared with baseline. (P=0.001, 0.003, respectively) (figure). Absolute numbers of all EPCs improved significantly after hiking. (all EPCs, P<0.001). There is no significant difference of blood pressure and baPWV (table).

Conclusions: Even single bout hiking improved vascular endothelial function and arterial stiffness and augmented the number of circulating EPCs in young healthy volunteers.

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008 / #664

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

SGLT2 INHIBITORS INCREASE ENDOTHELIAL VE-CADHERIN LEVEL REDUCED BY 25-HYDROXYCHOLESTEROL

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

Agnieszka Pawlos[1], Paulina Gorzelak-Pabiś[2], Łukasz Markiewicz[3], Ewelina Woźniak[4], Agnieszka Piastowska-Ciesielska[3], Marlena Broncel[2]
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Background and Aims: The exact mechanism of beneficial effects of SGLT2 inhibitors (empagliflozin-empa, canagliflozin-cana, dapagliflozin-dapa) in patients with cardiovascular diseases remains not fully understood. In our previous studies we have shown that SGLT2 inhibitors significantly improve endothelial integrity interrupted by 25-hydroxychoelsterol (25-OHC). The aim of this study was to assess whether SGLT2 inhibitors affect VE-cadherin level, the most important endothelial-specific protein that maintains endothelial barrier functions.

Methods: HUVECs were incubated with: 25-hydroxycholesterol 10 mg/ml, empa 1µM, cana 1µM, dapa 1µM and 25-OHC+ empa 1µM, 25-OHC+ cana 1µM, 25-OHC+ dapa 1µM and medium as control. VE-cadherin was assessed in confocal microscopy. Cells were stained for VE-cadherin (green), and DAPI (blue). Quantification of VE-cadherin protein levels measured as mean fluorescence intensity in cell membrane (n=30-40 cells).

Results: 25-OHC significantly reduced VE-cadherin level in endothelial cells 19.4±8 vs medium control 33.1±9 (Figure 1A/B). VE-cadherin level in HUVECs incubated with SGLT2i's was significantly higher than medium control, respectively empa 43.4±12, cana 47.2±17, dapa 33.09±9 vs. 33.09±9 medium control (Figure 1A/B). In HUVECs pre-incubated with 25-OHC and then stimulated with SGLT2i's VE-cadherin level was significantly higher than in cells incubated only with 25-OHC 19.4±8; 25OHC+empa 48.5±13, 25OHC+cana 42.9±13 or 25OHC+dapa 40.6±14 (Figure 1A/B).

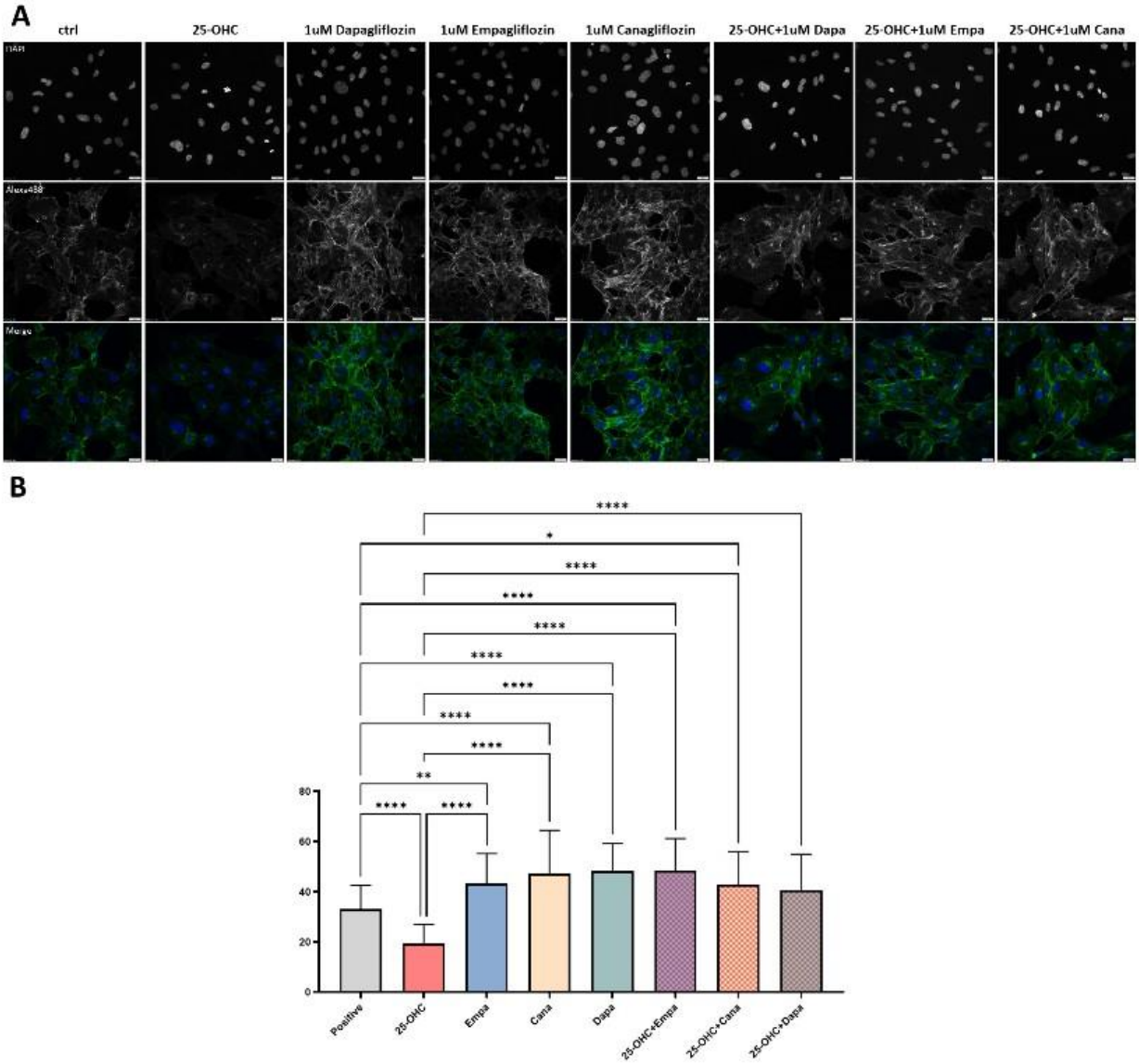

Figure 1: The expression and distribution of VE-cadherin in HUVECs. A Images from confocal microscopy B VE-cadherin protein levels measured as mean fluorescence intensity in cell membrane. Data presented as mean±SD. * p<0.1, ** p<0.01, ***p<0.00, **** p<0.0001.

Conclusions: Our results show that SGLT2 inhibitors significantly increase endothelial VE-cadherin level reduced by 25-OHC.

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009 / #931

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

TOWARDS UNDERSTANDING THE ROLE OF CHOLESTEROL IN VASCULAR REGENERATION: IMPLICATION TO THE FUTURE OF REGENERATIVE MEDICINE

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Atherosclerosis development results in damage of endothelial monolayer of vessel wall. Regeneration of endothelium is crucial to maintain vascular functionality and integrity. Cholesterol is one of the factors of biological origin suggested as an effectively stimulating agent involved in regeneration process. It is required for many cellular processes, it may promote cell migration, wound healing or neovascularization.

Methods: Explaining the mechanism of regeneration in atherosclerosis we performed an aortic ring assay. Rat aorta rings were coated with Geltrex™ with stimulators (cholesterol, VEGF) in 24-well plate and incubated with medium for 14 days. Sprouting cells were observed and photographed daily. We conducted transcriptomic analysis using isolated RNA of HMEC-1 stimulated with cholesterol. Moreover, we examined angiogenesis in an *in vivo* model (rat). Subcutaneous implantation of PLA-based composite modified with cholesterol (0,15 and 0,015%) was fixed and dyed with hematoxylin and eosine after 7, 30 and 90 days.

Results: In aortic ring assay cholesterol stimulated cells to sprout, even faster than VEGF. Transcriptomic analysis showed significant changes in up- and downregulation of genes involved in angiogenesis. Whereas histological analysis of implantations indicated that PLA-based composite modified with cholesterol (0,15%) stimulated angiogenesis which continued to progress over time.

Conclusions: We conclude cholesterol stimulates regeneration of endothelium after its damage in atherosclerosis. These studies were performed within the project “Multifunctional composites biologically active for applications in regenerative medicine of bone system (POIR.04.04.00-00-16D7/18)” carried out within the TEAM NET programme of the Foundation for Polish Science co-financed by the European Union under the European Regional Development Fund.

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010 / #548

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

INFLUENCE OF BREAST CANCER CELLS ON THE EXPRESSION OF ENDOTHELIAL CELL ADHESION MARKERS TO STUDY THE INTERPLAY BETWEEN ATHEROSCLEROSIS AND CANCER

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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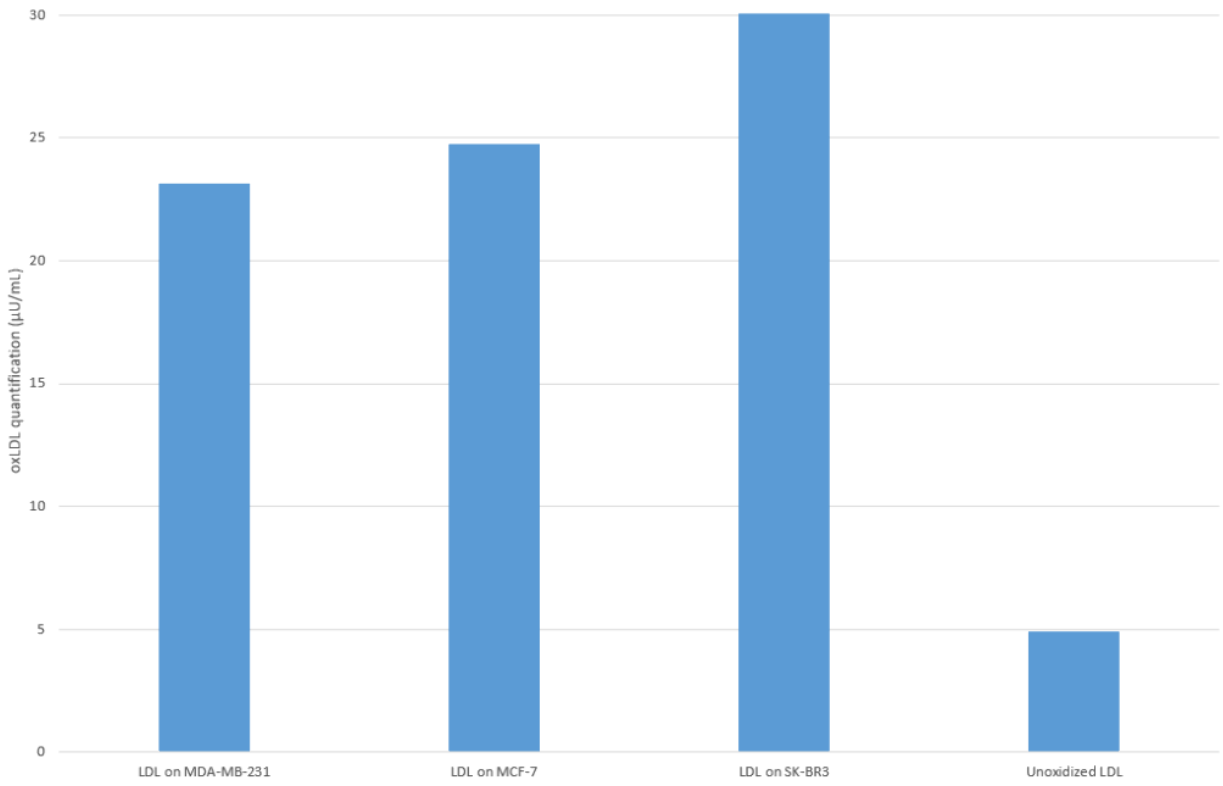
Background and Aims: Cardiovascular diseases are the leading causes of death worldwide closely followed by cancers. Among women, breast cancers (BC) are the most prevalent. We sought to investigate in vitro the influence of BC cells and their milieu on the expression of selectins and connexins involved in atherosclerosis.

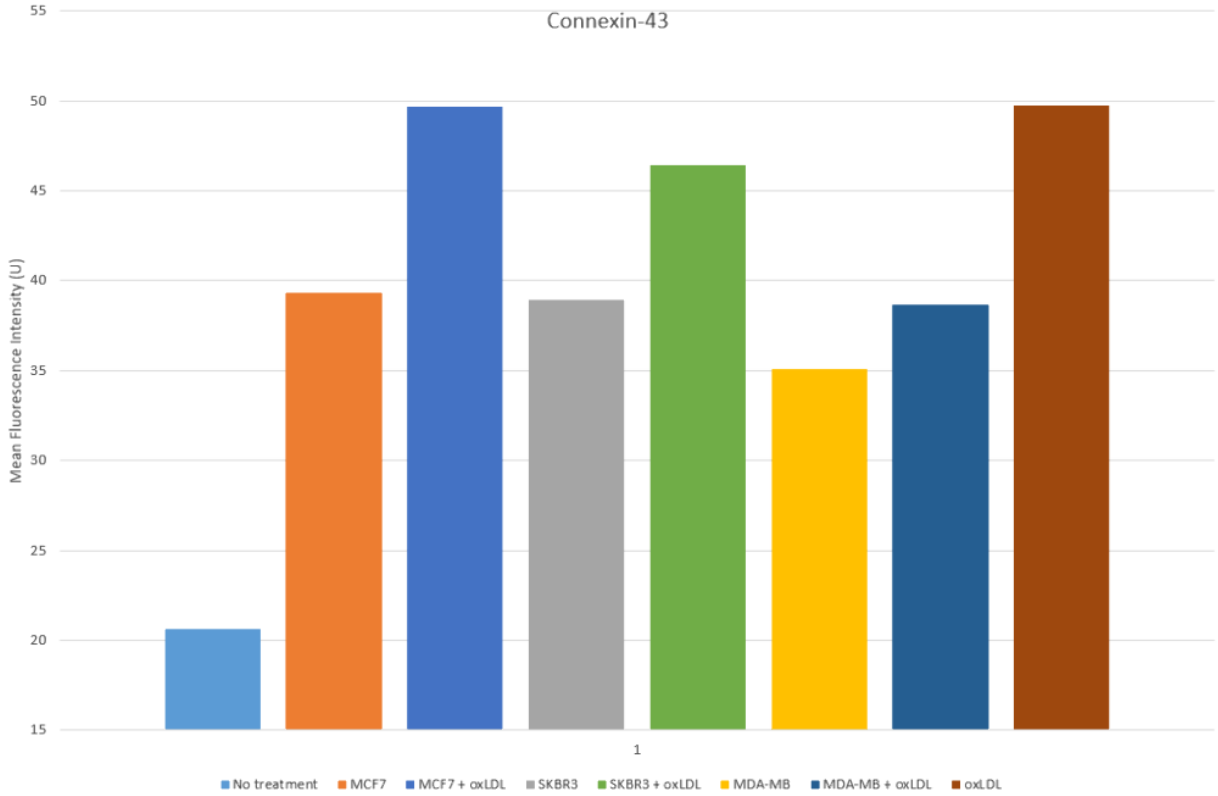
Methods: In order to study the influence of BC cell lines (SKBR3, MCF-7 and MDA-MB-231) on the expression of E-selectin, connexin-43 and ICAM-1 on endothelial cells (Human Umbilical Vein Endothelial Cells; HUVECs), a blended-medium containing 70% HUVEC medium and 30% BC conditioned-medium was prepared. This medium was exposed to HUVEC for 48h and negative control represents HUVEC exposed to a mix of 70% of HUVEC medium plus 30% of fresh DMEM. Moreover, homemade oxidized low-density lipoproteins(oxLDL)(Scalia et al. IJMS, 2022) were added or not to the blended-medium. An immunofluorescence was performed to highlight E-selectin, connexin-43 and ICAM-1 expression on HUVECs. We also exposed 50µg/mL unoxidized LDL on the three BC cell lines for 48 hours and observed oxLDL quantification with a commercial ELISA kit.

Results: 1)The expression of the 3 adhesion markers involved in the initiation of atherosclerosis was significantly increased when HUVEC were exposed to BC blended-medium. This expression was increased by oxLDL exposition. 2)We observed a significant increase in oxLDL levels when LDL was exposed to BC

cells.


30
25
20
15
10
5
0
oxLDL quantification (µU/mL)
LDL on MDA-MB-231
LDL on MCF-7
LDL on SK-BR3
Unoxidized LDL

Conclusions:



We successfully highlighted an increased oxidation of LDL in contact with breast cancer cells associated with an increased expression of atherosclerosis initiation receptors. This shed new lights on the clinically observed interplay between atherosclerosis and cancers.

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011 / #1030

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

MODULATING ENDOTHELIAL PENTOSE PHOSPHATE PATHWAY TO ATTENUATE VASCULAR INFLAMMATION

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Alterations in intracellular metabolic pathways have emerged as a crucial factor in supporting residual inflammation and high-risk plaque phenotype. Recently, it was demonstrated that pro-inflammatory macrophages rely on increased dependency on glycolysis and its interconnecting pentose phosphate pathway (PPP) to sustain their inflammatory phenotype. However, the role of endothelial PPP in driving vascular inflammation and progression of atherosclerosis is a largely unexplored disease mechanism.

Methods: Human aortic endothelial cells (HAECs) were stimulated with 0.5 ng/mL of IL-1β to mimic a residual low-grade inflammation. Next, in order to assess the role of PPP, the first rate-limiting enzyme of the pathway, glucose-6-phosphate dehydrogenase (G6PD) was pharmacologically inhibited with dehydroepiandrosterone (DHEA). After 48 hours, cytokine secretion and gene and protein expression of key inflammatory markers as well as transendothelial migration of monocytes were measured.

Results: Untargeted metabolomics analysis under residual low-grade inflammation revealed increase in several key metabolites, ribose-5P of non-oxidative PPP branch, suggesting an increased metabolic flux into the PPP under inflammatory conditions. Inhibition of G6PD activity reduced the secretion of pro-inflammatory cytokines IL-6 (1243±196 vs. 777±244 pg/mL, p=0.025) and IL-8 (8920±1689 vs. 5792±643 pg/mL, p=0.013), accompanied with a decreased gene and protein expression of the key adhesion molecules ICAM-1 and VCAM-1. Functionally, this resulted in reduced monocyte transendothelial migration capacity.

Conclusions: These findings suggest that reduced metabolic fluxes may attenuate residual inflammation in ECs. Future work is needed to uncover the functional mechanisms of rewired endothelial PPP in regulating vascular inflammation and progression of atherosclerosis, thereby providing insights for novel therapeutic approaches.

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012 / #813

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

EVALUATION AND SELECTION OF ANTIBODIES SUITABLE FOR ENDOGLIN DETECTION TO BE APPLIED IN THE STUDY OF LIVER AND AORTA PATHOLOGY ON MICE MODELS

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Endoglin (CD105, Eng) is a glycoprotein affecting the function of vascular endothelium and liver fibrosis. If immunoassay techniques that use antibodies for the specific detection of proteins are involved, finding a high-quality antibody is crucial. We found that some commercial anti-Eng antibodies show contradictory results regarding Eng expression during the development of atherosclerosis and non-alcoholic steatohepatitis (NASH). We aimed to evaluate the affinity and specificity of these antibodies and suggest the most suitable antibody detecting Eng in the aorta and liver in these pathologies.

Methods: Four different anti-Eng antibodies were tested for their affinity and specificity to mouse Eng. Affiblot (affinity and specific reaction with recombinant Eng), western blot (WB) and IHC (cross-reactivity with non-target proteins), and surface plasmon resonance (SPR, for affinity) were used. The antibodies were tested with pure recombinant Eng and with liver and aorta homogenates either from healthy mice or from mice with induced atherosclerosis or NASH.

Results: The antibodies showed significant differences in the number of bands detected by WB (cross-reactivity). In addition, the antibodies display different affinity to target where some antibodies fail to detect the significant differences in Eng expression in pathological liver and aorta, which resulted in false negative biological results.

Conclusions: Only one of the tested antibodies has suitable parameters regarding specificity, sensitivity, and cross-reactivity for the identification of Eng reflecting biological differences in control and atherosclerotic/NASH samples. Thus, this study reflects the need for proper characterization of antibodies prior to the analysis of samples. *The study was supported by GACR 22-14961S*

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013 / #1066

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

ENDOGLIN BLOCKAGE IS ESSENTIAL IN INFLAMMATION-INDUCED ENDOTHELIAL DYSFUNCTION IN HUMAN AORTIC ENDOTHELIAL CELLS

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Endoglin (Eng), the TGF-β co-receptor, was shown to play an important role in endothelial dysfunction and TRC105 is an antibody that can block Eng and its signaling. Our aim was to investigate the TRC105 effects on the Eng expression, signaling, and function in endothelial dysfunction induced by inflammation (simulated by tumor necrosis factor alpha [TNF-α]).

Methods: Human aortic endothelial cells (HAECs), passage 5, were treated with TNF-α (10 ng/mL) for 4 hours, followed by the addition of TRC105 (300 µg/mL) for 12 hours. Protein levels, adhesion, and transmigration of monocytes were assessed by flow cytometry, mRNA expression was measured by qRT-PCR.

Results: Inflammation induced by TNF-α resulted in decreased protein expression of Eng and increased protein expression of cell adhesion molecules (ICAM-1, VCAM-1), which was followed by increased adhesion of THP-1 monocytes to endothelial cells. Treatment with TRC105 led to further reduction of Eng protein expression, which was able to prevent inflammation-induced adhesion of monocytes to endothelial cells.

Conclusions: These results suggest that blockage of Eng by TRC105 can prevent the endothelial dysfunction induced by TNF-α in HAECs, suggesting that Eng participates on inflammation-induced endothelial dysfunction, but to which extent must be further investigated.

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014 / #552

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

THE PROINFLAMMATORY PHENOTYPE OF TYPE II DIABETES MELLITUS HUMAN ENDOTHELIAL CELLS INCLUDES INCREASED ENDOGLIN EXPRESSION AND SOLUBLE ENDOGLIN LEVELS

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Endoglin is a transmembrane glycoprotein that is present in two different forms - membrane endoglin (Eng) and soluble endoglin (sEng). Our previous experiments showed that stimulation of endothelial cells with high glucose resulted in increased levels of Eng and cell adhesion molecules, as well as increased adhesion and transmigration of monocytes through endothelial monolayer. We hypothesized that similar activation of Eng, endothelial dysfunction, and adhesion/transmigration markers could be detected in human coronary endothelial cells from diabetic patients (D-HCAEC). We aimed to evaluate the impact of hyperglycemia on Eng expression and function (adhesion/transmigration of monocytes) with respect to endothelial dysfunction and inflammation by comparing HCAEC and D-HCAEC.

Methods: HCAEC and D-HCAEC were cultured in EGM-2 media with appropriate supplements and 10% FBS. Western Blotting, ELISA, and flow cytometry were used for protein analysis of Eng, sEng, and markers of endothelial dysfunction/inflammation. For functional analysis (monocytes adhesion to endothelial cells and transmigration via endothelial cells), THP-1 monocytes were used.

Results: We showed increased levels of sEng, increased expression of Eng, inflammatory markers (VCAM-1 and ICAM-1), as well as adhesion and transmigration of THP-1 monocytes in D-HCAEC compared to HCAEC.

Conclusions: These results suggest that the presence of type II diabetes mellitus induces a proinflammatory phenotype and increases both membrane and soluble endoglin levels in endothelial cells suggesting the role of Eng in this disease, which will be further explored in prospective studies. Supported by GAUK 288322 and SVV 260549.

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015 / #589

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

INTERPLAY BETWEEN DNA METHYLATION AND METABOLISM: IMPLICATIONS IN PATHOGENESIS OF VASCULAR DISEASES

POSTER ON BOARD: AS01.01 ENDOTHELIAL CELL FUNCTION AND BIOLOGY

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Background and Aims: Atherosclerosis is a multi-genic and complex disorder associated with epigenetic and metabolic changes in cellular components of vessel wall such as endothelial cells (ECs) and vascular smooth muscle cells. ECs are physiologically quiescent and pathological stimuli during atherosclerosis (inflammation, high glucose) activate these cells causing vascular dysfunction. In the present study, we aim to address the influence of a) high glucose on DNA methylation and b) overexpression of DNMT isoforms on endothelial metabolism and functions.

Methods: In ECs immunoblotting was performed to assess the influence of high glucose on DNA methyltransferase isoforms. Global DNA methylation was measured by HPLC. ECs were overexpressed with DNMT isoforms using lentivirus. Cell cycle and angiogenesis assays were performed by flow cytometry and 3D spheroid models respectively. DNMT1 expression in aortic tissues of high fat diet (HFD) mice was quantified using immunofluorescence. Metabolic reprogramming in DNMT overexpressing ECs was assessed using untargeted LC-MS/MS followed by bioinformatic analysis.

Results: We observed high glucose induced significant (four-fold) increase in levels of the DNMT isoforms which was associated with elevation in DNA synthesis & global DNA hypermethylation. Functional analysis revealed high glucose and overexpression of DNMT isoforms induces cell proliferation and angiogenesis which was inhibited by the inclusion of 5-azacytidine. Aortal ECs exhibited increased levels of DNMT1 in HFD fed mouse models. Interestingly, we observed overexpression of DNMT1 and high glucose led to significant metabolic reprogramming in ECs associated with elevated nucleotide biosynthesis pathway intermediates.

Conclusions: Our data indicates high glucose breaks quiescence and activates ECs by DNMT1 dependent metabolic reprogramming.

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016 / #682

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.02 Smooth muscle cell biology*

FUROXANS, THANKS TO THEIR DUAL ACTIVITY, MAY AMELIORATE DIFFERENT ASPECTS OF ATHEROSCLEROSIS: AN IN VITRO STUDY ON SMOOTH MUSCLE CELLS

POSTER ON BOARD: AS01.02 SMOOTH MUSCLE CELL BIOLOGY

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Background and Aims: Atherosclerosis is a multifactorial disease in which NO unbalance and smooth muscle cell (SMC) proliferation play pivotal roles. To find a new pharmacological approach, we synthesized furoxans, which release NO in a controlled fashion and we tested their ability in inhibiting SMC proliferation, together with the comprehension of their mechanism of action.

Methods: We measured SMC proliferation by cell counting (Coulter Counter) after 72 hours of incubation or by thymidine incorporation (20 hours). Proteomics was assessed by SILAC followed by MetaCore analysis or western blot techniques.

Results: We demonstrated that furoxans inhibit SMC growth and vasodilate rat aorta rings, albeit with different potency. To comprehend their antiproliferative mechanism, after blocking the position 4 of their ring (phenyl), we found that their inhibitory potency paralleled with the electron-attractor capacity of the group in 3. Extending the study to related furoxans (groups in 3 and 4 interchanged) and furazans (analogues without ring-opening capacity, unable to release NO), we found that 4-Ph-3-R furoxans were the most potent inhibitors of proliferation, followed by 3-Ph-4-R furoxans. Furazans were not effective, documenting that the ring opening is essential for growth inhibition. We also demonstrated that NO is not the culprit of furoxans' effects on SMC proliferation. Finally, proteomics assessed that specific proteins (12) and networks involved in cell homeostasis (e.g. SUMO1, BANF1) are modulated by furoxans, probably by interaction with adducts generated by their ring opening.

Conclusions: Altogether, furoxans' pharmacological flexibility makes them eligible to be tested in animal models of atherosclerosis to assess their efficacy as antiatherosclerotic molecules.

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017 / #310

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.02 Smooth muscle cell biology*

INTERFERON GAMMA REPROGRAMS GLUTAMINE METABOLIC PATHWAYS IN HUMAN AORTIC SMOOTH MUSCLE CELLS

POSTER ON BOARD: AS01.02 SMOOTH MUSCLE CELL BIOLOGY

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Background and Aims: Cells within atherosclerotic lesions have a higher glutamine demand than cells in healthy vessel although glutaminase, the enzyme converting glutamine to glutamate, is significantly downregulated in human carotid lesions. This may suggest rewiring of glutamine metabolic pathways in atherosclerotic lesions, caused by infiltrating immune cells and or their cytokines. Here we aimed at exploring the enzymes and transporters involved in glutamine metabolism in human carotid atherosclerotic tissues and aortic smooth muscle cells (hAoSMCs) exposed to interferon gamma.

Methods: Protein and mRNA from interferon gamma-treated hAoSMCs were subjected to Western blot or qRT-PCR for quantification of enzymes and transporters involved in glutamine metabolism. H2DCFDA probe was utilized for detection of intracellular reactive oxygen species (ROS) using flow cytometry. The expression of these enzymes and transporters was also evaluated in human carotid lesions (GEO accession: GSE43292).

Results: Interferon-treated hAoSMCs display a significantly lower expression of glutaminase followed by an increase in the expression of glutamine transporters, glutamine synthetase and glutamine-fructose-6-phosphate transaminase-1 (GFPT1). The level of ROS and the expression of enzymes involved in *de novo* synthesis of glutathione are elevated in interferon-treated cells. A similar expression pattern for these genes, expect for GFPT1, is also evident in human carotid lesions where glutaminase mRNA shows a strong positive correlation with SMC markers and a strong negative correlation with macrophage markers.

Conclusions: Glutamine metabolism is disrupted in human carotid lesions and interferon gamma alters glutamine metabolism in hAoSMCs, which may favor the production of UDP-GlcNAc and reactive oxygen species.

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018 / #583

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.02 Smooth muscle cell biology*

THE ROLE OF THE MICRO RNA MIR-92B-3P IN VASCULAR SENESCENCE

POSTER ON BOARD: AS01.02 SMOOTH MUSCLE CELL BIOLOGY

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Background and Aims: Smooth muscle cells (SMC) are of central importance to vascular homeostasis and the development of vascular remodelling. They influence pathological processes induced by vascular aging and senescence like atherosclerosis. Here, we identified miR-92b-3p as a robustly regulated miR in senescent SMC *in vitro* and *in vivo*.

Methods: We used vascular smooth muscle cells (VSMC) and human umbilical vein endothelial cells (HUVECS) to assess the effect of miR-92b-3p on vasculature in vitro. Methods included expression analysis of miR-92b-3, multiple functional assays to assess proliferation, apoptosis and migration and identification of possible targets on mRNA and protein level.

Results: We demonstrate that contrasting the expression in HUVECS miR-92b-3p expression levels in SMCs were downregulated during replicative senescence. Similar changes of miRNA 92b-3p expression were observed in murine ECs and VSMCs. Elevating miR-92b-3p levels in senescent and non-senescent VSMCs, using miR-92b-3p mimics enhanced the migrational capacity in these cells. Degradation of the reduced expression levels of miR-92b-3p in VSMCs via specific antimiRs resulted in reduction of the proliferative and migrational capacities of senescent and non-senescent SMCs. Apoptosis was increased following knock down of miR-92b-3p. The determined target genes were confirmed to be altered in their expression following over expression or knock down respectively.

Conclusions: MiR-92b-3p differs in its expression in aging and in different vascular cell types. It is indicated that miR-92b-3p regulates senescence progression in SMC, since reconstitution of miR-92b-3p levels in SMC partially reduces senescence-induced functional impairments. The miR-92b-3p might be a target for future therapeutic options influencing vascular aging and subsequent pathologies.

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019 / #560

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.02 Smooth muscle cell biology*

IN AORTIC VASCULAR SMOOTH MUSCLE CELLS HIGH GLUCOSE INCREASES PCSK9 EXPRESSION: ROLE OF PCSK9 INHIBITORS

POSTER ON BOARD: AS01.02 SMOOTH MUSCLE CELL BIOLOGY

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Background and Aims: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is implicated in the regulation of cholesterol homeostasis and also in processes associated with atherosclerosis including vascular smooth muscle cells (VSMC) dysfunction. Aim of this study was to evaluate in VSMC under high glucose (HG): (i)PCSK9 expression; (ii)the role of PCSK9 on phosphatidylinositol 3-kinase (PI3-K) and mitogen-activated protein kinase (MAPK) pathways activation; (iii)the role of PCSK9 inhibition.

Methods: In cultured rat aortic VSMC incubated for 30 hours with 25mmol/L D-Glucose we measured: PCSK9 expression (by Western Blot), with or without PCSK9 inhibitors, specifically represented by the anti-PCSK9 monoclonal antibodies Alirocumab or Evolocumab (40 mug/mL) or the synthetic PCSK9-binding peptide PEP 2-8 (10 mumol/L)) and the effects of PCSK9 inhibitors on the HG-induced increase of pAKT and pERK-1/2.

Results: HG increased PCSK9 expression (n=6, $p<0.0001$) and this effect was reduced by Alirocumab (n=6, $p<0.001$), Evolocumab (n=6, $p<0.005$), and PEP 2-8 (n=6, $p<0.01$). The HG-induced increase of pAKT and pERK-1/2 levels were significantly attenuated by Alirocumab (n=5, $p<0.002$ and $p<0.005$ respectively), Evolocumab (n=5, $p<0.001$ and $p<0.0001$, respectively), and PEP 2-8 (n=5, $p<0.03$ and $p<0.001$, respectively).

Conclusions: In aortic VSMC, HG increases PCSK9 expression. HG effects on PCSK9 expression are reduced by monoclonal antibodies or PEP 2-8, indicating that PCSK9 can sustain its expression and secretion in an autocrine manner. Both PI3K and MAPK are involved in this process. Collectively, these findings suggest a new mechanism by which HG may impair vascular function and a positive effect exerted by Alirocumab and Evolocumab by opposing to the autocrine loop of PCSK9.

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020 / #1041

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.02 Smooth muscle cell biology*

THE ROLE OF PRDM16 DURING VASCULAR SMOOTH MUSCLE PHENOTYPIC SWITCHING IN ATHEROSCLEROSIS

POSTER ON BOARD: AS01.02 SMOOTH MUSCLE CELL BIOLOGY

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Background and Aims: Smooth muscle cell (SMC) phenotypic switching heavily underlies the development, progression, and outcome of atherosclerosis. During atherogenesis, SMCs dedifferentiate from their canonical, contractile state into “modulated” states, where SMCs take on e.g. fibrotic/synthetic, immunogenic, and osteogenic phenotypes. Dedifferentiated SMCs are associated with both favourable and deleterious effects on atherosclerosis progression and outcome. The mechanisms behind SMC-phenotypic switching and how SMC modulation impacts atherosclerosis remains unclear. PRDM16 is a powerful transcriptional activator and repressor which regulates many cellular processes, such as the activation of the thermogenic gene program during brown adipose tissue development. PRDM16 is extremely highly expressed in SMCs and has recently been identified as a major CAD risk allele. Therefore, we set out to characterise the role of PRDM16 in SMC phenotypic switching during atherogenesis.

Methods: Histology and analysis of publicly available scRNAseq datasets was used to determine the expression pattern of *PRDM16* during the progression of atherosclerosis. Atherosclerosis was induced by AAV8-PCSK9 D377Y injections and 12 weeks of western diet in SMC-specific PRDM16-KO mice. The effect of PRDM16 on SMC phenotypic switching was assessed *in vitro* using Lonza human aortic SMCs.

Results: *PRDM16* expression is inversely correlated with SMC modulation during atherosclerosis. Similarly, PRDM16 protein levels decrease in atherosclerotic lesions. In vitro, PRDM16 decreases SMC migration and the fibrotic response to TGFß. The *in vivo* results are not known yet.

Conclusions: We nominate PRDM16 as a promising regulator of SMC phenotypic switching during atherosclerosis.

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021 / #202

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

LOSS OF ARTERIAL RESIDENT LYVE-1 EXPRESSING MACROPHAGES EXACERBATES ATHEROSCLEROSIS

POSTER ON BOARD: AS01.03 MACROPHAGES IN LIPID METABOLISM AND ATHEROSCLEROSIS

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Background and Aims: Atherosclerosis is a chronic inflammatory disease characterized by plaque formation and lipid accumulation in the arteries, where the activation of immune cells including macrophages can contribute to pro-atherogenic environment and drive atherosclerosis progression. Tissue resident macrophages reside in most organs and act constitutively as guardians of tissue homeostasis. Distinct from pro-inflammatory macrophages, adventitial resident macrophages expressing Lymphatic Vessel Endothelial Hyaluronan Receptor-1 (LYVE-1) play vital role in maintaining arterial homeostasis and function. However, their contribution in atherosclerosis remains elusive. This study aimed to explore the role of arterial resident LYVE-1^{+} macrophages in atherosclerosis.

Methods: We examined LYVE-1^{+} macrophages distribution in human atherosclerotic aorta and Apolipoprotein E deficient (*Apoe*$^{-/-}$) mice. To study the impact of LYVE-1^{+} macrophages in atherosclerosis, we developed atherosclerotic *Apoe*$^{-/-}$ mice lacking LYVE-1^{+} macrophages (*Apoe*$^{-/-}$*Lyve1*$^{cre/wt}$*Csf1r*$^{flox/flox}$).

Results: LYVE-1^{+} macrophages were abrogated in human atherosclerotic aorta. In *Apoe*$^{-/-}$ mice, incremental loss of LYVE-1^{+} macrophages was observed as atherosclerosis worsened, particularly in adventitia of plaque regions, and it correlated with increased atherosclerotic plaque extent. Treatment of cholesterol-lowering ezetimibe in these mice to attenuate atherogenesis significantly increased adventitial LYVE-1^{+} macrophage number. *Apoe*$^{-/-}$*Lyve1*$^{cre/wt}$*Csf1r*$^{flox/flox}$ mice developed larger atherosclerotic plaques in aortic root, while plasma cholesterol and monocyte levels remained comparable to control *Apoe*$^{-/-}$ *Csf1r*$^{flox/flox}$ mice. Plaques in these mice were more vulnerable due to increased necrotic core area and lesion cap CD68 content. Contrastingly, plaque lipid and collagen content remained unchanged.

Conclusions: Arterial resident LYVE-1 expressing macrophages are protective against atherosclerosis progression and associated vascular remodelling. They may be targeted for anti-atherogenic therapeutic strategies.

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022 / #115

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

THE IN VITRO EFFECT OF MYELOPEROXIDASE MODIFIED LDL ON THP-1 DERIVED MACROPHAGES.

POSTER ON BOARD: AS01.03 MACROPHAGES IN LIPID METABOLISM AND ATHEROSCLEROSIS

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Background and Aims: Atherosclerosis is a chronic inflammatory disorder characterized by the accumulation of lipids and inflammatory cells inside the intima of arteries. Macrophages (Mφs) play a crucial role in the development of the disease by engulfing modified LDL particles and forming foam cells which constitute the hallmark of atherosclerosis. Many studies suggest that myeloperoxidase oxidized LDL (Mox-LDL) is an important patho-physiological model for LDL modification *in vivo*. Classically activated (M1) and alternatively activated (M2) Mφs are both implicated in the process of atherogenesis. Since little is known about the effects of Mox-LDL on Mφ biology and pathobiology, our study aimed at evaluating the *in vitro* effects of Mox-LDL at this level through making use of the well-established model of human THP-1-derived Mφs.

Methods: THP-1 monocytes were differentiated into M0-Mφs by treatment with phorbol12-myristate-13-acetate. Resting M0-Mφs were polarized toward M1- and M2-Mφs, then M0-, M1- and M2-Mφs were all treated with physiological concentrations of Mox-LDL in order to assess the effect of Mox-LDL treatment on Mφ polarization and repolarization as well as on the level of ROS generation and cholesterol uptake.

Results: Treatment of M0-Mφs with a physiological concentration of Mox-LDL had no significant effects at the level of their polarization. However, treatment of M1-Mφs with Mox-LDL resulted in a significant reduction in their IL-10 cytokine secretion with no significant effects at the level of ROS generation and cholesterol uptake.

Conclusions: Our results point to a potential role of Mox-LDL in increasing the pro-inflammatory state in Mφs through reducing the release of the anti-inflammatory cytokine IL-10.

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023 / #6

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

EFFECT OF ANTI-PECAM-1 VECTORIZED NANOCAPSULES CONTAINING DOCOSAHEXAENOIC ACID ON MACROPHAGES POLARIZATION

POSTER ON BOARD: AS01.03 MACROPHAGES IN LIPID METABOLISM AND ATHEROSCLEROSIS

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Background and Aims: The presence of pro-resolving M2 macrophages instead of pro-inflammatory M1 macrophages has been associated to wound healing and more stable atherosclerotic plaques. Omega 3 fatty acids, such as docosahexanoic acid (DHA; C22:6 n3) could promote the switch of M1 to M2 macrophages. Thus, our objective was firstly to evaluate the toxicity of lipid-core nanocapsules containing DHA (LNC-DHA), multi-wall nanocapsules containing DHA (MLNC-DHA) and the surface-functionalized (anti-PECAM-1) metal-complex multi-wall nanocapsules containing DHA (MLNC-DHA-a1) in HUVEC, U937 and RAW 264.7 cells; and after to determine the effect of these nanocapsules on macrophages uptake and polarization.

Methods: Cells were exposed to three concentrations: $0.14x10^{11}$, $0.75\ x10^{11}$ and $1.40x10^{11}$ nanocapsules/mL during 24, 48 and 72h, being the cell viability determined by flow cytometry. The uptake of MLNC-DHA and MLNC-DHA-a1 nanocapsules by RAW 264.7 macrophages and their polarization were determined at $0.7\ 5x10^{11}$ nanocapsules/mL.

Results: Cell viability was not changed according to the type of cells, suggesting absence of toxicity in the three concentrations evaluated in this study. It was observed that both MLNC-DHA and MLNC-DHA-a1 nanocapsules decreased the concentration of Tumor necrosis factor-alpha (TNFα) ($p=0.02$) compared with non-treated group (NT), with no changes in Interleukin-10 (IL-10) ($p=0.29$). The nanocapsules also showed an increase of M2 ($F4/80^+$ CD206) phenotype % ($p<0.01$) without M1 ($F4/80^+$ CD80) alteration ($p=0.25$).

Conclusions: This result suggests that DHA richer algae oil, as part of the lipid core of the nanocapsules, did not reduce cells viability and improved the macrophage phenotype, being a potential therapy to heal or stabilize atherosclerotic plaques.

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024 / #136

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

IDENTIFICATION OF A POTENTIAL MICRORNA AS AN IMPORTANT REGULATOR IN HHCY-RELATED ATHEROSCLEROSIS

POSTER ON BOARD: AS01.03 MACROPHAGES IN LIPID METABOLISM AND ATHEROSCLEROSIS

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Background and Aims: Increased serum levels of homocysteine (Hcy) are a risk factor for cardiovascular diseases, including atherosclerosis. However, the precise mechanisms by which Hcy contributes to this condition remain elusive. microRNAs influence the expression of several genes related to atherosclerosis. Interestingly, miR-30d-5p was found to be up-regulated in the plasma of patients with hyperhomocysteinemia (HHcy) and venous thrombosis. Moreover, *TIMP3* gene was a predicted target for miR-30d-5p. Thus, in this study, we aimed to determine whether miR-30d-5p plays a role in the pathophysiology of HHcy-induced atherosclerosis through the regulation of *TIMP3*.

Methods: Mouse peritoneal macrophages (MPM) were obtained from C57BL/6J mice and treated with different concentrations of Hcy for 24h to evaluate gene expression. Transfection experiments and dual luciferase reporter assays were performed. The *in vivo* mouse model was developed by adding 0.9 g/L of DL-Hcy to the drinking water of *ApoE*$^{-/-}$ mice, and the atherosclerotic lesion was analyzed by histological and immunohistochemical techniques.

Results: We demonstrated that miR-30d-5p was up-regulated in MPM treated with 50µM of Hcy, whereas *TIMP3* expression was significantly reduced. We identified *TIMP3* as a direct target of miR-30d-5p by repressing the activity of the 3'UTR-*TIMP3* reporter construct. Moreover, the specific inhibition of endogenous miR-30d-5p in both human and mouse macrophages was found to up-regulate the expression of *TIMP3*. The *in vivo* mice models of HHcy-induced atherosclerosis showed higher aortic lesion size when compared with control mice.

Conclusions: These results provide evidence that miR-30d-5p downregulates *TIMP3* and increases the activity of MMPs, representing a potential mechanism by which Hcy influences atherogenicity.

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025 / #765

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

EZH2 INHIBITION REDUCES MACROPHAGE INFLAMMATORY RESPONSES IN ATHEROSCLEROSIS

POSTER ON BOARD: AS01.03 MACROPHAGES IN LIPID METABOLISM AND ATHEROSCLEROSIS

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Background and Aims: Epigenetic processes are essential modulators of macrophage inflammatory responses. We postulate that interference in the epigenetic machinery of macrophages might offer novel approaches to combat atherosclerosis. Here, we investigate the repressive histone modification H3K27Me3 deposited by the polycomb repressor complex 2 (PRC2) with its catalytic component EZH2. We studied the therapeutic potential of macrophage EZH2 inhibition in the context of atherosclerosis.

Methods: Human monocyte-derived macrophages and murine peritoneal and bone-marrow derived macrophages were treated with EZH2-specific inhibitor GSK126 and subsequently activated with LPS to mimic TLR4-inflammatory responses. The impact of GSK126 on macrophage differentiation and activation compared to vehicle (DMSO) was assessed by RNA-seq, flow cytometry, western blot, ELISA, RT-qPCR, and ChIP-seq.

Results: GSK126 treatment lowered global H3K27Me3 levels without altering macrophage viability and differentiation, showing effective EZH2 inhibition. RNA-seq revealed that more than one-third of the LPS-induced genes were significantly downregulated by GSK126 treatment. Subsequent pathway analysis identified cytokine and interferon signaling, co-stimulation, and cell migration as the top down-regulated pathways (padj<0.05). Indeed, we confirmed that gene expression and cytokine secretion of the inflammatory mediators IL-6, IL-12, and TNF were reduced. Furthermore, membrane marker expression of co-stimulatory CD40, CD80, and CD86 were significantly decreased.

Conclusions: Overall, we show that EZH2 inhibition reduces inflammatory responses in human and murine macrophages. We are currently analyzing ChIP-seq data to identify direct targets of EZH2. Furthermore, we are performing *ex vivo* experiments on human endarterectomy plaques and an *in vivo* murine atherosclerosis study to assess the therapeutic potential of EZH2 inhibition on atherosclerosis development and progression.

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026 / #1237

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE EFFECT OF STATIN MONOTHERAPY OR ADD-ON EZETIMIBE TREATMENT ON NETOSIS IN DYSLIPIDEMIC PATIENTS

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: To investigate the effects of statin monotherapy or add-on ezetimibe treatment on netosis biomarkers, in particular plasma myeloperoxidase-DNA (MPO-DNA) complexes.

Methods: This was a prospective study conducted in the outpatient Metabolism and Lipid Disorders clinic of the University Hospital of Ioannina in collaboration with the Atherothrombosis Research Centre of the University of Ioannina. The primary end point of this analysis was the effect of statin monotherapy (Statin group) and add-on ezetimibe in patients already taking statin therapy (Ezetimibe group), on plasma MPO-DNA complexes measured by a specific sandwich-ELISA technique at baseline visit, and after 3 months of each treatment.

Results: We included 19 dyslipidemic patients, 9 males and 10 females with a mean age of 56 years, the majority of whom had moderate to high 10-year cardiovascular risk. Of those, n=10 subjects received treatment with moderate to high intensity statins alone for at least 3 months, and n=9 subjects received add-on ezetimibe to already stable statin therapy. Baseline characteristics did not significantly differ between the 2 groups nor did baseline levels of plasma MPO-DNA complexes. Statin treatment increased, albeit not significantly (by 32%), the plasma MPO-DNA complexes, while add-on ezetimibe induced a significant (by 53.5%) increase in these complexes ($p<0.05$ vs baseline) (Table 1). Changes in lipid parameters were not significantly correlated with alterations in MPO-DNA levels, during the 3-month

follow-up in both groups.

Table 1 The effect of statins and add-on ezetimibe on plasma MPO-DNA complexes and lipid profile during 3-month follow-up

	BASELINE VISIT	AFTER 3 MONTHS	%CHANGE
MPO-DNA complexes			
Statin group	0.08506 (0.05380-0.15840)	0.11265 (0.0831-0.21790)	32.0
Ezetimibe group	0.08190 (0.05710-0.11040)	0.12570 (0.08590-0.22530)	53.5*
TCHOL (mg/dL)			
Statin group	260 (212-337)	178 (134-242)	-31.6*
Ezetimibe group	171 (93-224)	150 (122-179)	-12.4
TGs (mg/dL)			
Statin group	125 (57-189)	88 (45-137)	-29.2*
Ezetimibe group	111 (44-154)	99 (49-158)	-10.1
HDL-C (mg/dL)			
Statin group	59 (38-76)	61 (37-86)	4.4
Ezetimibe group	51 (24-89)	53 (38-88)	4.1
LDL-C (mg/dL)			
Statin group	177 (134-250)	98 (76-129)	-44.4*
Ezetimibe group	98 (38-151)	77 (43-102)	-21.6*
non-HDL-C (mg/dL)			
Statin group	202 (151-273)	117 (92-156)	-42.0*
Ezetimibe group	120 (69-176)	97(72-122)	-19.5*

*p<0.05 for the comparison within each group

MPO-DNA: plasma myeloperoxidase-DNA, TCHOL: total cholesterol, TGs: triglycerides, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol

Conclusions: Add-on ezetimibe significantly increases MPO-DNA complexes independently of the effects in lipid parameters. Studies with a larger sample size and additional netosis biomarkers are needed.

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027 / #702

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

MYELOID DERIVED SUPPRESSOR CELLS: A NEW TARGET TO SUPPRESS INFLAMMATION IN ATHEROSCLEROSIS

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: In mature atherosclerotic lesions, failure of macrophage resolution mechanisms and increased immune responses by T-cells drive inflammation. Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature cells that, like macrophages, originate in the bone marrow (BM). During disease, MDSCs expand in BM and migrate to inflamed tissues and peripheral lymphoid organs (spleen) where they act as potent immunosuppressors. We previously showed that TNF-related apoptosis inducing-ligand (TRAIL)-expressing macrophages protect against atherosclerosis. We aimed to identify whether TRAIL could also influence MDSC-mediated inflammation suppression in atherosclerosis.

Methods: *Trail*$^{-/-}$*Apoe*$^{-/-}$ *and Apoe*$^{-/-}$mice were placed on a high fat diet for 12w. Atherosclerosis and MDSC populations were assesssed. To measure immunosuppressive activity, MDSC subsets were isolated from BM and co-cultured with CD3/CD28-activated T-cells. Finally TRAIL expression and MDSC content were assessed in carotid plaque from asymptomatic vs symptomatic patients.

Results: Total MDSC numbers were reduced in blood and spleen, ~50%, but increased 3-fold in aortae. This increase comprised predominantly of the PMN-MDSC subset, morphologically like neutrophils, suppressing T-cells by ROS. No differences in the M-MDSC subset (like monocytes; suppress T-cell function via NO) were found. Immunosuppression assays found TRAIL+ve PMN- and M-MDSCs reduced T-cell proliferation ~40% and ~30% compared to TRAIL-ve MDSC subsets. Indeed, TRAIL expression was significantly suppressed in symptomatic vs. asymptomatic carotid plaque, and in part, associating with increased MDSC content.

Conclusions: These findings indicate that TRAIL suppression promotes MDSC production but impairs their immunosuppressive capabilities. Because current treatments do not adequately address immune mechanisms driving atherogenesis, increasing TRAIL levels in MDSC may protect against atherosclerosis.

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028 / #1335

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR – ALPHA (PPARA) AND EXPRESSION OF CD36 RECEPTOR SCAVENGER ON CIRCULATING CELLS AS BIOMARKERS OF ATHEROSCLEROSIS

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Peroxisome Proliferator-Activated Receptor – Alpha (PPARα), member of the nuclear receptor superfamily of transcription factors, is critically involved in the management of lipid metabolism during homeostasis or inflammatory stresses in various cell types and represents one of the therapeutic targets in metabolic syndrome (MS).

Methods: This study included 1530 adult patients recruited under informed voluntary consent: MS group (389 patients) and the control group – non-MS (1141 subjects). Common clinical and laboratory parameters targeted in MS evaluation were determined for all the studied cases. We studied the expression of PPARα receptors, as a protective element, simultaneously with the expression of the scavenger receptor CD36.

Results: The fluorescence staining for PPARα were significantly dimmer when comparing the cellular expression in eosinophils ($p<0.05$) of MS group versus the control group. In patients with MS, the relative expression of PPARα in eosinophils was inversely associated with CD36 receptor expression, proving the anti-inflammatory role of PPARα receptors at the endothelial level. Furthermore, we noticed an increase plasma fibrinogen concentration and the high number of blood eosinophils in the MS group compared to the control group.

Conclusions: This study is the first to show that circulating eosinophils display significantly reduced PPARα protein expression in MS patients. The differences in key molecule expression in circulating leukocytes (like PPAR species, CD36 and other) might be evocatory for the endothelial dysfunction and obesity and might be of use in the therapeutic decision.

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029 / #605

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

DYSLIPIDEMIA ALTERS THE BINDING SPECIFICITY OF SECRETED IGM ANTIBODIES IN ATHEROSCLEROTIC MICE.

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: It is well established that both hypercholesterolemia and immunity contribute to atherosclerosis. Importantly, IgM antibodies have been shown protective in murine atherosclerosis, and epidemiological studies in humans demonstrate a negative correlation between IgM levels and cardiovascular events. However, the impact of hyperlipidemia and atherogenesis on the IgM repertoire is unknown.

Methods: We fed LDLR^{KO} mice a high-cholesterol diet or a chow diet for 13 or 18 weeks to investigate the impact of dyslipidemia on the IgM repertoire *in vivo* combining two complementary approaches. 1. We sequenced the variable regions of splenic and bone marrow resident IgM+ plasma cells (IgVH), which are mainly responsible for the IgM present in the circulation. 2. We analyzed the binding pattern of circulating and plaque derived IgM using a newly developed peptide array.

Results: We found that hyperlipidemic mice exhibit increased number of IgM+ antibody secreting cells in both spleen and bone marrow. B cell receptor sequencing of sorted IgM+ plasma cells in these tissues revealed differences in VJ usage and an increased occurrence of mutations, consistent with an alteration of IgM specificities in circulation. Furthermore, plasma IgM from hyperlipidemic mice displayed different binding patterns in the peptide array compared to IgM from control mice, consistent with a global change in IgM reactivity. Finally, we found that IgM reactivities defining the IgM signature of hyperlipidemic mice are also present in IgM eluted from plaques.

Conclusions: Hyperlipidemia induces alterations in the IgM repertoire of the plasma cell and humoral compartment that are associated with the specificity of plaque-associated IgM.

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030 / #998

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

EFFECT OF OMEGA 3 FATTY ACIDS SUPPLEMENTATION USING SURFACE-FUNCTIONALIZED NANOCAPSULES ON POST-RESOLUTION INFLAMMATION

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Several diseases can be caused by a maladapted homeostasis in the post-resolution phase of the inflammatory cycle. Omega 3 fatty acids, such as docosahexaenoic acid (DHA) have been consumed to control chronic inflammation. Thus, our objective was to evaluate an anti-PECAM-1 surface functionalized nanocapsule containing DHA as a strategy to improve the post-resolution phase.

Methods: Mice fed a Western diet was applied as model to promote chronic inflammation. After 24 weeks, the diet was replaced by a regular diet and the animals were fed for 8 weeks without supplementation (CONT group), supplemented with algae oil by gavage (DHA-D), treated once a week with a non-functionalized nanocapsule (LNC-MCT) and treated once a week with the surface-functionalized (anti-PECAM-1) metal-complex multi-wall nanocapsule containing algae oil in the lipid core (MLNC-DHA-a1).

Results: After 8 weeks of the Western diet replacement, excepted for IL1β, the cytokines measured in plasma and liver did not change when compared with a BASELINE group. No difference was observed among the groups the four groups towards body weight, showing that all interventions were well tolerated. However, compared with CONT group, MLNC-DHA-a1 increased Interleukin 6 , Interleukin 1β and Interleukin 10 in plasma.

Conclusions: It can be concluded that 5.36 x 10^8 MLNC-DHA-a1 nanocapsules containing 12 µL algae oil/mL were well tolerated, but strongly increased pro-inflammatory cytokines in plasma. In next studies, It will be important to identify the factors associated to the immune response, and also if this effect is necessarily negative in terms of infection's vulnerability.

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032 / #561

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

TIM-4 DEFICIENCY AGGRAVATES ATHEROSCLEROSIS

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: In advanced stages of atherosclerosis, the clearance of apoptotic cells is impaired, promoting the formation of necrotic cores and inflammatory responses that contribute to atherosclerosis progression. T-cell immunoglobulin and mucin domain protein-4 (TIM-4), present on macrophages, dendritic cells and B-cells, binds to phosphatidylserine on apoptotic cells and plays a critical role in apoptotic cell clearance. Moreover, TIM-4 regulates the number of phosphatidylserine-expressing activated T-cells. Given the immunosuppressive potency of TIM-4, we investigated the role of TIM-4 in atherosclerosis using TIM-4 deficient mice.

Methods: TIM-4$^{-/-}$ mice and control WT (C57/Bl6) mice received a single i.v. injection of rAAV8-D377Y-mPCSK9 and were fed a Western-type diet for 14 weeks.

Results: At sacrifice, no difference in body weight, cholesterol levels or plasma PCSK9 levels was observed. TIM-4 deficiency increased atherosclerotic lesion size with 3.7-fold in the aortic arch (1.67±0.28x10^{6}µm vs. 0.45±0.13 x10^{6}µm, P<0.001) and with 33% in the aortic root (6.19±0.24x10^{5}µm vs 4.66±0.38x10^{5}µm, P<0.01). Concomitant with impaired clearance of apoptotic cells, atherosclerotic lesions of TIM-4$^{-/-}$ mice contained significantly larger necrotic cores. Moreover, we found increased percentages of CD4$^+$ T-cells and activated CD4$^+$CD69$^+$ T-cells locally in the atherosclerotic lesions and in the circulation of TIM-4$^{-/-}$ mice compared to WT mice. Following antigen (oxLDL) or TCR stimulation (anti-CD3/CD28), TIM-4$^{-/-}$ T-cells proliferated more vigorously than WT T-cells. In addition, we found increased percentages and absolute numbers of CD19$^+$ B-cells in TIM-4$^{-/-}$ mice, caused by an increase in pro-atherogenic B2-cells.

Conclusions: In conclusion, TIM-4 deficiency enhances atherosclerosis through impaired clearance of apoptotic cells and hyperactive immune cell responses.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

CARDIOVASCULAR DISEASE (CVD) AND COVID-19 INFECTION: A DEADLY SYNERGISM

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Acute coronary syndrome (ACS) is the leading cause of death and disability in the US and COVID-19, the third. Many COVID patients admitted to BUSM with acute respiratory distress also had CVD, which increases the likelihood of ACS during hospitalization. Heart fatty acid binding protein (H-FABP), is a small soluble intracellular molecule unique to cardiomyocytes. It has been validated as a clinical measure of cardiac injury in patients and will provide rapid and reliable detection of CVD, which is crucial for COVID patients since myocardial infarction can occur as early as 2 days after infection.

Methods: The concentration of H-FABP will be measured in the buffer of cardiomyocytes by ELISA to quantify membrane injury and reduction by natural therapeutics. We applied the Endotoxin lipopolysaccharide (LPS) to induce cell membrane damage in cultures of immortalized cardiomyocytes and stem cell-derived cardiac cell systems.

Results: ELISA assays showed instantaneous concentration-dependent leakage of H-FABP after injury and decreased leakage after treatment with resolvins. Acute and chronic challenges to LPS produced the same extent of injury followed by a decrease of ~50% by resolvin E1. The sensitivity of H-FABP was much higher than cardiac troponin, and its rapid detection in ACS patients will save lives.

Conclusions: Plasma H-FABP is a sensitive mechanistic biomarker for heart injuries that will acutely impair lung function. Our studies have optimized conditions for application to SARS-CoV-2 and newly emerging COVID variants. These quantitative in vitro studies will optimize treatment for individuals upon hospitalization, and guide therapeutics for the most effective patient care.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

DIFFERENCES IN THE PERIPHERAL IMMUNE CELL LANDSCAPE IN ATHEROSCLEROSIS – INSIGHTS FROM THE LURIC SINGLE CELL RNA-SEQUENCING STUDY (LURNA)

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Atherosclerosis and its clinical sequelae, myocardial infarction and stroke, represent the main causes of death worldwide. Although preclinical evidence has suggested the existence of a sustained inflammatory and immune response driving disease and complications, the extend of cellular alterations in human atherosclerosis remains enigmatic. Here, we employ single cell RNA-sequencing (scRNA-seq) on peripheral blood mononucleated cells in a well-defined cardiovascular risk cohort from the the LURIC trial to define changes in the immune cell landscape in atherosclerotic patients.

Methods: Of 3317 patients enrolled in the LURIC trial, we selected individuals with stable coronary-artery disease (CAD) (n=31) and healthy patients (no CAD) (n=16) by propensity score matching, adjusted for CRP, NT-proBNP, Troponin T, LDL-C, and Cystatin-C, in a case-control design. Individual scRNA-seq data sets were integrated and changes between healthy individuals and patients with CAD were evaluated on numeric and transcriptional levels.

Results: We identified several regulated leukocyte populations that were differentially regulated between both conditions. Interestingly, NK cells and small cell populations like Tregs (both >1.4-fold more), platelets (>10-fold more), stem cells (>3-fold more), and proliferating cells (>2-fold-more) were significantly increased in PBMCs from patients suffering from CAD. Pathway analyses of distinct clusters in patients with CAD revealed increased signaling for cellular exhaustion, response to stress, and leukocyte activation.

Conclusions: Employing scRNAseq, we demonstrate that atherosclerosis is associated with a profound change in the immune cell landscape even in the absence of measurable differences in inflammatory biomarkers. These findings propose the usage of scRNAseq for the discovery of outcome-relevant cellular biomarkers in the future.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

COMPOUND SCREENING IDENTIFIES NOVEL INHIBITORS OF MONOCYTE PYROPTOSIS AND INTERLEUKIN 1-BETA RELEASE

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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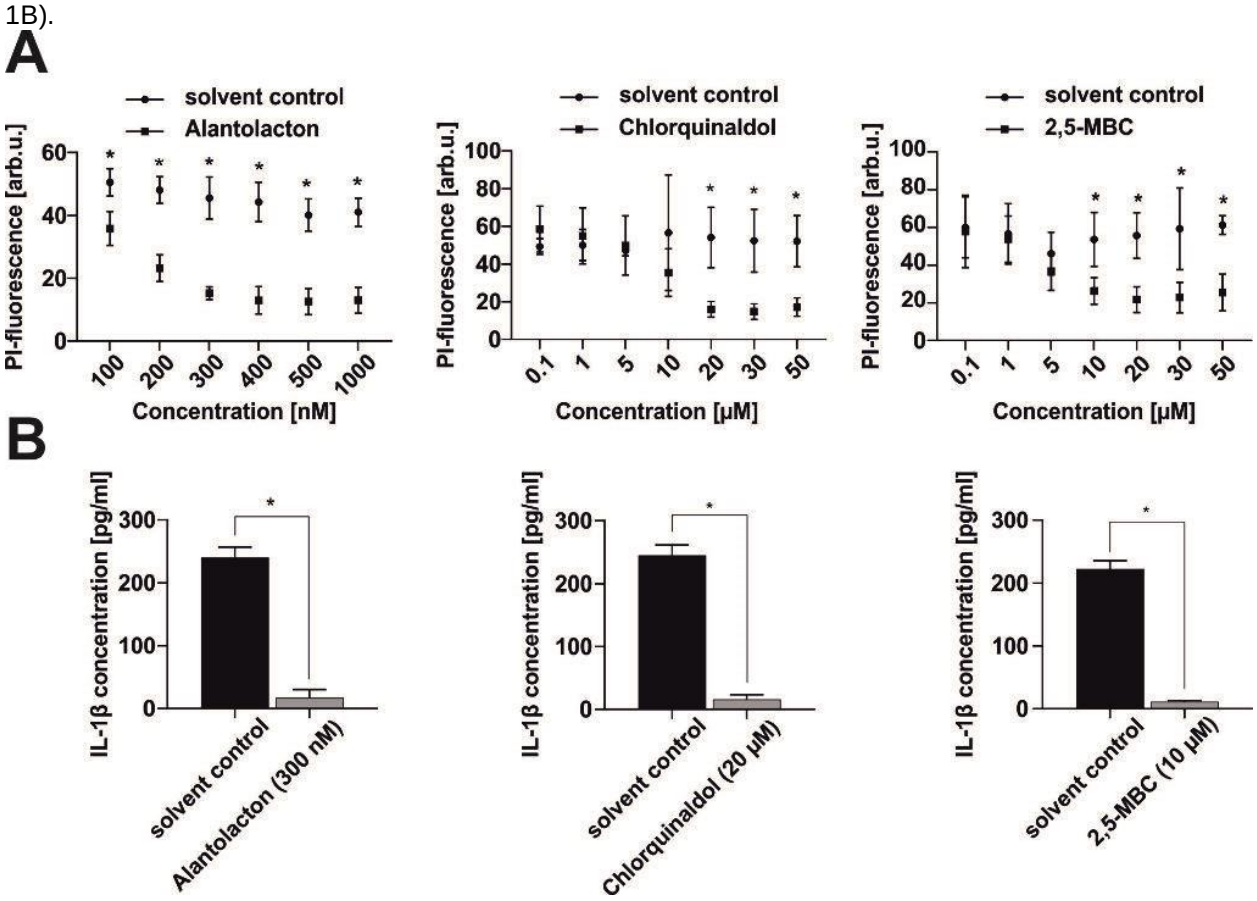
Background and Aims: Pyroptosis is an inflammatory cell death resulting in the maturation and release of inflammatory cytokines like Interleukin 1-ß. Pyroptosis contributes to sterile inflammatory pathologies like atherosclerosis, myocardial ischemia-reperfusion injury or diabetes. To date, no pharmacologic inhibitor of pyroptosis is available. By performing a compound screening for pyroptosis inhibitors, we aim to identify suitable targets for further characterization and potential drug development.

Methods: NLRP3-mediated pyroptosis was induced in THP1–ASC–GFP monocytes by lipopolysaccharide and nigericin treatment and quantified by propidium iodide staining. ASC expression was confirmed by fluorescence microscopy. Toxicity concerning the integrity of the cellular membrane was assessed by trypan blue staining. Effects on cell proliferation, viability, and chemosensitivity were measured by a WST1 assay. Interleukin-1 concentrations were quantified in cell supernatants, using an ELISA.

Results: Screening of approximately 6,280 drugs or drug-like compounds in the “Spectrum Collection” (Microsource) the “Bioactive Compound Library” (Selleckchem) revealed 22 potentially anti-pyroptotic substances. Of the identified compounds those already published as antipyroptotic or toxic as well as commercially unavailable compounds were discarded. Three compounds were proven ineffective after follow-up validation. Concentration curves of the remaining compounds revealed effective and non-toxic concentrations for alantolactone (300nM), chlorquinaldol (20µM), and 2,5-methoxybenzochinone (2,5-MBC; 10µM; Fig. 1A). Interleukin 1-ß release was strongly and significantly ($p<0.05$) inhibited by alantolactone (240pg/ml vs. 17pg/ml), chlorquinaldol (245pg/ml vs. 1 pg/ml) and 2,5-methoxybenzochinone (223pg/ml vs. 11pg/ml) (Fig.

1B).



Conclusions: Alantolactone, chlorquinaldol, and 2,5-methoxybenzochinone are inhibitors of pyroptosis and promising candidates for further characterization to pharmacologically target NLRP3-mediated inflammatory conditions such as atherosclerosis.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

EFFECT OF OMEGA-3 FATTY ACIDS, DOACS AND THEIR COMBINATION ON THE INFLAMMATORY STIMULATION OF ENDOTHELIAL CELLS, IN VITRO

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: A multitude of experimental and clinical data indicate the significant role of chronic inflammation in the pathophysiology of atherosclerosis. Omega-3 fatty acids exhibit pleiotropic effects, including anti-inflammatory and antiplatelet activities. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are commonly prescribed in patients with hypertriglyceridemia, often alongside Direct Oral Anticoagulants (DOACs). The present study aims to investigate the effect of the combination of omega-3 fatty acids and two DOACs on the inflammatory activation of Human Umbilical Vein Endothelial Cells (HUVECs), induced by Tumor Necrosis Factor-α (TNF-α).

Methods: HUVECs in culture were pre-incubated with various concentrations of EPA, DHA, Rivaroxaban, Dabigatran, or their vehicles for 10min, 37°C, 5%CO_2, followed by 0.5ng/ml TNF-α for 6h at 37°C, 5%CO_2. Intercellular Adhesion Molecule-1 (ICAM-1) membrane expression was determined by flow cytometry, using anti-CD54-PE.

Results: Omega-3 fatty acids inhibit ICAM-1 membrane expression in a dose dependent manner, with IC50 values of 157.04μM for EPA and 237.4μM for DHA. Rivaroxaban and Dabigatran displayed 20.3±5.4% and 16.3±4,3% maximal inhibitory activity at 10μM. The combinations of EPA at 100μM (38.67±5.2% inhibition) with Rivaroxaban and Dabigatran exhibit 30.47±14.3% and 20.66±10.2% inhibition, respectively. In addition, the combinations of DHA at 100μM (31.20±3.4% inhibition) with Rivaroxaban and Dabigatran exhibit 28.9±8.7% and 21.47± 11.4% inhibition, respectively.

Conclusions: EPA and DHA, displayed an inhibitory effect on ICAM-1 membrane expression on HUVECs, EPA having the more potent effect ($p<0.05$ against DHA). The inhibitory effect of omega-3 was not significantly altered in the presence of DOACs. The clinical significance of omega-3 in combination with DOACs needs further investigation.

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038 / #819

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

INCREASED PROPORTION OF CIRCULATING NEUTROPHILS WITH IMPAIRED PHAGOCYTOSIS CAPACITY IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Peripheral arterial disease (PAD) is a clinical manifestation of atherosclerosis, affecting arteries in the leg. Based on their symptoms and severity, PAD patients are characterized into three sub-groups: asymptomatic, intermittent claudication (IC) and critical limb ischemia (CLI). Despite its high prevalence, PAD remains under diagnosed and the role of immune cells in PAD pathophysiology remains poorly understood. In this study, we characterized the innate immune responses in PAD patients compared to healthy controls.

Methods: Blood samples were collected from 14 patients with PAD (IC) and 30 healthy controls, to assess the phenotype of monocytes and neutrophils by using 10-colour flow cytometry. Phagocytosis assay was performed with labelled *E.coli* particles. Mann-Whitney U non-parametrical test was used for statistical comparison between PAD patients and healthy controls.

Results: A significant higher proportion of leukocytes ($p<0.05$) and neutrophils ($p<0.01$) was observed in PAD patients compared to healthy controls, whereas monocyte subsets showed no significant differences. Interestingly, neutrophils showed a significantly impaired phagocytosis capability ($p<0.05$) and reduced expression of myeloperoxidase (MPO) ($p<0.05$) in PAD patients compared to healthy controls.

Conclusions: Taken together these results, suggest that PAD patients have an increased proportion of neutrophils in circulation, with impaired phagocytosis capability, compared to healthy controls.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

039 / #691

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE ANTI-INFLAMMATORY EFFECT OF THE COMBINATION TREATMENT OF DAPAGLIFLOZIN AND DULAGLUTIDE IN ATHEROSCLEROSIS DIABETIC MODEL

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: The synergistic effect of SGLT2 inhibitor and GLP1 agonist has been studied, but the mechanism is not well identified. Therefore, this study aims to investigate the mechanism to prevent an atherosclerosis combination therapy with Dapagliflozin and Dulaglutide.

Methods: A total of 45 ApoE knockout mice were administered low dose of streptozotocin for 5 days to induce diabetes, and fed a high fat diet to induce atherosclerosis. Dapagliflozin and Dulaglutide were administered during 8 weeks. The size of atherosclerosis lesions, serum lipid profile, body weight, and inflammation levels were analyzed. In vitro, we used human monocytic cell line THP-1 that PMA induced cell differentiation. Diabetes group was treated with high glucose. For cell stimulation, the cells were incubated with LPS, ATP and analyzed the level of inflammation.

Results: In vivo studies demonstrated combination treatment with Dapagliflozin and Dulaglutide showed favorable effect on reduced body weight, serum lipid profile, and fasting blood glucose. In addition, atherosclerotic aortic plaques were attenuated and NLRP3 inflammasome was reduced. In addition, in vitro studies showed NLRP3 inflammasome decreased when combination treated with Dapagliflozin and Dulaglutide compared to positive control group.

Conclusions: This study shows that combination treatment with Dapagliflozin and Dulaglutide improved atherosclerosis and attenuated NLRP3 inflammasome.

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040 / #534

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

CELL SURFACE IL-1A IS AN NLRP3-INDEPENDENT DRIVER OF EARLY ATHEROSCLEROSIS IN HYPERLIPIDEMIC MICE

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Previous studies have suggested differential effects of IL-1α and IL-1β on atherogenesis. As the presentation of pro-IL-1α on the surface of immune cells (cs-IL-1α) is an exclusive trait of this cytokine, we characterized its role as a driver of atherosclerosis using a non-genetic hyperlipidemic mouse model.

Methods: Atherosclerosis was induced in wild-type (WT), *Il1a*$^{-/-}$, *Nlrp3*$^{-/-}$, and *Il1b*$^{-/-}$ mice by a single injection of mutant Pcsk9-AAV8 virus and a high-fat western diet (WTD, 21% fat, 0.2% cholesterol) for 12 weeks. Mechanistic studies were performed in isolated BMDCs and human monocytes. Cell fractioning and proximity-ligation assays (PLA) were applied.

Results: Atherosclerosis was significantly reduced in *Il1a*$^{-/-}$ mice measured by lesion size (-62% vs. WT-WTD, $p<0.05$) and fat accumulation (Oil-RedO, -64% vs. WT-WTD, $p<0.05$). Cholesterol levels were similarly increased in all four groups, but only WT-WTD mice showed significantly increased serum concentrations (vs. normal chow, $p<0.05$) of pro-inflammatory cytokines (e.g., IL-1α, IL-1β, and IL-6), suggesting a redundant role of inflammatory cytokines in atherogenesis. To test the importance of csIL-1α, LPS-stimulated BMDCs from WT-WTD, *Nlrp3*$^{-/-}$, and *Il1b*$^{-/-}$ mice showed translocation of pro-IL-1α to the plasma membrane. Using a PLA, we found that activated monocytes bind to the IL1R on endothelial cells, leading to adhesion of monocytes to the endothelium, which was abolished by neutralization of either anti-IL-1α or IL1R.

Conclusions: This study demonstrated that csIL-1α mediates monocyte-to-endothelial adhesion and is the main driver of early atherosclerosis development in mice. These data underscore the importance of juxtacrine signaling through cs-IL1α in the absence of circulating pro-inflammatory cytokines.

91ST EAS CONGRESS
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041 / #554

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

PCSK6 ABLATION INCREASES ATHEROSCLEROTIC BURDEN, BUT PROVIDES PLAQUE STABILITY BY REGULATING TH17 AND SMOOTH MUSCLE CELL CONTENT

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: We have previously shown that PCSK6 is a key protease modulating smooth muscle cell activation in vascular disease. Its expression and localization also associated positively with typical markers of inflammatory cells in atherosclerotic plaques, leading to a hypothesis that PCSK6 may be involved in modulating immune responses.

Methods: Detailed immunophenotyping using histology, FACS-, OLINK- and ELISA-based analyses and primary cell cultures was used to compare *Pcsk6*$^{-/-}$mice and controls. Atherosclerosis was evaluated in a bone marrow transplant model.

Results: Plasma from Pcks6$^{-/-}$ mice showed increased levels of pro-inflammatory cytokines CCL2, CCL3 and in particular IL-17A and IL-17F. Pcsk6$^{-/-}$ spleens had an increased number of germinal centers and contained more CD8^{+} T cells. Splenocytes isolated from Pcsk6$^{-/-}$ mice secreted higher levels of IFN-g, IL-2, IL-17 and IL-10 upon stimulation and were more proliferative in vitro. Peritoneal macrophages from Pcsk6$^{-/-}$ mice also secreted more cytokines, including TNF-a, CCL2, IL-6 and IL-10 upon stimulation in vitro, while bone marrow derived macrophages from Pcsk6$^{-/-}$ mice were prone to lipid uptake. Finally, in vivo transplantation of Pcsk6$^{-/-}$ bone marrow to Ldlr$^{-/-}$ mice led to increased atherosclerotic plaque burden compared to Ldlr$^{-/-}$ receiving control bone marrow. However, these plaques presented more stable features, attributed to increased collagen deposition and SMC presence, and increased content of the fibrogenic IL-17 cytokine.

Conclusions: *Pcsk6*$^{-/-}$ ablation in bone marrow revealed its dichotomous role in atherogenesis, provoking higher atherosclerotic burden, but also increased plaque stability. Taken together, these results indicate that PCSK6 is a key regulator of the immune system.

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042 / #728

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE ANTIINFLAMMATORY EFFECT OF STATIN TREATMENT ON MACROPHAGES POLARISATION IN VITRO- PRELIMINARY STUDY

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: The aim of our study was to demonstrate the anti-inflammatory effect of statin treatment, documented in clinical studies, on the polarization of pro-inflammatory (M1) and anti-inflammatory (M2) macrophages *in vitro*.

Methods: Human peripheral blood (n=5) moncytes were differentiated into macrophages (via M-CSF), subsequently polarized into M1 (coincubation: LPS + IFNγ) and M2 (with IL-4 + IL-13) macrophages and treated with fluvastatin. Next, the macrophages were subjected to FACS, qPCR and Griess, ELISA assays and 1w-ANOVA analysis.

Results: Fluvastatin reduced the expression of surface marker Trem-2 on both macrophage subpopulations (CI 99%, p_{M1} <0.04, p_{M2} <0.0008). Moreover, fluvastatin reduced the expression of ABCA-1 on the surface of M1 (CI 99%, p=0.055), no effect on M2 macrophages. Likewise, results showed, fluvastatin upregulated the expression of the anti-inflammatory CD206 on the M2 (CI 99%, p<0.007) whereas M1 remained unaffected. Proinflammatory gene expression was significantly affected by fluvastatin solely in M1 macrophages, as the expression of NFκB (p<0.0001), IL-1β (p<0.0002), IL-6 (p<0.0009), iNOS (p<0.002) was reduced (CI 99%). Fluvastatin significantly decreased the activity of iNOS by M1 macrophages (CI 99%, p<0.0001), with no effect on M2 macrophages. Fluvastatin reduced the production of IL-6 (p<0.01), TNFα (p<0.003) (CI 95%) by M1 macrophages while increasing IL-10 production (CI 95%, p=0.052), M2 macropahges remained unaffected.

Conclusions: The anti-inflammatory effect of statin therapy on macrophage polarization and phenotype *in vitro* was documented. A more detailed *in vitro* study is currently being planned and designed. Supported by MH CZ - DRO („Institute for Clinical and Experimental Medicine – IKEM, IN 00023001“)

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043 / #1239

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

INTRALESIONAL INTERLEUKIN 6 IS ASSOCIATED WITH INTRAPLAQUE HEMORRHAGE IN CAROTID ATHEROSCLEROTIC PLAQUES

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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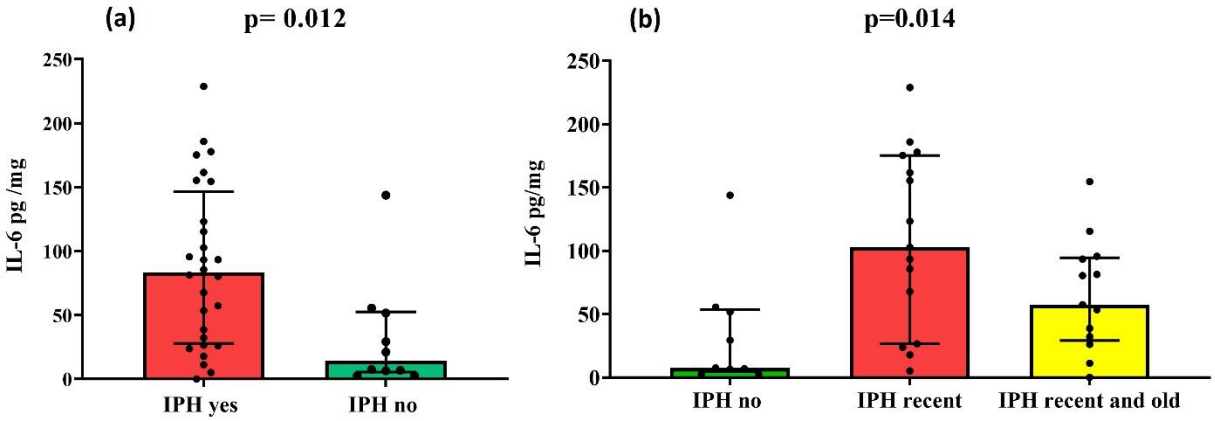
Background and Aims: Interleukin 6 (IL6) has been demonstrated as an important marker of atherosclerotic plaque progression. Intraplaque hemorrhage (IPH) is considered a marker of atherosclerotic plaque vulnerability. However, any connection between the carotid plaque IL6 and IPH remains scantly investigated. We aimed to determine whether intralesional IL6 concentration is related to the histologic evidence of IPH in carotid plaques.

Methods: We retrospectively enrolled 38 consecutive patients undergoing carotid endarterectomy (CEA) with symptomatic (ischemic stroke, TIA, amaurosis fugax) or asymptomatic ipsilateral carotid artery disease. Carotid plaques were collected at CEA. In each specimen, IL6 was measured using fluorescence detection on a Luminex 200, and its concentration was normalized to total protein (pg/mg). The specimen was also stained with H&E to identify IPH. We classified specimens as without IPH, with recent IPH (red blood cells and fibrin), old IPH (hemosiderin-laden macrophages), or both recent and old.

Results: IPH was identified in 28 patients (73.7%). Tissue IL6 was higher in carotid plaques with IPH vs without IPH (85.6 pg/mg [IQR 32.2-154.5] vs 7.5 pg/mg [IQR 4.5-5.5]; p=0.012). One section was excluded because not representative of plaque morphology. None of the sections had old IPH only. Intralesional IL6 was higher in specimens with recent IPH compared to those without IPH and with both recent and old IPH (respectively, N=15, 102.7 pg/mg [IQR 26.5-175.1]; N=9, 7.5 pg/mg [IQR 4.5-53.5]; N=13, 57.3 pg/mg [IQR 29.1-94.4];

p=0.014).



Conclusions: These findings suggest that IL6 is associated with IPH and may act as an initial inflammatory marker of IPH.

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044 / #952

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

PHENOTYPIC AND FUNCTIONAL CHARACTERIZATION OF T CELL IMMUNE RESPONSES IN PERIPHERAL ARTERIAL DISEASE

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Peripheral arterial disease (PAD) is a common manifestation of atherosclerosis, affecting the lower limbs. T cells are among the principal contributors to the development of atherosclerotic plaques. However, T cell immune responses in PAD pathophysiology are poorly understood and a detailed phenotypic and functional characterization of T cell immune responses in PAD is needed.

Methods: Blood samples were collected from PAD patients with claudicatio intermittens (n=14) and healthy controls (HCs, n=30). We assessed the phenotype of active, effector and memory T cell subsets by evaluating the expression of specific surface and intracellular markers analysed by 10-colour flow cytometry. Functional responses were evaluated by performing T cell receptor (TCR) stimulation of PBMCs in a 3D cell culture system to assess cytokine production by ELISA. Statistical analyses were performed using the Mann-Whitney U test.

Results: No differences were observed between PAD and HCs in terms of active, effector and memory T cell phenotypes and in the frequency of cells expressing CCR6 and CXCR3 (markers associated with T cells producing IL-17 and IFN-γ). However, lower frequencies of IFN-γ^+ cells among $CD8^+$ (P=0.04), and $CD4^+CD8^+$ cells (P=0.03) were observed in PAD compared to HCs. TNF-α production in PAD-derived PBMCs, via TCR stimulation was increased at both 48- (P=0.004) and 72-hour time points (P=0.003). No differences were observed in IL-1β, IFN-γ and IL-17 secretion.

Conclusions: Taken together these results suggest that increased TNF-α secretion by PBMCs in response to TCR activation might contribute to the pro-inflammatory environment in PAD pathogenesis.

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045 / #386

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

INTERLEUKIN-6 POLYMORPHISMS ARE ASSOCIATED WITH INCREASED CAROTID INTIMA-MEDIA THICKNESS AND CARDIOVASCULAR RISK FACTORS. GEA MEXICAN STUDY.

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Interleukin 6 (IL-6) is a pleiotropic cytokine associated with atherosclerosis. The study aimed to evaluate if three *IL-6* polymorphisms are associated with increased carotid intima-media thickness (CIMT) and cardiovascular risk factors.

Methods: We determined three *IL-6* polymorphisms (rs1800795, rs1800796, and rs2069827) in 178 individuals with and 906 without increased CIMT. We evaluated the associations employing logistic regression analyses, using inheritance models adjusted by confounding variables. The haplotypes were constructed and analyzed using the Haploview software. IL-6 concentrations were determined by a Bioplex system.

Results: The rs1800796 polymorphism was associated with a high risk of increased CIMT (OR=1.354, $p_{aditive}$=0.016; OR=1.803, $p_{recessive}$=0.014; OR=1.989, $p_{codominant2}$=0.008). One haplotype (*GGG*) was associated with a high risk (OR=1.288, p=0.008), and one (*GCG*) with a low risk of increased CIMT (OR=0.773, p=0.006). The rs2069827 was associated with a low risk of central obesity (CO), hypoalphalipoproteinemia, and low risk to present high concentrations of total cholesterol, non-HDL-C, LDL-C/HDL-C index, apolipoprotein B, and gamma-glutamyl transpeptidase, the rs1800795 with a low risk of insulin resistance of adipose tissue and the rs1800795 with a low risk of CO and hypoalphalipoproteinemia in individuals without increased CIMT ($p<0.05$). In individuals with increased CIMT, the rs2069827 was associated with a low risk of CO, hypertriglyceridemia, metabolic syndrome, and high TG/HDL-C index. The rs1800795 was associated with a low risk of fatty liver ($p<0.05$). IL-6 concentrations were similar in individuals with and without increased CIMT.

Conclusions: The rs1800796 polymorphism is associated with increased CIMT. The rs2069827 and rs1800795 are associated with cardiovascular risk factors.

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046 / #805

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

INTRONIC ALU RNA EDITING COUPLES MRNA STABILITY WITH PRE-MRNA PROCESSING OF INFLAMMATORY GENE EXPRESSION IN ATHEROSCLEROSIS

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Adenosine deaminase acting on RNA-1 (ADAR1) binds double-stranded RNAs (e.g *Alu* elements) and deaminates adenosine to inosine (A-to-I), a process called RNA-editing. Although most of the RNA-editing events are located in introns, the role of intronic RNA editing in gene expression and pathophysiology remains elusive.

Methods: RNA-sequencing, RNA-editing studies, gain/loss-of-function assays, gene expression analysis, individual cross-linking immunoprecipitation (iCLIP) and RNA immunoprecipitation (RIP) studies in human primary endothelial cells were employed. Cathepsin K (CTSK) and ADAR1 mRNA expression were measured by qRT-PCR in peripheral blood mononuclear cells and carotid plaques from patients with cardiovascular disease (n = 91) and healthy individuals (n = 131).

Results: RNA-sequencing and RNA-editing studies revealed editing events in CTSK, an inflammation-stimulated extracellular matrix degradation enzyme with an established role in atherosclerosis. CTSK is extensively edited within the *Alu* regions of intron 5, also enriched of HuR binding sites. Silencing of ADAR1 resulted in a 2-fold downregulation of CTSK mature mRNA and a 2-fold upregulation of pre-mRNA. ADAR1 overexpression exerted the opposite. Silencing of HuR reduced CTSK expression by >2-fold. iCLIP and RIP experiments confirmed that HuR interacts with intronic edited regions of CTSK. In the absence of RNA editing, HuR did not bind CTSK. ADAR1 and CTSK levels were significantly upregulated in patients compared to healthy subjects. CTSK levels closely correlated with the expression of ADAR1 in patients($p < 0.001$, $r = 0.707$).

Conclusions: Intronic *Alu* RNA-editing enables proper pre-mRNA processing by HuR, a primate-specific mechanism that plays a decisive part in inflammatory gene expression during atherosclerotic heart disease.

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047 / #734

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

NEUTROPHIL ACTIVATION STATUS AND LOW-DENSITY NEUTROPHIL FRACTIONS IN PATIENTS WITH CORONARY ARTERY DISEASE.

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Many patients with coronary artery disease (CAD) suffer from low-grade chronic inflammation indicating an increased risk of recurrent cardiac events. They also exhibit elevated neutrophil counts, however whether neutrophil activation is altered remains unclear. Recently, a new subset of neutrophils, the low-density neutrophils (LDNs) was described as more activated than normal-density neutrophils (NDNs). Here, we aimed to compare activation status of neutrophils, including LDN and NDN fractions, in CAD patients and healthy controls.

Methods: Blood was collected from 20 CAD patients aged 53-76 (50% female) and 20 age- and gender matched controls. Neutrophils were cultured in medium +/- LPS, TNF and IL-10 for 2h. Activation (CD66b expression) and LDN/NDN percentage were assessed by flow cytometry followed by Mann-Whitney or Wilcoxon-Signed-Ranks test.

Results: In all participants, LDNs expressed more CD66b compared to NDNs (all $p<0.001$). LPS and TNF increased CD66b expression in both LDNs and NDNs ($p<0.01$), while IL-10 reduced it, though only in NDNs ($p=0.01$). In CAD patients, CD66b expression was higher than in controls, in both LDNs and NDNs, independent of stimulus (all $p<0.05$). The LDN percentage in patients did not significantly differ from controls in medium, (6.0 vs 5.7%), medium+TNF (6.3 vs 4.9%) or medium+IL-10 (5.9 vs 5.2%). However, LPS treatment resulted in a larger LDN fraction in patients than in controls (9.5 vs 5.9%, $p=0.011$).

Conclusions: In conclusion, neutrophils from CAD patients exhibit a more activated phenotype and are prone to transform into highly active LDNs. Neutrophil activation may be an important contributor to chronic low-grade inflammation in CAD patients.

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048 / #574

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

IL-21R BLOCKADE REDUCES ATHEROSCLEROSIS DEVELOPMENT

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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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.

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049 / #989

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

ROLE OF NLRP3 INFLAMMASOME IN THE MACROPHAGES TRANSFORMATION INTO FOAM CELLS IN THE ENVIRONMENT OF HELICOBACTER PYLORI COMPONENTS

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: The transformation of macrophages into foam cells, which are the main components of atherosclerotic plaque, is initiated largely by oxidized lipids. The process of lipid oxidation can be initiated by reactive oxygen species formed as a result of the inflammatory response to acute or chronic infections. Previously done research by our scientific team has shown that the components of *Helicobacter pylori* (HP) stimulate the transformation of macrophages into foam cells. Literature suggest the role of the NLRP3 inflammasome in this process, therefore **the aim of the study was to determine the role of NLRP3 in the transformation of macrophages into foam upon HP components.**

Methods: Two cell lines were used for the study: THP1 (human monocytes) and THPKONLRP3 (human monocytes with the NLRP3 gene knockout). Monocytes of both cells lines were transformed into macrophages and then stimulated with HP bacterial agents and 7-KCH. Next cells were stained with hematoxylin and oil red O to be visualized under a light microscope.

Results: The results indicate the significant decrease in the percentage of foam cells among NLRP3 knockout cells stimulated with HP components and 7-KCH as compared to control cells. Moreover, in the group of knockout cells, the percentage of foam cells after stimulation with HP and 7-KCH remained at the level of spontaneous transformation.

Conclusions: Our results suggest the involvement of the NLRP3 inflammasome in the process of macrophage transformation into foams as a result of HP contribution to the development and progression of atherosclerosis. *Funding: Doctoral Research Grants, University of Lodz No. 8/DGB/IDUB/2022*

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050 / #338

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE CONCENTRATION OF PCSK9-LP(A) COMPLEXES AND THE LEVEL OF BLOOD MONOCYTES IN MALES WITH CORONARY ATHEROSCLEROSIS.

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: High level of lipoprotein(a) [Lp(a)] is a proven ASCVD risk factor, however the mechanisms of high atherogenicity of Lp(a) are mysteries till today. Elevated Lp(a) is associated with blood content of non-classic subset of monocyte. Lp(a) can transport cytokines and other molecules with immune-modulating activity, in particular PCSK9. In this study we analyzed the concentration of Lp(a), PCSK9-Lp(a) complexes and the circulating monocyte subsets in coronary atherosclerosis.

Methods: 238 male patients were categorized into two groups: “1” – patients (60 (55;66) years, n=54 without CHD and stenotic atherosclerosis in coronary, carotid and low limb arteries, “2” – patients (59 (53;65) years, n=184) with ASCVD. Monocyte subpopulations (classical CD14++CD16-, intermediate CD14++CD16+, non-classical CD14+CD16+) were analyzed by direct immunofluorescence and flow cytometry. Lp(a) and PCSK9-Lp(a) complexes in serum were detected by ELISA.

Results: Patients of both groups were comparable in traditional ASCVD risk factors. The concentration of Lp(a) was higher in group 2 compared to group 1 (31.7 (10.2;79.4) mg/dL versus 12.5 (4.7;30.2) mg/dL, $p<0.05$). There were no correlations between the level of Lp(a) and the concentration of PCSK9-Lp(a) complexes, and between the level of Lp(a) and the total number of monocytes. The positive correlation between concentration of complexes PCSK9-Lp(a) and the absolute content of monocytes was observed ($r=0.31$, $p<0.05$) in group 2 predominantly due to CD14+ subsets ($r=0.36$, $p<0.05$).

Conclusions: We hypothesize that complexes PCSK9-Lp(a) may be involved in monocyte activation in atherosclerosis. The physiological consequences of these phenomena require further investigation. The study was supported by RSF, grant № 22-25-00051.

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051 / #385

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

INTERLEUKIN-6 POLYMORPHISMS ARE ASSOCIATED WITH CARDIOVASCULAR RISK FACTORS AND IL-6 CONCENTRATIONS. STUDY IN PATIENTS AND CONTROLS OF THE GEA MEXICAN STUDY.

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Interleukin-6 (IL-6) is an acute-phase protein important in the inflammatory response, vascular inflammation, and atherosclerosis process. The study aimed to establish whether *IL-6* gene polymorphisms and IL-6 concentrations are associated with premature coronary artery disease (pCAD) and cardiovascular risk factors.

Methods: The IL-6 concentrations and the rs2069827, rs1800796, and rs1800795 *IL-6* polymorphisms were determined in 1150 pCAD patients and 1083 healthy controls. The associations were evaluated by logistic regression using inheritance models adjusted by confounding variables.

Results: The *IL-6* polymorphisms were not associated with pCAD; however, in controls, under the dominant model, the rs1800795 *C* and the rs2069827 *T* alleles were associated with a low risk of central obesity (OR=0.401, p=0.017, and OR=0.577, p=0.031, respectively), hypoalphalipoproteinemia (OR=0.581, p=0.027, and OR=0.700, p=0.014, respectively) and hypertriglyceridemia (OR=0.575, p=0.030 and OR=0.728, p=0.033, respectively). In pCAD, the rs1800795 *C* allele was associated with an increased risk of hypoalphalipoproteinemia (OR=1.370, $p_{additive}$=0.025) and increased C-reactive protein (CRP) concentrations (OR=1.491, $p_{additive}$=0.007). pCAD patients had significantly higher IL-6 concentrations compared to controls (p=0.002). In the whole population, individuals carrying the rs1800795 *GC* + *CC* genotypes had higher levels of IL-6 than carriers of the *GG* genotype (p = 0.025).

Conclusions: The *IL-6* polymorphisms were not associated with pCAD; however, they were associated with cardiovascular risk factors in pCAD patients and healthy controls. The rs1800795 *C* allele could determine the levels of IL-6 in carrier individuals.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

HUMAN ADP-RECEPTORS FAIL TO ASSEMBLE THE NLRP3-INFLAMMASOME

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Inflammasome activation through purinergic signalling plays an important role in the development of atherosclerosis. Recently ADP was found to activate the NLRP3-inflammasome via the $P2Y_1$ receptor in mice. As modulation of this axis could be of therapeutic interest, we assessed if the finding translates to humans.

Methods: Bone-marrow-derived macrophages (BMDMs) were generated from ASC-Citrine mice using M-CSF. THP1-ASC-GFP monocytes were differentiated to macrophages with 5ng/ml PMA for 48h. Human PBMCs were differentiated to monocyte-derived macrophages (MDMs) using M-CSF. The NLRP3-inflammasome was primed with 100ng/ml LPS for 4h and subsequently stimulated with 5mM ADP or ATP for 1h. The flow cytometric readout for inflammasome activation was ASC-speck formation. IL-1β release was assessed with ELISA. Expression of ADP-receptors was analyzed with qPCR and Western Blot.

Results: After confirming ADP-dependent NLRP3-inflammasome activation in murine BMDMs, we looked at the human THP1 cell line. Here, ADP did not activate the inflammasome after the priming step. Differentiation to macrophages lead to increased inflammatory capability, but ADP still did not induce ASC-speck formation. In primary human PBMCs, ADP did not activate the inflammasome despite the upregulation of its receptors $P2Y_{1, 12, 13}$ upon priming. The three ADP-receptors were also expressed on MDMs, but rather marked anti-inflammatory macrophages. Finally, ADP did not activate the inflammasome in MDMs.

Conclusions: Responsiveness of the NLRP3-inflammasome to ADP is very much species-dependent. This demonstrates again that results found to be true in the murine system have to be considered with caution and treated carefully when translated to humans.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

A CA2+-PERMEABLE CHANNEL TRPM2 PROMOTES ATHEROSCLEROTIC PROGRESSION IN MOUSE MODEL OF ATHEROSCLEROSIS

POSTER ON BOARD: AS01.04 INFLAMMATION, IMMUNITY AND INFECTION IN ATHEROSCLEROSIS

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Background and Aims: Atherosclerosis is a chronic inflammatory arterial disease characterized by excessive production of reactive oxygen species (ROS) in arterial walls. Transient receptor potential channel M2 (TRPM2) is a Ca^{2+}-permeable cation channel activated by oxidative stress. The aim of the present study is to study the role of TRPM2 in atherosclerosis in animal models.

Methods: High cholesterol diet was used in PCSK-overexpressing mice to induce atherosclerosis. Perivascular cuffs were also used to introduce mechanical damage-related vascular hyperplasia in mice. Primary isolated vascular smooth muscle cells were used for mechanistic study.

Results: Our study showed that TRPM2 knockout reduces the atherosclerotic plaque area in cuff-induced vascular hyperplasia model and hypercholesterolemia-induced atherosclerotic model. Mechanistic studies demonstrate that TRPM2 knockout reduces the expression of inflammatory cytokines, macrophage infiltration in vascular wall, smooth muscle cell proliferation and migration, and vascular smooth muscle cell death. In addition, a TRPM2 antagonist N-(p-amylcinnamoyl) anthranilic acid (ACA) was found to inhibit atherosclerotic development in ApoE-/- mouse model of atherosclerosis.

Conclusions: This study demonstrated that TRPM2 contributes to the progression of hypercholesterolemia-induced atherosclerosis. Mechanistically, TRPM2 channels may provide an essential link that can connect excessive ROS to Ca^{2+} and inflammation, leading to atherosclerotic progression.

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054 / #559

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.05 Extracellular matrix and calcification*

LYSYL OXIDASE (LOX) IN ECTOPIC CARDIOVASCULAR CALCIFICATION: IMPACT ON MATRIX MINERALIZATION AND VASCULAR CALCIFICATION ASSOCIATED TO ATHEROSCLEROSIS

POSTER ON BOARD: AS01.05 EXTRACELLULAR MATRIX AND CALCIFICATION

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Background and Aims: We have shown that the extracellular matrix (ECM)-modifying enzyme lysyl oxidase (LOX) contributes to the osteogenic differentiation and calcification of vascular smooth muscle cells (VSMCs). Our objective was to assess the impact LOX in ECM mineralization *in vitro* and in vascular calcification associated to atherosclerosis.

Methods: Conditioned media and ECM from cultures of valvular interstitial cells (VICs) transduced to over-express LOX were tested in calcification assays. In both wild-type (WT) and transgenic mice that overexpress LOX in VSMC ($TgLOX^{VSMC}$), atherosclerosis was induced by the administration of AAV-$PCSK9^{D374Y}$ and a high-fat diet. Body weight and plasma levels of cholesterol and triglycerides were analyzed. Atherosclerosis burden was quantified en face after O.R.O. staining. Aortic calcification was determined by NIRF reflectance imaging. Gene expression was analyzed by RT-PCR, and vascular calcification and collagen content by von Kossa and picrosirius red staining, respectively.

Results: VICs exposed to conditioned media from cells over-expressing LOX or cultured onto crosslinked matrices showed enhanced *in vitro* calcification. In atherosclerosis-challenged $TgLOX^{VSMC}$ mice both atherosclerosis burden and calcification in the whole aorta, as well as calcified area of atherosclerotic lesions in the aortic arch and brachiocephalic artery, were noticeably higher than in the WT mice. Osteogenic markers were similarly induced in the aorta of WT and $TgLOX^{VSMC}$ mice, but higher collagen cross-linking was observed in plaques from transgenic mice.

Conclusions: Our findings highlight the procalcifying properties of LOX and the key role of this enzyme on the mineralization of ECM associated to atherosclerosis. Funding by RTI2018-094727-B-100 (MICINN)

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.05 Extracellular matrix and calcification*

NEDDYLATION OF PARP-1 IS MEDIATED BY CBLB AND REGULATES ITS ACTIVITY IN VASCULAR CALCIFICATION

POSTER ON BOARD: AS01.05 EXTRACELLULAR MATRIX AND CALCIFICATION

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Background and Aims: Vascular calcification (VC) is mineral depositions on the walls of arteries and veins and highly correlated with cardiovascular disease mortality, especially in high risk patients with diabetes and chronic kidney diseases (CKD)**.** Neuronal precursor cell-expressed developmentally downregulated protein 8 (NEDD8) is a ubiquitin-like protein that is critical in various cellular functions by conjugating to target proteins. However, the roles of NEDD8-conjugated proteins in VC is not reported yet.

Methods: To induce VC, A10 cells were treated 4mM inorganic phosphate with growth medium for 3~4 days

Results: In our study, treatment of MLN4924, inhibitor of Nedd8 activating E1 enzyme, blocks Pi-induced calcium deposition and mRNA expression of osteogenic differentiation makers in VSMCs. By using LC-MS/MS analysis, we identified that poly (ADP-ribose) polymerase 1 (PARP-1) is conjugated with NEDD8 and increases PARP-1 activity under VC conditions. Furthermore, we discovered that PARP-1 neddylation is mediated by E3 ligase Cbl proto-oncogene B (CBLB) and removed by NEDD8-specific protease 1 (NEDP-1) in VC.

Conclusions: These results demonstrate that NEDD8-dependent activation of PARP-1 is a novel mechanism of vascular calcification and inhibition of PARP-1 activity may be a new therapeutic target in VC.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.05 Extracellular matrix and calcification*

CIRCULAR RNA CIRCSMOC1-2 REGULATES VASCULAR DISEASE BY ACTING AS A MIR-874-3P SPONGE

POSTER ON BOARD: AS01.05 EXTRACELLULAR MATRIX AND CALCIFICATION

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Background and Aims: CircRNAs are mainly formed by back-splicing reactions and are found to regulate diverse diseases including vascular diseases. Vascular calcification (VC), the calcium deposition inside the blood vessels, is common in patients with atherosclerosis, cardiovascular disease, and chronic kidney disease. Although several treatments are available to reduce calcification, the incidence of VC continues to rise. However, roles of circRNAs in VC have not yet been fully explored.

Methods: Inorganic phosphate(Pi) was treated to rat vascular smooth muscle cells(RVSMCs) to induce VC. The expression of circRNAs was analyzed by RNA-seq. We investigated the function of circSmoc1-2, one of the circRNAs generated from the Smoc1 gene, which is downregulated in response to VC. Gain and loss of function of circRNAs were investigated by creating overexpression(OE) and knockdown(KD) models. To investigate function of circRNAs in VC, calcium assay was performed. Additionally, to discover whether the selected circRNAs act as microRNA(miRNA) sponges, bioinformatic analysis and luciferase assay was conducted.

Results: CircSmoc1-2 is primarily localized to the cytoplasm and is resistant to exonuclease digestion. Inhibition of circSmoc1-2 worsens VC, while overexpression of circSmoc1-2 reduces VC, suggesting that circSmoc1-2 can prevent calcification. We went on to investigate the mechanism of circSmoc1-2 as a microRNA sponge, and noted that miR-874-3p, the predicted target of circSmoc1-2, promotes VC, while overexpression of circSmoc1-2 reduces VC through suppressing miR-874-3p. Additionally, we identified the potential mRNA target of miR-874-3p as Adam19.

Conclusions: We revealed that the circSmoc1-2/miR-874-3p/Adam19 axis regulates VC, suggesting that circSmoc1-2 may be a novel therapeutic target in the treatment of VC.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

CIRCULAR DECOYS SPONGE MIR-21 AND MIR-146A IN SENESCENT VASCULAR CELLS

POSTER ON BOARD: AS01.06 VASCULAR BIOLOGY OF THE ARTERIAL WALL: MISCELLANEOUS

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Background and Aims: Numerous studies have confirmed that microRNAs (miRs), including miR-21 and miR-146a, influence cellular function, and contribute to the pathogenesis of CVDs, especially in the context of cellular aging. Inhibition of these miRs through sponges, like antagomiRs and circular RNAs (circRNAs), could represent a promising therapeutic strategy. This project aims to establish a therapeutic approach using designed circRNAs to study their effect on miR-21 and miR-146a in senescent human umbilical vein endothelial cells (HUVECs), human coronary artery endothelial cells (HCAEC), and vascular smooth muscle cells (VSMCs).

Methods: CircRNAs were designed, produced and tested by northern blotting. Methods to characterize the effect of circRNA transfection and the effect on vascular cells included the quantification of target gene and protein expression and functional analysis of proliferation and migration.

Results: We showed that ECs and VSMCs have higher levels of miR-21 and miR-146a expression in replicative senescent cells compared to non-senescent cells ($P<0.05$). CircRNAs were designed as linear RNAs with four miRNA binding sides followed by a circularization step confirmed by norther blot analysis. In SMCs, significant target upregulation was achieved by the treatment with circRNAs showing a better effect than antagomiRs for both miR-21 and miR-146a. In ECs, circRNA transfection also affected target regulation. Effects on target regulation were further confirmed on protein level.

Conclusions: In summary, we demonstrate the efficiency of circRNAs by sponging miR-21 and miR-146a in senescent cells. CircRNAs are more stable and efficient compared to antagomiRs. CircRNAs might therefore be a better alternative and a realistic approach for future clinical studies.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

POSSIBLE ROLE OF SPP1 IN DEGENERATIVE ASCENDING AORTIC ANEURYSM FORMATION

POSTER ON BOARD: AS01.06 VASCULAR BIOLOGY OF THE ARTERIAL WALL: MISCELLANEOUS

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Background and Aims: Ascending aortic aneurysm (AscAA) is a silent, progressive and potentially fatal disease. AscAA is characterized by excessive fibrosis and inflammation, but the underlying molecular mechanism is not well established. Our objective was to characterize the cellular and molecular signature of degenerative AscAA and identify regulatory elements contributing to disease development.

Methods: Patients undergoing elective open-heart surgery for AscAA- and/or aortic valve repair at the Karolinska University hospital, Stockholm, Sweden, were included. Global gene expression was measured in the intima-media portion of ascending aortic tissue biopsies from non-dilated (n=22) and dilated (n=24) aortas. Protein expression and localization of candidate genes were assessed using immunohistochemistry (12 patients/group). Interacting distal regions (enhancers) were identified using high-throughput chromosome conformation capture (HiCap) in THP1 cells, followed by identification of predicted transcription factors binding sites (TFBS). *In vivo* validation of putative TFs was done by CUT&RUN analysis.

Results: Differential expression analysis of global gene expression profiles identified osteopontin (SPP1) as a potential candidate gene for aortic dilatation in degenerative AscAA, and its protein expression co-localised with CD68-positive cells. HiCap and subsequent TFBS analysis of interacting distals identified possible TFs for SPP1. Further validation of TFs binding to SPP1 in dilated aortic tissue is currently ongoing using CUT&RUN.

Conclusions: Our findings suggest that SPP1 may be of importance for degenerative AscAA development.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

MIR-31-5P INFLUENCES VASCULAR REGENERATION CAPACITY

POSTER ON BOARD: AS01.06 VASCULAR BIOLOGY OF THE ARTERIAL WALL: MISCELLANEOUS

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Background and Aims: MicroRNAs (miRs) play a crucial role in vascular regeneration, a key factor in CVD-development. Although few miRs are characterized in the cardiovascular context, consequently investigating new miRs could lead to new therapeutic strategies. Here, we evaluate miR-31-5p and its influence on cellular functions in vascular cells such as endothelial and smooth muscle cells, especially in the context of cellular aging.

Methods: Expressions of miR-31-5p in senescent and non-senescent vascular cells were assessed by qRT-PCR. Additionally, the effect of miR-31-5p on functional cell properties was investigated. Possible targets were identified and further investigated on mRNA and protein level.

Results: Expression of miR-31-5p was significantly upregulated in senescent human umbilical vein endothelial cells (HUVECs) and human coronary arterial endothelial cells (HCAECs) compared to non-senescent cells. Also, in coronary artery smooth muscle cells (CaSMCs) an enhanced expression was observable. Hypoxia highly influences the expression of miR-31-5p, particularly an upregulation after 72h of incubation in both senescent and non-senescent cells. Previously predicted target regulation by target scan was confirmed on mRNA and on protein level. Attenuating miR-31-5p in endothelial cells via anti-miR-31-5p transfection influences functional parameters such as proliferation and migration capacity.

Conclusions: First results showed that miR-31-5p might play a crucial role in vascular regeneration. Inhibiting miR-31-5p may thus present a therapeutic option to limit the progression and development of EC dysfunction, relevant to multiple disease settings, accentuating particularly coronary diseases due to the focus on coronary endothelial cells. However, further studies are needed to investigate its translational potential for establishing a new therapeutic target.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

ACTIVATION OF WNT/B-CATENIN SIGNALING IN ABDOMINAL AORTIC ANEURYSM: IMPACT OF PORCUPINE INHIBITION AND DISRUPTION OF CBP/B-CATENIN INTERACTION IN A MURINE EXPERIMENTAL MODEL

POSTER ON BOARD: AS01.06 VASCULAR BIOLOGY OF THE ARTERIAL WALL: MISCELLANEOUS

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Background and Aims: Atherosclerosis is frequently associated to abdominal aortic aneurysm (AAA), a life-threatening condition for which there is currently no medical treatment available. Wnt signaling is reactivated in multiple disorders; nevertheless, it is uncertain whether a disturbance of Wnt signaling could underlie aneurysm development and its therapeutic potential.

Methods: Wnt signaling was analysed in abdominal aortas from patients with AAA, healthy donors, and AngII-infused ApoE$^{-/-}$ mice (PCR/Western blot/ immunohistochemistry). Animals were treated with LGK974 (a porcupine inhibitor) and Pri-724 (that disrupts CBP/β-catenin interaction). Blood pressure, aortic diameter and cardiac function were analysed.

Results: β-catenin mRNA levels remained unaltered in human AAA; however, those of *WNT2*, *WNT5a* and *WNT5b* were significantly enhanced, associated with an altered expression of *SFRP2*, *SFRP4* and *SFRP3*. This abnormal profile was comparable to that detected in aneurysms from AngII-infused ApoE$^{-/-}$ mice. Interestingly, in both human and experimental AAA, the transcriptionally active form of β-catenin was dramatically increased, indicating the activation of the Wnt/β-catenin pathway. Treatment with LGK974 reduced vascular *Axin2* expression and limited cardiac hypertrophy, although it neither affected survival rate, nor modulated the progression, incidence or severity of AAA. Interestingly, PRI-724, effectively blocked canonical Wnt signalling, slightly delaying AAA progression and reducing aneurysm severity, as well as abolished the increase of LV mass induced by AngII.

Conclusions: Wnt signaling is reactivated in human and experimental AAA. Porcupine inhibition and CBP/β-catenin disruption limited cardiac hypertrophy, although minor benefit on AAA progression/severity was noticed. Our data suggest that targeting specific elements of this route could ameliorate aneurysm development.

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Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

IMPACT OF CHRONIC HOOKAH (WATERPIPE) SMOKING ON CENTRAL ARTERIAL STIFFNESS AND CARDIOVASCULAR DISEASE-RELATED EXPOSURE BIOMARKERS

POSTER ON BOARD: AS01.06 VASCULAR BIOLOGY OF THE ARTERIAL WALL: MISCELLANEOUS

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Background and Aims: Flavored tobacco smoking using a hookah (i.e., waterpipe) is a growing tobacco epidemic affecting young adults and effectively being marketed as a harmless tobacco alternative. The long-term vascular effects of flavored hookah smoking are not only lacking but are critical to strengthen the evidence base and inform regulatory efforts. Herein, we sought to determine the effect of chronic, intermittent hookah smoking on arterial stiffness and biomarkers of harm, as compared to cigarette smokers and non-smokers.

Methods: In 13 exclusive chronic hookah smokers, aged 21 to 49 years of age, who reported smoking hookah on average two times per week for 5±3 years, 18 exclusive cigarette smokers, and 21 non-smokers, we measured aortic stiffness, assessed as carotid-femoral pulse wave velocity and plasma biomarkers of harm, including: high sensitivity-C-Reactive Protein (hs-CRP), and fibrinogen.

Results: Hookah smokers and cigarette smokers exhibited significantly higher carotid-femoral pulse wave velocity, indicating increased arterial stiffness, than non-smokers (hookah smokers: 7.8±0.8 m/sec; cigarette smokers: 8.8±1.1 m/sec; non-smokers: 6.9±0.7 m/sec; mean±SE; $p<0.05$). Among hookah smokers, the vascular changes were accompanied by intermediate levels of fibrinogen and hs-CRP as compared to cigarette and non-smokers (fibrinogen: hookah 274.3±15.1; cigarette 303.3±2.5; non-smokers 249.8±10.5 mg/dL; hs-CRP: hookah 1.8±0.5; cigarette 2.4± 0.6; non-smokers 1.4±0.4 mg/L; $p<0.05$).

Conclusions: Though intermediate between cigarette smoking and non-smokers, long-term intermittent flavored hookah tobacco smoking increases central artery stiffness, evidenced by an increase in carotid-femoral pulse wave velocity, and increasing cardiovascular disease-related exposure biomarkers, suggesting, in stark contrast with social media claims, that hookah smoking is not without harm.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

062 / #1282

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

PROGNOSTIC VALUE OF ECHOCARDIOGRAPHIC DATA IN CHRONIC HEART FAILURE PATIENTS

POSTER ON BOARD: AS01.07 IMAGING TECHNOLOGY

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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. The data was analysed among HF functional class, outcome, RVDD and EF quartiles. Statistical analysis was performed using IBM SPSS statistics 16.0.

Results: 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.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

063 / #1072

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

HIV-INFECTION AND ATHEROSCLEROSIS. IS THERE A CONNECTION? DATA RECEIVED BY OCT.

POSTER ON BOARD: AS01.07 IMAGING TECHNOLOGY

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Background and Aims: Chronic infection by HIV evolves with a vascular inflammatory action causing endothelial dysfunction. The action of the virus as well as the side effects of antiretroviral drugs contributes to the progression of cardiovascular diseases. The study aimed to characterise the changes of the structure of the coronary wall by Optical Coherence Tomography in HIV-infected patients with or without symptoms of coronary heart disease.

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.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

064 / #692

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

WALL SHEAR STRESS ASSOCIATED WITH STROKE OCCURRENCE AND MECHANISM IN MIDDLE CEREBRAL ARTERY ATHEROSCLEROSIS

POSTER ON BOARD: AS01.08 PLATELETS, THROMBOSIS AND ATHEROSCLEROSIS

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Background and Aims: Various mechanisms are involved in stroke caused by atherosclerosis of the middle cerebral artery (MCA). However, the factors that affect stroke mechanism are unclarified. Here, we compared plaque nature and hemodynamic parameters according to stroke mechanism in patients with MCA atherosclerosis.

Methods: We recruited consecutive patients with asymptomatic and symptomatic MCA atherosclerosis (≥50% stenosis). Stroke mechanism was subdivided based on lesion patterns. MCA plaque characteristics (location and enhancement) and wall shear stress (WSS) were measured by high-resolution vessel wall and four-dimensional flow magnetic resonance imaging, respectively, at 5 points (initial, upstream, minimal lumen, downstream, and terminal). These parameters were compared among patients with asymptomatic and symptomatic MCA atherosclerosis with infarctions of different mechanisms (artery-to-artery embolism versus local branch occlusion).

Results: A total of 110 patients (46 asymptomatic, 32 artery-to-artery embolisms, and 32 local branch occlusions) were investigated. Plaques were evenly distributed in the MCA in asymptomatic MCA atherosclerosis, more commonly observed in the distal MCA in artery-to-artery embolism, and in local branch occlusion. The area of maximum WSS was closely correlated with the plaque enhancement area. Maximum WSS and plaque enhancement were more identified in the minimum lumen area in patients with asymptomatic MCA atherosclerosis or those with stroke due to local branch occlusion and were prominent in the upstream region in those with artery-to-artery embolism. Elevated variability of maximum WSS was related to artery-to-artery embolism.

Conclusions: Stroke caused by artery-to-artery embolism showed plaque enhancement and the highest maximum WSS at the upstream point of the plaque associated with elevated variability of maximum WSS.

91ST EAS CONGRESS
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065 / #601

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

UPSTREAM HIGH WALL SHEAR STRESS ASSOCIATED WITH ARTERY-TO-ARTERY EMBOLISM AND RECURRENT STROKE IN SYMPTOMATIC INTRACRANIAL ATHEROSCLEROTIC STENOSIS

POSTER ON BOARD: AS01.08 PLATELETS, THROMBOSIS AND ATHEROSCLEROSIS

Shuang Li[1], Linfang Lan[2], Xuan Tian[1], Haipeng Liu[3], Bonaventure Ip[1], Sze Ho Ma[1], Jill Abrigo[4], Yuying Liu[1], Yu Liu[1], Karen Ma[1], Florence Fan[1], Vincent Ip[1], Yannie Soo[1], Alexander Lau[1], Howan Leung[1], Vincent Mok[1], Thomas Leung[1], Xinyi Leng[1]
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Background and Aims: To investigate associations of local wall shear stress (WSS) with artery-to-artery embolism (AAE) and risk of stroke recurrence, in symptomatic intracranial atherosclerotic stenosis (sICAS).

Methods: Patients with 50-99% sICAS in M1 middle cerebral artery in CTA were included in this cohort study. AAE as a baseline stroke mechanism was determined by MRI infarct patterns. Computed fluid dynamics models were built based on CTA; relative WSS (rWSS) at any locus across the sICAS lesion was quantified, as relative to mean WSS at proximally normal vessel segment. For each sICAS lesion, high WSS score (HWSSs) was calculated as the mean rWSS multiplied by the proportional area in the high WSS regions (rWSS>3.0) across the lesion. HWSSs were also calculated in the upstream and downstream segments of the plaque divided at the stenotic throat. HWSSs ≥4th quartile was considered as high HWSSs. We associated HWSSs with AAE at baseline and the primary outcome (same-territory ischemic stroke within 1 year).

Results: Among 102 sICAS patients, 46 had AAE. Upstream high HWSSs (OR=5.133, 95% CI 1.334-19.751; p=0.017) was independently associated with AAE at baseline in multivariate logistic regression, and associated with higher risk of primary outcome in log-rank test (26.7% versus 5.36%; HR= 6.01, 95% CI, 1.06-34.07; p=0.043). Such association was not found with HWSSs across the entire plaque or in the downstream segment.

Conclusions: Upstream high HWSSs, i.e., higher WSS and/or larger area with high WSS in the upstream segment of sICAS plaque, was associated with increased risks of AAE and recurrent, same-territory stroke.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

066 / #558

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

THE ROLE OF TUMOR-NECROSIS RECEPTOR ASSOCIATED FACTOR 1 (TRAF-1) AND 5 (TRAF-5) IN PLATELET ACTIVATION

POSTER ON BOARD: AS01.08 PLATELETS, THROMBOSIS AND ATHEROSCLEROSIS

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Background and Aims: Platelet signalling pathways linking inflammatory and thrombotic circuits play a key role in atherosclerosis-related thrombotic events. However, the underlying mechanisms are only poorly understood. Here, we tested the role of the inflammatory signalling adapters TRAF-1 and TRAF-5 in freshly prepared tissues from wild type (WT), TRAF-1 (TRAF-$1^{-/-}$) and TRAF-5 (TRAF-$5^{-/-}$) deficient C57BL/6 mice.

Methods: The expression of TRAF-1 and TRAF-5 in WT-platelets was validated by fluorescence microscopy. TRAF-associated receptors TNFR-1 and CD40 were detected on WT-platelet surface by flow cytometry. Platelet aggregation was evaluated using a Multiple Analyzer (Roche) in whole blood.

Results: Automatic platelet count was not affected among different genotypes. Stimulation with TNF-α or an activating CD40-stimulating antibody resulted in platelet activation as assessed by P-selectin expression and GPIIbIIIa activation. ADP stimulation of aggregation-samples from both genotypes caused an increase in the area under the curve (AUC) compared to WT. This effect could be resembled in flow cytometry of ADP-stimulated platelets from TRAF-$1^{-/-}$ mice. In addition, we observed significantly lower plasma levels of fibrinogen and von-Willebrand-factor in TRAF-$5^{-/-}$ and in TRAF-$1^{-/-}$ mice. Additionally, levels of D-Dimers showed an increase in both knockout mice. Platelet-neutrophil-aggregates and platelet-Ly6C^{high}-monocyte-aggregates were differently regulated and showed a reduction in TRAF-$1^{-/-}$ and an increase in TRAF-$5^{-/-}$, indicating a proinflammatory and anti-inflammatory role of TRAFs, respectively.

Conclusions: Expression of pro-inflammatory receptors and down-stream TRAFs regulates platelet functionality and haemostasis, partially in opposing directions. The connection of inflammatory and platelet-specific signalling, therefore, provides a potential explanation for enhanced thrombotic complications in chronic inflammatory disease.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

067 / #1013

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

PLATELET SPECIFIC C5A RECEPTOR (C5AR) 1 DEFICIENCY IMPROVES CARDIAC FUNCTION IN A MURINE MODEL OF ACUTE MYOCARDIAL INFARCTION

POSTER ON BOARD: AS01.08 PLATELETS, THROMBOSIS AND ATHEROSCLEROSIS

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Background and Aims: Background: The complement system and its anaphylatoxin C5a play a key role in acute inflammation. Recently, the presence of the C5a receptor 1 (C5aR1) on platelets was implicated in controling tissue neovascularization. **Aim:** To investigate the effect of platelet C5aR1 on Left Ventricular (LV) remodeling following acute myocardial infarction.

Methods: The left anterior descending coronary artery (LAD) was permanently ligated in male mice aged 10-12 weeks to induce myocardial infarction (MI). We compared C5aR1flox/floxPf4Cre^{+} (platelet specific C5aR1-deficient) mice to their C5aR1flox/floxPf4Cre^{-} littermates (n=10). To investigate LV morphology and function, echocardiography was performed on day 1 and 13 after LAD ligation. On day 1 and 14, platelet-neutrophil-complexes (CD42b^{+} out of Ly6G^{+} events) and platelet activation markers (activated GPIIb/IIIa and surface P-selectin) were analyzed in whole blood by flow cytometry. Additionally, hearts from day 14 after LAD ligation were stained with triphenyl tetrazolium chloride to measure infarct size.

Results: Compared to the control mice, platelet-specific C5aR1$^{-/-}$ mice developed significantly smaller infarcts (12,92%±2,38 vs. 25,24%±3,38; n=4, p<0,05) along with significantly improved ejection fractions (47,66%±6,43 vs 35,22%±9,56; n=8-10, p<0,01) on day 13. We observed a profound decrease in the stimulated expression of activated GPIIb/IIIa (13.63±8.90 vs. 32.14±17.16, p<0.01, n=10) and surface P-Selectin on platelets one day after MI in the platelet-specific C5aR1$^{-/-}$ mice. Interestingly, this was accompanied by an increased percentage of circulating platelet-neutrophil-complexes (31.93%±13.09 vs. 19.30%±9.75; n=10 or 9, p<0,01).

Conclusions: Platelet specific C5aR1-deficiency improves myocardial outcome in a murine permanent LAD ligation model. The underlying mechanisms are subject of our ongoing investigation.

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068 / #491

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.09 Aortic valve stenosis*

A NEW RABBIT MODEL OF AORTIC VALVE STENOSIS INDUCED BY DIRECT BALLOON INJURY

POSTER ON BOARD: AS01.09 AORTIC VALVE STENOSIS

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Background and Aims: It is increasingly recognized that the appropriate animal model can contribute to a better understanding of the pathological mechanisms underlying aortic valve stenosis (AVS) due to the lack of access to reliable sources of diseased human aortic valves associated with the progression of AVS. This study aims to establish a new model of the rabbit AVS model, which induced by direct balloon injury onto the aortic valves to study the initiation and progression of aortic stenosis.

Methods: A rabbit model of aortic valve stenosis was established by direct balloon injury in male New Zealand White rabbits (3.5–4.0 kg) on aortic valves, followed by 0.5 % cholesterol enriched diet and 50,000 Unit vitamin D2 (HC+VitD2) for 8 weeks. Known as the diet-induced AVS model, the rabbit fed with HC+VitD2 was used as a control group.

Results: Echocardiography revealed that thickening of cusps and restriction of motion in the injured rabbit fed with HC+VitD2 diet were observed 8 weeks after aortic valve injury. According to histological analysis, the aortic valve stained with MT showed increased thickness of the aortic valve cusps in the injured group. In addition, while HC+VitD2 diet-induced group exhibited negligible calcium deposits in the valvular leaflets, significant calcific deposits were observed in the balloon injured group.

Conclusions: We described a new model for direct balloon injury on the aortic valves via fluoroscopic guidance in male NZW rabbits, which can mimic valvular aortic stenosis and have the potential to be used for studying the pathological mechanisms underlying AVS and developing therapeutic options.

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069 / #689

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.09 Aortic valve stenosis*

PROTECTIVE EFFECT OF NICLOSAMIDE ON CALCIFICATION OF AORTIC VALVE INTERSTITIAL CELLS AND ITS UNDERLYING MOLECULAR MECHANISM

POSTER ON BOARD: AS01.09 AORTIC VALVE STENOSIS

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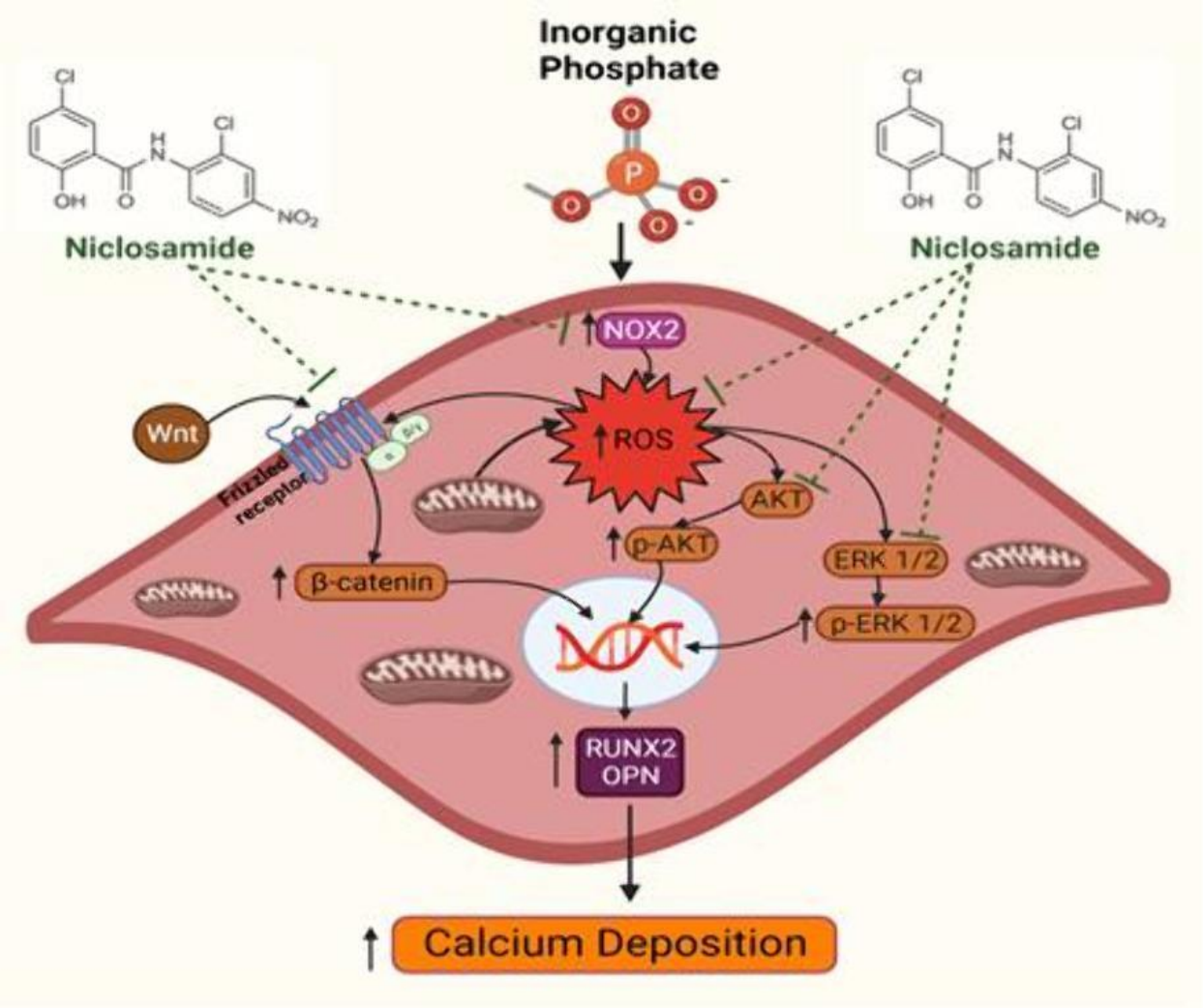
Background and Aims: The most common heart valvular disorder is calcific aortic valve stenosis (CAVS), which is characterized by a narrowing of the aortic valve. CAVS is known to impose a huge social and economic burden on patients. However, no pharmacotherapy for this condition has yet been established. Aortic valve replacement is the only treatment option, although its lifelong efficacy is not guaranteed and involves inevitable complications. Therefore, the purpose of this study is to see if niclosamide can reduce calcification in aortic valve interstitial cells (VICs).

Methods: Porcine hearts were obtained immediately after sacrifice and VICs are isolated using collagenase. To induce calcification, cells were treated with a pro-calcifying medium (PCM), different concentrations of niclosamide were added to the PCM-treated cells, and the level of calcification, mRNA, and protein expression of calcification markers was measured. The level of intracellular reactive oxygen species (ROS) was measured using a redox-sensitive cell-permeable dye, 2',7'-dichlorodihydrofluorescein diacetate (DCF-DA).

Results: Niclosamide reduced the level of calcium deposition in calcified VICs, along with reductions in the gene and protein expression of the calcification markers Runx2 and osteopontin. Niclosamide also decreased the formation of reactive oxygen species and the expression of Nox2 and p22phox. Furthermore, in calcified VICs, niclosamide inhibited the expression of β-catenin and phosphorylated glycogen synthase kinase (GSK-3β), as well as the phosphorylation of AKT and ERK.

Conclusions: Our findings suggest that niclosamide may alleviate PCM-induced calcification, at least in part, by inhibiting oxidative stress mediated activation of the GSK-3β/β-catenin/AKT/ERK signaling

pathway, and may be a potential treatment for CAVS.



91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

070 / #749

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.09 Aortic valve stenosis*

SIRT1 DIRECTLY REGULATES MYOFIBROBLASTIC ACTIVATION, EXTRACELLULAR-MATRIX REMODELING, AND CALCIFICATION IN AORTIC VALVE INTERSTITIAL CELLS

POSTER ON BOARD: AS01.09 AORTIC VALVE STENOSIS

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Background and Aims: Calcific aortic valve stenosis (CAVS) is one of the most common valve disorders. The well-known deacetylase SIRT1 could be involved in many pathways linked to CAVS development and progression. We aim to unveil if SIRT1 could represent a novel important player in the homeostasis of aortic valve leaflets.

Methods: RNA-sequencing of whole aortic valves or valve interstitial cells were used to identify the main regulated pathways linked to CAVS. SIRT1 knockdown (SIRT1-) and overexpressing (SIRT1+) immortalized valve interstitial cells (iVIC) were generated by CRISPR/Cas9 technology. Fibrosis was evaluated by quantitative PCR and immunofluorescence of well-known genes. A calcification assay was employed to evaluate the capability of mutant iVIC to produce calcium deposits.

Results: Whole tissue RNA-sequencing showed that many pathways which are linked to SIRT1 are modulated in CAVS specimens. Functional analysis of SIRT1 mutant iVICs revealed that inflammation, extracellular-matrix remodeling, and calcification mechanisms are significantly regulated. Validations showed that fibrosis-associated genes were down-regulated in SIRT1+ iVICs compared to wild-type ones (COL1A1 log2FC=-1.0±0.4; TGFB2 log2FC=-0.9±0.1; FN1 log2FC=-0.4±0.1; ACTA2 log2FC=-1.0±0.1; BGN log2FC=-1.0±0.08; TAGLN log2FC=-0.4±0.04; all $p<0.001$) as well as αSMA protein (-52%, $p<0.0001$), while SIRT1- iVICs showed a significant up-regulation of COL1A1 protein (+50.5% $p<0.0001$). Calcium assays unveiled a significant increment of calcification in SIRT1- iVICs (+50.8%, $p<0.01$), while SIRT1+ iVICs deposited less calcium (-23.6%; $p<0.01$) compared to wild-type ones.

Conclusions: Our data show that SIRT1 could represent a novel master regulator of fibro-calcific processes involved in CAVS progression.

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071 / #1499

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

ASSESSMENT OF THE DISTRIBUTION OF PCSK9 E670G GENETIC POLYMORPHISM IN PATIENTS WITH HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA DEPENDING ON THE PRESENCE OF DIABETES MELLITUS

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: To evaluate the distribution of PCSK9 E670G genetic polymorphism in patients with coronary artery disease and heterozygous familial hypercholesterolemia (heFH) depending on the presence of type 2 diabetes mellitus (DM2).

Methods: The 201 patients with chronic CAD, including those with heFH (n=57, group I) and without (n=144, group II). DLCN was used to diagnose heFH. The genetic typing at PCSK9 E670G (rs505151) polymorphism was performed with the PCR-RFLP method. The frequency of the studied genotypes corresponded to the equilibrium Hardy-Weinberg distribution in the group of patients and healthy individuals (P>0.05).

Results: There were 2 times more carriers of the G allele in group I (13.11.4%) than in group II (17.6.0%) and 3 times (1.3.0%) than in healthy people (control group), however, the differences were unreliable. DM2 was in 66 out of 201 (32.8%) examined patients, including 18/57 (31.6%) pts in group I, and in 48/144 (33.3%) pts in group II. However, in group I, among 18 patients with DM2, there were 9 (50.0%) carriers of the G allele (AG + GG) vs. 9 carriers of the AA genotype, while in group II there were fewer (P<0.05) - 9/48 (18.8%) vs 39/48 (81.2%) AA carriers. At the same time, in patients with heFH and CAD, there was a positive correlation between the carriage of the G allele and DM2 (Spearman's r 0.43, P<0.05).

Conclusions: In patients with heFH and CAD in the Uzbek population, DM2 was significantly more often associated with the presence of the “gain-of-function” G allele of the PCSK9 E670G genetic polymorphism.

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072 / #1064

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

IMPACT OF SMOKING AND SMOKING CESSATION ON DNA METHYLATION IN PATIENTS REFERRED FOR CORONARY ANGIOGRAPHY

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Smoking is a leading cause of morbidity and mortality worldwide and contributes to disease development and progression partly through epigenetic mechanisms.We analyzed the association of smoking with DNA methylation in the Ludwigshafen Risk and Cardiovascular Health (LURIC) study.

Methods: The LURIC study included 3316 individuals who had been referred for coronary angiography. Smoking status was assessed based on a questionnaire and verified by measurement of serum cotinine. DNA-methylation was assessed using the Illumina HumanMethylation EPIC Beadchip for 2423 participants. Analyses were conducted using the R-package “CpGassoc”. All analyses were performed using multivariable linear regression. In each model the methylation b-value was considered as the independent variable and smoking status as the dependent variable, with adjustment for sex, age, estimated cell count, surrogate variables and the array ID.

Results: In our study, we found 1071 CpGs that had significantly different levels of methylation when comparing active smokers with never smokers. The most significant loci were near the genes AHRR, ALPPL2, F2RL3, RARA, PRSS23, and IER3. For all loci, a decrease in methylation was observed starting from never smokers to ex-smokers to active smokers. Even in the ex-smokers who had already quit smoking more than 20 years ago, the methylation level was still significantly lower at the loci PRSS23, AHRR, ALPPL2 compared to never smokers. For F2RL3, RARA, IER3 there was at least a tendency.

Conclusions: Smoking induces long-lasting changes in DNA methylation and these may play a role in mediating the adverse health effects of tobacco.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

073 / #768

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

SOLUBLE ENDOGLIN IS A BIOMARKER OF VARIOUS TYPES OF LIVER DAMAGE

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Endoglin exists in two forms, membrane endoglin (Eng) and soluble endoglin (sEng) circulating in the blood. Although it has been established that Eng possibly plays an essential role in liver impairment, the precise impact of changing in Eng expression and sEng levels during liver injuries are still unknown. We aimed to analyze the expression of Eng and sEng levels with respect to biomarkers of fibrosis, inflammation, and endothelial dysfunction in two mouse models of liver alteration.

Methods: The liver damage was induced in 9-12-weeks-old C57BL/6 male mice by DDC (3,5-diethoxycarbonyl-1,4-dihydrocollidine) and CDAA-HFD (choline-deficient L-amino acid defined high-fat diet) diets, while control animals were fed with a chow diet for 4 weeks. DDC diet was used to develop intrahepatic cholestasis, and the CDAA-HFD diet induces NASH changes.

Results: The liver impairment was confirmed by the significant increase in the level of liver enzymes along with fibrosis and inflammation induction in both models. While a significant reduction in the Eng liver expression was observed in the DDC animals, there was a significant upregulation of Eng protein expression in the CDAA-HFD mice. Both diets significantly increased MMP14 protein expression which is supported by significantly increased sEng plasma levels.

Conclusions: We suggest both cholestasis and NASH induction result in cleavage of Eng by MMP-14, presenting sEng as a biomarker of these pathologies. According to contrasting results of Eng expression in these two liver injury mouse models, we propose the different potential role of endoglin in various liver pathologies.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

074 / #796

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

INVESTIGATION OF THE ANTIPLATELETS AND ANTI-INFLAMMATORY POTENCY OF BERRIES EXTRACTS

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Berries exert potent antioxidant properties. We studied the effect of 2 different extracts on the membrane expression of the adhesion molecule ICAM-1, on Outgrowth Endothelial Cells (OECs) activated with Tumor Necrosis Factor-alpha (TNF-α) and on platelet aggregation.

Methods: Extracts of *Morus alba* (MA) and *Blueberries* (BB) were prepared using H_2O/Acetic acid (99.5/0.5 v/v) and Isopropanol/H_2O/Acetic acid (60/39.5/0.5 v/v) as solvents, respectively. All extracts were treated with XAD-7 adsorbent resin. Both extracts were rich in flavonoids. MA's main compounds were alkaloids whereas BB was rich in anthocyanins as determined by LC-HRMS. To study their possible anti-inflammatory activity the extracts (200μg/ml) were incubated with OECs and activated with TNF-α (0.5ng/mL) for 6h, 37℃/5%CO_2. Cell activation was assessed determining the expression of ICAM-1 by flow cytometry, using anti-CD54-PE.The inhibitory activity of both extracts towards platelet aggregation in platelet rich plasma induced by ADP, TRAP-6 and Arachidonic Acid (A.A.) was determined by Light Transmittance Aggregometry.

Results: Both MA and BB exhibited a potent inhibitory effect of OECs activation, by 44±22% and by 51±8.3%, respectively. By contrast, neither MA nor BB exhibit inhibitory effect on platelet activation by all agonists. Specifically, MA exhibited 4.68±5.48%, 14.87±12.43% and 17.3±12.74% inhibition, respectively and BB 10.45±12.22%, 13.79±7.65% and 5.53±6.70% inhibition, respectively, for ADP, TRAP-6, and A.A.-induced platelet aggregation.

Conclusions: The extracts exhibit similar anti-inflammatory effect on OECs activation, despite their different phytochemical content. However, both extracts did not exhibit any significant inhibitory effect towards platelet aggregation. Further studies are necessary to investigate the compound(s) responsible for this activity and the underlying mechanisms

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

075 / #695

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

ACTIVE IMMUNIZATION USING TRPM2 PEPTIDE VACCINE ATTENUATES ATHEROSCLEROTIC PROGRESSION IN A MOUSE MODEL OF ATHEROSCLEROSIS

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Atherosclerosis is an immune-mediated inflammation disease with participation of both humoral and cellular immune system. It is tempting to consider specific strategies to modulate the immune responses to attenuate atherosclerotic TRPM2 is expressed in macrophages and vascular cells in vascular walls. Our recent study showed that TRPM2 has proinflammatory role in vascular walls, consequently promoting atherosclerotic progression. In this study, we aimed at developing TRPM2 peptide in vaccine platform to activate anti-TRPM2 immune response to protect against atherosclerosis.

Methods: We applied ApoE$^{-/-}$ mice to establish atherosclerotic model. Peptides were immunized to ApoE$^{-/-}$ mice subcutaneously and then sacrificed followed by serum component measurements and histologic analysis.

Results: We designed several peptide vaccines based on TRPM2 E3 sequences from different animal species' different region, Relative production of IgG antibodies against each antigen was analyzed, Results showed that P1 and R1 elicited modest antibody productions. We also applied immunization with different peptide antigens to suppress atherosclerotic progression in ApoE$^{-/-}$ mice. Results showed that the usage of peptide P1, peptide R1 and R1+R2 combination significantly suppressed the atherosclerotic progression. We further made comparison of different doses of peptide P1 and R1 antigens with two adjuvants in suppressing atherosclerotic progression in ApoE$^{-/-}$ mice. The results showed that P1 and R1 can significantly reduce the atherosclerotic progression at the dose of 67.5μg per mouse with either aluminium salts or with Freund's adjuvant.

Conclusions: Our present study developed a novel strategy of active immunization with TRPM2 E3 peptide in a vaccine platform to attenuate atherosclerotic progression.

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076 / #557

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

MONITORING B CELL ACTIVATION BY FLOW CYTOMETRIC DETECTION OF PHOSPHORYLATED BRUTON'S TYROSINE KINASE (BTK)

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Atherosclerosis and myocardial infarction are driven by autoimmune responses that involve B cell activation and autoantibody generation. BTK is a critical downstream mediator of B cell receptor (BCR) signalling in B cell activation, proliferation, and differentiation. Here, we aimed to develop a flow cytometry assay to monitor B cell activation in humans and mice by detecting BTK phosphorylation.

Methods: Human PBMCs were stimulated with anti-IgM antibody at several time points to evaluate the dynamics of BTK phosphorylation at phosphorylation sites Tyr551 and Tyr223. The specific BTK inhibitor Ibrutinib was used at 0.1 nM to 10 µM to prevent BTK phosphorylation. BTK Phosphorylation was assessed with phospho-specific antibodies (pBTK551 and pBTK223) by intracellular flow cytometry. Mice B cells were negatively isolated from splenocytes, pBTK551 was also detected after anti-IgM antibody stimulation.

Results: The mean fluorescence intensity (MFI) for pBTK223 and pBTK551 rose by up to 3.1- and 4.6-fold at 2 and 3.5 min after stimulation with anti-IgM, respectively, and reached a plateau at 10 min. With 100 nM Ibrutinib, the MFI of pBTK551 and pBTK223 decreased by 50%, indicating high specificity of the assay. The phosphorylation of Tyr551 and Tyr223 were regulated differently among different B cell subsets in humans. In mice B cells, MFI of pBTK551 was significantly increased in transitional 1 and 2, marginal zone, follicular, and plasma B cells ($p<0.05$), but not in memory B cells.

Conclusions: The detection of BTK phosphorylation by flow cytometry provides a valuable tool for monitoring B cell activation in humans and mice in cardiovascular disease.

91ST EAS CONGRESS
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077 / #1319

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

THE ATTENUATED METABOLIC SUPPRESSION AND ELEVATED MTOR LEVELS IN REPLICATIVELY AGED FIBROBLASTS MAY CONTRIBUTE TO ATHEROSCLEROSIS IN HUTCHINSON GILFORD PROGERIA

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Hutchinson Gilford Progeria (HGP) is characterized by accelerated aging and premature death caused by myocardial infarction or stroke. Enhanced metabolism and proliferation may accelerate senescence entry and atherogenesis. We therefore related cellular proliferation and exogenous stress to mTOR signaling in four control and four HGP fibroblast cell lines.

Methods: Cells were grown until they reached replicative senescence through progressive telomere shortening. Hydrogen peroxide served as non-replicative stressor. Semi-quantitative Western-blot analysis of mTOR and up-stream-protein Akt, and down-stream protein p70S6K were related to cell growth and senescence characteristics.

Results: HGP-fibroblasts revealed higher proliferation rates (+ 53±35%), premature (on average 226 days earlier) entries into growth arrest and higher percentages of senescent cells (73 ±18%), compared to healthy aged controls (40±3%). We observed 2-fold elevated levels of *TBC1D3*, an amplifier of EGF receptor response. All key proteins of the mTOR signaling pathway and their phosphorylated forms were suppressed in healthy aged cells (mTOR and phosphorylated mTOR down to 34±17%/26±3 %; AKT and phosphorylated AKT 40±23 %/2±2 %; p70S6K and phosphorylated p70S6K 36±24 %/16±11 % of the levels of young cells). In HGP cells, by contrast, suppression was absent or markedly reduced for mTOR (125±54%), phosphorylated mTOR (141±66%), Akt (122±31%), phosphorylated Akt (40±22%) and p70S6K (159±201%). Treatment with hydrogen peroxide had no modifying influence on these results.

Conclusions: In conclusion, these findings show that HGP cells have higher proliferation stress than controls. Altered mTOR signaling may contribute to attenuated metabolic suppression, accelerated senescence entry and premature atherosclerosis in HGP.

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078 / #1008

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

ABO BLOOD GROUPS, RHD-FACTOR, AND THEIR ASSOCIATION WITH SUBCLINICAL CARDIOVASCULAR DISEASE ASSESSED BY CAROTID ULTRASONOGRAPHY

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: ABO group system has previously been associated with several disease outcomes, where non-O blood group individuals have been associated with increased incidence of both venous and arterial thromboembolic events. However, studies assessing early atherosclerotic disease and also the influence of RhD are few. Some have stated that non-O blood groups are associated with higher severity of atherosclerosis assessed by angiography and also linked to CAD with myocardial infarction but no association between ABO and CAD without infarction was seen. This present study aimed to investigate whether the ABO blood group and RhD are associated with subclinical cardiovascular disease assessed by carotid ultrasonography in a healthy population.

Methods: Participants were all part of the VIP-VIZA trial], including 3532 participants with available carotid ultrasonography results to visually assess subclinical disease (prescence of carotid plaques and carotid intima media thickness [CIMT]). To determine ABO and RhD the Swedish-Danish database (SCANDAT-3) was used, including data on blood donors, transfusions, transfused patients and blood components where 85% of VIP-VIZA participants were registered.

Results: Among ABO blood groups 44% of participants had carotid plaques. There was no significant difference between Non-O and O individuals regarding plaque (OR 1.10 CI 95% 0.88-1,18) or CIMT quartiles (OR 1.065 CI 95% 0.86-1.31 when comparing Q4 to Q1). For RhD similar results were seen OR 1.12 CI95% 0.91-1.38 and OR 1.082 CI95% 0.08-1.45 respectively.

Conclusions: Our findings indicate that ABO and RhD is not associated with early atherosclerotic disease in a healthy population.

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079 / #291

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

IMMUNE CELL TEMPORAL DYNAMICS AFTER MYOCARDIAL INFARCTION IN THE MOUSE HEART

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Myocardial infarction (MI) caused by coronary artery disease is a major cause of death globally. The inflammatory response triggered by myocyte necrosis drives adverse ventricular remodeling that ultimately promotes heart failure. The temporal and spatial characteristics of cardiac immune cell infiltration after MI, however, are only partially understood. Here, we describe a systematic screening by flow cytometry to decipher the immune cell repertoire in murine experimental MI.

Methods: We characterized the dynamics of the immune cell repertoire in murine hearts following myocardial infarction by multi-color flow cytometry. Immune cell infiltrates in the heart were screened at 1, 3, 7, 14 and 28 days after MI induced by a surgical permanent ligation of the descending left coronary artery (LAD), transient ischemic/reperfusion injury (I/R) or sham surgery in C57BL6/J, 10 weeks old male mice. Also, we performed transcription analysis by bulk RNA sequencing of healthy hearts as well as remote and infarcted heart areas after 3,7 and 28 days focusing on immune activation and exhaustion markers.

Results: Our results identify a sequential shift in the resident heart leukocyte population after myocardial infarction, from a healthy state until end-stage heart failure and argue for an adaptive immune response, involving antigen-presenting DCs and effector T and B cells as well as potential new targets, including NK and γ/δ T cells. This is consistent with the build-up of a relevant immune memory after MI.

Conclusions: Our results clarify the immune cell subsets infiltrating the heart following myocardial infarction and throughout the development of ischemic heart failure.

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080 / #1525

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

DISEASE PROGRESSION IN A MOUSE MODEL OF DIET-INDUCED LETHAL ISCHEMIC HEART DISEASE: THE INFLUENCE OF PERIPHERAL BLOOD NEUTROPHIL AND MYOCARDIAL COLLAGEN DEPOSITS

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Myocardial infarction (MI) is a leading cause of death worldwide. Myocardial ischemia leads to a progressive increase in collagen depositions with changes in the relative proportion between collagen I and III, which has been associated with a worsening prognosis of patients with heart failure. Studies have reported that neutrophils could play a crucial role throughout the process of MI, however, if its peripheral levels are involved with the changes in myocardial collagen deposits after ischemic events need to be studied. We studied the peripheral blood neutrophil levels and myocardial collagen deposits in the SR-B1 KO/ApoeR61$^{h/h}$ mice, a murine model of diet-induced lethal ischemic heart disease, during the progression of the coronary disease.

Methods: Male SR-B1 KO/ApoeR61$^{h/h}$ mice were fed with an atherogenic diet (HFC; 15% fat, 1.25% cholesterol, 0.5% cholate) for 0, 7, and 21 days (n=3). Mice fed with normal diet were used as controls. Blood samples were obtained for analysis of neutrophils. Myocardial tissues were processed and stained for the evaluation of collagen deposits. Statistical analysis was performed with Kruskal-Wallis test and Spearman correlation.

Results: Blood neutrophil levels, myocardial collagen, and collagen I deposits were increased during the progression of the diseases and at day 21 there was a significant difference compared to 0 days (P=0.0264, P=0.0219, P=0.0338, respectively). There was a positive correlation between the blood neutrophil levels and the collagen deposits during the progression of the disease.

Conclusions: SR-BI KO/ApoeR61$^{h/h}$ mice have the potential to contribute to our understanding of myocardial ischemia, remodelling, and the disease prognostic.

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081 / #260

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

DYSFUNCTIONAL MITOPHAGY ASSOCIATED MUTATION IN THP-1 CELLS.

POSTER ON BOARD: AS01.13 OTHER

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Background and Aims: Dysfunctional autophagy (mitophagy) is associated with atherosclerosis progression. Dysfunctional mitophagy can promote apoptosis and lead to hyperactivation of inflammatory pathways in macrophages. Some mitochondrial mutations may provoke defective mitophagy in macrophages. One of this mutation, G15059A in CYB gene, was mainly found in atherosclerosis plaques and positively correlates with the age of patients with atherosclerosis and coronary artery disease. The aim of this study was to assess the role of this mutation in dysfunctional mitophagy on macrophages.

Methods: The control THP-1 cells and THP-1 cells with mitochondrial G15059A mutation (TCHSMAM1 cells) in CYB gene were used to assess mitophagy level. The mitoCAS9 vector and two sgRNAs to G15059A mutation was used to eliminate the mutation from TCHSMAM1 cells. Carbonyl cyanide-p-trifluoromethoxyphenylhydrazone (FCCP) was used to stimulate mitophagy. Mitophagy was assessed by a confocal microscopy in the presence of MitoTracker Green and LysoTracker Deep Red.

Results: G15059A mutation was removed from TCHSMAM1 cells by CRISPR/Cas9 editing. As a result, the heteroplasmy level was decreased was reduced up to 3.7% from initial 68% in TCHSMAM1 cells. The mitophagy activity was increased in 1.3-fold ($p<0.001$) in THP-1 and in 1.5-fold ($p<0.001$) in CRISPR-treated TCHSMAM1 cells under induction of mitophagy by FCCP. In the intact TCHSMAM1 cells the mitophagy was dysfunctional under the same conditions.

Conclusions: Mutation G15059A can contribute to the disruption of mitophagy processes in cells, which can lead to the preservation of dysfunctional mitochondria in macrophages. This study was supported by Russian Science Foundation, Grant # 22-15-00064.

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082 / #1577

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

HYPOLIPIDEMIC TREATMENT INCREASES LIPOPROTEIN(A) LEVELS IN PATIENTS WITH MIXED HYPERLIPIDEMIA

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: To compare the effect of hypolipidemic treatment on Lipoprotein(a) [Lp(a)] levels of patients with mixed hyperlipidemia.

Methods: We previously randomised patients with mixed hyperlipidemia [low density lipoprotein (LDL-C) >160 mg/dl and triglycerides >200 mg/dl) to rosuvastatin monotherapy 40 mg/day (R group, n = 30) or rosuvastatin 10 mg/day combined with fenofibrate 200 mg/day (RF group, n = 30) or omega-3 fatty acids 2 g/day (RΩ group, n = 30). In the present retrospective study, we included only the patients whose Lp(a) levels were assessed (16, 16 and 15 in the R, RF and RΩ groups, respectively). Lipid profile and Lp(a) were measured at baseline and after 3 months of treatment.

Results: A significant increase in Lp(a) levels was noted in the R ($p = 0.017$) and RF ($p = 0.029$) groups, while a slight increase was seen in RΩ group (p = NS). Regarding Lp(a) elevations, no differences were found between groups. In the R group, a strong negative correlation between the changes in Lp(a) and LDL-C ($r = -0.500$, $p = 0.049$) was observed, while a significant negative correlation between the changes in Lp(a) and triglycerides ($r = -0.531$, $p = 0.034$) was noted in the RF group.

Conclusions: Hypolipidemic treatment increases Lp(a) levels in patients with mixed hyperlipidemia. Novel therapies should target on Lp(a) levels reduction to decrease the residual atherosclerotic cardiovascular disease risk.

91ST EAS CONGRESS
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083 / #747

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

NANOPORE SEQUENCING WITH UNIQUE MOLECULAR IDENTIFIERS PRESERVES SNP HAPLOTYPES OF THE LPA KIV-2 COPY NUMBER VARIATION

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: About 90% of lipoprotein(a) [Lp(a)] variance is explained by the polymorphic kringle IV type-2 (KIV-2) copy number variation in *LPA*. Multiple functional SNPs in the KIV-2 region have been detected using short-read next-generation sequencing (NGS). However, NGS loses SNP haplotype information, therefore masking SNP-SNP interactions. We evaluated a long-range, single-molecule nanopore-sequencing approach using unique molecular identifiers (UMI) to preserve SNP haplotype information of each KIV-2 repeat.

Methods: Seven KIV-2 amplicon mixtures (50% to 0.5% level, 85 differences) and 13 individuals were used for method validation. UMIs are random oligonucleotides that act as single-molecule barcodes and allow creating intramolecular consensus sequences to compensate sequencing and polymerase error rate. All KIV-2 repeats in each sample were UMI-tagged and PCR-amplified. After nanopore-sequencing (chemistries R9 and V14), reads were mapped, iteratively clustered by their UMI-tags and a consensus for each KIV-2 molecule was created. Variants were called and haplotypes extracted.

Results: UMI-nanopore sequencing is comparable to NGS but retains full SNP haplotype information of each KIV-2 unit. False-positive rate per KIV-2 unit was <1 in 5,100bp (<0.02%). After noise filtering, we found 1,179 of 1,191 expected SNPs with only 14 false-positives (precision and sensitivity, mean±SD: 98.9%±0.03%). SNP levels of NGS versus UMI-nanopore were highly correlated (R^2=0.955-0.999) and variants were detectable down to 1% (R9 chemistry) and 0.5% level (V14 chemistry). 60,000 reads per sample were sufficient for accurate consensus and variant calling.

Conclusions: UMI-nanopore sequencing allows conserving the SNP haplotypes during KIV-2 sequencing and provides a novel instrument to dissect haplotype diversity and effects on Lp(a) concentrations.

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084 / #407

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

DISTRIBUTION AND VARIATION OF LIPOPROTEIN(A) IN PATIENTS ATTENDING A LIPID CLINIC IN GREECE

POSTER ON BOARD: AS02.01 LP(A)

Fotios Barkas[1], Amalia-Despoina Koutsogianni[2], Georgia Anastasiou[2], Petros Spyridonas Adamidis[2], Konstantina Kyrili[2], George Liamis[2], Evangelia Ntzani[1], Charalampos Milionis[2], Evangelos Liberopoulos[3]
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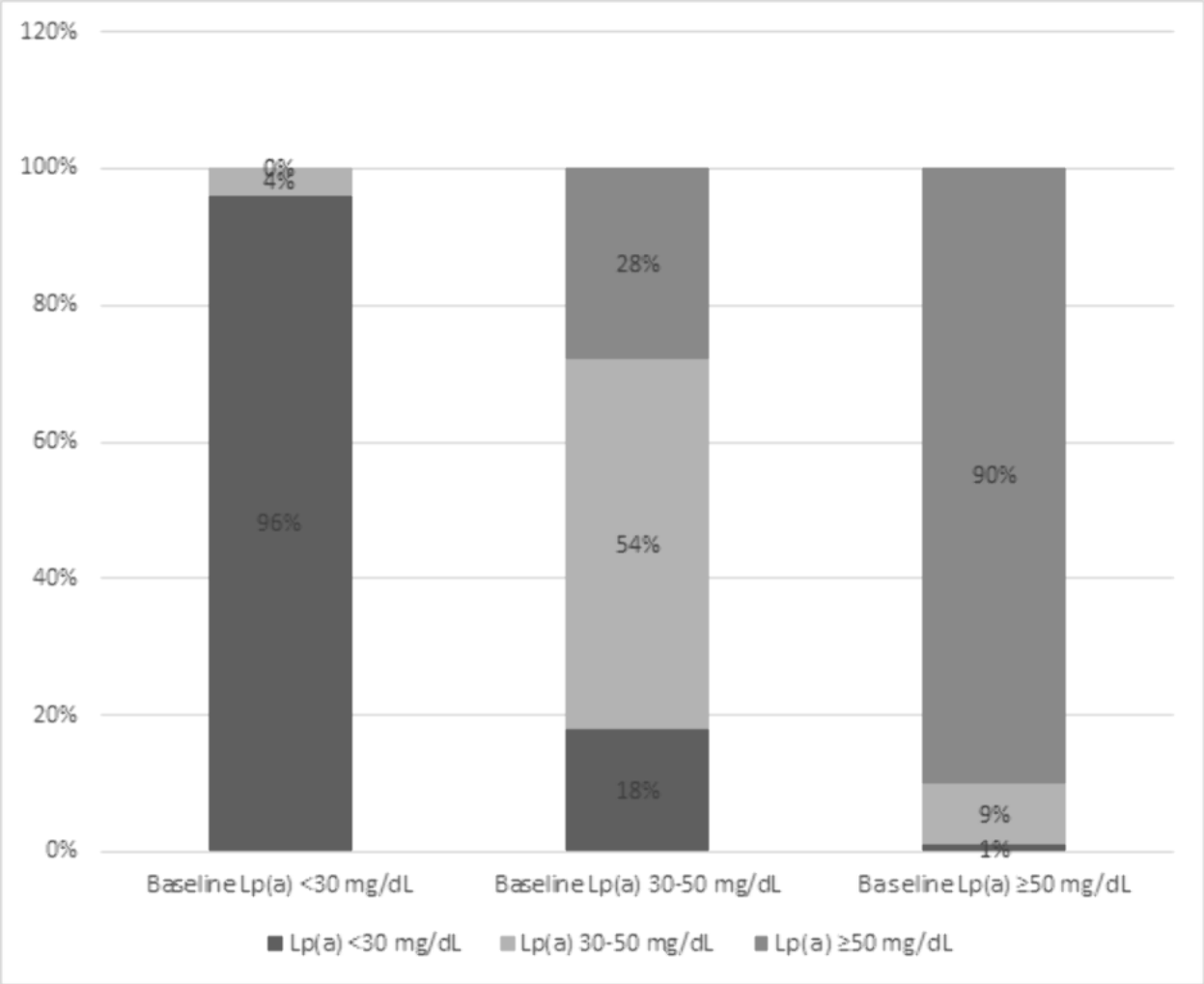
Background and Aims: To investigate the distribution and variation of lipoprotein(a) [Lp(a)] in patients with dyslipidemia attending a lipid clinic in Greece.

Methods: Retrospective observational study of patients with dyslipidemia attending a tertiary lipid clinic in Greece. Electronic health records were scrutinized for patients with available Lp(a) measurements from 2012 to 2022. Lp(a) variation was investigated in those having ≥2 heterochronized Lp(a) measurements during follow-up and were on stable hypolipidemic treatment.

Results: 1975 patients were included (51.3% females, 98% adults, median age 49 years [IQR: 37-60]). Median Lp(a) was 10.7 mg/dL (IQR: 4.4-27.8); values at 80th, 90th, and 95th percentiles were 35.9, 59.9 and 84.3 mg/dL, respectively. Of patients, 13.9% had Lp(a) ≥50 mg/dL. 775 patients had their Lp(a) measured twice during follow-up (0.6 [0.3-1.7] years). Lp(a) medians at 1st and 2nd visit were similar (13.5 [5.6-39] and 13.6 [5.6-39] mg/dL, p>0.05). Median intra-individual variation of Lp(a) was 13% (5-23%). As shown in Figure, 32% of patients were reclassified to a higher Lp(a) group and 28% to a lower Lp(a) group during follow-up. Higher Lp(a) variation was observed in children compared to adults (20% [13-26] vs 13% [6-24], p>0.05). Highest quartile of follow-up (>1.69 years) was associated with higher Lp(a) variation compared to the 1st quartile (15% [8-28] vs 11% [5- 23],

p<0.05).



Conclusions: Prevalence of Lp(a) >50 mg/dL in patients attending a lipid clinic in Greece is 13.9%. One in 4 patients showed a variation in Lp(a) over 20% during their follow-up. Childhood and duration of follow-up seem to be associated with increased Lp(a) variation.

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085 / #172

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

HYPOLIPIDAEMIC TREATMENT IN PATIENTS WITH ELEVATED LIPOPROTEIN (A)

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Aim: To evaluate the effect of hypolipidaemic therapies in patients with elevated levels of lipoprotein(a) [Lp(a)].

Methods: Materials and Methods: A prospective study including 70 patients at high cardiovascular risk with elevated Lp(a) levels (>30 mg/dL) attending a Lipid Clinic in Greece. Subjects were allocated to the following therapies according to national guidelines for cholesterol management: high-intensity statin monotherapy (n=28), ezetimibe added to high-intensity statin (n=31), and PCSK9 inhibitor added to high-intensity statin plus ezetimibe (n=11). Follow-up duration was 3 months. We investigated the effect of the lipid-lowering interventions on subjects' lipidemic and glycemic profile. Comparisons between two groups were adjusted for the baseline levels of the studied parameters.

Results: Results: Subjects' mean age was 51 ± 15 years, 40% were male, 39% were diagnosed with familial hypercholesterolaemia, 16% with atherosclerotic cardiovascular disease, while 36%, 33% and 15% were at very high, high, and moderate cardiovascular risk, respectively. All interventions significantly reduced apolipoprotein B, total and LDL cholesterol, but only PCSK9 inhibitors reduced significantly Lp(a) (Table). PCSK9 inhibitors achieved the highest reduction in LDL cholesterol (-56% vs -43% vs -22%, respectively, $p<0.05$) and Lp(a) levels (-28% vs +11% vs +17%, respectively, $p<0.05$) compared with ezetimibe and statin monotherapy, respectively (Table). No significant effect on subjects' glycemic profile

across treatment groups was

Table. Effect of hypolipidaemic drugs on the lipidemic and glycemic profile of patients with dyslipidemia

	Baseline Visit	After 3 Months	Absolute Change within each Group	% Change within each group
Total Cholesterol, mg/dl.				
Statin	256±38	177±35	-79±51 *	-29% *
Ezetimibe	176±23 *	151±22 *	-25±30 *	-14% *
PCSK9 inhibitors	217±52 *#	138±43 *	-78±20 *#	-35% *#
Triglycerides, mg/dl.				
Statin	97 (57-265)	78 (45-371)	-21 (-140 to 284) *	-25%
Ezetimibe	105 (44-198)	81 (45-254)	-8 (-98 to 74)	-13%
PCSK9 inhibitors	96 (72-270)	79 (44-365)	-20 (-119 to 93)	-19%
High-density Lipoprotein Cholesterol, mg/dl.				
Statin	60±15	58±13	3±7 *	4% *
Ezetimibe	54±16	54±14	-1±7	-1%
PCSK9 inhibitors	52±12	51±15	0	0
Low-density Lipoprotein Cholesterol, mg/dL				
Statin	174±34	99±27	-75±44 *	-41% *
Ezetimibe	101±19	79±15 *	-22±19 *	-21% *
PCSK9 inhibitors	140±45 *#	62±30 *#	-78±27 *#	-54% *#
Apolipoprotein B, mg/dl.				
Statin	102±27	70±18	-32±28 *	-28% *
Ezetimibe	85±26 *	65±13	-20±20 *	-20% *
PCSK9 inhibitors	107 ±22 *#	59±19	-47±28 *#	-43% *#
Lipoprotein (a), mg/dl.				
Statin	53,7 (30,9 168,8)	64.7 (23.6 145)	6±17	13%
Ezetimibe	57.8 (30,9 198)	69.1 (26.1 222)	10±18 *	10% *
PCSK9 inhibitors	79.2 (26,2 204)	48.8 (18.8 155)	22±12 *#	24% *#
Glucose, mg/dL				
Statin	90 (±8)	91 (±12)	1 (±11)	1%
Ezetimibe	97 (±11) *	98 (±10) *	0	0
PCSK9 inhibitors	91 (±6)	90 (±10)	-1 (±11)	-1%
Insulin, µU/mL				
Statin	7,2 (2,8-151,4)	7,3 (3,3-123,2)	0,4 (-28,1 to 18,4)	13%
Ezetimibe	6,7 (2,8-42)	8,2 (2,9-50,3)	0,1 (-21,8 to 18,8)	3%
PCSK9 inhibitors	10,8 (3,1-55,9)	9 (2,4-37,1)	-1,8 (-27,5 to 6,4)	-27%
HOMA Insulin Resistance Index				
Statin	1,7 (0,4 38,1)	1,6 (0,6 42,6)	0,1 (1,5 to 4,5)	12%
Ezetimibe	1,7 (0,7 10)	2,1 (0,7 7,6)	0	0
PCSK9 inhibitors	2,6 (0,7-12)	2 (0,5-9)	-0,5 (-6,3 to -0,6)	-29%

* p<0.05 for the comparison within each group

* p<0.05 for the comparison with patients treated with a high-intensity statin

# p<0.05 for comparison with patients treated with ezetimibe plus high-intensity statin

noted.

Conclusions: Conclusions: PCSK9 inhibitors achieved the highest LDL cholesterol reduction compared with high-intensity statin ± ezetimibe and the only to lower significantly Lp(a).

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086 / #1343

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

ATHEROGENIC LIPOPROTEINS, NEUTROPHIL-TO-LYMPHOCYTE RATIO AND SEVERITY OF AORTIC STENOSIS.

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: To assess the association of lipoprotein(a) [Lp(a)], low density lipoprotein cholesterol (LDL-C) concentration and inflammatory marker with severity of calcific aortic valve stenosis.

Methods: The study included 164 patients with aortic stenosis divided into 2 groups: group 1 of 64 patients with mild to moderate aortic stenosis and group 2 of 100 patients with severe and very severe aortic stenosis, according to the echocardiography data. Lipids, Lp(a) level were determined in all patients. Neutrophil-to-lymphocyte ratio (NLR) was used as an inflammatory marker.

Results: Patients with severe aortic stenosis were older than subjects with mild to moderate disease: 73.7±8.6 and 71.6±11.4 years old, respectively, $p<0.05$, the incidence of coronary heart disease (CHD) was higher in group 2 than in group 1; 78% vs 52%, $p<0.001$. The differences can probably be explained by the initial development of CHD that requires hospitalization, when the early stage of aortic stenosis was diagnosed. The concentration of LDL-C was higher among patients in the first group than in the second (3.4±2.3 mmol/l and 3.2±1.4 mmol/l, respectively, $p<0.01$) whereas there was no difference in Lp(a) level. According to univariate correlation analysis, Lp(a)≥30 mg/dL showed no association with aortic stenosis severity (Vmax and Gpmean) $r=-0.09$, $p=0.31$ and $r=-0.11$, $p=0.17$, respectively. NLR was higher in patients of group 1 than group 2: 2.4±2.0 and 2.1±1.1, respectively, $p<0.001$.

Conclusions: Elevated neutrophil-to-lymphocyte ratio and LDL-C concentrations but not Lp(a) level were associated with early stages of calcific aortic valve stenosis.

91ST EAS CONGRESS
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087 / #112

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LP(A) DETECTION DURING PREMATURE ACUTE VASCULAR EVENT

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Lipoprotein(a) [Lp(a)] is a genetical cardiovascular risk factor. The occurrence of an acute ischemic vascular event (coronary, cerebral, peripherical) is an opportunity to detect this specific dyslipidemia, mostly in the context of premature ischemic event.

Methods: All premature (women < 65 y/o, men < 55 y/o) acute ischemic vascular consecutive events from a single institution were recorded from 05/2022 to 12/2022. Demographic, clinical and biochemistry data were collected.

Results: 32 patients were detected with a premature acute ischemic vascular event (6 [19%] women, 26 [81%] male), mean age 56 y/o. 85% of the events were acute coronary syndrome and 15% acute peripheral artery disease events. Almost 45% of the patients were in secondary prevention (recurrent event). 9/32 (28%) had a value of Lp(a) elevated (mean value 71 mg/dL); none of the patients knew their Lp(a) value previously. Mean lipid profile: total cholesterol 154 mg/dL, HDLc 35 mg/dL, LDLc 90 mg/dL, triglyceride 146 mg/dL.

Conclusions: In this acute ischemic premature event setting, almost 1/3 of these patients were found to have an elevated lp(a) level, and nearly 50% had already a vascular event. This scenario is a unique opportunity to make awareness and detect patients with a high level of lp(a).

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088 / #991

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LIPOPROTEIN(A) SCREENING IN PATIENTS WITH ELEVATED CARDIOVASCULAR RISK

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Circulating levels of Lp(a) are mainly genetically determined. It is an undervalued but very important cardiovascular risk factor in patients with values ≥75nmol/L. National and international professional society guidelines have recommended measuring Lp(a) in select populations, while some have recommended that Lp(a) be measured at least once in the general population. The aim of the study was the screening assessment of the Lp(a) level in hospitalized patients and the comparison of groups with elevated and non-elevated Lp(a).

Methods: We performed 8 months screening of Lp(a) level in patients with elevated cardiovascular risk hospitalized at the Department of Internal Diseases. We included 110 patients. Lp(a) was measured at the day of the admission to the hospital.

Results: Average Lp(a) level for them was 84±135nmol/l, mean age 68±14.5years, mean LDL 91±64mg/dl. Regarding the Lp(a) level the patients were divided into two groups: 1) patients with Lp(a)≥75nmol/L, n=31 (28%), mean age 62.4±16 years; mean Lp(a) 254.7± 151.8nmol/l, mean LDL 91±51.4mg/dl, and 2) patients with Lp(a)<75nmol/L, n=79 (72%), mean age 69.9±13.2years; mean Lp(a) 16.7±16.9nmol/l, mean LDL 91.2±69.5mg/dl, there were 17(15%) cardiovascular incidents including: STEMI(n=4) at the average age of 54±18 years with mean Lp(a) levels 177.4±156nmol/l; NSTEMI(n=6), mean age 62±9, mean Lp(a) 143.3±183nmol/l and UA(n=7), mean age 48±11, mean Lp(a) 156.9±254 nmol/l. The frequency of cardiovascular incidents in two study groups: 1) with elevated Lpa(a) vs 2) with normal Lp(a) was: 7/17(41.2%) vs. 6/28(21.4%).

Conclusions: Lp(a) was elevated among 28% of patients. Elevated Lp(a) was associated with higher frequency of cardiovascular incidents regardless of age and LDL concentration.

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089 / #652

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

ASSESSMENT OF LIPOPROTEIN (A) LEVELS IN PATIENTS WITH ATHEROSCLEROTIC CARDIOVASCULAR DISEASE: SINGLE CENTER EXPERIENCE FROM TURKIYE

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Elevated lipoprotein (a) level is accepted as a cause of residual risk in patients with atherosclerotic cardiovascular disease (ASCVD). About 90% of Lp(a) level is determined genetically so levels may differ between different geographical regions. There is not enough data on Lp(a) levels in Turkish population.

Methods: Data of patients with ASCVD and had Lp (a) measurement were retrospectively collected. Diagnosis of ASCVD was established as; coronary revascularization either percutaneous or surgical or presence of at least one coronary lesion with > 50% stenosis on coronary angiography; peripheral arterial revascularization either percutaneous or surgical or presence of at least one arterial lesion with > 50% stenosis on imaging; carotid revascularization either percutaneous or surgical or presence of at least one carotid lesion with > 50% stenosis.

Results: In total, Lp(a) measurements of 1193 patients were analyzed (Table1). Mean Lp(a) was 28.2 mg/dL, median Lp(a) was 16 mg/dL and 25th percentile was 7 mg/dL and 75th percentile was 39 mg/dL. The highest Lp(a) level was 326 mg/dL. 18.7% of the cases had Lp(a) ≥ 50 mg/dL, 10.8% of the cases had Lp(a) ≥ 70 mg/dL and 5.8% of the cases had Lp(a) ≥ 90 mg/dL (Figure 1). Highest measured mean total cholesterol and LDL-c levels were as follows; 212± 54 mg/dL and 132± 47 mg/dL. There was weak but significant positive correlation between Lp(a) levels total cholesterol (r=0.075, p = 0.01) and LDL-c (r=0.106, p < 0.01) (Figure
2).

Figure 1.

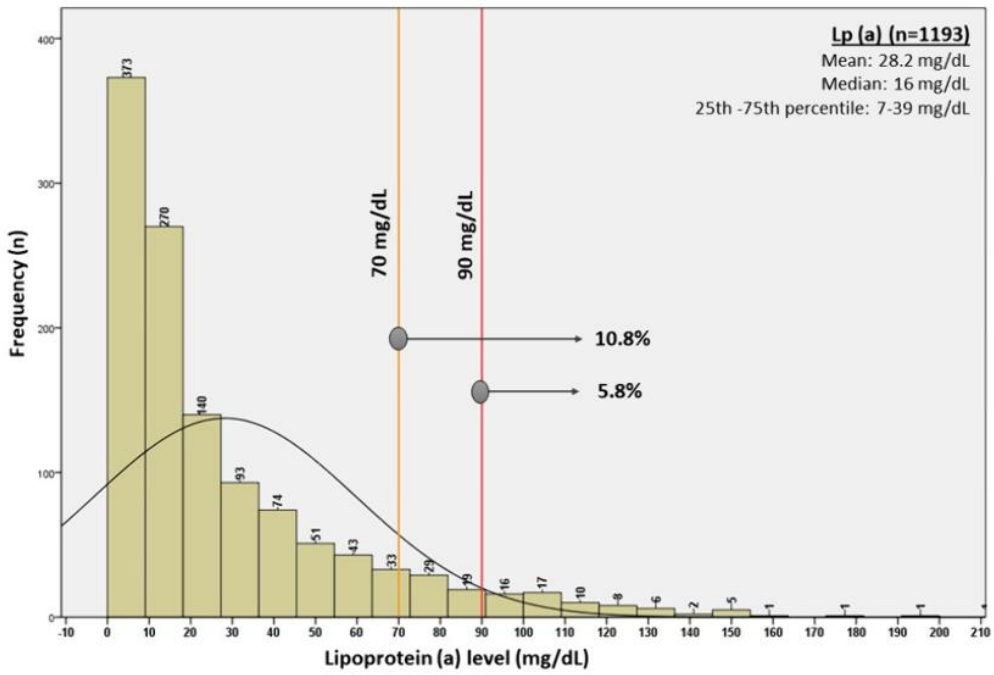
Lp (a) (n=1193)
Mean: 28.2 mg/dL
Median: 16 mg/dL
25th -75th percentile: 7-39 mg/dL
70 mg/dL
90 mg/dL
10.8%
5.8%
Frequency (n)
Lipoprotein (a) level (mg/dL)

Figure 2.

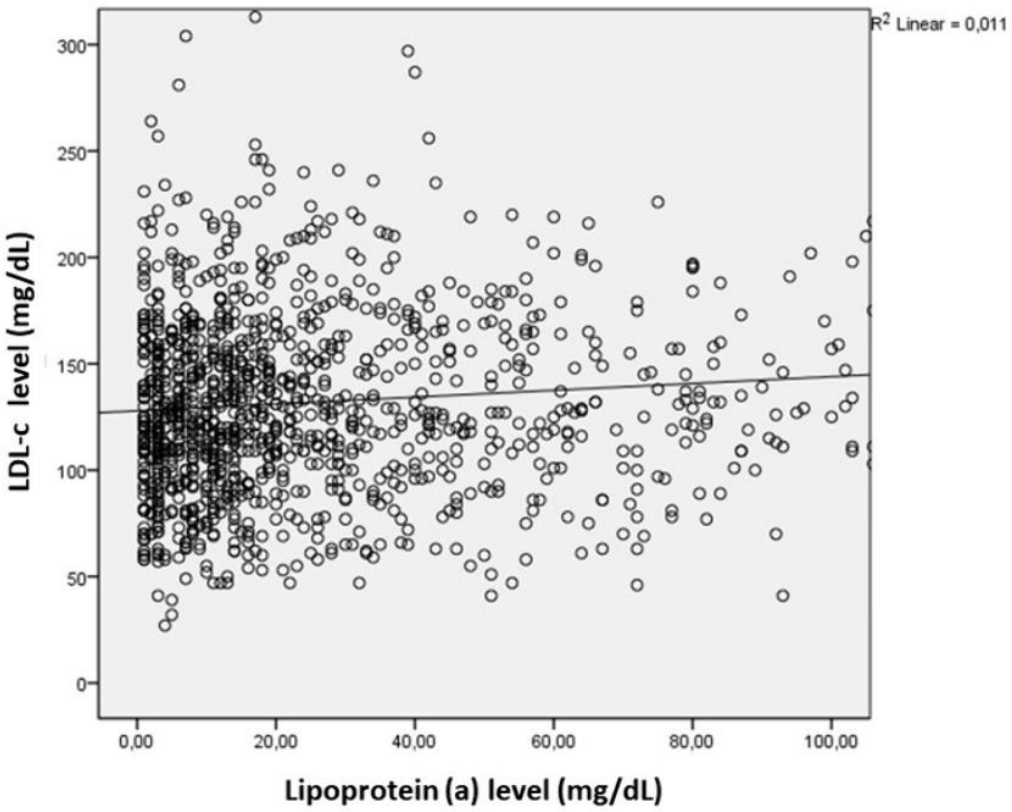
R² Linear = 0,011
LDL-c level (mg/dL)
300
250
200
150
100
50
0
0,00
20,00
40,00
60,00
80,00
100,00
Lipoprotein (a) level (mg/dL)

Table 1. The demographic, clinical, laboratory characteristics of the study population.

Variables	**All (n=1193)**
Age, years	53.6±8.5
Male gender, n (%)	923 (77.4)
Hypertension, n (%)	596 (49.9)
Diabetes mellitus, n (%)	363 (30.4)
Active Smoker, n (%)	420 (35.2)
ASCVD diagnosis	
Percutaneous coronary intervention, n(%)	963 (80.7)
Stroke, n(%)	18 (1.5)
Peripheral arterial disease, n(%)	56 (5.9)
Multiple territories, n(%)	70 ()
Laboratory parameters	
Total cholesterol, mg/dL	212± 54
LDL-C, mg/dL	132±47
Lipoprotein (a), mg/dL	16 [7-39]

Abbreviations: ASCVD atherosclerotic cardiovascular diseases; LDL low density lipoprotein

* Parametric variables are depicted as mean ± standard deviation and nonparametric variables are depicted as median [25th-75th percentile]

Conclusions: Here, we report the distribution of Lp(a) levels in ASCVD patients from Turkiye.

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090 / #1050

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LIPOPROTEIN(A) AND CAROTID INTIMA-MEDIA THICKNESS IN CHILDREN: A 20-YEAR FOLLOW-UP STUDY

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Elevated lipoprotein(a) [Lp(a)] is independently associated with cardiovascular disease (CVD). A long-term follow-up study in children with familial hypercholesterolemia (FH) showed that Lp(a) contributes significantly to early atherosclerosis, as measured by carotid intima-media thickness (cIMT). However, it is unknown if this holds true for children without FH. Therefore, we evaluated the contribution of Lp(a) to arterial wall thickening (cIMT) in children without FH during long-term follow-up.

Methods: For this 20-year follow-up study, unaffected siblings of children with FH that participated in a pravastatin-trial between 1997 and 1999, were eligible. We used linear mixed-effects models to evaluate the association between Lp(a) and cIMT during follow-up (baseline, and 10, 20 years thereafter).

Results: We included 88 children (mean age: 12.9 years). At baseline, median (IQR) Lp(a) was 16.2 (9.6-50.8) nmol/L and mean (SD) cIMT 0.439 (0.045) mm. No significant associations were found between Lp(a) and cIMT during follow-up (ß-unadjusted [95% CI]=0.006 [-0.005-0.017] mm per 50 nmol/L increase Lp(a), p=0.30; ß-adjusted [95% CI]=0.0001 [-0.008-0.008] mm per 50 nmol/L increase Lp(a), p=0.97).

Conclusions: In children without FH, Lp(a) did not contribute significantly to structural changes of the vessel wall during the 20-year follow-up period. Possibly, cIMT is not a suitable marker to detect potential (small) Lp(a)-mediated changes of the arterial wall in young, healthy individuals. However, it could also be that elevated Lp(a) is only a clinically significant risk factor for early atherosclerosis in the presence of other risk factors for atherosclerosis such as FH.

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091 / #744

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

ACTUAL DATA ON THE APOLIPOPROTEIN B PART TRANSPORTED WITH LIPOPROTEIN(A)

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: When measuring LDL-cholesterol (LDL-C) both compartments in LDL and lipoprotein(a) (Lp(a) are captured. When calculating the proportion of LDL-C of LDL a formula had been published: LDL-Ctrue (mg/dl) = LDL-C – (Lp(a) (mg/dl) * 0,3). Unfortunately, this formula has several problems and in some patients negative LDL-Ctrue concentrations are obtained. In a statement from the American Heart Association (Reyes-Soffer G, et al. Arterioscler Thromb Vasc Biol. 2022;42(1):e48-e60) it was suggested to calculate the apolipoprotein B (ApoB) that is in Lp(a).

Methods: We calculated this percentage in 125 patients who were treated with lipoprotein apheresis (LA) before and after an LA session.

Results: This percentage amounted to 11.3 % (IQR 6.9 / 14.6) before LA and to 9.8 % (IQR 5.1 / 18.0) after LA. The concentrations of ApoB transported with Lp(a) (ApoBLpa) were: before LA 8.8 mg/dl (IQR 6.3 / 11.4), after LA 2.15 mg/dl (IQR 1.45 / 2.9). The corresponding ApoB concentrations contained in VLDL and LDL (ApoBVLDL_LDL) were: before LA 71.25 mg/dl (IQR 58.95 / 84.00), after LA 21.95 (IQR 9.30 / 26.95). The following acute reduction rates induced by the LA session were seen: Lp(a) –75.64 % (IQR -79.63 / - 72.27), ApoBLpa -75.64 % (IQR -79.62 / -72.27), LDL-C -70.67 % (IQR -75.72 / -67.03), ApoBVLDL_LDL -70.13 % (IQR -79.82 / -65.57), total ApoB -70.79 % (IQR -79.62 / -72.27).

Conclusions: Calculating the percentage of ApoB that is contained in Lp(a) is a new approach to differentiate the effect of LA on various lipoprotein particles.

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092 / #181

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

THE ASSESSMENT OF CAROTID ATHEROSCLEROSIS MAY BE USEFUL TO RESTRATIFY PATIENTS WITH ELEVATED LIPOPROTEIN (A)

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Elevated Lipoprotein (a) (Lp(a)) is a independent and causal risk factor for cardiovascular disease. Subclinical atheromatosis is a predictor of vascular events in the general population.The aim of this abstract is to evaluate the association between carotid atherosclerosis (CA) and major vascular events (MACE) in a population with elevated Lp(a) and its performance in predicting events.

Methods: We retrospectively included patients >18 years of age evaluated in our center who presented Lp(a) > 75 nmol/l. Cardiovascular risk factors and the presence of carotid atheromatosis were analyzed by ultrasound. Univariate and multivariate analyzes were performed using logistic regression to determine the association between CA and a history of MACE. Carotid Doppler performance was evaluated to predict events by sensitivity (S), specificity (E), positive and negative likelihood (LR+, LR -). p <0.05 was considered significant.

Results: 61 patients were included, mean age 54 years (±13), 21% were women, 44% had MACE (Table 1). CA and male sex were associated with MACE (68.8% vs 12% p<0.001 and 53% vs 15% p0.015 respectively) (table 2). The multivariate model showed a significant association between MACE and AC

with an OR16.7 IC95 3.8 - 73, p<0.001. Carotid Doppler had an E64.7%, S88.9%, LR+ 2.52 and LR- 0.17

	Sin AC 26p(43%)	Con AC 35p(58%)	P
Edad (años)	49±13	57±13	0.02
Mujer	7(27%)	6(17%)	NS
Lp (a) (nmol/L)	172(Rg 394)	200(Rg 545)	NS
HTA	8(32%)	19(54%)	NS
TBQ	2(8%)	9(26%)	NS
EXTBQ	3(12%)	4(11%)	NS
DLP	16(64%)	24(68%)	NS
DM2	2(8%)	2(5.7%)	NS
CT	192±48	175±47	NS

TABLA1

	Con MACE (27p)	Sin MACE(34p)	p (significativa <0.05)
Presencia de AC	68.8%	12%	<0.001
Sexo masculino	53%	15%	0.015

TABLA 2

Performance	Resultado	Intervalo de confianza 95%
Especificidad	64.7%	IC95 47% -78%
Sensibilidad	88.9%	IC95 72% - 96%
Positive Likelihood Ratio	2.52	IC95 1.56 - 4
Negative Likelihood Ratio	0.17	IC95 0.06 - 0.5

(Table 3).

Conclusions: In patients with elevated Lp(a), a significant association was observed between CA and a history of MACE. Given the high sensitivity of this tool, it could be useful for the detection of individuals at higher risk. This information could guide the intensity of treatment in this population.

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093 / #170

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

IMPACT OF DIETARY N-3 AND N-6 POLYUNSATURATED FATTY ACIDS ON SERUM LIPOPROTEIN(A)

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Current evidence suggests that despite lowering LDL cholesterol (LDL-C), replacing dietary saturated fatty acids with unsaturated fatty acids might increase serum lipoprotein(a) [Lp(a)] by 10–15%. The current study aimed to examine the impact of polyunsaturated n-3 alpha-linolenic acid (ALA) and n-6 linoleic acid (LA) on serum Lp(a) and LDL-C concentrations in a randomized genotype-based intervention study.

Methods: We measured Lp(a) concentration at baseline and at the end of the 8-week intervention in 118 men homozygous for *FADS1* rs174550 SNP. After a 4-week run-in period, participants were randomized to consume either ALA-rich *Camelina sativa* oil (CSO) or LA-rich sunflower oil (SFO) 30–50 mL/day based on participants' BMI for eight weeks. Fasting plasma samples were analyzed using turbidimetric immunoassay or enzymatic colorimetric test for Lp(a) and LDL-C, respectively. Linear mixed models were used for data analysis.

Results: At baseline, the median Lp(a) concentration was 15.4 (IQR: 8.1, 37.6) mg/dL and the prevalence of elevated Lp(a) (>50 mg/dL) was 16%. With the intervention, dietary LA:ALA ratio changed from 4:1 to 1:1 in the CSO group and to 12:1 in the SFO group. Serum Lp(a) decreased by 9.4% (P=0.002) and 9.8% (P<0.001) in the CSO and SFO groups, respectively. LDL-C decreased more in the CSO group (10.9% [P<0.001] vs. 3.7% [P=0.02], P=0.001 for between-group difference). No gene × diet interaction was found for either variable.

Conclusions: A considerable increase in the intake of either n-3 or n-6 polyunsaturated fatty acids from vegetable oils has a beneficial effect on both serum Lp(a) and LDL-C concentrations.

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094 / #210

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LP(A) VALUES IN THE PORTUGUESE POPULATION

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Lp(a) is a cardiovascular risk factor (CVRF) predominantly determined by genetic factors. Its distribution in the Portuguese population has not yet been studied. To evaluate the distribution of Lp(a) and the prevalence of elevated values in the Portuguese population as well as its relationship with established atherosclerotic cardiovascular disease (ACVD).

Methods: Retrospective cross-sectional study with adult patients followed at our center whose levels of Lp(a) were dosed by immunoturbidimetric assay between August/2018 and June/2022. Lp(a) values <75nmol/L were considered low-risk and ≥125nmol/L high-risk. 1134 patients included, 50,4% of which were male, with a median age of 51(41-60)years.

Results: The median Lp(a) concentration was 42.0(12.8-148.5)nmol/L. 60.9% patients were in the low-risk category and 28.7% in the high-risk category. The Lp(a) concentration was significantly elevated in patients with dyslipidemia ($p<0.001$), elderly ($p=0.027$), with established ACVD ($p<0.001$), with a family history of premature ACVD ($p<0.001$), with chronic kidney disease ($p=0.002$) and post-menopause ($p=0.047$). No significant differences were found in patients with diabetes, acute inflammation or between the sexes. Patients with established ACVD, as well as patients with a family history of premature ACVD, more often had Lp(a) levels in the high-risk zone ($p<0.001$). Patients with established ACVD more often had Lp(a) concentrations >430nmol/L (cardiovascular risk equivalent to familial heterozygous hypercholesterolemia) ($p=0.018$).

Conclusions: Lp(a) elevation is a prevalent CVRF in the Portuguese population (>20%) and its association with ACVD is evident. In the absence of specific drugs to reduce Lp(a), it is important to invest in early and intensive treatment of traditional CVRFs if Lp(a) is high.

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095 / #570

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

PREVALENCE OF LP(A) IN ACUTE CORONARY SYNDROME AND ITS ASSOCIATION WITH SEVERITY OF DISEASE AMONG PATIENTS ADMITTED TO A TERTIARY CARE HOSPITAL

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: It is estimated that approximately 25% of the Indian population has elevated Lp(a). In India Acute coronary syndrome (ACS) occurs in young population. But the prevalence of elevated Lp(a) among ACS patients is not known. The aim of this study is to evaluate the prevalence of Lp(a) in ACS and to find the association between elevated Lp(a) levels and severity of disease. The study will also evaluate the prevalence of elevated Lp(a) among Familial hypercholesterolemia (FH) in ACS patients.

Methods: All ACS patients (n = 1021) were studied for Lp(a) levels, coronary angiography and screened for FH by DUTCH clinical lipid network criteria. Lp(a) levels of > 50mg/dl was considered as elevated. Gensini score more than 35 was considered to be associated with severe CAD. Correlations between Lp(a) levels and Gensini score was examined using Spearman correlation analysis.

Results: 34 % of ACS patients exhibited elevated Lp(a) levels. 37% of young ACS patients, exhibited elevated Lp(a) compared to 32% elderly patients. Elevated Lp(a) was observed in 40% patients with multivessel disease compared to 26% patients who had single vessel disease . 43% of FH patients had elevated Lp(a) There was significant , positive correlation of Lp(a) levels with Gensini score (p = 0.002)

Conclusions: Lp(a) was higher in young ACS patients. Patients with elevated Lp(a) exhibited severe disease angiographically based on Gensini score. Elevated Lp(a) was more common in FH suggesting it to be independent factor for accelerating the disease.

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096 / #1176

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LIPOPROTEIN(A) CONTRIBUTION TO TOTAL CIRCULATING APOB IN SEVERE HYPERCHOLESTEROLEMIC PATIENTS.

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Lp(a) is one of the atherogenic lipoproteins that contributes with its cholesterol (C) to the measured and/or calculated value of LDL-C, but so far there is no reliable commercial assay to determine Lp(a)-C neither conversion factors to estimate Lp(a)-C from particle number. Given that Lp(a) also contains one apoB molecule, is proposed to calculate the contribution of Lp(a) to total circulating apoB particles, which is more relevant when LDL-C is increased. Aim: to assess the contribution of Lp(a) to total apoB in severe hypercholesterolemic individuals.

Methods: this descriptive study includes 151 adult patients of both sexes with LDL-C>190 mg/dL. A lipid panel, apoB and Lp(a) particle number (Lp(a)-P) were measured. apoB-P was calculated converting the mass to molar concentration using apoB100 molecular weight (512 Kg/mol) and the percentage (%) of Lp(a)-P relative to apoB-P. Statistical tests applied: Spearman, ANOVA (Tuckey, Bonferroni).

Results: Median (range): Lp(a) 43 (1.3-618) nmol/L, % Lp(a) contribution to total apoB 1,6(0.07-38.1) increasing as Lp(a) increases: $r=0.85$ $p<0.001$, adjusted by triglyceride concentrations. Subdividing Lp(a)-P into deciles it was observed that from 113 nmol/L -corresponding to the P80th lower value- the contribution of Lp(a)-P in total apoB become significant $p<0.001$.

Conclusions: Conclusion: in hypercholesterolemic subjects it would be advisable to estimate the Lp(a)-apoB contribution when Lp(a) is above 113 nmol/L to handle more real values of apoB until having wide possibilities of measuring Lp(a)-C.

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097 / #672

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

RISK OF ATRIAL FIBRILLATION WITH LIPOPROTEIN (A) LEVEL: A META-ANALYSIS OF OBSERVATIONAL AND MENDELIAN RANDOMIZATION STUDIES

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Lipoprotein(a) (Lp[a]) is an established risk factor for atherosclerotic cardiovascular disease (ASCVD). However, its association with atrial fibrillation is still unknown.

Methods: We searched PubMed/Medline, Scopus, and EMBASE for studies evaluating Lp(a) association with the occurrence of AF till November 2022. Random effects models and I^2 statistics were used for pooled hazard ratios (HR), odds ratio (OR) and heterogeneity assessment. Subgroup analysis was performed based on cohort population and one out sensitivity analysis was performed. There was a partial overlap of the sample due to the UK Biobank cohort used in some mendelian randomization (MR) studies.

Results: Our final analysis incorporated 9 studies (5 observational, 5 MR) reporting the association of Lp(a) with AF. Age ranged from 56-70 years with a follow-up duration from 2-16 years. An increase in Lp(a) was associated with an increased risk of AF in MR studies (OR 1.024, 95%CI: 1.007-1.042, I^2=87.72%, p<0.001) **(Fig 1),** but the association did not achieve significance for observational data (OR 1.006, 95%CI: 0.912-1.110, I^2=84.26%, p<0.001). Leave-one-out sensitivity analysis confirmed equivalent results in MR studies and observational data. Subgroup analysis of MR studies revealed a higher risk of AF in the European cohort (OR 1.023, 95%CI: 1.007-1.040, I^2=89.05%, <0.001) and low risk (OR 0.940, 95%CI: 0.893-0.990) in Chinese population **(Fig.**

2).

Figure 1. Risk of Atrial Fibrillation with Increased Lipoprotein A

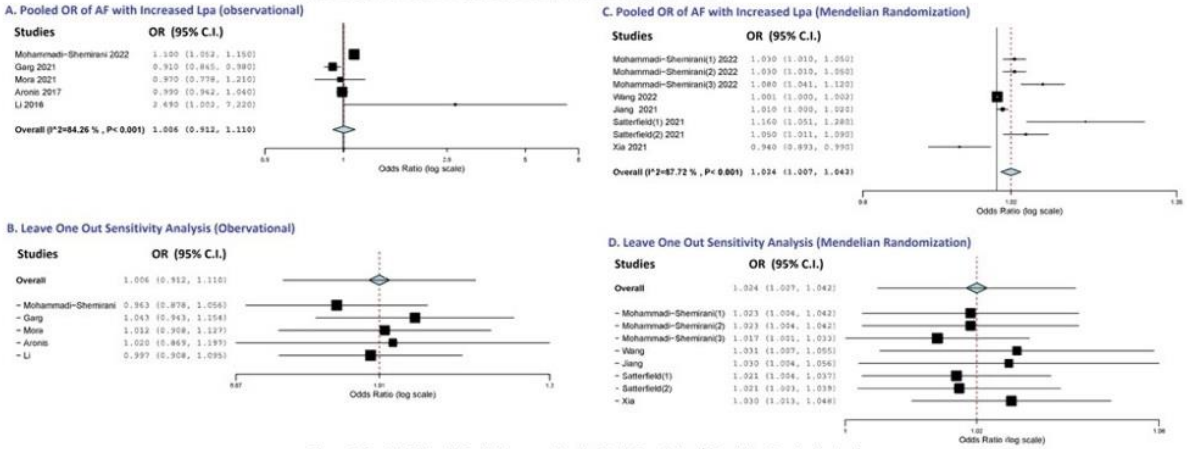
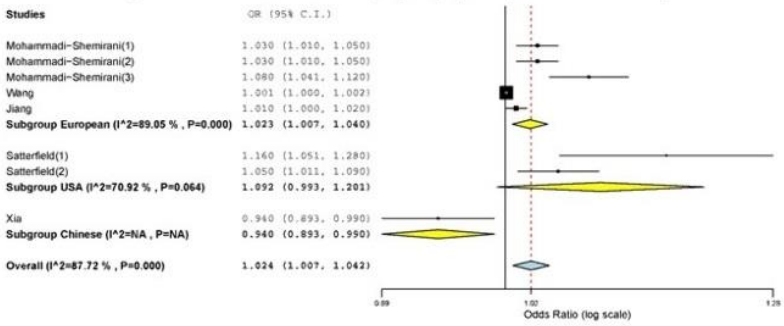


Figure 2. Pooled Odds of AF with Increased Lpa by Study Population [Mendelian Randomization]



Conclusions: Meta-analysis of the MR data suggested that higher levels of Lp(a) were associated with increased risk of AF, however, no association was noticed in data from observational cohorts. Future robust studies are warranted to validate these findings.

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098 / #1475

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

DISTRIBUTIONS OF SERUM LIPOPROTEIN(A), LIPIDS AND APOLIPOPROTEINS AND IDENTIFICATION OF EXTREME VALUES SUGGESTING GENETIC LIPID DISORDERS IN CHINESE UNIVERSITY STUDENTS IN MACAU

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Detailed profiles of lipids, apolipoproteins (Apo), and lipoprotein(a) [Lp(a)] are not available for the Macau population and the prevalence of familial hypercholesterolaemia (FH) and other genetic lipid disorders is not known. The aim of this study was to examine the extended lipid profile in apparently healthy new university students in Macau and to identify extreme values which may represent monogenic conditions.

Methods: Serum samples from new Chinese students from Macao and southern China at Macau University of Science and Technology were analysed retrospectively for the lipid profile, Apo AI, Apo B and Lp(a) and the distributions were plotted and extreme values identified.

Results: In 999 subjects with mean age 24.3 years, Lp(a) values showed a skewed distribution and were higher in females than males (median values 11.40 vs. 8.20 mg/dL, P <0.001). Lp(a) values ≥30 mg/dL were present in 188 (18.8%) subjects. All other lipid parameters were more favorable in females than males and a large proportion of subjects had lipid values above the ideal range. There were 4 subjects (0.4%) with outlying values of low-density lipoprotein cholesterol (5.96 to 8.01 mmol/L), which may suggest monogenic FH, and 6 subjects with triglyceride values >10 mmol/L (12.3 to 28.5 mmol/L) which may represent monogenic or polygenic hypertriglyceridaemia.

Conclusions: This first detailed report of lipid and Lp(a) values in Macau shows a substantial number of subjects have undesirable levels. The prevalence of monogenic FH may be about 0.4% and clinical assessment and genetic testing will be required to confirm this.

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099 / #942

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LIPOPROTEIN(A), LYMPHOCYTE-MONOCYTE RATIO AND PROGRESSION OF CAROTID ATHEROSCLEROSIS

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Lipoprotein(a) [Lp(a)] is an independent risk factor for carotid atherosclerosis and ischemic stroke, leading to the induction and maintenance of systemic inflammation. The ratio of different leukocyte subpopulations is the most available marker of systemic inflammation. The aim of the study was to evaluate the association of Lp(a) and lymphocyte monocyte ratio (LMR) with the progression of carotid atherosclerosis

Methods: The study included 102 patients aged 62±10 years, 78% men. All patients initially underwent duplex scanning (DS) of the carotid arteries. The median time to repeat DS was 5 [3; 8] years. Patients with carotid progression were more often on statin therapy than patients without progression. Criteria for the progression of carotid atherosclerosis was: detecting plaque in a new segment, increased degree of stenosis in at least one of the segments over 10%. Lp(a) concentration, lipids, leukocyte count and their ratios were determined.

Results: Patients were divided into two groups depending on the presence (n=70) or absence (n=32) of carotid atherosclerosis progression. The groups didn`t differ in age, sex, classical risk factors, and lipid panel at baseline and on therapy. Lp(a) level were significantly higher in the group with carotid atherosclerosis progression: 69 [18;116] mg/dL vs 16[9;53], p=0.003. Patients with Lp(a) ≥30 mg/dL and LMR <4.17 when compared with patients with Lp(a) <30 mg/dL and LMR ≥4.17 had the highest risk of carotid atherosclerosis progression (OR=4.3 (1,1-17.2), p=0.03) regardless of sex and LDL-C level.

Conclusions: Elevated Lp(a) levels and a decreased LMR are associated with an increased risk of progression of carotid atherosclerosis.

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100 / #955

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LOW MOLECULAR WEIGHT PHENOTYPE APO(A) AS A RISK FACTOR OF MYOCARDIAL INFARCTION IN PATIENTS WITH CHD

POSTER ON BOARD: AS02.01 LP(A)

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Background and Aims: Lipoprotein(a) [Lpa(a)] is a genetic risk factor of ASCVD. PCSK9 is related to vascular inflammation and detected in atherosclerotic plaques. A temporary increase in circulating concentration of PCSK9 and Lp(a) was shown in patients with myocardial infarction (MI).

Methods: In a prospective study with retrospective data collection, we included 116 patients with premature CHD (males<55 years, females<60 years) who were followed for a median 12 years. Medical history and information on major adverse cardiovascular events (MACE) after initial exam, as well analyses for levels of lipids, Lp(a), apo(a) phenotype, PCSK9 and PCSK9-Lp(a) complex were obtained from all patients.

Results: All patients were divided into two groups depending on the presence of low (LMW, n=52) or high molecular weight (HMW, n=64) apo(a) phenotype. There was no difference in all characteristics, excepting Lp(a) level. Lp(a)>50 md/dL was associated with risk of MACE (HR=1.7(95%CI 1.0-2.8), p<0.05) despite effective management of other risk factors. On the contrary, LMW apo(a) (2.3(1.1 to 5.0), p=0.03) but not elevated Lp(a) (1.9 (0.8-4.6), p=0.13), was an independent predictor of earlier development of MI after adjustment for sex, age of CHD debut, initial lipids levels and lipid-lowering treatment. Apo(a) phenotype also determines the relationship between Lp(a) and PCSK9 concentrations. PCSK9-Lp(a) complex was higher in the presence of LMW apo(a) patients. PCSK9 levels were related to MACE, but not MI, only in patients with LMW apo(a).

Conclusions: The apo(a) low molecular phenotype is a predictor of MI in patients with premature CHD and this link could be mediated via PCSK9.

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101 / #767

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

ICOSAPENT ETHYL SUPPLEMENTATION RAPIDLY REDUCES CARDIOVASCULAR DISEASE RISK MARKERS AND IMPROVES PLASMA AND LIPOPROTEIN LIPIDOME REDUCING THEIR ATHEROGENICITY IN HUMANS

POSTER ON BOARD: AS02.02 TG RICH LIPOPROTEINS METABOLISM AND LIPASES

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Background and Aims: Icosapent ethyl (IPE) -supplementation has postulated benefits in improving cardiovascular health. Here we assessed how IPE-supplementation affects lipoproteins subclass profile, and the lipidome and proatherogenic properties of plasma lipoproteins.

Methods: 39 healthy, normolipidemic volunteers received a 4 g daily dose of IPE for 4 weeks. Plasma samples collected prior, during, and after the supplementation were analysed by NMR spectroscopy.

Results: Total circulating eicosapentaenoic acid (EPA) increased 4-fold, while omega-6 fatty acids reduced, decreasing the omega-6/omega-3 ratio from 7.9 to 2.8. Plasma triglycerides (TG) (0.89±0.38 mmol/L vs. 0.72±0.34 mmol/L) and apolipoprotein-B (apoB) (0.75±0.15 g/l vs. 0.71±0.16 g/l) were significantly decreased already after 7-days of IPE-supplementation. The concentrations of VLDL-TG, VLDL-C, VLDL particles and total lipid were significantly decreased after IPE-supplementation. The concentration of XXL-VLDL lipids and particles decreased by more than 50%, while XS-VLDL lipids and particles decreased only by 5% and 6%, respectively. IPE-supplementation also decreased the level of lipoprotein lipase inhibitor ANGPTL3 as well as the binding of plasma lipoproteins to human aortic proteoglycans. IPE-supplementation also decreased cardiovascular disease risk, as assessed by lipid-based Coronary Event Risk Test 2 (CERT2).

Conclusions: IPE-supplementation led to rapid increase in total circulating EPA, reducing the omega-6/omega-3 ratio, improving the plasma lipidome. In addition, TGs and especially TG-rich apoB particles and their probability to bind to proteoglycans were reduced. The CERT2 risk score was improved even after 7-day washout period, suggesting a long-lasting benefit from IPE-supplementation. Our data highlights mechanisms that may explain the previously identified IPE-induced reduction in cardiovascular disease risk.

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102 / #246

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

HYPERTRIGLYCERIDEMIA COMPROMISES HDL ANTI-OXIDANT CAPACITY AND AGGRAVATES RHEUMATOID ARTHRITIS IN HUMAN APOC-III TRANSGENIC MICE

POSTER ON BOARD: AS02.02 TG RICH LIPOPROTEINS METABOLISM AND LIPASES

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Background and Aims: Dyslipidemia and low-level chronic metabolic inflammation co-exist with atherosclerosis in cardiovascular disease (CVD) patients. Patients with chronic inflammatory diseases, such as rheumatoid arthritis (RA), have increased incidence of CVD compared to the general population. ApoC-III, a main component of triglyceride-rich lipoproteins (TRLs), has been reported to activate a non-canonical inflammasome pathway in monocytes. RA patients with high triglycerides (TG) and low HDL-cholesterol (HDL-C) levels present limited response to anti-TNFα treatment together with systematic inflammation. Our aim was to investigate the role of hypertriglyceridemia caused by apoC-III overexpression in RA pathogenesis.

Methods: We used the apoC-III Tg mouse strain which overexpresses human apoC-III and is characterized by combined dyslipidemia (high TG and total cholesterol, low HDL-C), as well as control mice (non carriers of the same genetic background) in an antigen-induced arthritis protocol. HDL properties were estimated by density gradient ultracentrifugation of serum, immunoblotting and PON-1 activity. Gene expression analysis in peritoneal macrophages was performed by RT-qPCR.

Results: ApoC-III Tg mice had combined dyslipidemia characterized by abnormal distribution of apoA-I and apoC-III in lipoprotein fractions. HDL from these mice had compromised anti-oxidant capacity. Importantly, apoC-III Tg mice developed more severe antigen-induced arthritis compared to control mice, which was evident at four days post knee inflammation onset. Expression analysis in peritoneal macrophages revealed downregulation of *Arg1* and upregulation of *iNOS* and *Cd36* mRNA levels in apoC-III Tg mice.

Conclusions: Our results signify that combined dyslipidemia aggravates RA possibly via changes on HDL functionality, fatty acid transport and the establishment of M1-like characteristics on macrophages.

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103 / #1124

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

VOLANESORSEN TO TREAT SEVERE HYPERTRIGLYCERIDEMIA: A POOLED ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

POSTER ON BOARD: AS02.02 TG RICH LIPOPROTEINS METABOLISM AND LIPASES

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Background and Aims: Patient with severe hypertriglyceridemia (sHTG) are often refractory to lipid lowering therapy. Apolipoprotein (Apo) CIII inhibition could be promising to treat subjects with sHTG. The antisense oligonucleotide against APOC3 mRNA volanesorsen was recently introduced to treat sHTG. We performed a systematic review and meta-analysis of RCTs on efficacy and safety of volanesorsen as compared to placebo treatment in patients with severe HTG.

Methods: Studies were systematically searched in the PubMed, Web of Science, Scopus databases according to PRISMA guidelines. Last search performed on 07thFeb2022.

Results: Four studies showed significant reduction in TG after 3 month of treatment with volanesorsen as compared with placebo (MD: -73.9%; 95%CI: -93.5%, -54.2; P<0.001 I2= 89.05%; P<0.001); VLDL-C level (MD: -71.0%; 95%CI: -76.6%, -65.4%; P<0.001 I2= 94.1 %; P<0.001); Apo-B48 level (MD: -69.03%; 95%CI: -98.59.4%, -39.47%; P<0.001, I2=93,51%; P<0.001); Apo-CIII level (MD: -80.0%; 95%CI: -97.5 %, -62.5; P<0.001 I2= 94.1 %; P<0.001**)** with an increase in HDL-C level (MD: +45.92.5%, 95%CI: +37.24%, +54.60%; P<0.001 I2= 94.34%; P<0.001) and in LDL-C level (MD: +68.6%, 95%CI: +7.0%, +130.1%; P<0.001 I2= 96.18%; P<0.001) without a significant elevation of Apo-B100 level (MD: +4.58%, 95%CI: -5.64%, +14.79%; P=0.380 I2= 95.09%; P<0.001) in 139 volanesorsen patients as compared to 100 placebo-treated controls. Most of adverse events were mild and related to local injection site reactions.

Conclusions: In patients with severe HTG, volanesorsen is associated with a significant reduction in TG, VLDL-C, Apo-B48, non-HDL-C, and increment of HDL-C as compared to placebo. Documented efficacy is accompanied by an acceptable safety profile.

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104 / #1022

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

A STRUCTURE FUNCTION ANALYSIS OF NATURALLY-OCCURRING VARIANTS IN ANGIOPOIETIN LIKE 3 (ANGPTL3) TO IDENTIFY REGIONS INVOLVED IN THE INHIBITION OF LPL AND EL FUNCTION

POSTER ON BOARD: AS02.02 TG RICH LIPOPROTEINS METABOLISM AND LIPASES

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Background and Aims: ANGPTL3 is a liver-secreted protein which circulates both as a homomeric complex and in complex with ANGPTL8 and inhibits both lipoprotein lipase (LPL) and endothelial lipase (EL), thus increasing levels of TG, LDL-C and HDL-C. The structural bases of LPL and EL inhibition are only partially understood. In this study we evaluated the relationship between naturally-occurring variants of ANGPTL3 and lipid markers of LPL and EL activity, to identify protein regions required for the regulation of lipase enzymatic activity.

Methods: We evaluated lipid biomarker levels, assessed by NMR, in human carriers of selected ANGPTL3 variants and non-carrier controls from the Penn Medicine and UK Biobanks (PMBB and UKBB, application number 70653). The association of biomarkers with carriers status was determined using adjusted linear regression models.

Results: The screening of PMBB identified 678 carriers (451 females, 227 males). Carriers of nonsense, frameshift or splice-site variants, had a biomarker profile compatible with complete loss of ANGPTL3 function. Carriers of missense or in-frame deletion variants had variable phenotype. Interestingly, variants located within the regions involved in the formation of the ANGPTL3-8 complex displayed a more marked alteration of ApoB-containing lipoprotein composition, compared to HDL composition. Data from the UKBB were consistent with this observation.

Conclusions: Our preliminary analysis suggests that variants which alter the ANGPTL3 protein region involved in the formation of the ANGPTL3-8 complex may be associated with increased LPL, rather than EL activity. However, additional analyses are required to confirm whether this phenotype is unique of this class of variants.

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105 / #224

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

OUTCOME OF SEVERE HYPERTRIGLYCERIDEMIA IN HOSPITAL PRACTICE. A SINGLE CENTRE EXPERIENCE FROM SINGAPORE

POSTER ON BOARD: AS02.02 TG RICH LIPOPROTEINS METABOLISM AND LIPASES

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Background and Aims: Severe hypertriglyceridemia(HTG) >10mmol/l is usually caused by hyperchylomicronaemia. Monogenic severe HTG is rare and majority of cases are polygenic/multifactorial in nature .Common secondary causes are insulin resistance and alcoholism. . Treatment of severe HTG is primarily to prevent pancreatitis. Aim To assess the demographics, etiological factors, management and short term major sequelae of individuals with severe HTG, presented to our institution during the specified period

Methods: Electronic medical records (EMR) of individuals who had at least one triglyceride (TG) level greater than 10mmol/L during the 6-month study period (March to August 2019) were scrutinized retrospectively until August 2021.

Results: . A total of 13595 individuals' blood samples for triglyceride measurements were received. Of these, 23 patients (0.15%) had TG greater than 10mmol/L. Three (13%) were female and 20 (87%) were male. 78% (n=18) patients were obese while 65 % (n=15) had type 2 Diabetes. Three patients (13%) did not have identifiable risk factors. Majority received combination treatment. 4 out of 23 (17%) individuals developed pancreatitis. The median TG level of individuals who developed pancreatitis was 30.7mmol/l while in others 15.6mmol/l. [30.7mmol/L vs 15.6mmol/L, p<0.001]. The median TG improvement was 11.9mmol/L and 81% decrease from baseline. Nine out of 18 patients (50%) achieved TG of <3mmol/L at follow up.

Conclusions: Severe hypertriglyceridemia was rare in individuals in whom TG was tested. Pancreatitis was not uncommon with severe HTG especially with significantly high TG levels. Obesity and type 2 diabetes accounted for most cases. Half of the patients on treatment were able to maintain satisfactory TG levels.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

106 / #1139

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

GENETIC AND HUMORAL CHARACTERISTICS OF PATIENTS WITH MODERATE AND SEVERE HYPERTRIGLYCERIDEMIA WITHOUT SECONDARY ETIOLOGY

POSTER ON BOARD: AS02.02 TG RICH LIPOPROTEINS METABOLISM AND LIPASES

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Background and Aims: Background: Primary causes of hypertriglyceridemia (HTG) such as genetic defects i and autoimmune causes are rare. Certain genetic disorders such as LPL deficiency, Apo C-II deficiency, Apo A-V mutation, GPIHBP1 mutation, LFM1 mutation were related to HTG. Autoimmune disorders such as anibodies against apolipoprotein C-II, lipoprotein lipase, and GPIHBP1 were described as a rare cause of HTG.In this study we systematically examined genetic and humoral causes for patients with hypertriglyceridemia with no identifiable secondary causes.

Methods: We evaluated patients who had moderate to severe HTG (above 500 mg/dl) without a secondary cause. Patients underwent whole exome sequencing (WES), and tests for the presence of GPIHBP1 autoantibodies.

Results: Six patients were found to fulfill the inclusion criteria tion. Mean patients' age was 24 years, 3 were females, mean BMI was 21. The mean fasting plasma triglyceride level was 3399 [r1] mg/dl, 2 had a prior pancreatitis event. Three had a family history of dyslipidemia. Mutations were found in 4 individuals; homozygote for LPL deletion, APO E difficiency (Apo E kochi), a mutation in the SLC10A2 bile trabsporter, and a coumpound heterozygore for LMF1. Two others had no identifiable genetic defects. Testing for the presence of GPIHBP1 autoantibody was done showed only a single borderline positive result in one patient. This patient had a history of thrombocytopenic purpura (ITP).

Conclusions: Conclusion: Our findings suggest that patients with hypertriglyceridemia without a secondary cause should be offered genetic and humoral tests to identify the etiology as treatment options might be available.

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107 / #1612

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

CLASSIFICATION OF HYPERTRIGLYCERIDEMIA SEVERITY AND ESTIMATED PREVALENCE OF CHYLOMICRONEMIA SYNDROME IN MEDELLÍN, COLOMBIA.

POSTER ON BOARD: AS02.02 TG RICH LIPOPROTEINS METABOLISM AND LIPASES

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Background and Aims: Introduction: Severe hypertriglyceridemia i.e.; triglyceride values greater than 885 mg/dL indicate chylomicronemia that in persistent cases may be of monogenic origin as in familial chylomicronemia syndrome. **Purpose:** To determine the frequency of hypertriglyceridemia, chylomicronemia and possibly its primary forms in adults evaluated on a health system in Medellin, Colombia.

Methods: Methods: This is a retrospective study comprising data of 164,874 triglyceride samples, collected in a 4- month interval. Fasting triglyceride levels were categorized according to the ATP III and the Endocrine Society classifications. In addition, the number of patients with persistent values > 885 mg/dL, especially in those whose secondary causes were excluded were identified .

Results: Of 164,874 samples, 43.41% (n=71,576) had triglyceride levels greater than 150 mg/ dL with a median (%25:75%) of 207 mg/dL (173;266 mg/dL). According to the ATP III classification: 1.63% (n= 2,703) had values > 500 mg/dL, while 0.04% (n=70) had values > 2000 mg/dL according to the Endocrine Society. Regarding the laboratory parameters for chylomicronemia, 0.32% (n= 531) had values > 885 mg/dL. Of these 74 patients presented at least three samples with values > 885 mg/dL; 29 patients were excluded thus, 45 (0.02 %) patients were suspected of primary chylomicronemia syndrome.

Conclusions: In most patients hypertriglyceridemia was not severe and chylomicronemia syndrome of possible primary origin had a very low prevalence

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108 / #56

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

THE INCREASED ANTIOXIDANT ACTION OF HDL IS INDEPENDENT OF HDL CHOLESTEROL PLASMA LEVELS IN TRIPLE-NEGATIVE BREAST CANCER

POSTER ON BOARD: AS02.03 HDL

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Background and Aims: The association between HDL cholesterol (HDLc) with breast cancer (BC) is controversial and can be affected by HDL functionality. The composition and antioxidant activity of isolated HDL isolated from women with triple-negative BC (TNBC) compared to controls were addressed.

Methods: Total HDL was isolated from 27 women with a recent diagnosis of TNBC, without prior treatment, and 27 healthy women (control group) paired by age and body mass index (BMI). Plasma lipids and HDL composition (total cholesterol, triglycerides, HDLc, and phospholipids) were determined by enzymatic methods, and apoB and apo A-I by immunoturbidimetry. HDL antioxidant activity was determined by measuring the lag time phase (LTP) for LDL oxidation and the maximal rate of conjugated dienes formation (MRCDF) in LDL (from a healthy donor) incubated with copper sulfate solution (234 nm absorbance monitored for 4 h, at 3 min intervals).

Results: Comparisons by Mann Whitney and Kruskal Wallis test. Menopause, plasma lipids, and HDL composition were similar between controls and TNBC. The ability of HDL to retard LDL oxidation was 22 % greater in the TNBC group as compared to the control (P=0.019) and positively correlated with apoA-I in HDL(r=0.45; P=0.018). The LTP was greater in the advanced stages of TNBC compared to the control group (P=0.017). The MRCDF was similar between groups and among clinical stages of the disease.

Conclusions: The improved antioxidant activity of HDL could contribute to limiting oxidation and inflammation in the advanced stages of TNBC. Results highlight HDL as an antioxidant defense in TNBC independently of HDLc plasma levels.

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109 / #1142

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

TANGIER DISEASE IN ISRAEL; COMPLICATED BY MOBILE LIPOMATOUS MASS ON MITRAL VALVE AND ACUTE STROKE

POSTER ON BOARD: AS02.03 HDL

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Background and Aims: Tangier disease (TD) is a rare genetic disease which causes very low or even deficient HDL in plasma and accumulation of cholesterol in different tissues throughout the body. The disease is related to early onset of atherosclerotic disease and other clinical sequelae, previous articles described increased incidence of stroke in tangier patients. Valvular involvement in Tangier's disease was never described before .

Methods: exome sequencing analysis to define mutation.

Results: We describe a case of 77-year old female patient of Ashkenazi descent genetically diagnosed with Tangier Disease which presented with acute stroke and found out to have a vegetation highly suspicious of lipomatous nature on the mitral valve by echocardiography, conservative management was administrated.

Conclusions: .Tangies disease is now descibed among the Askenazi Jeiwhs population

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110 / #264

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

INTERPRETATION OF THE STRUCTURE-FUNCTION RELATIONSHIPS IN SYNTHETIC HDL NANODISCS

POSTER ON BOARD: AS02.03 HDL

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Background and Aims: HDL have inspired many synthetic HDL(sHDL)-based therapies to reduce the risk of cardiovascular diseases, but still the mechanism behind the activation of lecithin-cholesterol acyltransferase (LCAT) by apoA-I and its synthetic fragments (apo-AI mimetic peptides) remains enigmatic. The objectives of the research are the study of: sHDL with different compositions; apoA-I mimetic peptides in sHDL with/without LCAT; location, orientation and positioning of LCAT on sHDL; how apoA-I mimetic peptides modulate LCAT activity. The final aim is the design of enhanced sHDL for cardiovascular diseases.

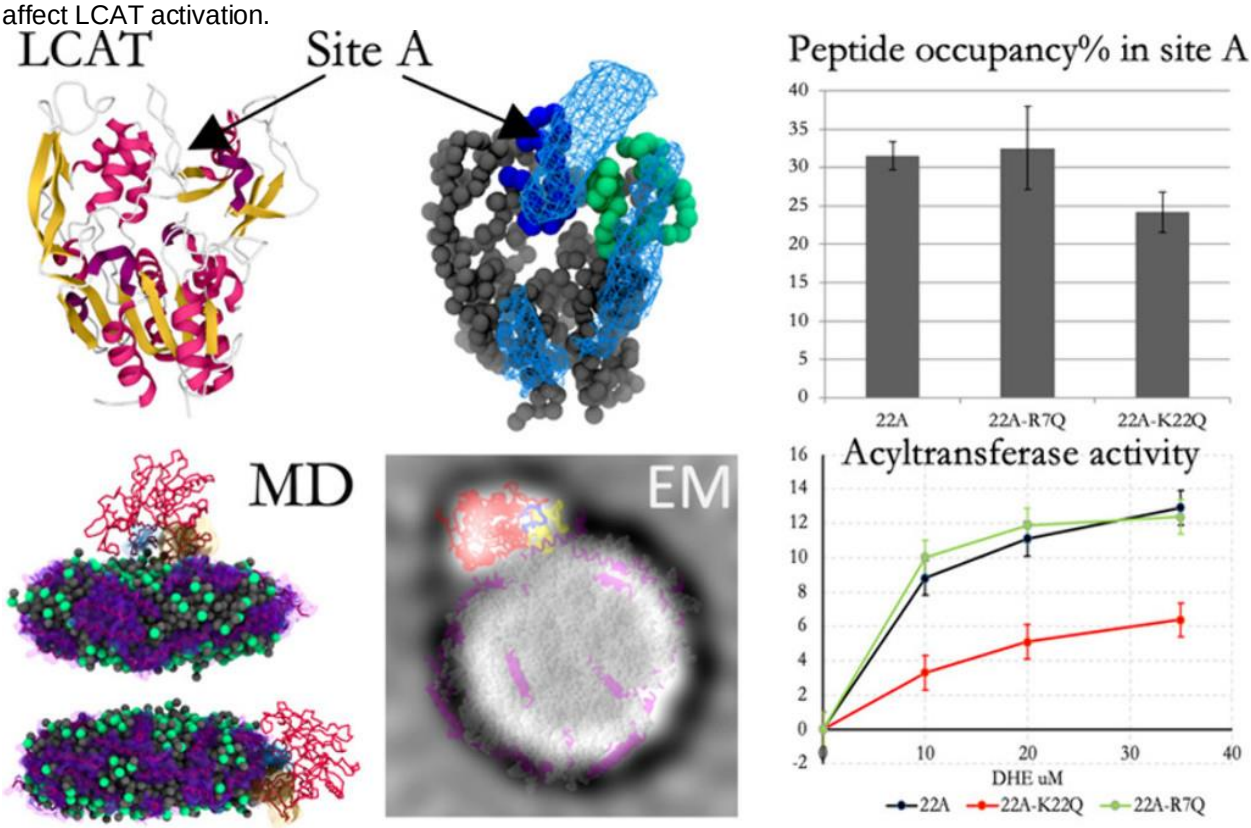
Methods: Molecular dynamic (MD) simulations were conducted with GROMACS using Martini 3.0 force field. Each simulated nanodisc comprised 200 phospholipid molecules and 28 peptide molecules. sHDL were synthetized by Thermal Cycling method (lipid:protein molar ratio 7:1) and characterized by DLS and EM. sHDL activity was evaluated by the LCAT Activity Assay. LCAT-sHDL binding strength was compared by

QCM.

Material for MD		*Material for experiments*	
ApoA-I mimetic peptides:	Phospholipids:	ApoA-I mimetic peptides:	Phospholipids:
22A PVLDLFRELLNELLEALKQKLK	1,2-dimyristoyl-sn-glycerol-3-phosphocholine (DMPC)	**22A** PVLDLFRELLNELLEALKQKLK	1,2-dimyristoyl-sn-glycerol-3-phosphocholine (DMPC)
22A-K PVLDLFRELLNELLEALKQKL (22A variant without the final K)			1,2-dipalmitoyl-sn-glycerol-3-phosphocholine (DPPC).
22A-K22Q PVLDLFRELLNELLEALKQKLQ (22A variant with the substitution of the final K with a Q),		**22A-K22Q** PVLDLFRELLNELLEALKQKLQ (22A variant with the substitution of the final K with a Q),	
22A-R7Q PVLDLFQELLNELLEALKQKLK (22A variant with the substitution of the R in position 7 with a Q).		**22A-R7Q** PVLDLFQELLNELLEALKQKLK (22A variant with the substitution of the R in position 7 with a Q).	

Results: All 22A variants studied had a specific interaction site (site A) in LCAT; they showed different tendencies to form antiparallel dimers when bound to site A. Simulated LCAT matched location and orientation of experimental LCAT in the rim of the nanodiscs in EM images. LCAT prefers to localize to the rim of nanodiscs, orientating its active side towards the lipid surface of the sHDL. The substitution of the K22 with Q lowered the activation of LCAT by 50%, while the substitution of the R7 seems to not

affect LCAT activation.



Conclusions: Results and methodology reported provide a blueprint that can be utilized to design novel drug formulations against cardiovascular diseases.

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111 / #31

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

IMPROVING HDL FUNCTIONS BY INTERACTION WITH NOVEL BIOACTIVE LIPIDS.

POSTER ON BOARD: AS02.03 HDL

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Background and Aims: High density lipoprotein (HDL) with its complex structure, plays an important role in preventing atherosclerosis due to its antiatherogenic properties. Improving HDL function and quality are expected to attenuate atherosclerosis and reduce CVD risk.

Methods: we isolated a novel active compound from Nannochloropsis microalgae (Lyso-DGTS), which increased activities of the main antioxidant enzyme associate to HDL, (paraoxonase 1-PON1). Our aim is to examine the effect of lyso-DGTS on rePON1 and HDL activities in vitro, in vivo and ex vivo.

Results: Lyso-DGTS increased activities of PON1 and increased HDL cholesterol efflux from macrophages in a dose-dependent manner and significantly increased the ability of HDL to induce nitric oxide (NO) production from endothelial cells. In an ex-vivo experiment, HDL obtained from5 patients, with plaque stenosis > 50% as determined by cardiac CT, was incubated with without lyso-DGTS and measured for its HDL efflux ability. In average, HDL efflux significantly increased in a dose dependent matter after incubation with lyso-DGTS. In serum obtained from apoEKO mice treated with Lyso –DGTS for 28 days, Lyso-DGTS increased activities of PON1 and enhanced HDL cholesterol efflux.

Conclusions: Novel bioactive lipids based on Lyso-DGTS derivatives interact selectively with HDL components and alter its structure and functions. Improving HDL functions using Lyso-DGTS and its derivatives might be a novel approach for reducing atherosclerosis development and decreasing CVD risk.

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112 / #818

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

REDUCED CAPACITY OF HDL TO ACQUIRE FREE CHOLESTEROL UPON LIPOLYSIS OF TRIGLYCERIDE-RICH LIPOPROTEINS REFLECTS SEVERITY OF MYOCARDIAL INFARCTION

POSTER ON BOARD: AS02.03 HDL

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Background and Aims: Both low and extremely high concentrations of HDL-cholesterol (HDL-C) are associated with elevated cardiovascular risk. To explain this U-shape relationship, we have recently proposed the reverse remnant cholesterol transport (RRT) hypothesis featuring, as a key step, transfer to HDL of free cholesterol (FC) from triglyceride-rich lipoproteins (TGRLs) upon lipolysis. To further assess our hypothesis, we evaluated whether the rate of FC transfer to HDL upon TGRL lipolysis was associated with disease severity and mortality in patients with acute myocardial infarction (AMI).

Methods: Cases who died on follow-up of up to 9.5 years (n=110) and sex- and age-matched controls who survived (n=220) were randomly selected from a total of 1,398 consecutive patients with AMI enrolled in the ePARIS study. Patients treated by statins before admission were excluded. After admission, large part of the population (82.6%) was treated with statins.

Results: Capacity of HDL to acquire FC from TGRL upon LPL-mediated lipolysis decreased with increasing KILLIP class of AMI. KILLIP class was the only variable significantly (p=0.016020) associated with FC transfer to HDL among all parameters studied. In a multivariate regression, only cardiac arrest (p=0.000006) and FC transfer to HDL (p=0.021138) were significantly associated with KILLIP class. No relationship of all-cause mortality and survival time with the FC transfer to HDL evaluated at baseline was observed.

Conclusions: Reduced FC transfer to HDL upon TGRL lipolysis in a pathway of RRT reflected severity of AMI but did not predict all-cause mortality and survival on follow-up in a cohort of patients largely treated by statins during hospitalisation.

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113 / #1595

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

BOTH LOW AND EXTREMELY HIGH MONOGENIC HDL-CHOLESTEROL STATES ARE CHARACTERISED BY DEFECTIVE CAPACITY OF HDL TO ACQUIRE FREE CHOLESTEROL UPON TRIGLYCERIDE LIPOLYSIS

POSTER ON BOARD: AS02.03 HDL

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Background and Aims: Both low and extremely high concentrations of HDL-cholesterol are associated with elevated cardiovascular risk. The reverse remnant cholesterol transport (RRT) hypothesis developed by us posits that transfer to HDL of free cholesterol (FC) from triglyceride-rich lipoproteins (TGRLs) upon their lipolysis is impaired both in low and extremely high HDL-cholesterol states. To further assess this hypothesis, we evaluated whether this pathway was impaired in subjects with genetically altered HDL-cholesterol.

Methods: Low HDL-cholesterol subjects with homozygous (2 males, 2 females) and heterozygous (3 males, 2 females) lecithin-cholesterol acyltransferase (LCAT) deficiency and extremely high HDL-cholesterol subjects with heterozygous endothelial lipase (EL) deficiency (3 females) were recruited together with healthy normolipidemic controls (7 males, 6 females). Capacity of HDL to acquire FC during lipolysis of normolipidemic TGRL by lipoprotein lipase was determined in vitro using fluorescent TopFluor cholesterol.

Results: While levels of HDL-cholesterol were reduced in homozygous (5±1 mg/dl) and heterozygous (41±12 mg/dl) LCAT deficiency vs. controls (54±13 mg/dl), they were greatly elevated in EL-deficient subjects (109±17 mg/dl). The capacity of HDL to acquire FC from TGRL upon lipolysis was reduced in subjects with heterozygous (-31%, $p<0.05$), but not with homozygous (-14%, $p>0.05$), LCAT deficiency and was similarly reduced in EL-deficient subjects (-31%, $p<0.05$). Cholesterol esterification was undetectable in LCAT-deficient homozygotes and was normal in both LCAT-deficient heterozygotes and EL-deficient subjects, revealing negative correlation with FC accumulation in HDL.

Conclusions: FC accumulation in HDL upon TGRL lipolysis is impaired in both low and extremely high monogenic HDL-cholesterol states. Cholesterol esterification is essential for FC removal from HDL.

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114 / #1259

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

OBESITY AFFECTS MATERNAL AND NEONATAL HDL METABOLISM AND FUNCTION

POSTER ON BOARD: AS02.03 HDL

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Background and Aims: Pre-gravid obesity is one of the major risk factors for pregnancy complications such as gestational diabetes mellitus (GDM), increased risk of congenital heart defects in their children, and premature death from cardiovascular events. However, the biological mechanisms, which underpin these adverse outcomes, are not well understood. High-density lipoproteins (HDL) are anti-atherogenic by promoting efflux of cholesterol from macrophages and suppression of inflammation. Functional impairment of HDL in obese and GDM-complicated pregnancies may have long-term effects on maternal and fetal health. In the present study, we assessed metrics of HDL function in sera of overweight/obese pregnant women and in cord blood at delivery.

Methods: In this study, 186 obese and 34 normal weight women were included. We assessed arylesterase-activity of PON1, LCAT activity, HDL cholesterol efflux capacity, and anti-oxidative-capacity of maternal serum and in cord blood.

Results: We observed that pre-gravid obesity was associated with impaired serum anti-oxidative capacity and LCAT activity in both mothers and offspring, whereas maternal cholesterol efflux capacity was increased. Functionalities of maternal and fetal HDL correlated robustly. Gestational diabetes did not further alter HDL functionality in obese women.

Conclusions: Obesity affects functional parameters of HDL in mothers and children. We observed that serum antioxidant capacity was significantly reduced in obese mothers and their offspring. Maternal and fetal HDL-related functions correlate between mothers and their children.Gestational diabetes did not significantly further alter the parameters of HDL functionality in obese women, so obesity itself appears to have a major impact on HDL functionality in mothers and their offspring.

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115 / #703

Topic: *AS02 Lipids and Lipoproteins / AS02.04 Lipoprotein receptors*

SOLUBLE LDL-RECEPTOR IS INDUCED BY TNF-A AND INHIBITS HEPATOCYTIC CLEARANCE OF LDL-CHOLESTEROL

POSTER ON BOARD: AS02.04 LIPOPROTEIN RECEPTORS

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Background and Aims: LDL-c is cleared from the circulation mainly by hepatic LDL-receptor mediated endocytosis. Defective LDL-c clearance and hence its elevation in circulation is one of the risk factors for myocardial infarction (MI). A soluble LDL-R (sLDL-R) exists in human plasma and exhibits strong correlation with circulating LDL-c and conditions that promote chronic inflammation. However, the mechanistic interplay between sLDL-R, inflammation and MI remains to be investigated.

Methods: *In vitro* studies using HepG2 cells treated with TNF-α, and a nested case-control study was conducted to investigate the relationship between plasma sLDL-R, TNF-α and risk of future MI.

Results: Stimulation of HepG2 cells with TNF-α induces release of sLDL-R with limited effect on surface expression of LDL-R. TNF-α induces gene expression of peptidases ADAM17 and MMP14 in HepG2 cells, and inhibition of ADAM17 and MMP-14 significantly reduces the TNF-α induced sLDL-R release. Although TNF-α treatment of HepG2 cells has limited effect on LDL-c endocytosis, HepG2 cells incubated with recombinant sLDL-R showed reduced LDL-c uptake in a dose-dependent manner. In a nested case-control study, baseline sLDL-R in plasma was positively correlated with plasma total cholesterol level. Further, a 2-fold increase in plasma sLDL-R was associated with 2.1x higher risk of future MI. Using mediation analyses, we determined that significant proportion of the association is mediated by elevation in plasma cholesterol level.

Conclusions: Our study suggests that sLDL-R is generated by TNF-α via membrane shedding. Further, an increase in sLDL-R could inhibit hepatic clearance of LDL-c increasing its half-life in the circulation and contributing to the pathogenesis of MI.

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116 / #253

Topic: *AS02 Lipids and Lipoproteins / AS02.05 Bile acids*

SOLUBLE ENDOGLIN EXACERBATES BILE ACID RETENTION DURING LABETALOL TREATMENT IN MICE WITH ETHINYLESTRADIOL-INDUCED CHOLESTASIS

POSTER ON BOARD: AS02.05 BILE ACIDS

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Background and Aims: Intrahepatic cholestasis (ICP) is a serious complication of pregnancy, threatening the fetuses by the toxicity of cumulating bile acids (BA). ICP can coincidence with preeclampsia, which is characterized by high plasma concentration of soluble endoglin (sEng) levels. In addition, labetalol, is used for therapy of hypertension in preeclampsia. In this study, we hypothesized that ICP increases plasma levels of sEng and that both labetalol and increased sEng levels worsen BA cumulation in estrogen-induced cholestasis, the mice model of ICP.

Methods: Four-month-old transgenic mice overexpressing human sEng and wild-type female mice were administrated with ethinylestradiol (EE) for 5 days (estrogen-induced intrahepatic cholestasis model), and/or labetalol during the same period to simulate ICP and antihypertensive treatment in pregnancy. Plasma was also collected from healthy pregnant women and patients with ICP.

Results: Increased plasma levels of sEng were observed in EE cholestasis and patients with ICP. Administration of labetalol to mice with EE cholestasis aggravated the increase in BA plasma concentrations by induction of hepatic Mrp4 efflux transporter and potentiated the increment of sEng plasma levels. Moreover, increased plasma levels of sEng in transgenic mice exacerbated the increase in BA plasma concentrations during labetalol treatment.

Conclusions: These data demonstrate that both labetalol treatment and increased plasma levels of sEng aggravate estradiol-induced cholestasis, and result in increased systemic exposure to BA predisposing mother and fetus for adverse pregnancy outcome. Thus, these data suggest the importance of monitoring sEng and BA plasma concentrations of pregnant woman prone to preeclampsia and/or cholestasis. *Supported by [GAUK1166119] and [GACR 22-1496S].*

91ST EAS CONGRESS
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117 / #718

Topic: *AS02 Lipids and Lipoproteins / AS02.06 Cholesterol efflux and reverse cholesterol transport*

PCSK9 INHIBITORS ALTER THE DISTRIBUTION OF MACROPHAGE-DERIVED CHOLESTEROL EFFLUX TO FAMILIAL HYPERCHOLESTEROLEMIA LIPOPROTEINS AND PROMOTE MACROPHAGE-SPECIFIC REVERSE CHOLESTEROL TRANSPORT IN VIVO

POSTER ON BOARD: AS02.06 CHOLESTEROL EFFLUX AND REVERSE CHOLESTEROL TRANSPORT

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Background and Aims: Macrophage cholesterol efflux is a key step in the macrophage-specific reverse cholesterol transport (mRCT) pathway, which culminates in the fecal excretion of macrophage-derived cholesterol. We reported that LDL particles from familial hypercholesterolemia (FH) patients and FH mice were the major acceptors of macrophage-derived cholesterol and, thus, LDL receptors (LDLr) were essential to sustain functional mRCT pathway. In this study, we aimed to evaluate the ability of PCSK9 inhibitors to restore the HDL-mediated macrophage cholesterol efflux in FH subjects and to determine the potential of these drugs to promote the mRCT pathway in heterozygous LDLr–deficient mice expressing human apoB100.

Methods: We assessed macrophage [^{3}H]cholesterol efflux induced by plasma from FH patients before and after PCSK9 inhibitor treatment and the distribution of macrophage-derived cholesterol in plasma lipoprotein fractions. Next, we injected [^{3}H]cholesterol-labeled macrophages into the peritoneal cavity and evaluated the mRCT rate in mice treated with a PCSK9 antibody or vehicle.

Results: The capacity of FH plasmas to induce macrophage cholesterol efflux was not altered by PCSK9 inhibitor treatment. However, analysis of the distribution of lipoprotein [^{3}H]cholesterol showed that, after PCSK9 inhibitor treatment, LDL particles contained less and HDL particles contained more radiolabeled cholesterol. In FH mice, PCSK9 inhibition promoted the flow of macrophage-derived cholesterol to feces and also enhanced the transfer of LDL-derived cholesterol to feces.

Conclusions: In FH subjects, PCSK9 inhibitors reduce and increase the capacities of LDL and HDL particles, respectively, to act as macrophage-derived cholesterol reservoirs. In mice, the treatment with PCSK9 antibodies increases macrophage-to-feces RCT in vivo.

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MANNHEIM GERMANY | MAY 21-24, 2023

118 / #114

Topic: *AS02 Lipids and Lipoproteins / AS02.06 Cholesterol efflux and reverse cholesterol transport*

CAN HUMAN TRANS INTESTINAL CHOLESTEROL EXCRETION BE STIMULATED USING URSODEOXYCHOLIC ACID AND EZETIMIBE: A RANDOMIZED PLACEBO CONTROLLED CROSS-OVER STUDY.

POSTER ON BOARD: AS02.06 CHOLESTEROL EFFLUX AND REVERSE CHOLESTEROL TRANSPORT

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Background and Aims: The Trans Intestinal Cholesterol Excretion (TICE) pathway is a novel therapeutic target to reduce low-density lipoprotein cholesterol (LDL-C). TICE encompasses the direct excretion of cholesterol by enterocytes into feces. In mice TICE has been shown to be stimulated by hydrophilic bile acid, resulting in increased fecal neutral sterols (FNS) and reduced plasma cholesterol levels. We investigated whether the combined therapy of ezetimibe and ursodeoxcycholic acid (UDCA), a hydrophilic bile acid, would increase FNS in humans as proxy for TICE.

Methods: We performed a randomized double-blind placebo controlled cross-over trial. 20 male participants aged >18 years, with plasma LDL-C levels ≥2.6mmol/L were included. Patients started with 3 weeks of ezetimibe 20mg treatment, after which they were randomized to UDCA 600mg orally once daily, or matching placebo once daily for two weeks. The study included a three week wash-out between treatment periods. Blood and fecal samples were collected at each study visit.

Results: Mean (SD) age, BMI and LDL-cholesterol were 59 (11.3) years, 26.4 (3.1) kg/m2, and 3.9 (0.8) mmol/L, respectively. After UDCA treatment, plasma bile acid hydrophilicity increased (297%, $p<0.01$). A non-significant reduction in FNS concentration was observed (-6.2%, $p=0.83$). Total cholesterol and LDL-C levels increased on UDCA treatment when compared with placebo (4.5%, $p<0.001$ and 9%, $p<0.001$ respectively).

Conclusions: UDCA in combination with ezetimibe does increase bile acid hydrophilicity. Unexpectedly, this resulted in decreased FNS, with a concomitant increase in plasma cholesterol in hypercholesterolemic subjects. Research into other pathways which may promote TICE humans is warranted.

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119 / #687

Topic: *AS02 Lipids and Lipoproteins / AS02.06 Cholesterol efflux and reverse cholesterol transport*

ALTERATION OF HDL SUBCLASSES DISTRIBUTION AFFECTS THEIR CAPACITY TO MEDIATE CHOLESTEROL EFFLUX.

POSTER ON BOARD: AS02.06 CHOLESTEROL EFFLUX AND REVERSE CHOLESTEROL TRANSPORT

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Background and Aims: HDL has many anti-atherosclerotic properties. Their main beneficial activity is linked to their ability to promote “reverse cholesterol transport”, a process that contributes to the elimination of excess cholesterol. We hypothesize that the age-related decline capacity to mediate cholesterol efflux is largely due to an alteration in the distribution of HDL subclasses. This study aimed to investigate the effect of an alteration of HDL subclasses distribution on their functionality, and how extra-virgin olive oil (HOEV) may regulate the principal anti-atherosclerotic activity of HDL.

Methods: 87 healthy subjects were recruited and distributed in two age groups: 27 young and 57 elderly subjects. Participants were subjected to 12 weeks of HOEV-rich diet. The distribution of HDL fractions was measured using the Lipoprint system. HDL functionality was assessed by measuring their cholesterol efflux capacity (CEC) from J774 macrophages.

Results: Our results show that HDL from the elderly subjects presents a lower CEC (-11.12% $p<0.003$) compared to young subjects. Analysis of the distribution of HDL subclasses shows that older adults have less large HDL (L-HDL) ($p<0.003$) and high levels of small HDL (S-HDL) ($p<0.002$) compared to young people. Multiple linear regression analysis showed an inverse correlation between HDL-mediated CEC and S-LDL [$r = 0.27$; $p <0.01$] levels and a positive correlation between CEC and L-HDL levels [$r = 0.35$; $p <0.001$].

Conclusions: Our results demonstrate that the decrease in HDL functionality is due to an alteration in their subclasses’ distribution. HOEV intake improves both HDL functionality and particle distribution.

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120 / #429

Topic: *AS02 Lipids and Lipoproteins / AS02.06 Cholesterol efflux and reverse cholesterol transport*

IMPAIRED HDL-MEDIATED CELL CHOLESTEROL REMOVAL IN ADVANCED BREAST CANCER

POSTER ON BOARD: AS02.06 CHOLESTEROL EFFLUX AND REVERSE CHOLESTEROL TRANSPORT

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Background and Aims: HDL cholesterol (HDLc) and breast cancer (BC) association is partially controversial because its plasma levels do not reflect HDL particle's functionality. HDL removes cell cholesterol and oxysterols limiting tumor growth and metastasis.

Methods: It was addressed in newly diagnosed, treatment-naïve BC women (n=163) as compared to control women (n=150) the HDL ability in removing cell cholesterol and its composition in lipids, apolipoprotein A-I and oxysterols. HDL was isolated by ultracentrifugation; lipids (total cholesterol, TC; triglycerides, TG; and phospholipids, PL) were determined by enzymatic assays, apo A-I by immunoturbidimetry, and oxysterols (27, 25, and 24-hydroxycholesterol), by gas chromatography coupled with mass spectrometry. HDL-mediated cholesterol removal was determined in macrophages previously overloaded with cholesterol and ^{14}C-cholesterol. Comparisons were done by Mann-Whitney and Kruskal-Wallis tests.

Results: Lipid profile was similar between control and BC groups after adjustment per age. In BC, HDL composition in TC, TG, PL, and 27-hydroxicholesterol was reduced (respectively 84%, 93%, 89%, and 61%; $P<0.05$) as compared to controls, but cell cholesterol removal was similar. Reduced cholesterol efflux (28%; $P=0.01$) was observed in HDL from advanced BC cases (stages III and IV), as compared to stages I and II, independently of BC histological type.

Conclusions: The impaired ability of HDL in removing cell cholesterol and its reduced content in lipids and oxysterol is independent of HDLc plasma levels and may contribute to worsening BC prognosis.

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121 / #1169

Topic: *AS02 Lipids and Lipoproteins / AS02.07 Lipidomics*

TREATMENT WITH PCSK9 INHIBITORS IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA LOWERS PLASMA LEVELS OF PLATELET ACTIVATING FACTOR AND ITS PRECURSORS: A COMBINED METABOLOMIC AND LIPIDOMIC APPROACH.

POSTER ON BOARD: AS02.07 LIPIDOMICS

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Background and Aims: Familial hypercholesterolemia (FH) is characterized by extremely high levels of circulating low-density lipoprotein cholesterol (LDL-C) and is caused by mutations of genes involved in LDL-C metabolism, including LDL receptor (LDLR), Apolipoprotein B (APOB) or Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9). Accordingly, PCSK9 inhibitors (PCSK9i) are effective in LDL-C reduction. However, no data are available on pleiotropic effect of PCSK9i. To this end we performed an untargeted metabolomics approach to gather a global view on changes in metabolic pathways in patients receiving a treatment with PCSK9i.

Methods: FH patients starting a treatment with PCSK-9i were evaluated by untargeted metabolomics approach at baseline (before PCSK9i treatment) and after 12 weeks of treatment.

Results: 25 FH subjects were enrolled on maximal tolerated lipid-lowering therapy prior to study entry. After a 12-week treatment with PCSK9i, we observed an expected significant reduction in LDL-cholesterol levels (from 201.0±69.5 mg/dl to 103.0±58.0 mg/dl, $p < 0.001$). The LDL-C target was achieved in 36% of patients. After peak validation and correction, after 12-week PCSK9i treatment as compared to baseline, we observed an increment of creatine (p-value = 0,041), indole (p-value = 0,045) and indoleacrylic acid (p-value= 0,045) concentrations. Conversely, a significant decrease in choline (p-value = 0,045) and phosphatidylcholine (p-value <0.01) together with the reduction of platelet activating factor (p-value = 0,041) was observed.

Conclusions: aking advantage of untargeted metabolomics, we first provide evidence of a concomitant reduction of inflammation and platelet activation metabolites in FH patients receiving a 12-week treatment with PCSK9i.

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122 / #350

Topic: *AS02 Lipids and Lipoproteins / AS02.07 Lipidomics*

LIPIDOMICS OF TRIGLYCERIDE-RICH LIPOPROTEINS DETERMINES PARTICLE/THP-1 MACROPHAGES INTERACTION AND SYSTEMIC INFLAMMATORY PROFILE ASSESSED BY 1H-NMR

POSTER ON BOARD: AS02.07 LIPIDOMICS

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Background and Aims: High plasma triglyceride (TG) levels and chronic inflammation are important factors related to metabolic diseases, including diabetes. We aimed to study the lipidomic profile of triglyceride-rich lipoproteins (TRL) derived from patients with metabolic syndrome and the inflammatory effects mediated *in vivo* and *in vitro*.

Methods: Sequential preparative ultracentrifugation was used to isolate the TRL fraction from patients with metabolic alterations. Proton nuclear magnetic resonance (^{1}H-NMR) was used to study the TRL lipidomic profile and the plasma circulating levels of glycoprotein acetyls;; THP-1-derived macrophages were used as an *in vitro* model to study the molecular inflammatory effects mediated by TRL.

Results: *In vivo*: the highest content of TG on TRL was associated with higher circulating levels of NMR-measured acute-phase glycoproteins. The lipidomic analysis showed that TRL-TG enrichment was associated with an increase in omega-9 and a decrease in saturated fatty acids. *In vitro*: incubation of THP-1 derived macrophages with the higher concentrations of TRL-TG increased both the intracellular lipid content and cytokines secretion (IL-1β, TNF-α and CD206). This proinflammatory response was partially mediated by MAPK and Akt/NFκB activation.

Conclusions: High TG levels in TRLs were associated with higher inflammatory responses both *in vivo* and *in vitro*. Changes in the distribution of the fatty acids could mediate this inflammatory response. These results could explain the chronic inflammatory status observed in patients at metabolic risk.

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123 / #667

Topic: *AS02 Lipids and Lipoproteins / AS02.08 Cellular lipid metabolism and lipid droplets*

IN VITRO EXTRACELLULAR VESICLES' HETEROGENEITY-RELATED BIOLOGICAL PROPERTIES MAY BE DEFINED BY A NEW METHOD OF SEPARATION AND CHARACTERIZATION

POSTER ON BOARD: AS02.08 CELLULAR LIPID METABOLISM AND LIPID DROPLETS

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Background and Aims: Extracellular vesicles (EVs) participate to pathophysiological processe by transferring their cargo from cell to cell, but unproper separation and characterization methods make difficult to fully comprehend their functions. To overcome this problem, we optimized an ultracentrifugation method to size-separate different EV populations in vitro, following an algorithm developed by Livshits.

Methods: We characterized EVs secreted by a melanoma cell line by transmission electron microscopy, atomic force microscopy and dynamic light scattering. Fatty acid (FA) profile and protein content were evaluated by GLC and MS. Purity from external proteins was assayed by the CONAN method.

Results: Dimensional analysis confirmed the existence of different EV populations and the theoretical sizes calculated by the algorithm. GLC analysis revealed a continuous percentage increase in saturated FA ranging from parental cells to smaller EVs (33.61%-64.79%), suggesting different membrane rigidity and properties among populations. MS analysis identified 2003 proteins with quali/quantitative differential distribution among the populations. As expected, the MetaCore pathway analysis performed on individual cargos evidenced, besides common signaling pathways, molecular properties that specifically characterize each fraction, suggesting distinctive behaviors and functions for different EVs. Finally, the interactomic analysis performed on identified proteins from the smallest EV fraction (exomeres) evidenced a complex and highly integrated network involved in a fine regulation of target-cell and environmental plasticity.

Conclusions: Our separation method may be applied to any cell line, being helpful in defining the role of specific EV populations in cardiovascular diseases and in finding new pharmacological treatments able to modulate EV functions. *Supported by EXTRALIPO Bando SEED 2019.*

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MANNHEIM GERMANY | MAY 21-24, 2023

124 / #270

Topic: *AS02 Lipids and Lipoproteins / AS02.08 Cellular lipid metabolism and lipid droplets*

NONSENSE MUTATION IN MITOCHONDRIAL CYTB GENE AND MACROPHAGE LIPID METABOLISM.

POSTER ON BOARD: AS02.08 CELLULAR LIPID METABOLISM AND LIPID DROPLETS

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Background and Aims: Mutation m.15059G>A in the mitochondrial Cytb gene was found in lipofibrous plaques from patients with atherosclerosis. To study this mutation, we created cybrid cells HSMAM1, which has 68% heteroplasmy level of this mutation. The aim of this research was to examine the association of m.15059G>A mutation with macrophage lipid metabolism.

Methods: Human monocyte-like cell line THP-1 used as reference, cybrid line HSMAM1 with m.15059G>A mutation (CytB gene), and cybrid line HSMAM1 with eliminated m.15059G>A mutation (HSMAM1-Cas) by CRISPR/Cas9 editing were used to assess intracellular lipid metabolism. The intracellular lipid metabolism was assessed by the expression of cholesterol esterase (*LIPA*), acyl-coenzyme A:cholesterol acyltransferase (*ACAT1*) and fatty acid synthetase (*FASN*) genes by qPCR. Cholesterol accumulation was measured by spectrophotometry.

Results: Atherogenic LDL increased cholesterol accumulation in HSMAM1 and HSMAM1-Cas cybrids compared to the THP-1 cells. However, cholesterol accumulation between the HSMAM1 and HSMAM1-Cas cybrids did not differ ($p>0.05$). The basal expression of *LIPA, ACAT1* and *FASN* was decreased in HSMAM1 and HSMAM1-Cas cells compared with the THP-1 cells ($p<0.001$). Incubation of macrophages with atherogenic LDL leads to an increased expression of the *FASN*, as well as a decreased expression of *LIPA* in HSMAM1 cells compared to the THP-1 cells. Moreover, decreased expression of *ACAT1* and *FASN* as well as an increased expression of *LIPA* in response to cholesterol accumulation were observed in HSMAM1-Cas cells compared to HSMAM1 cells.

Conclusions: The m.15059G>A mutation may affect intracellular lipid metabolism in macrophages. This work was supported by Russian Science Foundation Grant # 22-25-00274.

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Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

ANALYSIS OF STEATOSIS BIOMARKERS AND INFLAMMATORY PROFILE AFTER ADDING ON PCSK9 INHIBITOR TREATMENT IN FAMILIAL HYPERCHOLESTEROLEMIA SUBJECTS WITH NONALCOHOLIC FATTY LIVER DISEASE

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: NAFLD may be crucial in subjects with FH. We aimed to evaluate the effect of the PCSK9-i on steatosis biomarkers such as TyG and HSI and analyse the role of TG/ HDL in this population before and after adding-on PCSK9-i.

Methods: In this observational study, we evaluated 26 genetically confirmed FH patients with NAFLD and an LDL-C off-target despite high-intensity statins plus ezetimibe. All patients added PCSK9-i treatment and obtained biochemical analysis and TyG and HSI evaluation at baseline and after six months of PCSK9-i.

Results: No difference of steatosis biomarkers was found after adding-on PCSK9-i therapy. In a secondary analysis, we divided the study population in two groups according to TG/HDL median value: high TG/HDL group (H-TG/HDL) and low TG/HDL group (L-TG/HDL). TyG and HSI were significantly lower in the L-TG/HDL than H-TG/HDL group (for TyG 9.05 ± 0.34 vs 9.51 ± 0.32; for HSI 38.43 ± 1.35 vs 41.35 ± 1.83, p value for both < 0.05). After six months of PCSK9-i therapy, TyG and HSI were significantly reduced in the L-TG/HDL group after PCSK9-i therapy (7.5% and 8.4% respectively, p value for both < 0.05) and these biomarkers were lower compared to H-TG/HDL group (for TyG 8.37 ± 0.14 vs 9.19 ± 0.12; for HSI 35.19 ± 1.32 vs 39.48 ± 1.33, p value for both < 0.05).

Conclusions: PCSK9-i therapy significantly ameliorate steatosis biomarkers in FH patients with low TG/HDL; results may be consistent with a beneficial role of PCSK9-i on steatosis biomarkers in FH subjects with NAFLD.

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126 / #1615

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

THE CONTEMPORARY MANAGEMENT OF PATIENTS WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA: THE EXPERIENCE OF THE ITALIAN LIPIGEN REGISTRY AND A SYSTEMATIC REVIEW OF THE LITERATURE

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Aim. The treatment of HoFH is rapidly changing in recent times and how such changes may affect LDL-C control and cardiovascular prognosis in HoFH is almost completely unknown.

Methods: Methods. Demographic, biochemical characteristics and clinical (including ASCVD and lipid lowering therapies, LLT) were collected from 139 HoFH included in the Italian LIPIGEN-FH registry. A systematic review of literature was performed to estimate the pooled prevalence of ASCVD in HoFH.

Results: Results: The LIPIGEN-HoFH included 37 true-HoFH, 11 ARH, 63 CHE/DHE, and 28 clinical HoFH showing a mean untreated LDL-C of 490.7±149.3mg/dl. At last follow-up, the 77% of patients were using innovative therapies (PCSK9i, lomitapide and evinacumab), some in combinations between them and/or with conventional LLT. After 6 years, last visit LDL-C dropped to 124.1±70.8mg/dl with a % reduction from baseline of 58.4±26.9%. The 33.3% of HoFH patients were referring past ASCVD history at baseline and 21.8% experienced incident ASCVD during follow-up (*P*=NS). Overall, the lifetime prevalence of ASCVD was 41.3% with the mean age at first ASCVD event being 41.4±13.9years. The systematic review included 14 study for a total of 1922 HoFH patients showing a median untreated LDL-C of 579.8±45.7mg/dl. This cohort provided a crude lifetime ASCVD prevalence of 35.0% (95% IC 32.9-37.1) with the first event occurring at 29.1±8.5years.

Conclusions: Conclusions: Although in the LIPIGEN cohort we observed a delay in the appearance of first ASCVD event, the cardiovascular risk in HoFH remains very high. These findings underline that a further improvement is necessary in the clinical management of HoFH patients.

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127 / #929

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

A FIVE-YEAR FOLLOW-UP IN HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA PATIENTS OF THE RUSSIAN FAMILIAL HYPERCHOLESTEROLEMIA REGISTRY

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Homozygous familial hypercholesterolemia (FH) is a rare genetic condition characterized by markedly elevated low-density lipoprotein cholesterol (LDL-C) concentrations from birth and extreme risk of premature atherosclerotic cardiovascular disease. The aim of this study was to evaluate the effectiveness and adherence to lipid-lowering therapy, the frequency of major adverse cardiovascular events (MACE) in homozygous FH patients during a five-year follow-up within the Russian FH registry.

Methods: The study included 17 homozygous FH patients (mean age 22±13 years, 65% females) from the Russian FH registry: 71% (n=12) adults and 29% (n=5) children. Genetic testing was performed in 82% (n=14) subjects: compound heterozygous FH was verified in 11 subjects and true homozygous FH in three persons. MACE included fatal and non-fatal cardiovascular events.

Results: The mean age of diagnosis homozygous FH was 10±8 years. Ischemic heart disease was detected in 9 (53%) patients and aortic valve stenosis in 6 (35%) patients. During mean follow-up 74±13 months non-fatal myocardial infarction was registered in two patients and two patients had sudden cardiac death. One patient died due to complications of COVID-19. Initial LDL-C level was 16.1±2.7 mmol/L. During the observation period we found a decrease mean LDL-C level by 29%, none of the patients reached the LDL-C target level. The description of the lipid-lowering treatment is presented in the Table. Three patients were approved for therapy with lomitapide therapy (not registered in the

Russia).

Table. Dynamic of lipid-lowering treatment in 17 homozygous FH patients.

Lipid-lowering treatment	Baseline	Follow-up	p
None	1 (6%)*	1 (6%)	1.0
Statin+ezetimibe	16 (94%)	2 (12%)	<0.001
Statin+ezetimibe+PCSK9 inhibitor	0 (0%)	7 (40%)	<0.01
Statin+ezetimibe+lipoprotein apheresis	0 (0%)	4 (24%)	0.1
Statin+ezetimibe+PCSK9 inhibitor+ lipoprotein apheresis	0 (0%)	3 (18%)	0.2

** A child of two years old.*

Conclusions: The using of combined therapy among Russian homozygous FH patients is increased, but new therapeutic agents are needed for better LDL-C levels control.

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Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

AGE EXACERBATES TRIGLYCERIDE-INDUCED HDLC-LOWERING IN WOMEN

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Elevated concentrations of HDL cholesterol (HDLc) protect against atherosclerotic cardiovascular disease. There are important age and gender differences both in cardiovascular risk and HDL metabolism. One immediate effect of elevated triglycerides is a decrease in HDLc. Our hypothesis is that the inverse relation between TG and HDLc is age and sex-dependent.

Methods: We studied 4.754 adults from the general population participating in the Di@bet.es study (n=2020 men and n=2734 women). Lipoprotein particles were determined by NMR. To estimate the association between HDLc and TG we used linear regression models, and known confounders (age, gender, BMI, alcohol, diet, physical activity, smoking, diabetes mellitus) were included in multivariable regression models.

Results: We identified interactions between TG and gender (p=0.001) and TG and age (p=0.001). Consequently, we stratified the population by gender and age. In women at 20 and 30 years of age, TGs did not affect HDLc. However, as they became older, the decrease in HDLc per 1mmol/L increase of TG doubled from -0.102 mmol/L at the age of 50 to -0.204 at the age of 80. Interestingly in men the effect of TGs on HDLc remained constant at all ages. The NMR data showed that HDLc decrease was mostly induced by large VLDL and affected only middle and small HDL particles.

Conclusions: Although at early ages the decrease in HDLc associated with an increase in TG is lower in women than in men, after 50s the effect on HDLc due to such increase in TG becomes significantly higher in women.

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129 / #117

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

SYSTEMATIC REVIEW ON THE EFFICACY OF CURRENT TREATMENTS FOR THE MANAGEMENT OF HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLAEMIA

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Homozygous familial hypercholesterolaemia (HoFH) is a rare genetic disorder characterized by profoundly elevated levels of LDL cholesterol (LDL-C) leading to premature atherosclerosis and cardiovascular complications. Despite multiple lipid-lowering treatments, most patients do not achieve LDL-C targets. This systematic review evaluated the efficacy of individual treatments for the management of HoFH.

Methods: A mixed-methods review was performed to identify and characterize primary interventional studies for HoFH management, including ezetimibe, PCSK9 inhibitors, lomitapide, evinacumab, and LDL apheresis. The primary outcome was change in LDL-C compared with baseline or placebo.

Results: Twenty-five studies were identified; four were double-blind, randomized controlled trials (RCTs) and the remainder were single-arm trials or observational registries. Of the three placebo-controlled RCTs with low risk of bias, evinacumab demonstrated the greatest efficacy with a 49.0% reduction in LDL-C, followed by the PCSK9 inhibitors alirocumab (-35.6%) and evolocumab (-30.9%), which are minimally effective (or not effective) for patients with null/null variants. Interpretation of the remaining studies was limited because of the study designs employed, which are prone to a high risk of bias and confounding. Comparing longitudinal data, evinacumab resulted in rapid, sustained reductions in LDL-C; PCSK9 inhibitors had a rapid but less substantive effect; and lomitapide had a more gradual effect that plateaued at a smaller percent reduction in LDL-C compared with evinacumab. Equivalent longitudinal data were not reported for LDL apheresis or ezetimibe.

Conclusions: All interventions lowered LDL-C, but with varied evidence certainty and magnitude of effect. The characteristics of each intervention should be considered when managing HoFH.

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130 / #88

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

IMPACT OF WEIGHT LOSS AFTER A BARIATRIC SURGERY ON THE LOW-DENSITY LIPOPROTEIN-PROTEOGLYCAN INTERACTION

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Obesity is increasing worldwide, representing a major public health issue. Dyslipidemia, oxidative stress, and chronic inflammation are common in obesity, increasing the risk of cardiovascular disease. Weight loss strategies to reduce obesity are increasingly important. Our goal is to determine how weight loss in obesity influences the interactions of low-density lipoproteins (LDL) with proteoglycans. These interactions initiate the pro-atherogenic lipoprotein retention in the arterial wall matrix.

Methods: LDL was isolated by density ultracentrifugation from 6 obese patients before and after one-year bariatric surgery (basal BMI 42.9 kg/m^2; post-surgery BMI 29.4 kg/m^2). Thirteen healthy subjects were included in the control group. Lipoprotein binding to proteoglycans was assessed by heparin affinity chromatography and ELISA.

Results: Before surgery, LDL from obese patients showed increased binding to various matrix proteoglycans including heparin, heparin sulfate, chondroitin sulfate, and hyaluronic acid at both acidic and neutral pH (pH 5.5 and 7.4) compared to control group. One year after surgery, the binding to chondroitin sulfate and hyaluronic acid decreased dramatically at both pH. However, there was only a small reduction in the binding affinity to heparin at neutral pH and no change at acidic pH compared to control group. These results suggest that obesity induces irreversible modifications in LDL, which affect electrostatically driven binding to highly sulfated matrix proteoglycans.

Conclusions: Bariatric surgery has different effects on LDL binding to different proteoglycans. This might stem from irreversible structural changes in apoB potentially via lipid modifications. The impact of these effects will be determined in the follow-up patients' studies. lipid modifications.

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131 / #103

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

TOTUM-070, A COMBINATION OF PLANT EXTRACTS, REDUCES HYPERCHOLESTEROLEMIA TROUGH INHIBITION OF INTESTINAL CHOLESTEROL ABSORPTION IN HAMSTERS AND HUMAN CACO2 CELLS

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: TOTUM-070 (T070) is a polyphenol-rich substance designed to prevent hypercholesterolemia composed by 5 plant extracts. Previous study in dyslipidemia models demonstrated that supplementation with T070 at 5% in the diet reduced serum non-HDL cholesterol compared to high fat high cholesterol diet (HFHCD) group (-47%, p<0,001,) and serum triglycerides (-46%, p<0,05). We aimed to characterize the mechanisms of action of T070 in animal and cell culture studies.

Methods: For in vivo investigation of lipoprotein metabolism, Syrian hamsters were fed either normal diet (ND) or HFHCD with or without T070 at 5% for 12 weeks (n=16 per group). For in vitro studies, [1,2-3H(N)]-cholesterol uptake and secretion assays were performed in differentiated human Caco2 cells.

Results: Quantification of fecal neutral sterols in hamsters after 12 weeks indicated a 17% increase (ns) of sterols excretion in feces from T070 5% group compared to HFHCD. Intestinal [4-14C]-Cholesterol absorption test showed a 12% reduction (ns) with T070 5% compared to HFHCD group. Furthermore, an oral fat tolerance test showed that post-prandial hypertriglyceridemia was significantly reduced by 40% (p<0,01) in T070 5% group following olive oil gavage compared to the HFHCD hamsters. Finally, gut microbiota analysis highlighted strong impact of T070 supplementation on alpha and beta diversity compared to ND and HFHCD. In enterocytes, incubation with T070 at 1g/l for 1h reduced [1,2-3H(N)]-cholesterol uptake by 30% (p<0.01). Moreover, cholesterol secretion was decreased by 38% (p<0.001) after overnight incubation with 0.5 g/l T070.

Conclusions: These results highlight the potential Totum-070 for the management of hypercholesterolemia through inhibition of intestinal cholesterol absorption

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Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

BEMPEDOIC ACID-STATINS AND APOE-BASED NANOPARTICLES COMBINATION INCREASES LDLR EXPRESSION AND LDL UPTAKE IN HEPATIC CELL LINES

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Familial hypercholesterolemia (FH) is the most common autosomal dominant dyslipidemia characterized by elevated plasma LDL-C levels.Today the gold standard treatment in FH patients are statins, which inhibit the cholesterol biosynthetic pathway inducing and increasing uptake of plasma ApoB containing lipoproteins. Recently, bempedoic acid (BA), an inhibitor of ATP citrate lyase, has been approved for the management of FH patients in combination with statins increasing their lipid-lowering efficacy. Moreover, BA has been designed to avoid myalgias, one of the most common side effects of the statin therapies. However, during clinical trials several adverse effects such as upper respiratory tract infections, muscle spasms, and back pain… were also described. The aim of the work is to study *in vitro* the effect of a BA-statin combinatory therapy when added into ApoE-based nanoparticles.

Methods: Flow cytometry, qRT-PCR.

Results: Delivery of statins and BA by nanoparticles increases the expression of LDLr mRNA and its membrane protein availability as measured by qRT-PCR and flow cytometry when compared to non-nanoparticle therapy or the combination of the nanoparticles with only one of the drug. LDL uptake was also significantly enhanced.

Conclusions: The increased LDL uptake using the combinatory therapy based on statins, BA and ApoE-based nanoparticles indicates that the effects showed in the clinical trials are reproducible using ApoE-based nanosystem. Moreover, the use of ApoE-based nanoparticles as carriers could reduce extrahepatic side effects of the treatment and improve patient prognosis.

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Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

SIZE IS NOT EVERYTHING: CHARACTERIZING LIPOPROTEIN LIFETIME IN ZEBRAFISH USING A PHOTOCONVERTIBLE APOB FUSION PROTEIN

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: The size, density, and cargo composition of apolipoprotein B (ApoB)-containing lipoproteins (B-lps) are known to influence their atherogenic character. The lifetime of B-lps in circulation can also contribute to the atherogenicity of B-lps. The longer B-lps are in circulation, modifications accumulate, which increase B-lp adherence to the vasculature and lower B-lp specificity to the LDL receptor (LDLR). The factors that control B-lp turnover have yet to be fully elucidated in part because measurement of turnover is difficult and mainly indirect.

Methods: We developed zebrafish in which endogenous ApoB is fused to the photoconvertible protein Dendra2. After UV exposure, ApoB-Dendra2 irreversibly converts from its green state into its red state. We can directly track the red-converted ApoB-Dendra2 labeled B-lps and measure their turnover rate and localization in optically-clear larvae.

Results: During development, zebrafish receive nutrients solely from the maternally deposited lipid-rich yolk, which is packaged into B-lps. We discovered that B-lp turnover becomes faster as development proceeds, correlating with increased growth rates and decreasing yolk lipid availability. Ldlr mutants exhibit higher levels of B-lps (up to 1285.43%), which are small in size and have significantly decreased turnover (1.7-2 fold). Similarly, apolipoprotein C2 mutants, which cannot liberate triglycerides from B-lps, show significantly increased numbers of large-sized B-lps (up to 1387.55%) and delayed turnover (2.21-4.37 fold). Microsomal triglyceride transfer mutants have smaller B-lps due to lipid-loading deficits, but increased turnover rates (0.36-0.73 fold).

Conclusions: These data underline the importance of including B-lp turnover studies when determining the atherogenic characteristics of B-lps.

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Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

LONG-TERM FASTING EFFECT ON HDL CHOLESTEROL EFFLUX AND SERUM CHOLESTEROL LOADING CAPACITY: PRELIMINARY RESULTS FROM A SINGLE-ARM INTERVENTIONAL TRIAL

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Long-term fasting (LF), defined as lasting from 4 days to several weeks, induces changes in metabolism leading to improvements in cardiovascular (CV) risk factors. We aim to evaluate whether LF affects lipoprotein CV-related functions, such as HDL-cholesterol efflux capacity (HDL-CEC) and serum cholesterol loading capacity (CLC) that are anti- and pro-atherogenic parameters.

Methods: We report preliminary results for 20 patients out of the 40 patients recruited within the GENESIS study for the analysis of cholesterol metabolism (age: 47.9 ± 12.1 years; BMI: 27.3 ± 4.2 kg/m^2; NCT05031598), who underwent 9 ± 3 days LF period (250 Kcal/day). Serum samples were collected before (baseline: BL), at the end of the LF period (END), and 1 month after food reintroduction (follow-up: FUP). HDL-CEC mediated by ATP-binding cassette A1 (ABCA1), G1 (ABCG1) transporters and aqueous diffusion (AD) and CLC were evaluated through cell-based radioisotopic and fluorimetric assays.

Results: CEC through AD was similar at BL and END of LF (-1.3%, ns), but increased at FUP as compared to the END of LF (7.2%, significant). ABCA1-mediated HDL-CEC decreased from BL to END of LF (31.9%, significant), then increased at FUP (35%, significant). ABCG1-mediated HDL-CEC did not significantly change across the analysed endpoints. Serum CLC decreased at the end of LF (11%, significant), then at FUP returned at levels similar to BL (10.8%, significant).

Conclusions: Our preliminary analysis of HDL-CEC and CLC during LF suggests an impact on cholesterol metabolism which might affect pro-atherogenic CV-related lipoprotein functions.

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135 / #1216

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

EVINACUMAB REDUCES EU APHERESIS ELIGIBILITY IN PATIENTS WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disorder associated with impaired low-density lipoprotein cholesterol (LDL-C) clearance from the circulation, leading to extremely elevated LDL-C levels and resulting in increased cardiovascular events and premature mortality. Evinacumab, a fully human monoclonal antibody against angiopoietin-like 3, has demonstrated LDL-C reductions of approximately 50% in patients with HoFH. This post-hoc analysis assessed the effect of evinacumab on the change in apheresis eligibility based on predefined EU apheresis criteria in patients with HoFH.

Methods: An ongoing, single-arm, open-label, phase 3 study (NCT03409744) enrolled and treated patients aged ≥12 years with HoFH. All evaluable patients (n=106) received intravenous evinacumab 15 mg/kg every 4 weeks.

Results: At baseline, 78.3% (83/106) of patients qualified for apheresis and 21.7% (23/106) of patients did not qualify for apheresis using predefined EU criteria (LDL-C >160 mg/dL [primary prevention] or LDL-C >120 mg/dL [secondary prevention]; **Table**). Overall, evinacumab treatment reduced mean (SD) LDL-C by 130.6 (109.3) mg/dL from baseline at Week 56. Of the 83 patients who initially qualified for apheresis at baseline, over one half (58.1% [43/74]) no longer qualified for apheresis following 56 weeks of evinacumab treatment (data missing for 9 patients). The observed reduction in the proportion of patients qualifying for apheresis was overall maintained through to Week 184 (results not

shown).

Table. Baseline qualification and shift in qualification for predefined EU apheresis criteria[a] according to apheresis status at baseline

Qualified for predefined EU apheresis criteria[a] at baseline		Total (n=106)	
Yes		83	
No		23	
Visit		**Baseline qualification status**	
	Evaluation	**Qualified**	**Not qualified**
Week 56	Qualified	31 (29.0)	2 (1.9)
	Not qualified	43 (40.2)	17 (15.9)
	Missing	9 (8.4)	4 (3.7)

[a]LDL-C >160 mg/dL [primary prevention] or LDL-C >120 mg/dL (secondary prevention).
LDL-C, low-density lipoprotein cholesterol.

Conclusions: Based on predefined EU apheresis eligibility criteria, evinacumab substantially reduced the proportion of patients who would qualify for apheresis.

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Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

PCSK9 INHIBITORS HAVE ANTI-INFLAMMATORY ACTIVITY ASSESSED BY 1H-NMR GLYCOPROTEIN PROFILE IN SUBJECTS AT HIGH OR VERY HIGH CARDIOVASCULAR RISK

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: Atherosclerosis is a chronic inflammatory disease lead by accumulation of cholesterol in the intima. Proprotein convertase subtilisin/kexin type 9 inhibitors (iPCSK9) can reduce low density lipoprotein (LDL) cholesterol levels by 60%, but have not been proven to lower markers of systemic inflammation such as high-sensitivity C-reactive protein (hsCRP). Acute-phase serum glycoproteins are upregulated in the liver during systemic inflammation and their role as inflammatory biomarkers is under clinical evaluation. In this observational study we evaluate the effects of iPCSK9 on GlycA, B and F.

Methods: Thirty-nine patients eligible for iPCSK9 therapy were enrolled. One sample before and after 1 to 6 months of iPCSK9 therapy with alirocumab was obtained from each patient. Lipids, apolipoproteins, hsCRP and PCSK9 levels were measured by biochemical analyses, and the lipoprotein and glycoprotein profiles were measured by 1H-NMR.

Results: PCSK9 inhibitor reduced total (36.27%, $p<0.001$), LDL (55.05%, $p<0.001$) and non-HDL (45.11%, $p<0.001$) cholesterol, apolipoprotein (apo) C-III (10%, $p<0.001$), triglycerides (9.92%, $p<0.001$) and glycoprotein signals GlycA (11.97%, $p<0.001$), GlycB (3.83%, $p=0.017$) and GlycF (7.26%, $p<0.001$). It also increased apoA-I (2.05%, $p=0.043$) and HDL cholesterol levels (11.58%, $p<0.001$). Circulating PCSK9 levels increased 6-fold (626.28%, $p<0.001$). The decrease in Glyc signals positively correlated with the decrease in triglycerides and apoC-III.

Conclusions: In addition to LDL cholesterol, iPCSK9 therapy also induces a reduction in systemic inflammation measured by 1H-NMR-glycoprotein signals, which correlates with a decrease in triglycerides and apoC-III.

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Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

EFFECT OF PCSK9 INHIBITION WITH EVOLOCUMAB ON THE CONCENTRATION AND COMPOSITION OF LDL SUBFRACTIONS IN HIGH-RISK PATIENTS WITH CARDIOVASCULAR DISEASE

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: LDL comprises a heterogeneous group of particles, of which the dense subfraction is considered the most atherogenic. The aim of our study was to investigate the effect of PCSK9 inhibition on LDL subfraction concentration and composition in patients at high risk for cardiovascular disease.

Methods: LDL subfractions were analysed in 68 patients of a phase IV, randomized (1:1), prospective, double-blind, placebo controlled, parallel-group study. Patients were recruited at the Clinical Research Unit (CRC) of the Department of Nephrology and Hypertension in Erlangen. Main inclusion criteria were LDL cholesterol ≥70 mg/dl and a history of clinically evident atherosclerotic cardiovascular disease. Lipoproteins were analysed at the Medical University of Graz using praparative ultracentrifugtion methods.

Results: Total LDL cholesterol and apoB were reduced by 63 and 57%, respectively, after 8 weeks of Evolocumab treatment in addition to optimised lipid lowering therapy. The changes were significant compared to the group without Evolocumab. The primary outcome measure, apoB in dense LDL particles, was reduced by 58%. The effect on apoB in buoyant (-54%) and medium (- 66%) LDL particles was similar. Analysis of triglyceride-rich lipoproteins (VLDL and IDL) revealed evidence that Evolocumab alters the composition of these particles by reducing predominantly apoE- and cholesterol-rich remnant particles. First, the cholesterol reduction in VLDL and IDL was higher than the reduction of the triglyceride content. Second, apoE was significantly lowered, but not apoCII and apoCIII.

Conclusions: Treatment with Evolocumab significantly reduced all LDL subfractions, but did not alter the distribution and composition of LDL subfractions.

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138 / #820

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

CURRENT LDL-C MANAGEMENT IN GERMANY – THE VICTORION-IMPLEMENT STUDY

POSTER ON BOARD: AS02.09 LIPID AND LIPOPROTEIN METABOLISM

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Background and Aims: The VICTORION-Implement study aims to characterize the LDL-C management in patients with atherosclerotic cardiovascular disease (ASCVD) initiating a new oral lipid lowering therapy (LLT) or the PSCK9 siRNA inclisiran. The study assesses clinical characteristics, utilization of healthcare resources and patient reported outcomes.

Methods: n = 2030 patients with established ASCVD newly initiating an oral LLT or inclisiran on top of statins or inclisiran on top of lipoprotein apheresis (LA) will be documented over 21 months. This interim analysis reports the first 469 participants (cut-off 15-Nov-2022).

Results: The analysis shows no major differences with regard to the time since first cardiovascular event, quality of life (WHO-QoL-BREF) or treatment satisfaction (TSQM-9) regarding the respective pre-treatment. Patients starting an oral LLT had mean LDL-C levels 91 mg/dl (min-max: 54-266). Patients with inclisiran initiation had mean LDL-C of 118 mg/dl (53 – 292) in PCSK9i naive and 148 mg/dl (45 – 383) in PCSKi pre-treated individuals. Ezetimibe was chosen as new oral LLT in addition to a statin (n=288) in 94% of the patients. In the inclisiran cohorts, 60% (PCSK9i naive) and 40% (PCSK9i pre-treated) also received ezetimibe and/or bempedoic acid, n=67 and 13 respectively. Interestingly, only 66% (PCSK9i naïve, n=73) and 30% (PSCK9i pre-treated, n=6) received any statin at

baseline.

		Oral LLT	Inclisiran, PCSK9i naiive	Inclisiran, PCSK9i pre-treated
n		321	121	24
Age, years	mean	70,5	64,7	69,0
	min	41,0	44,0	47,0
	max	88,0	84,0	84,0
Sex	% male	72%	59%	39%
	% female	28%	41%	61%
CV event, years	mean	7,4	8,0	8,1
	min	0	0	1
	max	43	26	28
LDL-C mg/dl, BL	mean	91	118	148
	median	83	100	120
	min	54	53	45
	max	266	292	383
Treatment history	Any statin history	98%	84%	65%
Treatment at baseline	Any statin	97%	66%	30%
	Statin + ezetimibe	87%	NA	NA
	Statin + ezetimibe+ bempedoic acid	4%	NA	NA
	Ezetimibe only	3%	NA	NA
	Inclisiran only	NA	20%	45%
	Inclisiran + statin	NA	15%	10%
	Inclisiran + ezetimibe/bempedoic acid, no statin	NA	12%	25%
	Inclisiran + ezetimibe/bempedoic acid + statin	NA	47%	15%

Conclusions: This interim analysis provides timely information contributing to a better understanding of ASCVD patients in Germany. These results will be updated in the respective poster presentation including 600 patients at baseline and a more detailed analysis of patient history, demographics and treatment history.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

140 / #1192

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

SERUM SLOX-1 LEVELS NEGATIVELY CORRELATE WITH GRAY-SCALE MEDIAN (GSM) SCORING IN PATIENTS UNDERGOING CAROTID ENDARTERECTOMY.

POSTER ON BOARD: AS02.10 MODIFIED LIPOPROTEINS

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Background and Aims: Oxidation of LDL plays a significant pathogenic role in atherosclerosis. Lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) is the main receptor for Ox-LDL in vascular endothelial cells, and the circulating soluble LOX-1 (sLOX-1) reflects of LOX-1 expression. We analyzed the oxLDL/sLOX-1 system in relation to GSM score in patients undergoing carotid endarterectomy (CEA).

Methods: Seventy seven consecutive patients undergoing CEA were enrolled in the study group. The control group consisted of 15 patients without symptoms of atherosclerosis undergoing abdominal aortic aneurysm repair. The stability of carotid plaques was assessed using GSM scoring system, and the study group was divided into three subgroups: GSM<35, GSM 35-50 and GSM>50, according to echogenicity of the plaque. GSM<35 was considered as a feature of plaque instability, whereas GSM>50 reflected the stable carotid plaque. Serum oxLDL and sLOX-1 levels were determined using commercial ELISA kits. Statistical analysis were performed using Statistica ver.10 computer software.

Results: There were no diferences between oxLDL levels in the studied groups. sLOX-1 concentration was higher in subgroup with GSM<35 compared to controls (p=0.007) and subgroup with GSM>50 (p=0.008). There was an inverse correlation between sLOX-1 in the whole patients' group (R= -0.220, p=0.048), and in subgroup with GSM<35 (R= -0.435, p=0.035).

Conclusions: The increased levels of sLOX-1, but not oxLDL, were associated with the features of unstable plaques. Our study demonstrates that circulating sLOX-1 could be used to evaluate the carotid plaque instability in patients undergoing carotid endarterectomy.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

141 / #396

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

SIGNALING PATHWAYS IN FOAM CELL FORMATION

POSTER ON BOARD: AS02.10 MODIFIED LIPOPROTEINS

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Background and Aims: To determine regulatory pathways that are potentially responsible for cholesterol accumulation in human macrophages after the exposure to multiple-modified atherogenic naturally occurring low-density lipoprotein (mmLDL), we used transcriptome analysis.

Methods: The mmLDL was isolated from atherosclerotic patients' plasma by ultracentrifugation. Lipoprotein was added to primary culture of human monocyte-derived macrophages for 24 hrs. Intracellular cholesterol was measured by biochemical technique. Monocyte-derived macrophages were transfected with lipofectamine RNAiMax (Invitrogen, Waltham, MA, USA) following the instructions of the manufacturer for achieving gene knockdown. Target gene-specific siRNA: IL15, EIF2AK3, or F2RL1 (Dallas, TX, USA, Santa Cruz Biotechnology) or 50 nM of a control scrambled siRNA were used for the transfection.

Results: We have identified at least three genes (F2RL1, EIF2AK3, and IL15) encoding inflammatory molecules and associated with signaling pathways that were upregulated in response to the interaction of mmLDL with macrophages. Knockdown of two of these genes, EIF2AK3 and IL15, completely suppressed cholesterol accumulation in macrophages. Correspondingly, the upregulation of EIF2AK3 and IL15 promoted cholesterol accumulation.

Conclusions: These data confirmed our hypothesis of the following chain of events in atherosclerosis: LDL particles undergo atherogenic modification; this is accompanied by the formation of self-associates; large LDL associates stimulate phagocytosis; as a result of phagocytosis stimulation, pro-inflammatory molecules are secreted; these molecules cause or at least contribute to the accumulation of intracellular cholesterol. This work was supported by the Russian Science Foundation (Grant # 23-45-00031).

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

142 / #832

Topic: *AS02 Lipids and Lipoproteins / AS02.11 Liver metabolism and steatosis*

REPEATED WEIGHT CYCLING IN OBESE MICE IMPROVES HEPATIC INFLAMMATION

POSTER ON BOARD: AS02.11 LIVER METABOLISM AND STEATOSIS

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Background and Aims: Lifestyle interventions remain the treatment of choice for non-alcoholic steatohepatitis (NASH), yet are difficult to maintain and often lead to cycles of weight loss and regain. Literature on weight cycling remain controversial, hence we evaluated the association between weight cycling and NASH.

Methods: Ldlr-/-.Leiden mice received a high fat diet (HFD) for 20 weeks to induce obesity, NASH and atherosclerosis. Mice next received HFD for 16 weeks (control group) or were subjected to 4 weight cycling episodes (using diet change). Another group was sacrificed after the initial 20 weeks (HFD reference group). At the study endpoint, effects on plasma variables, body composition, NASH and atherosclerosis were evaluated.

Results: Weight cycling tended to decrease body weight and significantly decreased fat mass (-15%, $p<0.05$) relative to HFD control mice. Adipocyte size tended to increase (+10%, $p=0.0502$) and adipose tissue inflammation was similar. Weight cycling did not significantly affect blood glucose or plasma insulin, yet significantly reduced plasma ALT levels (-40%, $p<0.05$). Hepatic macrovesicular steatosis was similar in weight cycled and HFD control mice (28% and 29%, respectively) while microvesicular steatosis tended to increase (HFD control: 17%; weight cycled: 24%; $p=0.077$), but not relative to HFD reference mice (20% microvesicular steatosis). Weight cycling strongly decreased hepatic inflammation compared to HFD control mice (-67%, $p<0.01$) and HFD reference mice (-60%, $p<0.05$). Hepatic fibrosis and atherosclerosis development were not affected by weight cycling.

Conclusions: These results argue against the postulate that weight cycling leads to unfavorable metabolic effects and actually revealed beneficial effects on hepatic inflammation.

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143 / #542

Topic: *AS02 Lipids and Lipoproteins / AS02.11 Liver metabolism and steatosis*

ANGPTL3 SILENCING INDUCES FAT ACCUMULATION IN HEPATIC HUH7 CELL LINE

POSTER ON BOARD: AS02.11 LIVER METABOLISM AND STEATOSIS

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Background and Aims: ANGPTL3 is an hepatokine acting as negative regulator of lipoprotein lipase (LPL) and targeted by multiple therapies. Vupanorsen, ANGPTL3 directed antisense oligonucleotide, has been discontinued from phase 2b clinical trial due to an unexpected increase in liver fat fraction. The aim of this project is to shed new insights on the intracellular mechanism causing fat accumulation.

Methods: We utilized hepatocarcinoma Huh7 cells treated with siRNA-ANGPTL3, human recombinant ANGPTL3 (hrecANGPTL3) or the combination of the two (siRNA+hrec). By western blot, Oil red-O, biochemical assays and ELISA assays, we analysed the expression of genes and proteins involved in lipid metabolism.

Results: Oil red-O analysis demonstrated that lipid content increased after ANGPTL3 silencing (5.89±0.33 fold), hrecANGPTL3 administration (4.08±0.35 fold) and the combination of both (8.56±0.18 fold) compared to untreated cells. We observed an increase in pro-SREBP1 and fatty acid synthase, respectively by 100% and by 45% both after siRNA-ANGPTL3 and combined treatment. PCSK9 protein levels increased after silencing (4.32±0.43) but no significant differences were found in other treatments. Cellular LPL activity doubled with siRNA-ANGPTL3 treatment as expected. No differences in secreted ApoB and total cholesterol were found in the different conditions. Treatment after oleic acid supplementation showed comparable results.

Conclusions: Efficient lipid accumulation following gene silencing emerged from our experiments, mirroring what was seen in patients treated with vupanorsen. The investigation led us to hypothesize an increase in triglyceride synthesis and lower secretion rate when ANGPTL3 is silenced. Moreover, silencing and administration appear to behave in an addictive manner, following two different pathways that are currently under analysis.

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144 / #1603

Topic: *AS02 Lipids and Lipoproteins / AS02.12 Adipose tissue biology and pathology*

EFFECT OF LPS-INDUCED PERIVASCULAR ADIPOSE TISSUE (PVAT) INFLAMMATION ON VASCULAR REACTIVITY OF ISOLATED RAT AORTA

POSTER ON BOARD: AS02.12 ADIPOSE TISSUE BIOLOGY AND PATHOLOGY

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Background and Aims: Perivascular adipose tissue (PVAT) which surrounds the vessels is assessed as an organ with autocrine, paracrine and endocrine features. In physiological conditions, PVAT has an anti-inflammatory effect and regulates vascular tone. In pathopysiological conditions such as T2DM, hypertension and atherosclerosis PVAT dysfunction occurs. Inflammation is an important underlying factor in many cardiovascular diseases. We aim to investigate the relationship between LPS-induced inflammation and PVAT function on vascular reactivity.

Methods: Current study is the first to examine the influence of in vitro LPS-incubation (100ng/ml,overnight) on PVAT mediated vascular reactivity of thoracic aorta isolated from male wistar rats (n=8-12). The effect of the presence of PVAT(+/-) on contractile reactivity as well as endothelium-dependent/independent responses were evaluated in control and LPS-incubated rings. Statistical-analysis was performed by two-way-ANOVA.

Results: In control aortic rings the presence of PVAT significantly decreased the contractile reactivity to Phe and KCl ($p<0.05$). LPS-incubation did not change Phe responses whereas furtherly decreased the contractile response to KCl ($p<0.001$). The endothelium-dependent relaxant response to ACh in control rings was not modified in the presence of PVAT but significantly decreased in LPS-incubated rings($p<0.05$). In addition, PVAT did not modify the relaxant responses to SNP in control rings, while significantly increased the maximum response to SNP in LPS-incubated rings($p<0.05$).

Conclusions: Our results indicate that in-vitro LPS-induced inflammation may influence PVAT function on KCl contraction as well as endothelium-dependent and independent vascular responses. Therefore, clarifying the crosstalk between inflammation and PVAT function on vascular reactivity may comprise a novel therapeutic target in the treatment of vascular diseases.

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145 / #634

Topic: *AS02 Lipids and Lipoproteins / AS02.13 Incretins and lipid metabolism*

LIPID FRACTIONS CHANGES IN PREDICTING THE DEVELOPMENT OF NONALCOHOLIC FATTY LIVER DISEASE

POSTER ON BOARD: AS02.13 INCRETINS AND LIPID METABOLISM

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Background and Aims: Introduction. Dyslipidemia, oxidative stress (OS), and subclinical inflammation are the main mechanisms of nonalcoholic fatty liver disease (NAFLD) and hypertension (HTN) pathogenesis. Mostly lipid infiltration and lipotoxicity of hepatocytes precede the development of OS against the background of increased lipid peroxidation. Selenoprotein P (Sel P) plays a decisive role in maintaining antioxidant protection as a leading source and transporter of selenium in the body. **Aim:** to identify possible predictors and form a model for predicting the development of NAFLD in healthy individuals.

Methods: Materials and methods. The study included: main group — 49 patients (67.3% women) with NAFLD and HTN; comparison group (G2) — 51 with isolated NAFLD (58.8% women), control group (G3) — 20 individuals (55.0% women). The median age was 51.0 [45.0; 56.0] (p_{1-3} = 0.980), 52.0 [47.0; 54.0] (p_{1-2} =0.610) and 51.0 [45.0; 55.5] years (p_{2-3} = 0.564), respectively. Blood parameters were measured by standard methods. Selenoprotein P levels were measured by immunoassays (ELISA Kit). IBM SPSS 25.0 for Windows was used for statistical calculations.

Results: The studied parameters are listed in Table
1

Table 1

Levels of possibly NAFLD predictors

Index	Main group	Comparison group	Control group
Body mass index (BMI), kg/m²	27.8 [26.6; 28.5] ($p_{1-2} = 0.008$)	27.3 [24.2; 28.3] ($p_{2-3} = 0.277$)	24.3 [21.9; 26.0] ($p_{1-3} = 0.049$)
Systolic blood pressure, mm Hg	150.0 [145.0; 158.0] ($p_{1-2} < 0.001$)	125.0 [115.0; 130.0] ($p_{2-3} = 0.012$)	120.0 [110.0; 120.0] ($p_{1-3} < 0.001$)
Diastolic blood pressure, mm Hg	90.0 [85.0; 90.0] ($p_{1-2} < 0.001$)	80.0 [70.0; 80.0] ($p_{2-3} < 0.918$)	80.0 [70.0; 80.0] ($p_{1-3} < 0.001$)
White blood cells (WBC) × 10⁹/l	5.3× 10^9/l [4.5; 7.7] ($p_{1-2} = 0.110$)	6.4× 10^9/l [5.2; 7.2] ($p_{2-3} = 0.002$)	5.3× 10^9/l [4.7; 5.6] ($p_{1-3} = 0.420$)
Cholesterol, μ/l	**5.5 [4.8; 6.3]** ($p_{1-2} < 0.001$)	**5.2 [4.6; 5.9]** ($p_{2-3} < 0.001$)	**3.2 [2.6; 3.7]** ($p_{1-3} < 0.001$)
TG, μ/l	1,5 [1,2; 1,8] ($p_{1-2} \leq 0,01$)	2,4 [1,7; 2,9] ($p_{2-3} \leq 0,01$)	1,3 [0,9; 1,5] ($p_{1-3} \leq 0,01$)
VLDL, μ/l	0,75 [0,56; 0,83] ($p_{1-2} \leq 0,01$)	0,60 [0,46; 0,67] ($p_{2-3} \leq 0,01$)	1,07 [0,7; 1,5] ($p_{1-3} \leq 0,01$)
SelP, ng/ml	**19.7[8.0; 26.7]** ($p_{1-2} < 0.001$)	**43.1 [41.3; 45.4]** ($p_{2-3} < 0.001$)	**71.0 [54.3; 76.1]** ($p_{1-3} < 0.001$)

Predictors associated with the development of NAFLD in healthy individuals were determined (Table 2).

Table 2

Predictors associated with the development of NAFLD

Predictors	Enter of variables method			Backward Wald method		
	OR	95.0 % CI	p	OR	95.0 % CI	p
SBP, mm Hg.	1,066	1,009–1,127	**0,023**		—	
BMI, kg/m²	1,305	1,078–1,579	**0,006**		—	
WBC, 10⁹/л	2,303	1,279–4,148	**0,005**	7,733	1,148–52,101	**0,036**
Thrombocytes, 10⁹/L	0,724	0,606–0,866	**<0.001**		—	
Cholesterol, μ/l	7,069	2,754–18,147	< 0,001	9,944	1,433–68,990	**0,020**
TG, μ/l	15,579	3,590–67,595	< 0,001		—	
VLDL, μ/l	0,015	0,002–0,135	< 0,001		—	
SelP, ng/ml	0,233	0,127–0,429	< 0,001	0,254	0,101–0,639	**0,004**

The prognostic characteristics of the developed model are shown in table

3.

Table 3

Predictive characteristics of the developed model

Index	Value	Sensitivity, %	Specificity, %
The highest sensitivity	-3,9727	100,0	50,0
The highest specificity	1,0634	96,1	100,0
Optimal value	-0,6277	98,0	88,9
Model	NAFLD = –12,261 + + [2,045 × WBC, 10^9/L] + + [2,297 × cholesterol, μ/l] – [1,372 × Sel P, ng/ml]		

Conclusions: The presence of reliable associations of cholesterol, WBC and Sel P allows to consider them as predictors of the development of NAFLD in healthy individuals. The proposed model has high classification characteristics and can be used as an auxiliary tool for forecasting the development of NAFLD.

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146 / #1500

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

EFFECT OF COMBINED CARRIAGE OF POLYMORPHIC MARKERS APOE (E2/E3/E4) AND APOA1 (G-75A) ON THE APOB/APOA-I RATIO IN CAD PATIENTS IN THE UZBEK POPULATION

POSTER ON BOARD: AS02.14 OTHER

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Background and Aims: To compare the effect of combined carriage of ApoE (ε2/ε3/ε4) and ApoA1 (G-75A) polymorphic markers on the ApoB/ApoA-I ratio in patients with coronary artery disease in the Uzbek population.

Methods: The study included 140 patients (75 men and 65 women) with chronic coronary artery disease. The genetic typing at ApoE (ε2/ε3/ε4) and ApoA1 (G-75A) polymorphisms was performed with the PCR-RFLP method. The distribution of studied polymorphic markers in CAD patients and healthy people were in Hardy-Weinberg equilibrium.

Results: In 35 patients, carriers of the ε4 ApoE allele (group I) had a significantly higher level of ApoB ($P<0.05$) and the ratio of ApoB/ApoA1 ($P<0.01$), while among carriers of the "wild" GG genotype and carriers allele A of ApoA1 (group II), there were no differences in the level of apolipoproteins. In group I, the level of ApoB/ApoA1 was significantly higher in ε4- and A-carriers (1 subgroup, n=15) than in ε4-non-carriers (n=105) as in the case of GA/AA (n=45, $P<0.01$) and GG-carriers of ApoAI genotypes (n=60, $P<0.05$). However, in group I, when the ε4 ApoE allele was combined with the GG ApoA1 genotype (subgroup 2, n=20), the ApoB/ApoAI ratio did not differ from ε4-non-carriers due to a higher level of ApoA1 ($P=0.01$) than in subgroup 1.

Conclusions: Carrying the “wild” GG ApoA1 genotype can protect against an increase in the ApoB/ApoA-I ratio in patients with CAD, carriers of the ε4 allele of the ApoE gene in the Uzbek population.

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MANNHEIM GERMANY | MAY 21-24, 2023

147 / #71

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

SAFETY AND EFFICACY OF PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 INHIBITORS AFTER ACUTE CORONARY SYNDROME; A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

POSTER ON BOARD: AS02.14 OTHER

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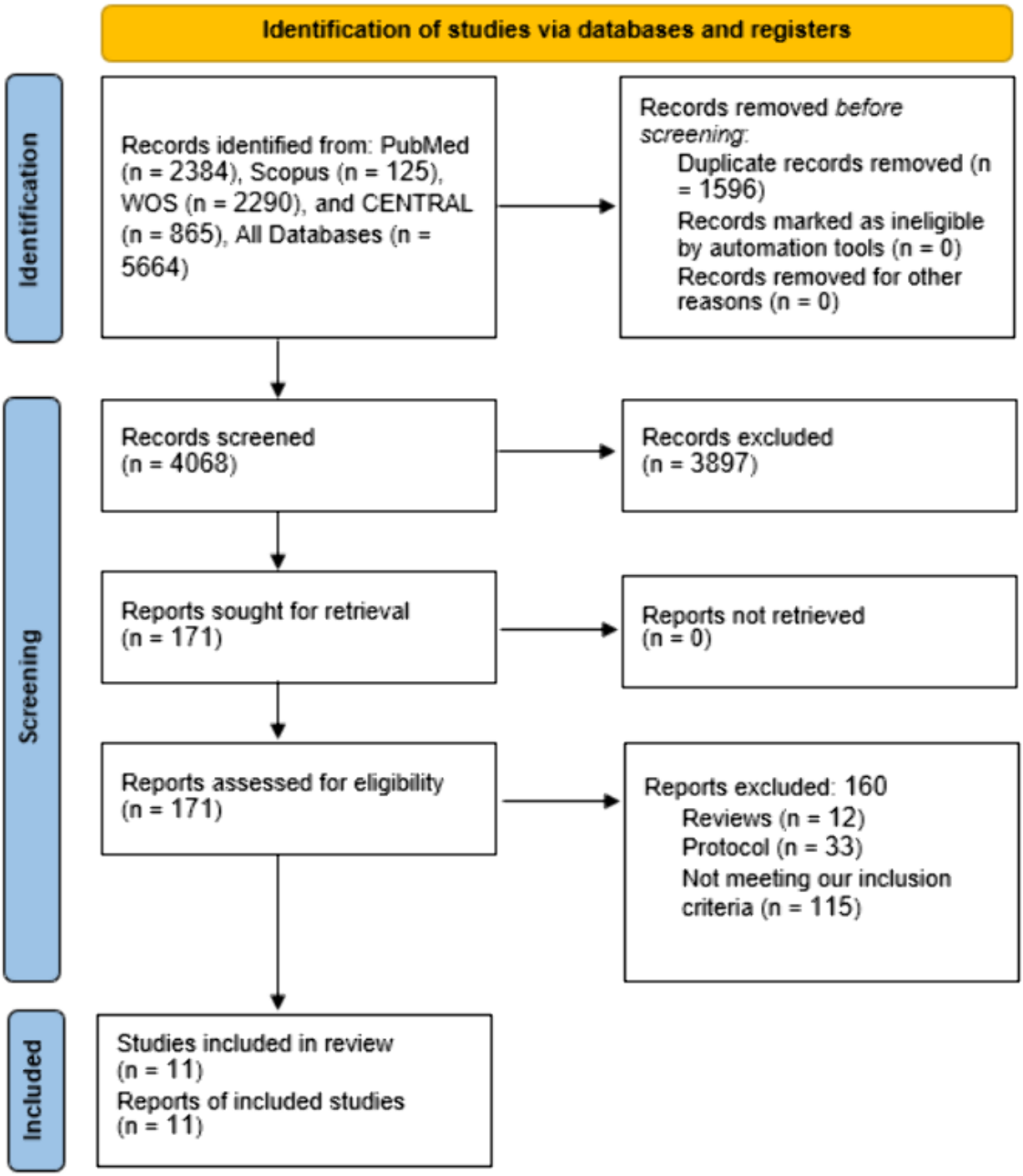
Background and Aims: Patients with a history of acute coronary syndrome (ACS) are at a higher risk of recurrent ischemia episodes. Elevated circulating cholesterol levels in patients with atherosclerotic cardiovascular disease increase morbidity and mortality. Recent studies reported that PCSK9 inhibitors (PCSK9i) have a beneficial influence on various domains of patients' lipid profiles; thus, we sought to study their safety and efficacy on post-ACS patients.

Methods: We performed a comprehensive electronic search of PubMed, Scopus, Web of Science, and Cochrane CENTRAL to identify relevant published randomized controlled trials. Data were extracted and analyzed using the Review Manager software (version 3.5 for Windows).

Results: Eleven studies (n=24,732) were included in this meta-analysis. Compared with the control group, PCSK9i may decrease the myocardial infarction (MI) events (RR 0.87[0.78, 0.96], P= 0.006), and also the lipid measurements as follows in mg/dl: LDL-C (SMD -1.30[-1.60, -1.00], P<0.0001), total cholesterol (SMD -1.29[-1.70, -0.88], P<0.0001), Triglycerides (SMD -0.26[-0.37, -0.14], P<0.0001), non-HDL-C (SMD -2.80[-3.63, -1.97], P<0.0001), HDL-C (SMD 0.33[0.23, 0.42], P<0.0001), Lipoprotein-A (SMD -6.37[-10.28, -2.46], P=0.001), Apo-A1 (SMD 0.30[0.25, 0.36], P<0.0001), and Apo-B (SMD -1.50[-1.85, -1.15], P<0.0001). For coronary heart disease events, coronary revascularization, cerebrovascular events, cardiovascular deaths, or all-cause deaths there was no strong evidence that confirms which group is better as illustrated in Figure
[3].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Identification
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Records marked as ineligible by automation tools (n = 0)
Records removed for other reasons (n = 0)
Screening
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Records excluded (n = 3897)
Reports sought for retrieval (n = 171)
Reports not retrieved (n = 0)
Reports assessed for eligibility (n = 171)
Reports excluded: 160
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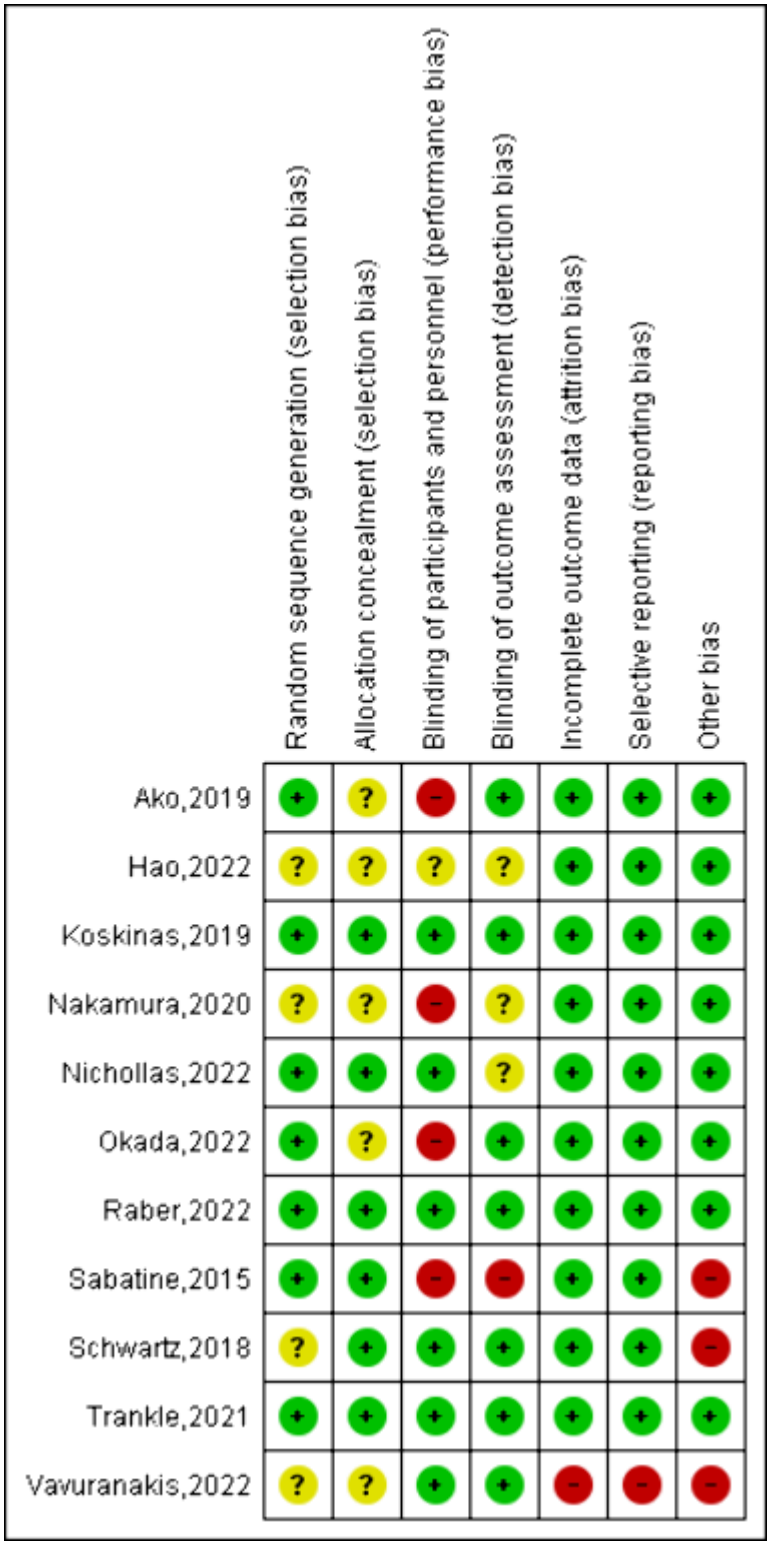
Protocol (n = 33)
Not meeting our inclusion criteria (n = 115)
Included
Studies included in review (n = 11)
Reports of included studies (n = 11)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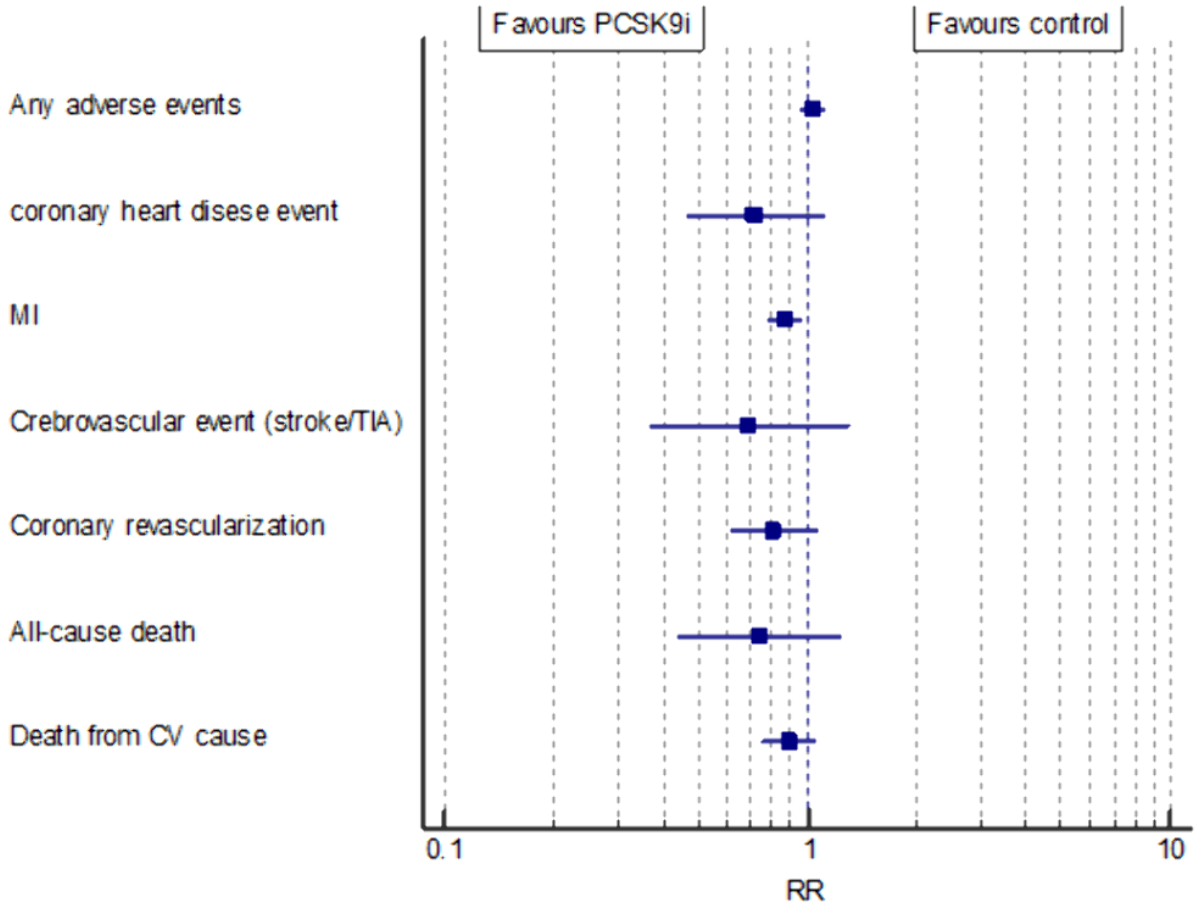
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Ako,2019
Hao,2022
Koskinas,2019
Nakamura,2020
Nichollas,2022
Okada,2022
Raber,2022
Sabatine,2015
Schwartz,2018
Trankle,2021
Vavuranakis,2022



Conclusions: Based on current evidence, PCSK9i may assist in decreasing further MI events and improving all lipid measurements significantly in post-ACS patients. Nevertheless, we recommend not using PCSK9i as a monotherapy, as it has no remarkable improvement on other cardiovascular events and deaths.

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MANNHEIM GERMANY | MAY 21-24, 2023

148 / #730

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

LONG-TERM EFFECTS OF STATINS ON HEMOGLOBIN A1C AND RELATED PARAMETERS

POSTER ON BOARD: AS02.14 OTHER

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Background and Aims: Statins increase the risk of new-onset diabetes mellitus (DM). Clinical characteristics of this phenomenon are poorly understood. This study investigated long-term effects of statins on hemoglobin A1c (HbA1c) and parameters associated with its changes.

Methods: This study enrolled patients who were managed with statins (n=421) and for hypertension or other cardiovascular diseases (n=240) for 1 year or more. Patients were followed up till 10 years (59.9±32.3 months). Patients with DM or other diseases influencing blood sugar level and HbA1c were excluded. HbA1c, FBS and lipid variables were measured at baseline and every year. If DM occurred, the case was excluded from further analysis.

Results: DM was observed in 5.4% and 4.8% patients in control and statin groups, respectively (p=ns). Kaplan-Meier analysis showed no difference between 2 groups (p=0.27, right figure). Changes of HbA1c were significantly higher at 1 year (p<0.005) in statin group than in control group (left figure). The difference disappeared from 2 years with exclusion of patients in whom DM occurred. Increase of HbA1c at 1 year adjusted by baseline level was independently associated with high fasting blood sugar (FBS, r=0.25, p<0.001), statin therapy (r=0.18, p<0.0001), body weight gain (r=0.13, p<0.001), and lower high density lipoprotein cholesterol (HDL-C, r=-0.12, p<0.005).

Conclusions: Statin therapy increased HbA1c level in patients with high risk for DM, such as higher FBS, lower HDL-C, and body weight gain. The education for low calorie diet is mandatory in these patients. In the other patients, long-term statin may not increase the risk of DM.

91ST EAS CONGRESS
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149 / #1280

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

THE SMASH PROGRAM: AN INITIATIVE FOR GREATER ACCESS TO INNOVATIONS FOR RARE OR SEVERE HYPERLIPIDEMIA

POSTER ON BOARD: AS02.14 OTHER

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Background and Aims: Rare diseases are often ignored, and patients have little access to effective treatments. Once marketed, novel therapies developed through clinical trials are often expensive and their use is limited by payers claiming lack of sufficient data on the natural history of the disease and of benefit from these novel therapies. As rare diseases involve small numbers, it makes it difficult to generate trial evidence. It is therefore necessary to make use of a collective effort to document the clinical expression of rare diseases and to ensure access to effective, safe, and affordable therapies. We aim to build a collaborative network grouping stakeholders involved in the management of patients with rare or severe lipid disorders to document the natural history of the diseases and ensure access to affordable therapies.

Methods: The SMASH program (System and Molecular Approaches of Severe Hyperlipidemia) is creating an international network of top-level researchers, clinicians, patient organizations and stakeholders. We plan to connect SMASH to Lipid Clinic Networks to provide larger sample sizes, improve comprehension of rare dyslipidemias and the impact of emerging therapies, document the natural history of rare diseases through a systems approach and ensure access to innovations to patients.

Results: The SMASH network will improve the understanding of the issues, causes and consequences of rare dyslipidemias and favor and promote access to personalized treatments for patients.

Conclusions: A collaborative network is mandatory to document rare dyslipidemias and provide patient access to emerging treatments in both developed countries and emerging economies.

91ST EAS CONGRESS
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150 / #95

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

TOTAL CHOLESTEROL LEVEL IN A SAMPLE OF EGYPTIAN CHILDREN AND THE NEED FOR PRIMORDIAL PREVENTION PROGRAMS.

POSTER ON BOARD: AS02.14 OTHER

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Background and Aims: Atherosclerosis is the main cause for cardiovascular disease worldwide as wellas in Egypt. The high prevalence of premature atherosclerosis had been shown in the Egyptian cardiorisk project. Early detection of lipid abnormalities and Primordial prevention is needed for proper prevention OF ASCVD. The aim was o identify the range of total cholesterol in a sample of Egyptian healthy children.

Methods: 10 hours fasting blood samples were obtained, allowing water intake till 2 hours before the samples. 220 children aged from 6 to 12 years were included after parents consent.

Results: 52% of the children were male . The mean values ± SD for total cholesterol was 182±24.07 mg/dl in male comparing to 181± 23.09 mg/dl in female. A mean values 212 ± 8.75 mg/dl, was detected in 27% of the studied group with no significant difference in values between both female and male participant children

Conclusions: The relatively high cholesterol level among the studied sample of Egyptian children necessitate appropriate screening, as well as Primordial prevention programs.

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151 / #1003

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

RISK OF CARDIOVASCULAR DISEASE IN PATIENTS WITH GENETICALLY VERIFIED FAMILIAL HYPERCHOLESTEROLEMIA AND MENTAL ILLNESS

POSTER ON BOARD: AS02.14 OTHER

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Background and Aims: Mental illness, including schizophrenia, bipolar and major depressive disorder, is associated with a pronounced increase in risk of cardiovascular disease (CVD). This is concordant with the reduced ability/capacity of self-care. Familial hypercholesterolemia (FH) also increase risk of CVD, however, implementation of treatment of FH depend on adequate risk and disease perception by the patient. Here, we study if mental illness increase the risk of CVD in patients with FH.

Methods: This is a prospective matched cohort study of 5,635 subjects with genetically verified FH and 112,589 age and sex matched controls. We used Norwegian Health registers to identify patients either hospitalized or treated in specialized care with the ICD10 codes F20-F29 (delusional disorders) or F30-F39 (affective disorders) during 2008-2019. We also identified all hospitalizations for CVD as well as use of lipid lowering medication in the same period. An incident event of CVD was defined as a hospitalization with CVD as primary or secondary diagnosis or a death with CVD as underlying cause of death without any prior hospitalizations with CVD. Using Cox proportional hazards regression with stratification on matched case-set, HR comparing risk of CVD in FH versus controls will be calculated

Results: We identified 40 and 408 patients with ICD10 codes F20-F29 and F30-F39, respectively, in FH patients and 974 and 7,403 in the age and sex matched controls.

Conclusions: For the first time, to our knowledge, data on CVD risk in genetically verified FH patients suffering of mental illness is compared to age and sex adjusted controls will be presented

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MANNHEIM GERMANY | MAY 21-24, 2023

152 / #1292

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

CONSENSUS PANEL ABOUT IMPLEMENTATION OF GUIDELINES ON LIPID-LOWERING MANAGEMENT AFTER ACUTE CORONARY SYNDROME AND UP TO ONE YEAR FOLLOW-UP

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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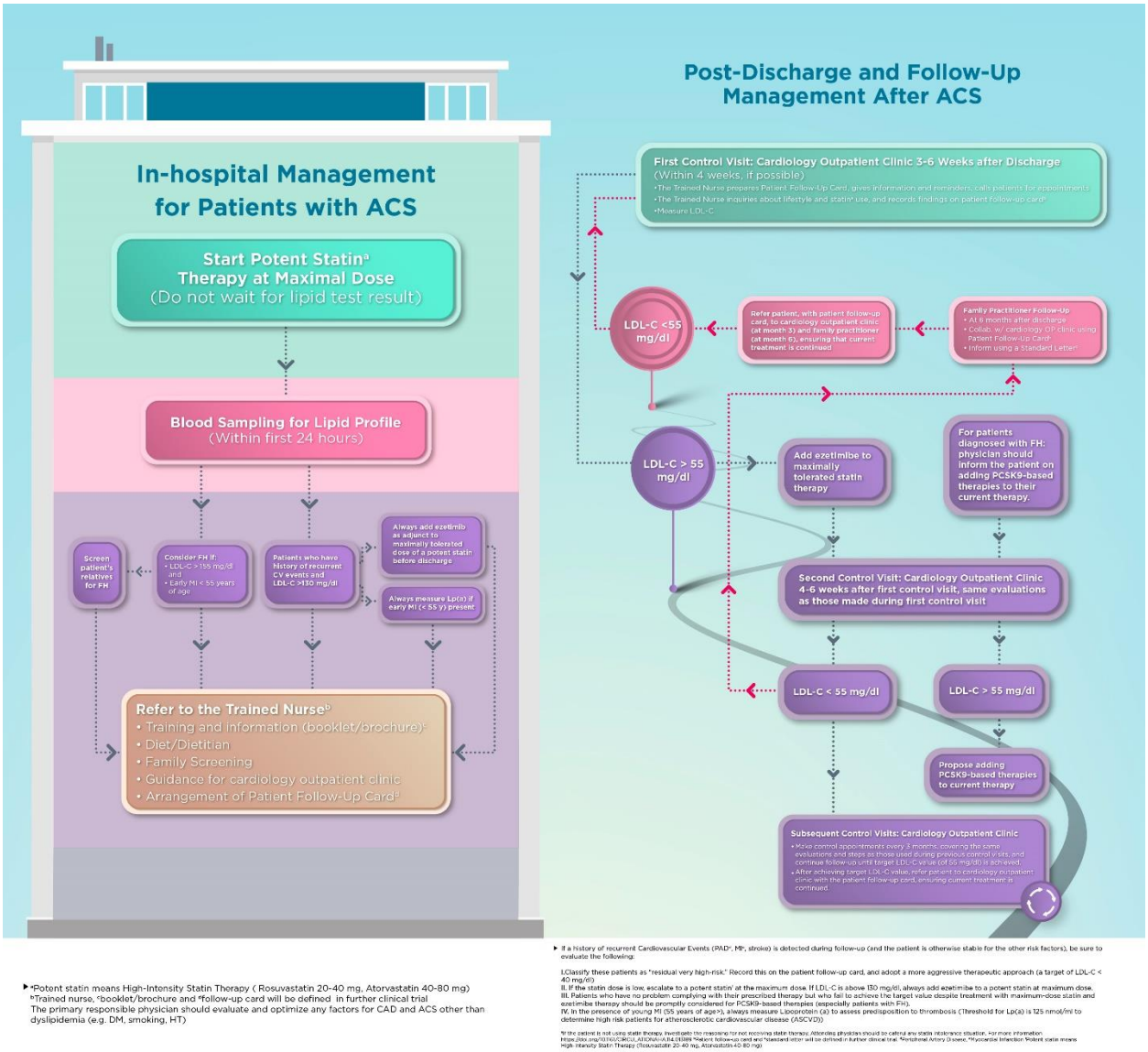
Background and Aims: There is still a significant proportion of patients with acute coronary syndromes (ACS) that could not reach the recommended targets of LDL-C suggested by the latest dyslipidemia guidelines. Country-specific recommendations as an expert consensus report for implementation of guidelines may be useful to provide better lipid-lowering management (LLM).

Methods: Four Consensus Panel meetings were held in 2022 by Cardiovascular Prevention and Lipid Working Group to achieve consensus for potential problems and solutions in LLM. Systematic literature review, guidelines, facilities and resources in clinics, clinical practices, reimbursement settings were evaluated. We assumed a standardized LLM algorithm after ACS up to one year period and discussed the impacts on behavioral change of physicians.

Results:



▸ *Potent statin means High-Intensity Statin Therapy (Rosuvastatin 20-40 mg, Atorvastatin 40-80 mg)
[b]Trained nurse, [c]booklet/brochure and [d]follow-up card will be defined in further clinical trial
The primary responsible physician should evaluate and optimize any factors for CAD and ACS other than dyslipidemia (e.g. DM, smoking, HT)

▸ If a history of recurrent Cardiovascular Events (PAD[a], MI[b], stroke) is detected during follow-up (and the patient is otherwise stable for the other risk factors), be sure to evaluate the following:

I.Classify these patients as "residual very high-risk." Record this on the patient follow-up card, and adopt a more aggressive therapeutic approach (a target of LDL-C < 40 mg/dl)
II. If the statin dose is low, escalate to a potent statin[c] at the maximum dose. If LDL-C is above 130 mg/dl, always add ezetimibe to a potent statin at maximum dose.
III. Patients who have no problem complying with their prescribed therapy but who fail to achieve the target value despite treatment with maximum-dose statin and ezetimibe therapy should be promptly considered for PCSK9-based therapies (especially patients with FH).
IV. In the presence of young MI (55 years of age>), always measure Lipoprotein (a) to assess predisposition to thrombosis (Threshold for Lp(a) is 125 nmol/ml to determine high risk patients for atherosclerotic cardiovascular disease (ASCVD)

*If the patient is not using statin therapy, investigate the reasoning for not receiving statin therapy. Attending physician should be called any statin intolerance situation. For more information: https://doi.org/10.1161/CIRCULATIONAHA.118.038889 [b]Patient follow-up card and [c]standard letter will be defined in further clinical trial. [a]Peripheral Artery Disease, [b]Myocardial Infarction [c]Potent statin means High-Intensity Statin Therapy (Rosuvastatin 20-40 mg, Atorvastatin 40-80 mg)

High-intensity statin therapy should be administrated without waiting the lipid test results for all ACS patients at hospital. Ezetimibe should be added as adjunct to maximally tolerated dose of a potent statin (rosuvastatin 20-40 mg, atorvastatin 40-80 mg) before discharge for those patients who have history of recurrent cardiovascular events and LDL-C >130 mg/dl. Second control visit should be made at 4-6 weeks later then the first control visit (3-6 weeks after discharge), if LDL-C is still > 55 mg/dl, PCSK9-based therapies could be considered as an add-on therapy. Novel strategy is implicated for more collaboration between cardiologists, primary care physicians, nurses, dietician, and patients.

Conclusions: Therapeutic inertia and lack of patient adherence are the main problems to reach recommended LDL-C levels of the international guidelines for ACS. These factors can be improved via country-specific recommendation and implementation science models.

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153 / #1302

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

INVESTIGATING THE IMPACT OF DOXORUBICIN ON PLAQUE FORMATION IN A MOUSE MODEL OF ATHEROSCLEROSIS

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Epidemiological data reveal a higher incidence of atherosclerosis in cancer survivors. In addition to its well-recognised cardiotoxicity, the chemotherapeutic agent doxorubicin (DOX) impairs endothelial function and increases arterial stiffness, which are key antecedents for atherosclerosis development. DOX may therefore accelerate atherosclerotic plaque formation, yet this has not been investigated so far. The current study therefore investigated whether DOX accelerates atherosclerotic plaque formation.

Methods: 24 male and 24 female apolipoprotein E-knockout ($ApoE^{-/-}$) mice (age 6 weeks) were fed a high-fat (HF) diet for 17 weeks. Starting at week 3, DOX (4 mg/kg) was administered intraperitoneally to half of the mice in each group once a week for 3 weeks. After 17 weeks, mice were humanely killed to assess the amount and the content of plaque in the thoracic aorta, proximal aorta and brachiocephalic artery.

Results: DOX increased arterial stiffness in male and female mice after 2 weeks, validating our model. Overall, total plaque amount and plaque content did not differ in the thoracic aorta and brachiocephalic artery of DOX-treated mice while sex differences in plaque size were observed. Paradoxically, DOX treatment resulted in smaller plaques in female mice, but not male mice.

Conclusions: In contrast to epidemiological reports, DOX does not seem to accelerate atherosclerotic plaque formation, although this study needs to be confirmed in a treatment study with shorter follow-up.

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154 / #1322

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

PREMATURE MYOCARDIAL INFARCTION: A POPULATION-BASED COHORT STUDY

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Background and aim: Premature myocardial infarction (MI) seems to be the one of the most pressing global issues in the modern cardiology due to its greater impact on the patient's psychology, ability to work and the socioeconomic burden. The aim of this study was to assess the trends in incidence and prevalence of premature MI and cardiac risk factors profile in a population-based cohort.

Methods: Methods. We studied a population-based cohort of prevalent premature MI and cardiac risk factors profile among residents in Kosovo County, during a 7-year period from January 1, 2014 through December 31, 2020.

Results: Results: Of 7349 MI cases age 63.2±1, 405 were premature MI (<45 years, 17.5% women). Premature MI had more prevalent smokers (72.3 vs. 50.4%; p<0.001), dyslipidemia (13.3 vs. 7.2%, p=0.01), family history for CV disease (50.4 vs. 37.4; p<0.001) and less frequent the diabetes and arterial hypertension (p<0.001 for both) compared to older age. The incidence of premature MI had similar trends through those years. Among premature MI, with regard to cardiac risk factors profile, the prevalence of hyperlipidemia and smokers was similar in women and men.

Conclusions: Conclusions. In this large community-based study, the incidence rates of premature MI had similar trends. The dyslipidemia and smoking were more prevalent regards risk factors profile. These results highlight the importance of primary prevention in young adults.

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155 / #417

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

CARDIOVASCULAR RISK IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: The aim of the study was to assess cardiovascular risk in patients with nonalcoholic fatty liver disease (NAFLD) compared to patients without NAFLD, and to identify the factors which account for this relationship.

Methods: This prospective study included 310 patients (111 patients with NAFLD and 199 non-NAFLD controls) admitted at the 2nd Internal Medicine Clinic, Emergency Clinical Hospital "Sf. Spiridon" Iasi, Romania. Data regarding patients' history, anthropometric parameters, biological profiles, and comorbidities were collected from medical records.

Results: This study included 59% women (gender ratio 1.4:1) with an average age of 70.23±14.08 and a range of 19-98 years. The studied risk factors elements were compared in NAFLD patients vs non NAFLD: obesity – body mass index (BMI) 30.48 vs 27.19 kg/m^2 (p=0.001), triglycerides – 150.95 vs 114.16 mg/dl (p=0.001), total cholesterol – 169.97 vs 189.90 mg/dl (p=0.025), ferritin – 133.88 vs 256.32 µg/l (p=0.041), glomerular filtration rate (GFR) – 84.30 vs 70.96 mL/min/1.73 m^2 (p=0.001). Good NAFLD predictors have been shown to be triglycerides (AUC=0.748; IC95%: 0.609-0.888; p=0.003), GFR (AUC=0.750; IC95: 0.518-0.982; p=0.043) and blood glucose (AUC=0.626; IC95%: 0.470-0.781; p=0.027). Higher BMI values had a sensitivity of 70% and a specificity of 54% for the NAFLD prediction.

Conclusions: In conclusion, patients with NAFLD are at significantly higher cardiovascular risk due to higher BMI, triglycerides, GFR, and blood glucose values. Timely identification of these cardiovascular risk factors will facilitate specific treatment initiation and thus improve the NAFLD patients' prognosis.

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156 / #970

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

APO E GENOTYPING AND CARDIOVASCULAR RISK RE-CLASSIFICATION OF SUBJECTS, A SINGLE CENTER EXPERIENCE 2008-2021

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Apolipoprotein E (apoE) is a glycoprotein, associated with the metabolism of triglyceride-rich lipoproteins and their clearance in the liver. ApoE exists in three isoforms: ApoE2, ApoE3 (most common) and ApoE4. ApoE2 is considered favorable regarding cardiovascular and neurological health and individuals with ApoE4 are at increased risk for cardiovascular disease outcomes. Genotyping of apoE may have a role in personalized medicine and individualized cardiovascular risk-assessment

Methods: Testing for Apo E genotyping was performed as a part of cardiovascular risk stratification in patients, at the Strassburger Lipid Center, Sheba Medical Center, Tel-Hashomer , Israel

Results: 435 genotyping were performed in adult patients from January 2008 until December 2021. Two participants had Apo E of 2/2 (0.5 %), seven had Apo E of 2/3 (1.6 %), four had Apo E of 2/4 (1%), 314 participants had Apo E of 3/3 (72%), 99 participants had Apo E of 3/4 (23%) and nine had Apo E of 4/4 (2 %).(Figure 1). Cardiovascular risk assessment was done by the ACC/AHA cardiovascular risk calculator. Among the 112 carriers of ApoE4 isoforms 33 (29.5%) were females and the mean age at the test was 52.8 ±16.4 years. Re-classification of risk and lowering the low-density lipoprotein cholesterol therapeutic target was found in 62 patients (55%).

Conclusions: ApoE gene polymorphisms is associated with cardiovascular morbidity and affect the lipid profile. In our experience, Apo E genotyping was valuable tool that assisted in the identification of certain patients at higher cardiovascular risk.

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157 / #17

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

COULD A LIPID OXIDATIVE BIOMARKER BE APPLIED TO IMPROVE RISK STRATIFICATION IN PREVENTION FOR CARDIOVASCULAR DISEASE?

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: There is evidence demonstrating the influence of oxidative stress on atherosclerosis progression and cardiovascular diseases (CVD). However, different from dyslipidemia and inflammation, non-oxidative biomarkers have been applied to analyze the primary or secondary prevention treatment of these patients. Many factors can explain this paradox: the higher complexity of the methods applied to quantify oxidative markers, the high variability observed among the studies, lack of reference values and weak correlation with clinical endpoints.

Methods: In this review, data from 116 treatments in 55 studies that evaluated oxidative stress markers under the atherosclerotic context were included

Results: showed that antioxidant capacity measured as Ferric Reducing Antioxidant Power (FRAP), Superoxide Dismutase (SOD), Glutathione (GSH), Malondialdehyde (MDA), oxidized LDL (oxLDL) and Isoprostanes (F_2-IsoP) were the oxidative markers more present. From them, MDA, IsoPs and oxLDL are directly formed from lipid oxidation, while FRAP, SOD and GSH have their values associated to general oxidative conditions. Among the lipid oxidative markers, MDA had the highest proportion among the treatments. A higher concentration of MDA (p=0.041) in patients with CVD (17.05 ± 37.24 µmol/L, n=51) was found than in healthy individuals (5.07 ± 7.54 µmol/L, n=21), despite the high general variability (235.85%).

Conclusions: Multivariate analysis suggested that MDA was an independent factor compared with traditional markers used in the algorithms to stratify the patient's risk. Thus, it is necessary to achieve a reference value for patients under prevention, and correlate MDA increase according to the disease's progression before including it in the algorithms applied to estimate CVD risk.

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158 / #1563

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

COMPLIANCE OF HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA PATIENTS: 5-YEARS FOLLOW-UP OF THE RUSSIAN FAMILIAL HYPERCHOLESTEROLEMIA REGISTRY

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: The aim of the study was to evaluate compliance of heterozygous familial hypercholesterolemia (FH) patients for the 5-year period of Russian FH registry existence.

Methods: The Russian FH registry is an open, national, observational study and includes FH patients. Atherosclerosis risk factors, history of CVD and adherence to LLT were taken into consideration. Concentrations of TC, TG, HDL-C were measured in blood serum. LDL-C level was defined according to Friedewald formula.

Results: The study included 2317 heterozygous FH patients, 59% are with high cardiovascular risk, 58% female. Follow-up visits were conducted for 47% of subjects, median follow-up time was 24 months (IQR, 11–42 month). Such patients more often had a definite heterozygous FH and a hereditary history of CVD, they were younger and diagnosed with FH at an earlier age in comparison with the patients without follow-up who had more common modified risk factors ($p<0.05$). In the group with high cardiovascular risk 54% received LLT, in the group with very high cardiovascular risk − 86%. During follow-up the number of patients taking LLT increased from 59% to 78%, including PCSK9 inhibitors from 4% to 14% ($p<0.001$ for all). The target LDL-C level was reached by 13% of patients. Simulation analysis data showed that for adequate LDL-C control, at least 92.5% of patients with heFH in the registry must receive combination LLT with PCSK9 inhibitors.

Conclusions: A five-year follow-up of participants in the Russian FH registry shows an increase in the use of combination LLT, which is, however, insufficient for adequate LDL-C control.

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159 / #1572

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

LIPOPROTEIN(A) DISTRIBUTION AMONG SUBJECTS WITH GENETIC DYSLIPIDEMIAS: DATA FROM A SINGLE CENTER RETROSPECTIVE STUDY.

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

Antonina Giammanco[1], Chiara Scrimali[1], Federica Brucato[2], Teresa Maria Grazia Fasciana[1], Marina Lanza[1], Rosalia Caldarella[3], Marcello Ciaccio[3], Maria Carola Gagliardo[1], Carlo Maria Barbagallo[1], Angelo Cefalù[1], Davide Noto[1], Maurizio Averna[4]
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Background and Aims: Lipoprotein(a)[Lp(a)] is a well-recognized risk factor for atherosclerotic cardiovascular disease (ASCVD). However, the distribution of Lp(a) levels among subjects at different cardiovascular risk (mild, moderate, high and very high) remains unclear. In addition, Lp(a) levels do not univocally correlate in different forms of dyslipidemia. The aim of this study was to investigate the distribution of Lp(a) plasma levels in subjects belonging to a free-living population and patients with high and low LDL-C levels [Familial Hypercholesterolemia (FH) and Familial Hypobetaliporoteinemia (FHBL)].

Methods: The whole study population included 1205 subjects (M:554/F:651): 212 genetically characterized FH subjects, 144 with clinical FH (mutation negative - FHneg), 52 FHBL and 797 free-living subjects. Clinical features and CV risk were also evaluated.

Results: Lp(a) levels were significantly higher in FH subjects (both FH and FHneg) (median 12.46 mg/dl and 14.0 mg/dl, respectively) compared to FHBL and controls (7.68 mg/dl and 7.18 mg/dl, respectively). More, Lp(a) levels were similar in FH subjects carrying LDLR defective mutations and in those with LDLR null mutations. Subjects at high and very high CV risk exhibited significant higher Lp(a) levels (median 10.68 mg/dl and 9.20 mg/dl, respectively) compared to low and moderate CV risk (median 5.72 mg/dl and 7.80 mg/dl, respectively) ($p<0.0008$).

Conclusions: Combined evaluation of Lp(a) levels in subjects with other traditional risk factors could identify high-risk individuals who may benefit from early aggressive treatments to avoid premature CV events.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

160 / #834

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

LOW ADHERENCE TO CARDIOVASCULAR MEDICATIONS IS FREQUENT IN AN OUTPATIENT CARDIOLOGY SERVICE

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

María Perez, Martín Schitter, Rodrigo Esparza Iraola, Martín Maidana, Lucas Muller, Gustavo Giunta, Alejandro Hershson
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Background and Aims: Lack of adherence is one of the main limitations for the implementation of pharmacological treatment in cardiovascular prevention. The objective of this study was to establish the level of adherence of patients receiving cardiovascular medication.

Methods: Observational, descriptive, prospective study, carried out in the framework of a Health institution in Argentina. We included patients over 18 years of age who attended to the cardiology consultation. Patients not receiving cardiovascular medication were excluded. The eight-question Morisky-Green Test was used as a validated scale to assess adherence. Those patients who obtained results with less than six points were considered non-adherent.

Results: A total of 214 pacs completed the survey (mean age 65 ± 13, 50.4% female). Regarding cardiovascular risk factors, 62% presented high blood pressure, 27% high cholesterol, 53% reported having smoked, of which 12.1% reported being active smokers. 15% had a history of ischemic heart disease. When asked “Do you sometimes forget to take your medicine?” 31.3% were satisfied that they were. 12.6% responded that they have sometimes taken fewer pills or have stopped taking them without telling their doctor. 15% of the total admitted not remembering their medications, and 7.5% had not taken their entire medication the day before. Low adherence was observed in 44 patients (20.7%). Table 1 shows the characteristics of adherent and non-adherent pac. We observed an association between female sex and non-adherence.

Conclusions: In our study, 1 out of 5 patients showed low adherence. These results constitute a call of attention for cardiologists treating cardiovascular risk factors.

91ST EAS CONGRESS
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161 / #1252

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

CARDIOVASCULAR RISK FACTORS AMONG MEN AND WOMEN OVER 70 YEARS

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Worldwide, there is an increase in the proportion of older adults. Knowing the characteristics of this population is decisive in cardiovascular health care. The aim of the present study was to evaluate differences between sex among cardiovascular risk factors prevalence, in primary prevention older patients.

Methods: In an observational design, we analyzed data from patients (pat) who attended a health prevention program in Argentina. Participants of both sexes older than 70 years and with no history of cardiovascular disease were included. The clinical history was used as a source for the collection of general data, anthropometric measurements and laboratory values. The NCEP criteria were used to define the presence of Metabolic Syndrome (MS). Doppler ultrasound was used to assess the presence of carotid plaques.

Results: A total of 725 pat were included (49.1% female). Women were older (74.3 ± 4.3 yo vs. 73.9 ± 4 yo; p< 0.01). Male pat had a higher prevalence of hypertension (61% vs. 54%; p< 0.05), diabetes mellitus (17.9% vs. 12.6%; p< 0.05) and former smoking (17.6% vs. 28.4%; p<0.005). There were similar frequence of smoking (M 7% vs. W 6.2%; p=ns), use of statins (M 32.8% vs. W 31.4%; p=ns) and obesity (M 36% vs. W 33%; p=ns). The prevalence of MS were also similar (M 41.2% vs. W 35.6%; p=ns). Carotid plaques were more frequent in men (M 84.8% vs. W 74.2%; p<0.005).

Conclusions: Older people, particularly men, are at increased cardiovascular risk. Cardiovascular risk factors and subclinical atherosclerosis are frequent in this age group.

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162 / #756

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

CARDIOVASCULAR THERAPY. WHAT IS THE PATIENT'S PERCEPTION?

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Cardiovascular therapy has been shown to reduce the rate of major events. However, lack of adherence to treatment compromises its effectiveness. The objective of this study was to evaluate the patient's perception about the use of cardiovascular medication.

Methods: Observational, descriptive, prospective study, carried out in the framework of a Health institution in Argentina. We included patients over 18 years of age who attended to the cardiology consultation. The validated scale "The Beliefs About Medicines Questionnaire" (BMQ) were used.

Results: A total of 268 pac completed the survey. The average age was 64 ± 14, 122 (45.5%) were female. In the general BMQ questionnaire, 33.8% considered that physicians use too many medications, 42.6% stated that if physicians had more time in the consultation would prescribe less medication. As to the perception of eventual harm, 19.5% affirmed that patients should stop their treatment for a while from time to time, 19.2% that most medications are addictive, and 12.7% that natural remedies are safer. When asked about the use of aspirin and statins in primary prevention, 53% considered that aspirin would be beneficial in this context, while only 27% said the same regarding statins ($p < 0.0001$). In the question about if the benefits of these drugs outweigh the risks, 46.8% responded affirmatively for aspirin and 26% for statins ($p < 0.0001$).

Conclusions: We detected negative perceptions regarding cardiovascular medication, also it was observed that they perceived greater benefits with the use of aspirin than with statins. Our results highlight the necessity to optimize education in cardiovascular prevention

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MANNHEIM GERMANY | MAY 21-24, 2023

163 / #1281

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

RATIONALE AND DESIGN OF IMPLEMENT FOR LIFE STUDY: A VALIDATION STUDY OF A NATIONAL LIPID LOWERING STRATEGY AFTER ACUTE CORONARY SYNDROME

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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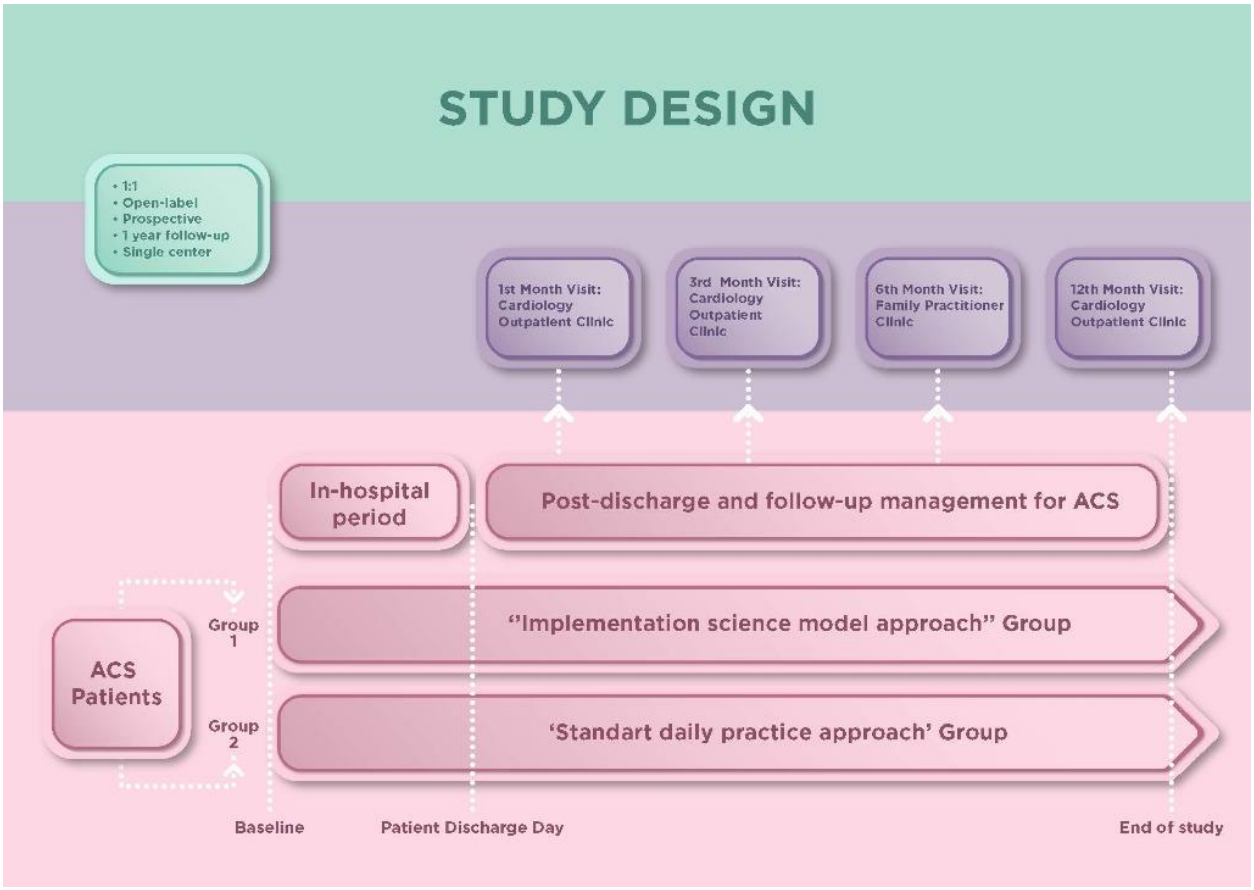
Background and Aims: Achieving adherence to lipid lowering therapies (LLTs) and attainment of LDL-C targets in patients after an acute coronary syndrome (ACS) is a major research area for implementation science in cardiology. In Turkey, national cardiology experts have established an Expert Consensus Report for Lipid-Lowering Strategy after ACS due to low rates of implementation of guidelines. Common causes of low implementation are: restricted reimbursement settings, more frequent young MI according to EUROASPIRE, high turnover rates of patients at busy hospitals, limited examination time at outpatient clinics, lack of recipe for family practitioners in post-ACS. We are designing a clinical study to validate the effectiveness and clinical applicability of this consensus report. The primary objective of the study; proportion of reaching the optimal LDL-C levels in ACS patients, and the secondary objectives; behavioral change in physicians and patients practice considering to lipid lowering therapy adherence, and major adverse cardiovascular events.

Methods:


STUDY DESIGN
• 1:1
• Open-label
• Prospective
• 1 year follow-up
• Single center
1st Month Visit: Cardiology Outpatient Clinic
3rd Month Visit: Cardiology Outpatient Clinic
6th Month Visit: Family Practitioner Clinic
12th Month Visit: Cardiology Outpatient Clinic
In-hospital period
Post-discharge and follow-up management for ACS
ACS Patients
Group 1
Group 2
''Implementation science model approach'' Group
'Standart daily practice approach' Group
Baseline
Patient Discharge Day
End of study

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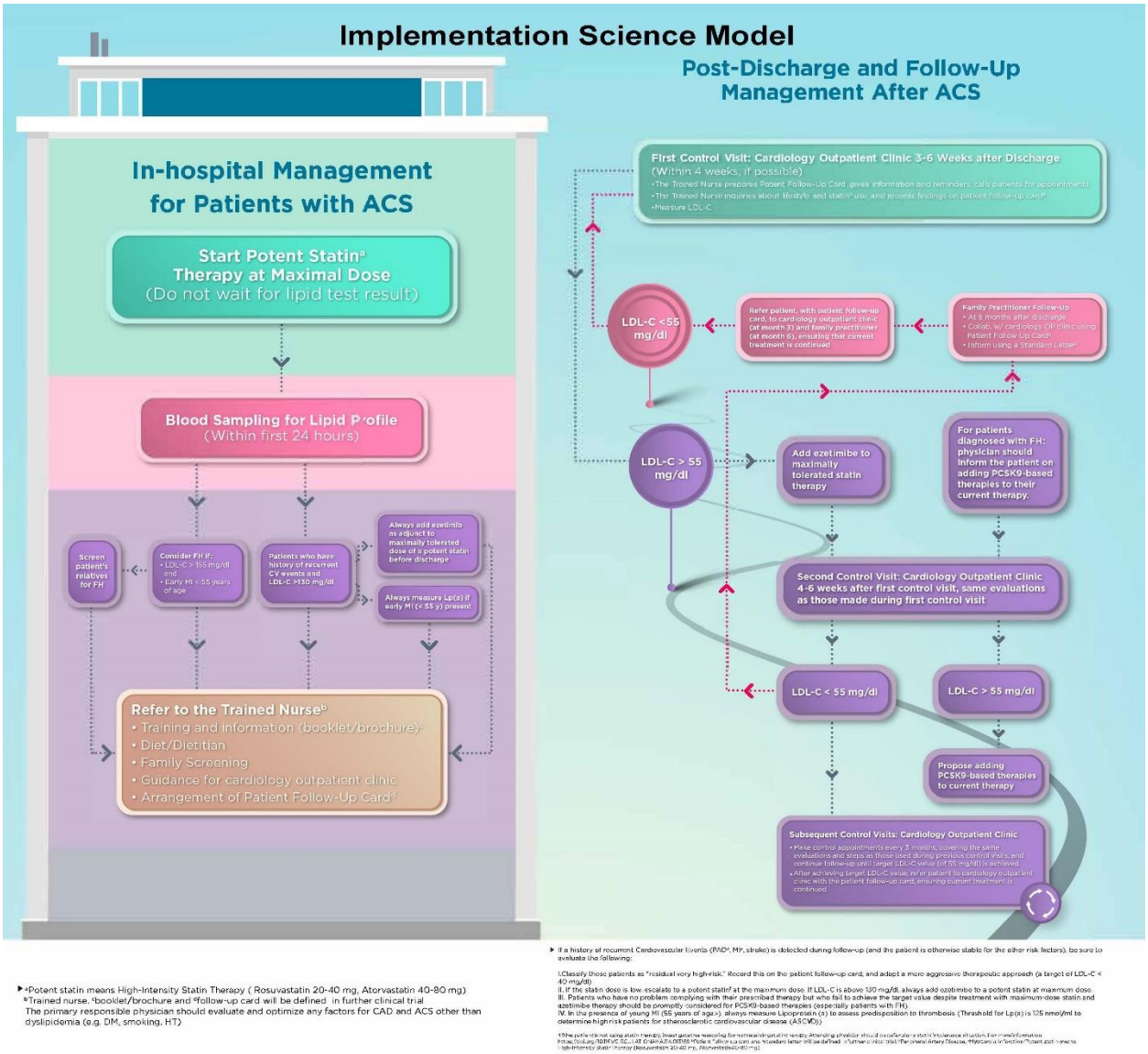

The study is open-label, prospective, one year follow-up, interventional, single center study(figure 1). Patients hospitalized with diagnosis of ACS will be recruited from a single heart center and will be randomly included in two study groups; 1-standart daily practice approach, and 2-using new implementation science model (figure 2) approach. The rates of adherence to LLTs, and achievement of LDL-c targets will be investigated.

Results: Implementation science also cover the improving the quality, disseminate and increasing effectiveness of health services and beyond all these mentioned topics.

Conclusions: Clinical trials are needed to demonstrate for effectiveness of any new algorithms on daily practice in dyslipidemia management.

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164 / #1530

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

A RETROSPECTIVE STUDY TO IDENTIFY THE PREVALENCE OF PERIPHERAL ARTERIAL DISEASE IN DIABETIC PATIENTS ATTENDING DIABETES AND NEUROPATHY CENTER IN EGYPT USING MESI-MED DEVICE

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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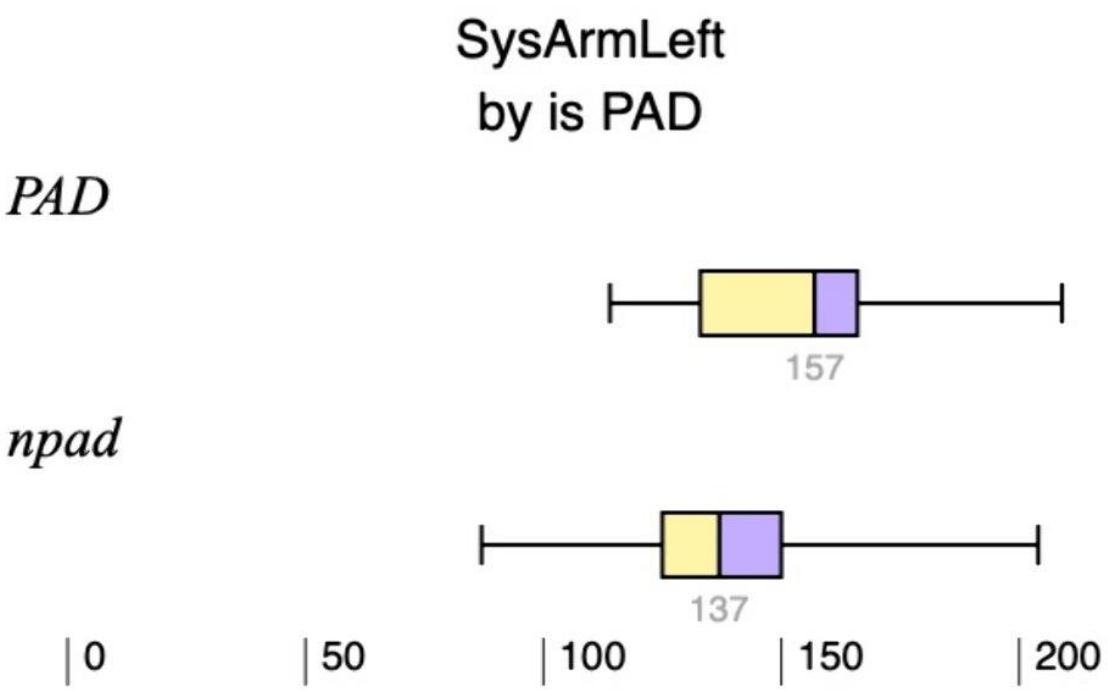
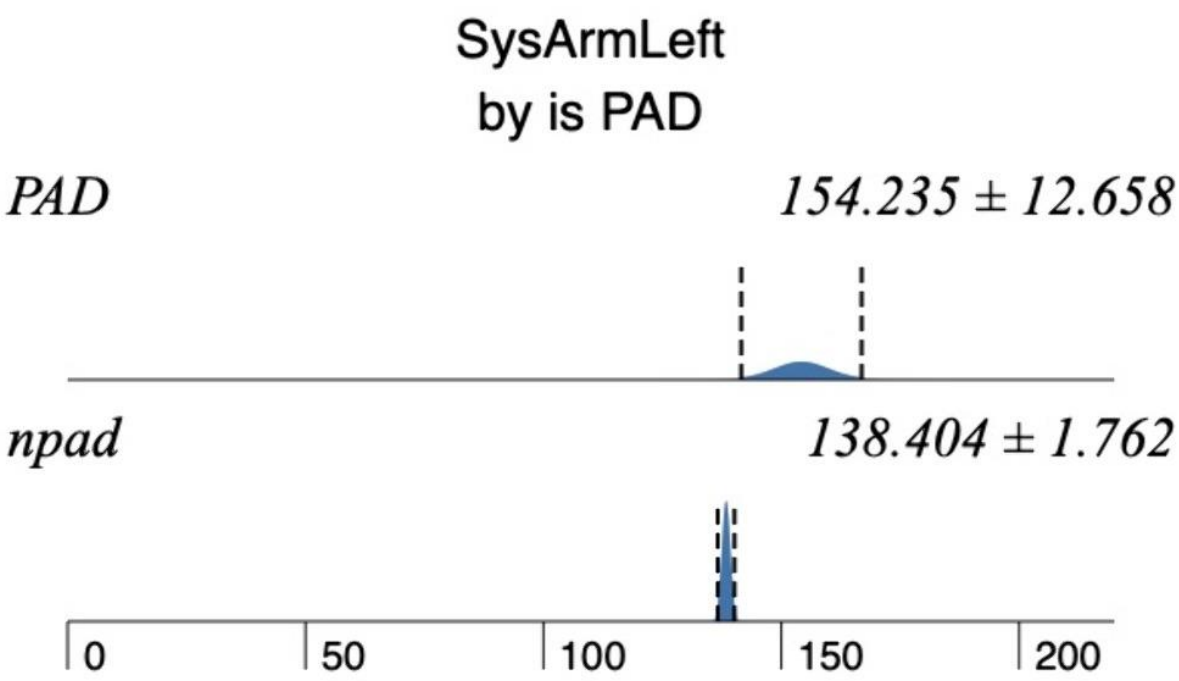
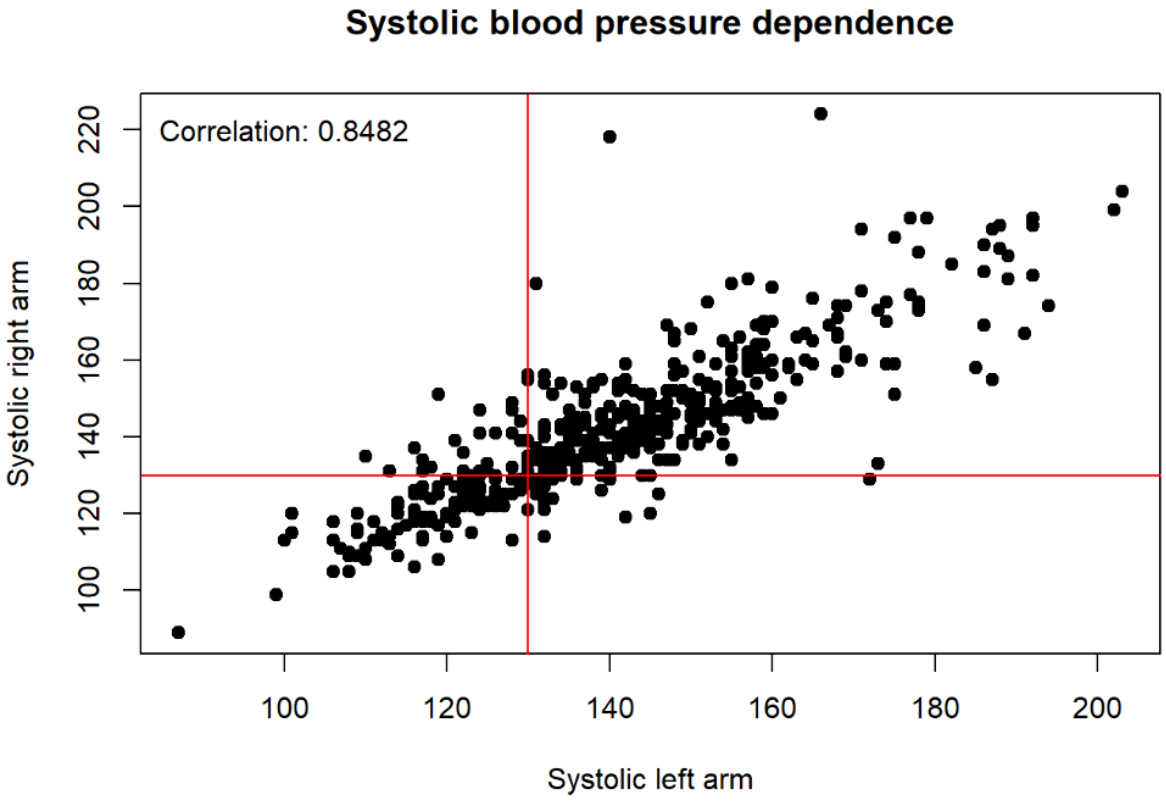
Background and Aims: To detect PAD in a small cohort with diabetes to identify its prevalence and correlating risk factors.

Methods: We looked at the records of patients who had been tested for PAD using the Mesi-Med device at our clinic and identified them into 2 groups according to the presence of PAD.

Results: 500 patients were included in this cohort, 20 had PAD (4%), and tested for correlations to different factors. There were no records on smoking status, so it was not included. Even though HbA1c, high Cholesterol, LDL, and LPa were numerically higher in the PAD group they did not reach significance due to sample size. The only correlation was with systolic and mean BP in both arms (P<0.001)


SysArmLeft
by is PAD
PAD
157
npad
137
0
50
100
150
200


SysArmLeft
by is PAD
PAD
154.235 ± 12.658
npad
138.404 ± 1.762
0
50
100
150
200



). We also checked for the rate of systolic BP control (<130 according to recent guidelines). 182 subjects had right arm systolic BP<130 (36.4%). Yet when cross-matched with the Left arm systolic pressure, 131 patients out of 500 (26.2%) had both arms systolic pressure <130 mmHg. The mean of Systolic BP in the uncontrolled group was 150.3 SD 15.2

Conclusions: High Blood pressure seemed to be the strongest risk factor for PAD thus giving positive statistical significance in a such small sample. Yet almost 73.8% of the studied population had systolic blood pressure >130 in at least one arm. We plan to continue this cohort for a larger sample in order to examine determinants for atherosclerosis. We recommend the measurement of Blood Pressure in both arms so as not to miss 10% of patients with uncontrolled BP.

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165 / #1298

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

A STUDY DESIGNED TO DETERMINE THE STATUS OF ATTITUDES AND BEHAVIORS OF PHYSICIANS TOWARDS ATHEROSCLEROSIS AND DYSLIPIDEMIA IN DIFFERENT CLINICS ACROSS TURKEY

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Most of the patients failing to meet recommended LDL-C goals. Investigating physicians' attitudes and behaviors may show the root causes of non-achievement. An attitudes and behaviors study involving a sufficiently representative population of physicians in Turkey, to reveal primary concerns in dealing with dyslipidemia has not been conducted. The study aims to reveal attitudes and behaviors that may be consistent to manage patients with dyslipidemia.

Methods: The questionnaire with 26 questions was developed to understand physician attitudes and behaviors without interfering decisions of physicians and patients. We aim to reach a total of 850 physicians (150 cardiologists, 100 endocrinologists, 250 internal medicine specialists, 50 nephrologists, 150 general practitioners, 100 family medicine specialists, 50 cardiovascular surgeons/ neurologists) based on NUTS-1 regional classification in Turkey. The survey will be conducted in 12 provinces to ensure the representation of Turkey. The margin of error for the survey is 3.3 percentage points with 95% confidence interval for each population. All physicians will complete the questionnaire in face to face with an interviewer. Research-related data and evaluation criteria data will be summarized using descriptive statistics. Categorical data will be displayed as absolute and relative frequencies for each category.

Results: Achieving the currently recommended lipid levels, awareness of adverse reactions to drug therapy and priority in atherosclerotic cardiovascular disease (ASCVD) appears to vary depending on medical specialty and health care center.

Conclusions: Our survey research in physicians will refer strategic plans to strengthen harmonization between patient and physicians. A survey research reflecting patients' attitudes and behaviors is also needed.

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166 / #645

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

FAMILY HISTORY SCREENING FOR PREMATURE CARDIOVASCULAR DISEASE AND HYPERCHOLESTEROLAEMIA IN NEWBORNS: AN ECONOMIC, SUSTAINABLE AND FAST STRATEGY TO IDENTIFY HIGH CARDIOVASCULAR DISEASE RISK SUBJECTS

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: the aim of our survey is to find families at increased cardiovascular disease (CVD) risk due to a positive family history for hypercholesterolaemia and/or premature CVD seeing the birth of a child as a starting point.

Methods: in two Northern Italy Neonatology Units, over a three-months period (ongoing study), a CVD oriented tailored family history was collected from parents of all newborns through a written survey for: own lipid profile, normal lipid values, family history for hypercholesterolaemia and/or premature CVD. Inclusion criteria were term birth, parents speaking either Italian, English, French, Spanish, no major abnormalities at birth. 900 subjects (450 couples of parents) were considered, 880 were eligible and 642 completed the survey.

Results: Mean age (mean±sd) was 31.9±5.3 years for mothers, 35.4±6.5 for fathers. 64.2% were Italian, 14% rest of Europe, 12.4% Africa, 5.9% Asia, 3,5% South America; 160/642 (25%) parents knew their own lipid profile, 256/642 (40%) knew the correct values. 230/642 (36%) declared to have positive family history for hypercholesterolemia and 192/642 (30%) for premature CVD in first or second degree relatives of which 62/192 (32%) knew their own lipid profile.

Conclusions: CVD oriented family history collected at birth is economic, sustainable, fast and reproducible and it enables to identify families at increased CVD risk and to start prevention at an early stage for both the child and the young relatives. The percentage of parents knowing their lipid values was low even when there was a positive family history of an early CVD event, so further preventive strategies are needed.

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MANNHEIM GERMANY | MAY 21-24, 2023

167 / #1055

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

CHARACTERISTICS OF ACUTE CORONARY SYNDROME DURING COVID 19 PANDEMIC

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: It seems that Covid 19 infection leads to a more significant occurrence of atherosclerotic diseases. Our aim is to investigate the characteristics of ACS patients with Covid 19.

Methods: Retrospective study during three months period , data were collected from medical records from Cantonal Hospital Zenica,B&H. Inclusion criteria were Covid 19 infection and ACS.Following parameters were STEMI, NSTEMI, therapeutic methods(angiography vs thrombolysis), risk factors (high LDL, hypertension, smoking).Statistical analysis was performed with SPSS 19.

Results: There were 214 pts with ACS , STEMI 34,58% (n=74),NSTEMI 65,42% (n=140) . Thrombolysis were performed at 35,51% (n=76), angiography 57% (n=122). 7%pts(n=15) had Covid 19 infection and among them 30% STEMI, and 70% NSTEMI. Mortality was je 6,07% (n=13), all pts with Covid 19 survived. 36%pts(n=77) had LDL-C>3mmol/l. 60,28% (n=129) pts were smokers .98pts(46%) had hypertension.

Conclusions: During the Covid 19 pandemic, the leading risk factors for the occurrence of ACS are still hypertension and elevated LDL. Smoking was a more pronounced risk factor, probably as a result of people's isolation. NSTEMI was more common than STEMI, and a special feature is the lower number of primary PCIs and increased thrombolytic therapy due to the need for testing for Covid 19. The Covid19 infection itself did not prove to be a significant risk factor for ACS and for mortality in this study. It seems that stress in this period had a more pronounced role in the worsening of atherosclerotic manifestations.

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168 / #511

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

A BODY SHAPE INDEX (ABSI) AND SMOKING ASSOCIATION IN MIDDLE-AGED LITHUANIAN MEN. RESULTS FROM 2009-2016 LITHIR STUDY.

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: The aim of this study was to evaluate the association between ABSI - measure of body composition which represents waist circumference (WC) adjusted for body mass index (BMI), and smoking status in middle-aged men who participated in the Lithuanian High Cardiovascular Risk primary prevention program between 2009-2016.

Methods: This community-based cross-sectional study comprised 38,412 men aged 40 to 54 years without overt cardiovascular disease. BMI, waist circumference, A body shape index (ABSI) and ABSI z-score mortality risk were analysed with respect to smoking status.

Results: 40.52% of subjects were current smokers. A similar proportion of subjects had obesity based on BMI and WC (28.36% and 28.25% respectively). The prevalence of smoking was highest in individuals with BMI <18.5 kg/m^2 and with normal WC (61.11% and 48.8% respectively). Analysis of ABSI and ABSI Z-score mortality risk demonstrated that ABSI values associated with a higher risk of mortality were more prevalent in smokers compared to non-smokers ($p < 0.001$).

Conclusions: Although the prevalence of smoking was highest in men who had low weight characterized by BMI or normal WC, our analysis including ABSI and ABSI z-score demonstrated that mortality risk was higher among smokers than non-smokers.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

RESULTS FROM THE NATIONWIDE FRENCH LIPIDS (LI PIDS PREVENTION IN DAILY PRACTICE SURVEY): CURRENT APPROACHES IN SECONDARY AND PRIMARY PREVENTION BY CARDIOLOGISTS.

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

Pierre Sabouret[1], Antonio Gallo[1], Ali Sharareh[2], Serge Cohen[2], Eric Parrens[2], Jérome Schwartz[2], Charlotte Cohen[2], Benoit Lequeux[2], Olivier Hoffman[2], Jean Claude Dib[2], Patrick Khanoyan[2], Serge Assouline[2], Philippe Durand[2], Lale Tokgozoglu[3], Giuseppe Biondi-Zoccai[4], Maciej Banach[5], Nicolas Lellouche[6], François Dievart[2]
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Background and Aims: Background: New ESC guidelines and statement by EAS have recently been published based on recent advances in lipid lowering treatments. However, real world data are lacking regarding the implementation among the community of French cardiologists. Objective: To determine the current approach and strategies concerning lipid lowering treatments in secondary and primary prevention in France.

Methods: : The French LIPIDS (LI pids Prevention In Daily practice Survey) was performed during October and November 2022 in France with an online questionnaire. Four mailings were sent to cardiologists to invite them to answer to the questionnaire.
A total of 323 answers of cardiologists were collected during this 2 months period.

Results: : for ASCVD patients, cardiologists agree with a LDL-C goal below 55 mg/dL in 69%, below 70 mg/dL in 16.5% , and 14.5% between 70 mg/dL and 100 mg/dL.
An upfront strategy using fixed lipid lowering combinations was prescribed in less than 5% of patients, whereas high-intensity statins was prescribed in more than 90% of ASCVD patients.
Answers concerning several clinical situations in primary prevention were very heterogenous highlighting the lack of knowledge.

Conclusions: Conclusion: in this survey, an excellent agreement of lipid goals in secondary prevention is observed whereas goals in primary prevention aren't implemented. Despite the consensus concerning the low levels of LDL-C in coronary patients, lipid lowering strategies are still mainly represented by the use of high intensity statins, whereas a combination of statins and ezetimibe is applied only for a minority of patients, and the use of PCSK9i remains marginal.

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170 / #1210

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

ELIGIBILITY OF ICOSAPENT ETHYL (EPA) IN A FRENCH POPULATION OF CORONARY OUTPATIENTS WITH TYPE 2 DIABETES.

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Background: Icosapent ethyl (EPA) is a lipid lowering treatment with proven clinical efficacy on major events in JELIS and REDUCE-IT studies. This innovative treatment has just been approved in France for ASCVD patients. But french data about clinical profiles of CAD outpatients with diabetes type 2 are lacking.

Methods: We included 574 consecutive coronary patients with T2D in our prospective registry, most of our population was male (81%) with a high prevalence of other risk factors (81% with hypertension) and numerous cardiovascular comorbidities: mean age was 71 year-old, history of myocardial infarction was present in 47%, coronary revascularization in 78% or peripheral arterial disease in 16% of cases.

Results: The lipid values were : mean serum total cholesterol 156 mg/dL, LDL cholesterol 85 mg/dL and triglycerides 148 mg/dL, with a mean glycated haemoglobin was 7.1%. 82% of patients received statins, with only 52% of high intensity statins, fibrates were prescribed for 1% of the population and ezetimibe only in 9% of cases despite guidelines, as only 37% reached a LDL-C below 70 mg/dL, and 19% under 55 mg/dL.
According to the criteria of the National Lipid Association, 31% of coronary patients with T2D were eligible to a treatment by icosapent ethyl 4 grammes per day.

Conclusions: In this contemporary survey with a non-selected coronary patients with diabetes, mainly treated by statins, 31% are potentially eligible to benefit from Icosapent Ethyl. These data also underline that only a minority reached LDL-C targets due to under prescription of lipid-lowering combinations.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

171 / #1333

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

COMMON PERINATAL CHARACTERISTICS AND ADVERSE OBSTETRIC COMPLICATIONS LEADING TO OVERWEIGHT IN ADOLESCENCE: ASSESSMENT OF INDEPENDENT AND SHARED MATERNAL-OFFSPRING PATHWAYS

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: The effects of early life exposures on offspring life-course health are well established. These exposures are associated with maternal health potentially through common pathways (i.e., genetic and environmental). In this study we aim to first examine whether perinatal characteristics, reflecting the normal distribution, are associated with offspring overweight in adolescence, independent of adverse complications, and vice versa. We then assess whether shared or independent mechanisms underlie the association of exposure scores with offspring overweight and excess maternal mortality.

Methods: We used 1974-1976 Jerusalem Perinatal Study (JPS) birth cohort, with extensive perinatal data, offspring overweight (BMI>25kg/m^2) at age 17 and maternal mortality from population registry through 2016. Two perinatal scores were constructed: (1) obstetric complications (OC) score, counting obstetric adverse events (range 0-6); and (2) common perinatal characteristics (PC) score, generated by principal component analysis (n=10 variables), comprised of 3 primary components reflecting maternal body size, parental socioeconomic position & lifestyle and fetal growth. Logistic regressions were used adjusting for covariates.

Results: Both OC and PC scores were independently associated with offspring overweight (OR_{OC}=1.15,95%CI:1.07,1.24; $OR_{PC1\text{-}Maternal\ body\ size}$=1.15,95%CI: 1.08,1.22; $OR_{PC2\text{-}SEP\ and\ lifestyle}$=0.84,95%CI: 0.79,0.90; $OR_{PC3\text{-}Fetal\ growth}$=1.15,95%CI: 1.07,1.23). Maternal mortality was associated with offspring overweight (OR=1.28,95%CI:1.02,1.61) as well as with both scores. When OC and maternal mortality were included in the same model, their associations with offspring overweight remained unchanged. Yet, coefficient for maternal mortality was attenuated when included with PC scores.

Conclusions: While adverse obstetric complications seem to affect maternal health and offspring obesity through independent mechanisms, common perinatal exposures likely share underlying pathways.

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172 / #15

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

ASSOCIATION OF PARENTAL OBESITY AND BODY MASS INDEX IN CHILDREN OF PATIENTS WITH EARLY ISCHEMIC HEART DISEASE

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: To investigate the association between parental obesity and body mass index (BMI) in children of patients with early (onset ≤55, men; ≤60, women, years) ischemic heart disease (IHD).

Methods: This analysis includes 272 children aged 5-34 years from the Moscow region (55.9% male). Only children whose two parents (proband with early IHD and consort) were examined were included in the analysis. We conducted an age-sex adjusted analysis of variance, with BMI as the dependent continuous variable and the number of obese parents (BMI ≥30 kg/m2 [WHO criteria, 2022]) as an independent ordinal variable. Association was evaluated separately in younger (5-19, n=132) and older (20-34 years, n=140) groups of chidren, where the cutoff was the median age.

Results: Table. Association of parental obesity and BMI in children of patients with early IHD

	Number of Obese Parents	
	0	1
	mean (SE*)	mean (SI
	Children, 5-19 years	
	n=52	n=59
BMI, kg/m2	18.9 (0.46)	20.3 (0.4
	Children, 20-34 years	
	n=64	n=47
BMI, kg/m2	23.6 (0.62)	25.5 (0.7

*SE – standard error, ±F-criterion, ≠p – p-level

Conclusions: The association of parental obesity and body mass index was found only in a younger group of children, it had positive and linear character and could be partially explained by the effect of cohabitation. Children of older group with positive parental history, who in many cases created their own families, were more likely to have pre-obesity.

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173 / #1057

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

CHALLENGES IN REACHING GUIDELINE RECOMMENDATIONS IN CORONARY ARTERY DISEASE PATIENTS

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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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. 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 check-ups between May 2019 and July 2020. All patients had been diagnosed with acute coronary syndrome or stable angina pectoris. Laboratory analyses were drawn before the current visit as part of the local standard of care.

Results: 81% were males with the mean age 61.7 years old. 93.4% of the patients had undergone PCI and 4.4 % had CABG. 17.6% of the patients had had a hospital admission in the last year due to CHD. 25% were current smokers, while 50% former smokers and mean BMI value was 29.9 (±6.07). Most patients (73.5%) had no family history of cardiovascular diseases. However, 67.6% of the patients interviewed claimed to be doing moderate physical activity 3-5 times/week. While 80.1% revealed no previous history of dyslipidaemia, 62.5% no history of arterial hypertension and 84.6% no 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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174 / #762

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

A REAL-WORLD ASSESSMENT OF LIPID-LOWERING THERAPY IN PATIENTS WITH ATHEROSCLEROTIC CARDIOVASCULAR DISEASE AND HYPERCHOLESTEROLEMIA: A RETROSPECTIVE DATABASE ANALYSIS IN GERMANY

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: ESC/EAS guidelines suggest that greater reductions in low-density lipoprotein cholesterol (LDL-C) lead to greater cardiovascular risk reduction. The aim was to characterize the patients (pts), lipid-lowering treatment (LLT) patterns and LDL-C outcomes of pts with atherosclerotic cardiovascular disease (ASCVD) and hypercholesterolemia in Germany.

Methods: This descriptive, non-interventional, retrospective cohort study identified ASCVD pts from general physician practices available in the electronic medical record database Disease Analyzer in Germany for 2021. Pts were included if they had a recorded ASCVD diagnosis in 2019 to 2021 and a hypercholesterolemia diagnosis (ICD-10 diagnoses E78.0, .2, .4, .5, .9) in 2021. LLT and corresponding LDL-C levels in this year were evaluated. LDL-C values were analyzed, if those were recorded within the therapy episodes matching the reach of the pack size allowing up to 20% additional buffer. If no therapy has been prescribed/allocated as above, the last available LDL-C value in 2021 has been evaluated.

Results: The population is characterized the table. Median age was high (74 years) and 39% of patients were females. Most patients received also therapies for hypertension and/or diabetes mellitus. Most present LLT were statins in monotherapy. For 45% of patients an LDL-C measurement was documented of whom 9% achieved LDL-C levels <55

mg/dl.

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	ASCVD populations								
	SAP	UAP	MI	PCI/CABG	IS	TIA	PAD	CHD	Total*
N patients in database	8.520	1.526	16.185	10.198	18.901	5.019	7.117	67.699	95.017
Demographics									
Median age (years)	72	72	72	74	77	76	74	75	74
Proportion of females	45%	40%	30%	26%	45%	50%	38%	36%	39%
Proportion of pts. with concomitant cardiovascular medication									
Antidiabetics	2%	1%	4%	6%	3%	2%	7%	3%	3%
Antihypertensives	55%	58%	52%	48%	48%	52%	42%	51%	50%
Antihypertensives + Antidiabetics	21%	23%	22%	23%	20%	16%	25%	21%	20%
No such concomitant therapy	22%	18%	22%	23%	29%	30%	26%	25%	27%
Proportion of pts. with LLT									
Statins low intensity	2%	2%	2%	1%	2%	2%	2%	2%	2%
Statins medium intensity	36%	37%	31%	30%	42%	43%	38%	36%	37%
Statins high intensity	20%	22%	25%	24%	19%	17%	19%	20%	19%
Statins low intensity + other LLT	0%	0%	0%	0%	0%	0%	0%	0%	0%
Statins medium intensity + other LLT	3%	4%	4%	4%	2%	2%	3%	3%	3%
Statins high intensity + other LLT	6%	9%	10%	10%	2%	2%	5%	7%	5%
Statins medium intensity + other LLT + PCSK9i	0%	0%	0%	0%	0%	0%	0%	0%	0%
Statins high + other LLT + PCSK9i	0%	0%	0%	0%	0%	0%	0%	0%	0%
Other LLT	2%	2%	2%	2%	1%	1%	2%	2%	2%
Other LLT + PCSK9i	0%	0%	0%	0%	0%	0%	0%	0%	0%
Statins medium intensity + PCSK9i	0%	0%	0%	0%	0%	0%	0%	0%	0%
Statins high intensity + PCSK9i	0%	0%	0%	0%	0%	0%	0%	0%	0%
PCSK9i	0%	0%	0%	0%	0%	0%	0%	0%	0%
no documented LLT	31%	24%	26%	27%	31%	32%	32%	30%	31%
Proportion of pts. with LDL-C measurement									
LDL-C measurement available	50%	51%	49%	47%	38%	43%	50%	46%	45%
LDL-C measurement not available	50%	49%	51%	53%	62%	57%	50%	54%	55%
LDL-C level achieved in pts. with LDL-C measurement									
0-39 mg/dl	2%	2%	2%	3%	2%	2%	2%	2%	2%
40-54 mg/dl	6%	6%	9%	9%	7%	5%	7%	8%	7%
55-69 mg/dl	14%	16%	19%	20%	15%	13%	14%	17%	16%
>= 70 mg/dl	78%	76%	70%	68%	76%	80%	77%	73%	75%

SAP stable angina pectoris (ICD-10 I20.8, .1, .9); UAP unstable angina pectoris (ICD-10 I20.0); MI myocardial infarction (ICD-10 I21, I25.2, I24.1, I23, I22); PCI/CABG percutaneous coronary intervention/coronary artery bypass graft (ICD-10 Z95.1, Z95.5); IS ischemic stroke (ICD-10 I63, I64, I69.3, I69.4); TIA transitory ischemic attack (ICD-10 G45); PAD peripheral arterial disease (ICD-10 I70.2); CHD chronic ischemic heart disease (ICD-10 I25 excluding I25.2); "PCSK9i" includes PCSK9i mAbs and inclisiran; "Other LLT" includes ezetimibe, bempedoic acid, bile acid sequestrants; * in the total column patients with multiple diagnoses were just counted once

Conclusions: LLT in this ASCVD population was dominated by statin monotherapy. For most patients, no LDL-C measurement was documented in 2021, and available LDL-C levels were <55 mg/dl only in a small proportion. The findings indicate a discrepancy between ESC/EAS guidelines recommendations and daily practice in Germany.

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175 / #610

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

LIPID-LOWERING TREATMENT OF PATIENTS WITH STATIN INTOLERANCE – INTERIM ANALYSIS OF AN OBSERVATIONAL, PROSPECTIVE, MULTICENTER REGISTRY

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: The medication history of patients with statin intolerance (SI) is incompletely known.

Methods: The statin intolerance registry (SIR) is an observational, prospective, multicenter study (NCT04975594). This interim analysis includes the baseline analysis of all completed patient records until December 2022 (N=630).

Results: 58.4% of patients with SI were female. The mean age was 66.7 (SD ± 10.2) years and BMI was 27.3 (SD ± 4.9) kg/m^2. 88.6% had established atherosclerotic diseases. The median *Statin-Associated Muscle Symptom Clinical Index* (SAMS-CI) was 9.0 out of 11 indicating that the muscle symptoms are likely related to statin use. Pain intensity of SAMS was rated ≧ 7 on a scale of 1 to 10 by 60.7% of patients. 30.7% of patients took painkillers for treatment. 34.8% of patients reported exposure to negative messages about statins by doctors, pharmacists, or family/friends. 49.2% had tried nutraceuticals. 59.1% of patients reported side effects under one other non-statin LLT drug, the most frequently reported was ezetimibe (80.7%). In 71.6% of these patients the reported symptoms were very similar to the statin-associated complaints. At baseline, 25% of patients reported to tolerate a statin therapy despite previous intolerance to at least two different statins. Rosuvastatin was the most common of the tolerated statins (61.6%), followed by atorvastatin (16.8%) and simvastatin (6.4%). 56.6% of all patients were treated with PCSK-9 inhibitors.

Conclusions: Most patients with SI can tolerate a LLT. The follow-up of the SI registry will show how baseline characteristics correlate with future treatments and clinical events.

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176 / #233

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

PROSPECTIVE OBSERVATIONAL STUDY ON THE EFFECTS OF VISCERAL FAT ACCUMULATION AND MULTIPLE RISKS ON ATHEROSCLEROTIC DISEASE DEVELOPMENT IN THE MIDDLE-AGED AND ELDERLY JAPANESE

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Obesity is a major risk factor for metabolic abnormalities and atherosclerosis. This study aimed to evaluate the effects of visceral fat accumulation (VFA) on development of atherosclerotic disease in the middle-aged and elderly Japanese.

Methods: Starting in 2013, annual health checkups were conducted for rural Wakayama Prefecture residents aged ≥40 years. Baseline analysis was conducted on data from initial visits (n=3649), and repeat participants were included in follow-up analysis (n=1000, mean follow-up 3.2 years). Apart from general examinations, assessments of visceral fat accumulation and arterial stiffness by brachial-ankle pulse wave velocity (baPWV) were conducted. Metabolic abnormalities and multiple risks were diagnosed according to the Japanese criteria. A self-administered questionnaire was used to investigate cardiovascular disease incidence. The effects of VFA and multiple risks on arterial stiffness and cardiovascular diseases were examined using logistic regression

analysis.

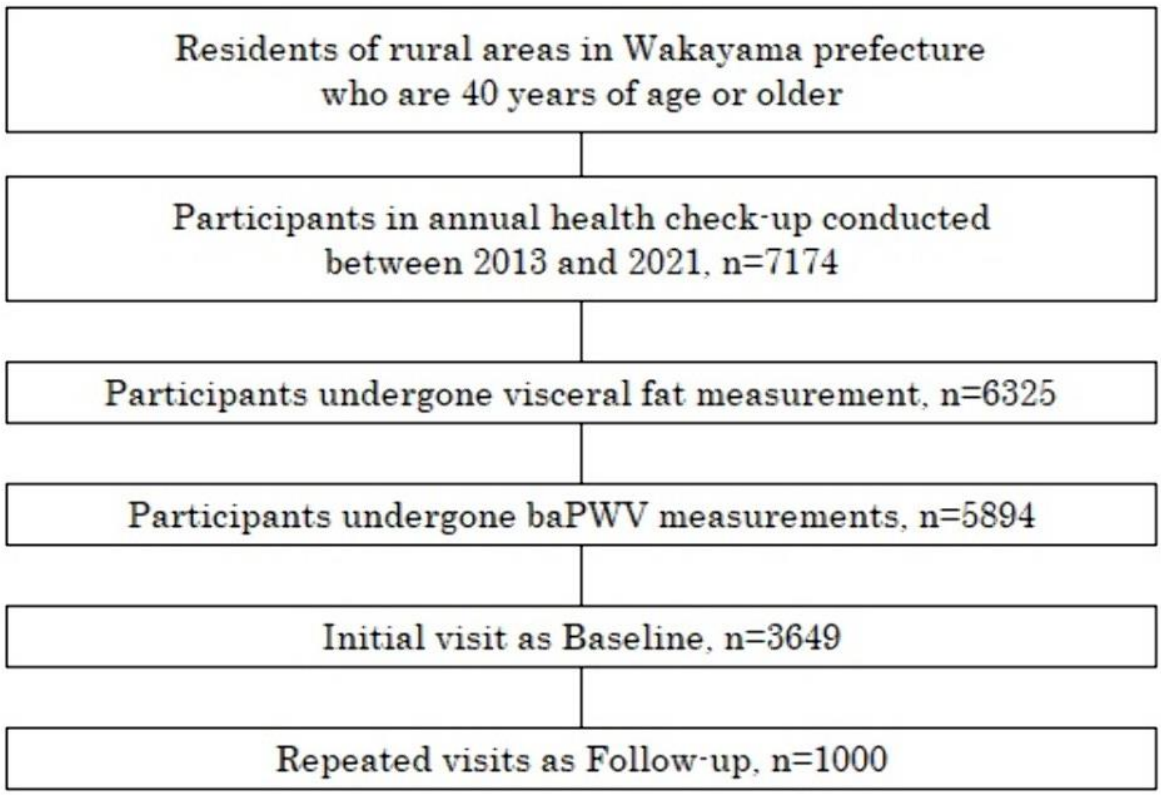

Figure 1. Flow of participants selection

Results: Baseline analysis revealed that the odds ratios of VFA for the incidence of multiple risks was significant in all sexes and ages (Table 1). Multiple risks significantly increased incidences of arterial stiffness and cardiovascular disease (Table 2). Follow-up analysis showed that incremental VFA during follow-up period increased the odds ratio for the development of new incidence of multiple risk in middle-aged (Table 3). Multiple risks during follow-up periods significantly increased new incidence of arterial stiffness in middle-aged participants (Table
4).

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Table 1. Odds ratio of VFA for the incidence of multiple risks at baseline

Sex	Age (year)	VFA Cutoff (cm^2) [1]	Odds ratio[2]	95% CI	
Male	<65	110	4.34	3.15	5.97
	≧65	110	3.10	2.33	4.13
Female	<65	65	6.44	4.40	9.43
	≧65	65	3.11	2.37	4.08

1) Optimal cuttoff that maximize sensitivity+specificity by receiver operating characteristic analysis

2) Logistic regression analysis adjusted for habitual smoking, alcohol consumption, physical activity, and walking

Table 2. Odds ratio[1] of multiple risks for the incidence of arterial stiffness and cardiovascular diseases at baseline

		Arterial stiffness[2]			Cardiovascular diseases[3]		
	age (year)	Odds ratio	95% CI		Odds ratio	95% CI	
Male	<65	2.74	1.78	4.24	2.90	1.59	5.28
	≧65	1.80	1.36	2.37	1.67	1.10	2.55
Female	<65	5.30	3.18	8.82	2.12	0.91	4.95
	≧65	2.04	1.57	2.66	1.40	0.79	2.50

1) Logistic regression analysis with adjustment by habitual smoking, drinking, physical activity and walking

2) baPWV≧1800cm/s

3) Self-administered medical questionnaire

Table 3. Odds ratio of increased VFA for newly onset multiple risks during follow-up period.

Sex	Age (year)	Odds ratio[1]	95% CI	
Male	<65	2.31	0.94	5.71
	≧65	0.83	0.36	1.93
Female	<65	2.15	0.79	5.89
	≧65	1.38	0.60	3.18

1) Logistic regression analysis with adjustment by habitual smoking, drinking, physical activity and walking

Table 4. Odds ratio of baseline multiple risks for newly onset vascular diseases during follow-up period.

			Mean follow-up	Arterial stiffness[1]			Cardiovascular diseases[2]		
	age (year)	n	Year	Odds ratio[3]	95% CI		Odds ratio	95% CI	
Male	<65	219	3.14±1.61	6.25	1.92	20.38	1.49	0.29	7.59
	≧65	229	3.14±1.58	0.58	0.26	1.29	1.51	0.36	6.35
Female	<65	294	3.25±1.54	4.93	1.59	15.32	1.78	0.31	10.14
	≧65	258	3.38±1.53	0.51	0.22	1.21	4.23	0.89	20.01

1) baPWV≧1800cm/s

2) Self-administered medical questionnaire

3) Logistic regression analysis with adjustment by habitual smoking, drinking, physical activity and walking

Conclusions: VFA poses a significant risk for atherosclerotic disease by accelerating onset of multiple risks. Proper management of VFA may be important in the prevention of atherosclerotic disease in middle-aged.

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177 / #545

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

PREVALENCE AND RISK FACTORS OF INTRACRANIAL AND EXTRACRANIAL ATHEROSCLEROTIC STENOSIS IN CHINESE PATIENTS WITH ACUTE MINOR STROKE OR TRANSIENT ISCHEMIC ATTACK

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: To investigate differences in prevalence and risk factors between intracranial and extracranial atherosclerotic stenosis (ICAS and ECAS) in patients with acute minor stroke or transient ischemic attack (TIA).

Methods: This was a cross-sectional study based on an ongoing, hospital-based, regional stroke registry consecutively enrolling stroke patients (predominantly Chinese). Patients with acute minor ischemic stroke (NIH Stroke Scale≤3) or TIA admitted in 2011-2015 were analyzed. Presence of ICAS or ECAS was defined as ≥50% atherosclerotic stenosis or occlusion in major intra- or extracranial arteries in transcranial Doppler, carotid duplex ultrasound or MR/CT angiography, with at least one vascular risk factor. Logistic regression analyses were employed to reveal independent predictors of ICAS and ECAS, respectively.

Results: Among 825 patients (median age 67 years; 60.5% males), 289 (35.0%) had ICAS, 88 (10.7%) had ECAS, and 50 (6.1%) had concurrent ICAS and ECAS. Independent predictors for ICAS included diabetes (odds ratio [OR] 1.61, 95% CI 1.00-2.59), prior stroke/TIA (OR 2.43, 1.56-3.79), systolic blood pressure (OR 1.01, 1.00-1.02), non-high-density lipoprotein (OR 1.48, 1.22-1.79) and presence of ECAS (OR 2.33, 1.33-4.09). Independent predictors for ECAS included age (OR 1.07, 1.04-1.10), ischemic heart disease (OR 2.76, 1.33-5.70) and presence of ICAS (OR 2.39, 1.37-4.17).

Conclusions: The prevalence and risk factors differ between ICAS and ECAS in Chinese patients with acute minor stroke or TIA, suggesting possibly different pathogenesis of ICAS and ECAS. The findings may inform prevention and management strategies for ICAS and ECAS.

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178 / #1046

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

FAMILIAL HYPERCHOLESTEROLEMIA, RISK FACTORS INFLUENCING DIAGNOSIS, AND CARDIOVASCULAR RISK. AN OBSERVATIONAL STUDY OF 106,507 INDIVIDUALS FROM THE GENERAL POPULATION.

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Individuals with familial hypercholesterolemia(FH) are at high risk of developing cardiovascular disease due to high cholesterol concentrations. Other cardiovascular risk factors may add to this risk.

Methods: We used the Dutch Lipid Clinic Network(DLCN) criteria to diagnose FH in 106,507 individuals from the Copenhagen General Population Study. We investigated the effect of cardiovascular risk factors on assignment to DLCN FH-categories; risk of myocardial infarction(MI) within each DLCN FH-category by additional cardiovascular risk factors; and the absolute ten-year risk of MI in DLCN FH-categories by the risk factors.

Results: Risk of being diagnosed with possible or probable FH was higher in individuals who smoked, had hypertension, body mass index(BMI)≥30kg/m^2, triglycerides≥2mmol/L, and lipoprotein (a)>50mg/dL compared to individuals who did not(all p<0.04). Risk of MI was higher in possible FH if individuals were men(odds ratio[OR]: 8.95; 95% confidence interval[95%CI]: 7.67-10.4), smoking(5.97[4.90-7.28]), had hypertension(8.22[7.04-9.59]), diabetes (9.11[6.94-12.0]) and high lipoprotein(a) levels(5.05[4.15-6.14]). Ten-year risk of MI stratified on DLCN FH-category was stepwise higher in individuals who smoked, had diabetes, and with higher blood pressure. Highest risk of MI was 44.3% in men who smoked, had diabetes, and a systolic blood pressure of 160-179mmHg, and a probable/definite FH diagnosis. Corresponding ten-year risk for women was 25.3%.

Conclusions: Risk of being diagnosed with FH by the DLCN criteria was influenced by smoking, hypertension, BMI, and triglyceride and lipoprotein(a) concentrations in the general population. For individuals within the same possible or probable FH-category, male sex, smoking, hypertension, and diabetes independently added to the risk of MI.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

179 / #656

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

LIPOPROTEIN (A) CONCENTRATION AND CARDIOVASCULAR DISEASE IN A GROUP OF PATIENTS WITH HYPERLIPIDEMIA – A LIPID OUTPATIENT CLINIC EXPERIENCE.

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: High lipoprotein(a), Lp(a) concentrations have been linked to increased risk of ischemic cardiovascular disease. However more evidence is needed to assess causality and potential clinical benefits of Lp(a) lowering therapies. The aim of the study was to assess the prevalence of increased Lp(a) levels in hyperlipidemic patients and association between Lp(a) levels and cardiovascular disease in this group of patients.

Methods: We examined 223 consecutive patients, 111 (49,8%) women with primary hyperlipidemia from lipid outpatient clinic. The mean (SD) age of patients was 48.8 (15.2) years, LDL-C 3.49 (1.8) mmol/l, median (IR) of Lp(a) 0.15 (0.53)g/l.

Results: Cardiovascular disease(CVD) was present in 24.2%, coronary artery disease(CAD) in 21.0%, type2 diabetes in 17%, hypertension in 39.5% of examined persons. Patients with CVD and patients with CAD had higher Lp(a) levels than patients without (p=0.0403 and p=0.0063 respectively). 42.3% patients, in whom carotid usg was performed, had carotid plaques. We didn't observe differences in Lp(a) levels between patients with or without plaques, nor correlation of Lp(a) with carotid IMT. 28.3% of patients have Lp(a) concentration in high risk category - Lp(a) > 0.5 g/dl, 9,9% in moderate risk category (0,3-0,5 g/l). Interestingly, we observed association between Lp(a) risk categories and presence of CVD (p=0.003), while not with presence of carotid plaques. There were no differences between patients with vs without family history of CVD, presence of diabetes or arterial hypertension in Lp(a) levels.

Conclusions: We found high prevalence of increased Lp(a) levels and strong associations of Lp(a) risk categories with CVD, but not with carotid atherosclerosis.

91ST EAS CONGRESS
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180 / #290

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

REMNANT CHOLESTEROL AND RISK OF MYOCARDIAL INFARCTION IN PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING REVASCULARIZATION

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Despite substantial reduction in low-density lipoprotein cholesterol (LDL-C), patients develop recurrent cardiovascular events. Remnant cholesterol (RC), the cholesterol content of triglyceride-rich lipoproteins, is a potential contributor to this residual risk. We aimed to investigate the association between RC and risk for myocardial infarction (MI) in patients with coronary artery disease, and examine whether the predictive value of RC is retained beyond LDL-C.

Methods: Data on 9,451 patients undergoing coronary revascularization in a single center. RC was calculated as total cholesterol minus high-density lipoprotein cholesterol minus LDL-C (estimated using Martin-Hopkins equation). Adjusted Cox-regression models were used to estimate the association between RC and risk for MI. Discordance analyses were performed to examine the correlation between RC and LDL-C in relation to MI risk.

Results: Mean age was 65±11 years; 67% presented with acute coronary syndrome. During median follow-up of 9.6 years, 1,690 patients developed MI. After multivariable adjustment including lipid-lowering therapies and LDL-C, RC was associated with higher MI risk: hazard ratio (95% confidence interval): 1.30 (1.15-1.46) and 1.51 (1.29-1.86) in those with RC levels ≥75th (32.6 mg/dL) and ≥90th (41.8 mg/dL) percentile, in comparison to individuals with RC levels <50th percentile (25.5 mg/dL). When RC and LDL-C levels were discordant, the level of RC reflected the risk for MI more than LDL-C.

Conclusions: Elevated RC is a risk factor for MI independent of lipid-lowering therapies and LDL-C, providing further support that RC may serve as a residual cardiovascular risk marker and potential treatment target in patients with coronary artery disease.

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181 / #1561

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

SUPPRESSING EFFECT OF HDL-CHOLESTEROL ON THE ASSOCIATIONS OF ACCELEROMETER-BASED SEDENTARY TIME WITH LOW-GRADE INFLAMMATION: A 13-YEAR LONGITUDINAL STUDY FROM CHILDHOOD THROUGH YOUNG ADULTHOOD

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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Background and Aims: Low-grade inflammation has been associated with atherosclerosis and metabolic disorders in youth. However, the long-term contribution of sedentary time (ST) assessed with accelerometer on low-grade inflammation is unknown. Similarly, whether high-density lipoprotein cholesterol (HDL-c) could potentially attenuate any deleterious effect of ST on inflammation remains uninvestigated in the pediatric population. This study examined the mediating or suppressing role of HDL-c on the association of ST with inflammation.

Methods: This study included 792 British 11-year-olds (58% females) followed up for 13 years from the Avon Longitudinal Study of Parents and Children, UK, who had at least twice measurement of accelerometer-based ST during ages 11, 15, and 24 years clinic visits with complete high-sensitivity C-reactive protein (hsCRP) and HDL-c measures at 15, 17, and 24 years. Mediating associations were examined using structural equation models adjusting for sex, age, low-density lipoprotein cholesterol, insulin, triglyceride, heart rate, systolic blood pressure, glucose, fat mass, lean mass, smoking status, family history of hypertension/diabetes/high cholesterol/vascular disease, socioeconomic status, and moderate-to-vigorous physical activity. When the magnitude of the association between exposure and outcome is increased upon inclusion of a third variable suppression occurred but mediation, if decreased.

Results: Cumulative exposure to ST from ages 11–24 years was positively associated with hsCRP progression, standardized regression coefficient total effect 0.24 [95% CI 0.19 – 0.28; p=0.003]. HDL-c had a 7.6% suppression effect on the relationship resulting in a direct effect of 0.26 [0.21 – 0.30; p = 0.003].

Conclusions: Cumulative increase in HDL-c may partially protect against the long-term inflammatory process of sedentariness.

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182 / #1593

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

INADEQUATE AWARENESS AND ATTENTION TO NON-HDL CHOLESTEROL: UNDERTREATMENT OF HIGH-RISK PATIENTS IN CARDIOLOGY PRACTICE

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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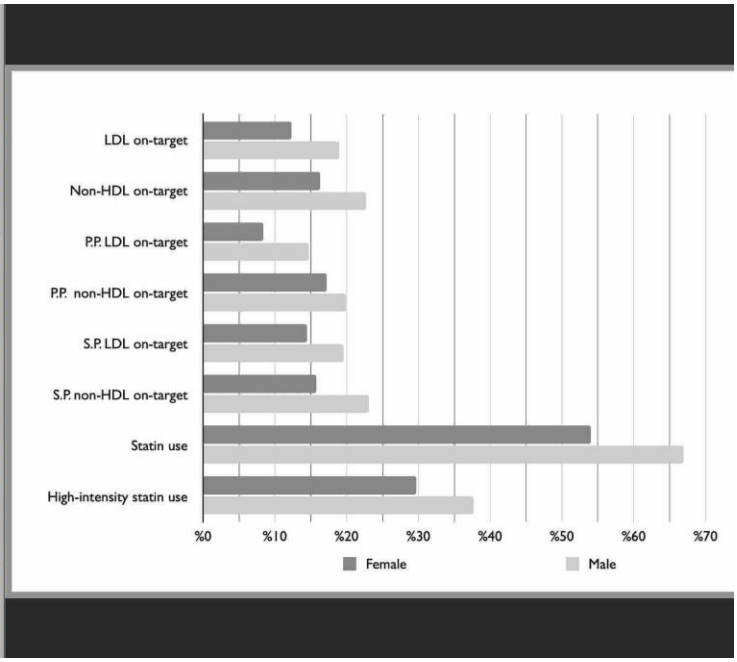
Background and Aims: The relationship between LDL-C and ASCVD is well-established. However, non-HDL-C has also been validated as a substantial predictor of ASCVD and has been confirmed to be superior to LDL-C, particularly in individuals with mild to moderate hypertriglyceridaemia. EPHESUS trial aimed to assess the real-life management of hypercholesterolemia in secondary and primary prevention in high-risk groups in cardiology outpatient clinics.

Methods: 1868 consecutively enrolled patients' data were analyzed to assess the proportion of patients achieving cholesterol goals, statin adherence, and physicians' perceptions. This analysis focused on evaluating the awareness of non-HDL-C in cardiology practice as a substantial predictor of ASCVD, patients' adherence to LLT, and clinicians' perceptions of LLT. Associations between patient demographics, co-morbidities, and statin adherence were examined.

Results:

Table 1: Patient demographics, characteristics and comorbid features

	Non-HDL off-target n=1490	Non-HDL on-target n=378	P-value
Demographic Characteristics			
Age (years)	61.8±9.9	63.3±10.4	0.013
Female (n, %)	597 (40.1)	116 (30.7)	0.001
Secondary Prevention (n, %)	1174 (78.8)	308 (81.5)	0.249
Body mass index (kg/m2)	29.1±4.8	28.5±4.5	0.038
Smoking (n, %)	1108 (74.4)	289 (76.5)	0.403
Place of residence, rural (n, %)	397 (26.8)	106 (28.1)	0.604
Family history for coronary heart disease (n, %)	609 (41.5)	135 (35.9)	0.052
Comorbidities (n, %)			
Atrial fibrillation	102 (6.8)	26 (6.9)	0.982
Chronic Renal Disease	96 (6.4)	34 (9.0)	0.082
Diabetes Mellitus	707 (47.4)	166 (43.9)	0.219
Hypertension	1049 (70.4)	245 (64.8)	0.035
Coronary heart disease	1131 (75.9)	302 (79.9)	0.101
Coronary Bypass	294 (19.7)	76 (20.1)	0.870
Congestive heart failure	218 (14.9)	62 (16.5)	0.418
Peripheral Vascular Disease	66 (4.4)	9 (2.4)	0.070
Carotid Arterial Disease	119 (8.0)	19 (5.0)	0.050
Stroke/Transient ischemic attack	85 (5.8)	16 (4.3)	0.269
Medication (n, %)			
Acetylsalicylic acid	1091 (73.2)	285 (75.4)	0.391
Anticoagulant therapy	86 (5.8)	23 (6.1)	0.817
Statins	860 (57.7)	298 (78.8)	<0.001
High intensity statin	279 (33.0)	121 (40.9)	0.015
Ezetimibe	2 (0.1)	1 (0.1)	0.493
Fenofibrate	61 (4.1)	10 (2.6)	0.188
Oral antidiabetics	594 (39.9)	141 (37.3)	0.362
Insulin	250 (16.8)	58 (15.3)	0.502
Beta blockers	1016 (68.2)	259 (68.5)	0.902
ACE inhibitors/ARBs	962 (64.6)	244 (64.6)	0.996
Calcium channel blockers	246 (16.5)	71 (18.8)	0.293
Lipid Parameters			
LDL cholesterol on-target (n, %)	66 (21.4)	242 (78.6)	<0.001
Total cholesterol (mg/dL)	205 (177.5-237)	131 (118-146.3)	<0.001
LDL cholesterol (mg/dL)	124 (98-180)	66 (54-76)	<0.001
HDL cholesterol (mg/dL)	43 (36-51)	44 (37-51)	0.323
Triglycerides (mg/dL)	165 (125-232)	110 (80.75-142)	<0.001
Non-HDL cholesterol (mg/dL)	162 (134-191)	88 (78-96)	<0.001



Among the study population, 20.2% achieved non-HDL-C and 16.5% achieved LDL-C goals. In primary prevention, 18.1% reached non-HDL-C and 10.6% reached LDL-C goals, while in secondary prevention, 20.8% and 18.0% attained these respective goals. High-intensity statin therapy was observed in 21.2% of patients, with 30.3% and 24.3% achieving non-HDL-C and LDL-C targets, respectively. Statin use was lower in women. Women achieved non-HDL-C and LDL-C goals less frequently in both primary and secondary prevention groups.

Conclusions: The achievement of non-HDL-C goals remains suboptimal in patients with hypercholesterolemia both in primary and secondary prevention. Suboptimal treatment is more prominent in women with a lower rate of statin use and goal attainment. Overall, our study highlights the need for increased awareness, education, and improved treatment strategies for managing hypercholesterolemia to reduce residual risk and improve patient outcomes.

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183 / #389

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

ADMISSION OF PATIENTS WITH SEVERE HYPERTRIGLYCERIDEMIA TO OUTPATIENT CLINICS

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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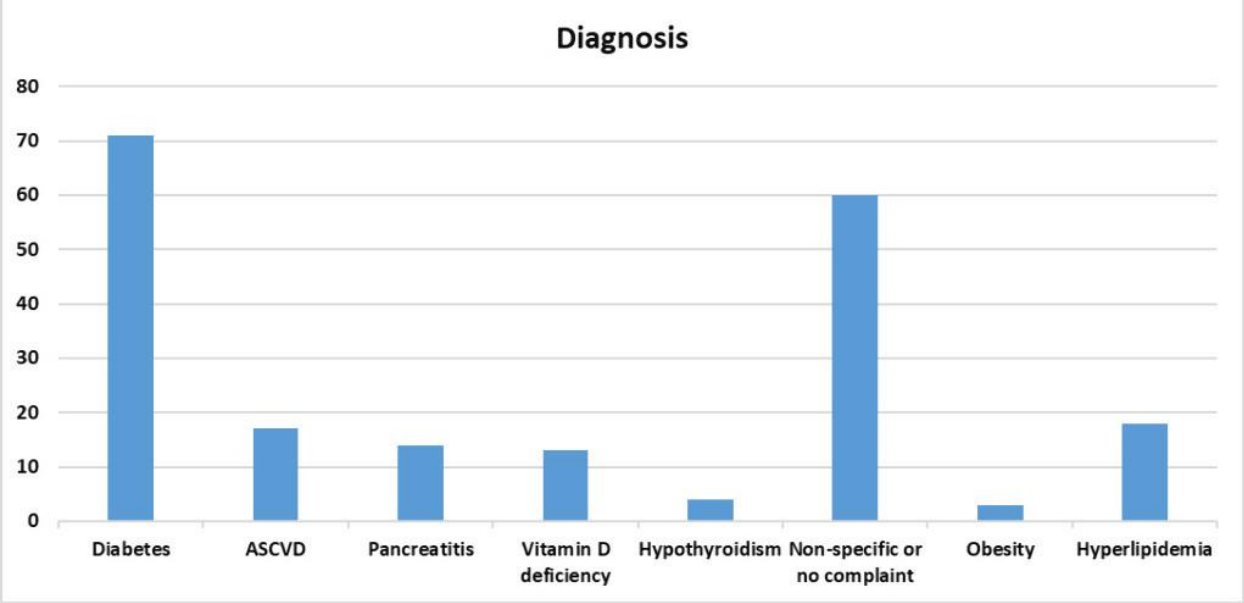
Background and Aims: Hypertriglyceridemia (HTG) usually accompanies to metabolic syndrome and diabetes. Although mild to moderate HTG is known to be associated with atherosclerotic cardiovascular disease (ASCVD), its role in ASCVD is still not clear. However, severe HTG is a rare lipid disorder which could lead to acute-chronic pancreatitis.

Methods: We retrospectively screened patients who were examined in our hospital outpatient clinics over one-year period with a triglyceride level of >1000mg/dL. We noted diagnostic codes of the patients and the type of outpatient clinic that they admitted.

Results: A total of 200 patients were enrolled to the study. The mean age was 51.1 ± 11.4 and 117 (58.5 %) were male. Most of the patients admitted to internal medicine (52.5%) followed by cardiology (14%) and endocrinology (10.5%) clinics. Although, diabetes was more frequently (35.5%) diagnosed in these patients, 30% of them had non-specific symptoms or did not have any complaints and were diagnosed during their routine follow-up (Figure). Patients with very high triglyceride levels were also diagnosed while routine follow up in cardiology outpatient clinics (14%) and 8.5% of them had a history of ASCVD. Those patients with severe HTG were rarely admitted to gastroenterology department with abdominal

pain and diagnosed with pancreatitis (7%).



Conclusions: Although the relationship of severe HTG with cardiovascular events is not clear, a substantial number of patients with very high levels of triglycerides had a history of ASCVD. Besides diabetes was the most important secondary cause of severe HTG, patients with very high levels of triglycerides might also be asymptomatic.

91ST EAS CONGRESS
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184 / #759

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

PREVALENCE OF DYSLIPIDAEMIA IN GERMANY

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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Background and Aims: Cardiovascular diseases (CVD) are a leading cause of death in Germany and often accompanied by dyslipidaemia, which contributes to the development of atherosclerosis.

Methods: Aim of our study was to estimate the prevalence of dyslipidaemia in Germany based on 2.13 million blood samples that were collected between 2018 and 2021 and sent to four SYNLAB laboratories for analysis. The laboratory parameters low-density lipoprotein cholesterol (LDL-C), triglycerides (TG) and lipoprotein (Lp) (a) were considered. Samples were from 1.08 million women and 1.04 million men. The mean age of women was 58.44 ± 19.24 years and that of men 58.04 ± 18.41 years.

Results: Our data show that 57.7 % of men and 66.8 % of women have LDL-C values above the threshold of 115 mg/dl. In men, median LDL-C concentrations increase to the age of 45 years and in women to the age of 55 years. On average, women have higher LDL-C (131 mg/dl) than men (123 mg/dl). For TG, 38.2 % of men`s and 28 % of women`s values are above the normal range (> 150 mg/dL). On average, women have lower TG (111 mg/dl) than men (125mg/dl). 1.23 % of all values exceed the threshold for severe hypertriglyceridemia of 500 mg/dl. Notably, Lp(a) values increased with age.

Conclusions: Our results demonstrate that a large percentage of the German population has elevated lipid levels. On average, women reach highest LDL-C significantly later than men. The correlation of Lp(a) levels with age suggests that Lp(a) does not remain constant throughout life.

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185 / #161

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

EVALUATING A RISK-BASED ALLOCATION STRATEGY FOR PCSK9 INHIBITORS – RESULTS FROM A SIMULATION STUDY IN A CONTEMPORARY ASCVD COHORT

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

Christopher Blaum, Alina Goßling, Benjamin Bay, Lukas Köster, Julia Rohde, Thiess Lorenz, Tanja Zeller, Renate Schnabel, Moritz Seiffert, Paulus Kirchhof, Stefan Blankenberg, Fabian Brunner, Christoph Waldeyer
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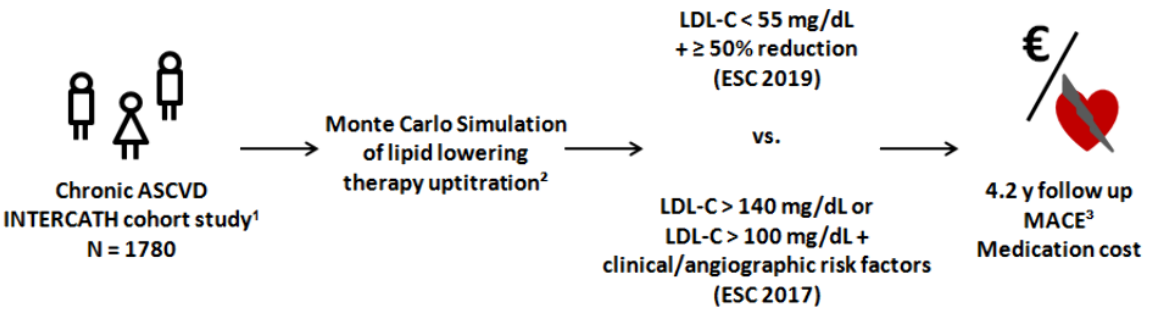
Background and Aims: Targeting PCSK9 inhibitors (PCSK9i) to patients with high LDL-cholesterol (LDL-C) and/or a high cardiovascular event rate is more cost effective and sustainable from a health economic perspective compared to strategies based on LDL-C alone. Such risk-based allocation criteria require evaluation.

Methods: We simulated the cost/preventable cardiovascular event for PCSK9i initiation in target populations according to the ESC 2019 guideline on dyslipidaemias compared to a risk-based use determined by residual LDL-C and clinical/angiographic risk factors, as proposed by the ESC consensus update on PCSK9i from 2017. The study flow is summarised in *Figure 1*.



1) recruitment 2015-2021, University Heart Centre Hamburg/Germany
2) algorithm with consideration of statin intolerance (Blaum et al., *Eur J Prev Cardiol* 2021)
3) MACE = cardiovascular death, non-fatal myocardial infarction (MI), non-fatal stroke

Results: We included 1780 patients (mean age 69.5 years, median baseline LDL-C 85.0 mg/dL). The need for PCSK9i was simulated to be 5.0% (ESC 2017) vs. 42.0% (ESC 2019). 3 year cardiovascular event rates were observed to be only slightly higher in the LDL-C/risk factor-based PCSK9i target population compared to the current guideline-based target population (13.2% vs. 11.3%), driven by an increase in the rate of non-fatal myocardial infarction (6.9% vs. 4.5 %). Cost/preventable event p.a. differed by more than factor 2 (326,000 € vs. 708,000 €), driven mainly by pre-PCSK9i LDL-C levels in the different target populations (125.8 mg/dL vs. 67.7 mg/dL). (*Table*

1).

	Need for PCSK9i	Median LDL-C pre-PCSK9i / mg/dL	3 year MACE rate	3 year non-fatal MI rate	Cost /preventable cardiovascular event p.a. (€)
1. ESC 2019 (LDL-C < 55 mg/dL)	42.0%	67.7	11.3%	4.5%	708,000
2. ESC 2017 (LDL-C/risk-based)	5.0%	125.8	13.2%	6.9%	326,000

Conclusions: Clinical/angiogiographic criteria for risk classification such as used in the ESC 2017 consensus statement offer limited discrimination for the identification of subpopulations at highest cardiovascular risk. Development of accurate risk prediction tools and their integration into risk-based allocation strategies, both requisites for a cost effective use of PCSK9i, remain a challenge.

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186 / #131

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

THE PREVALENCE OF FAMILIAL DYSBETALIPOPROTEINEMIA IN ONE OF THE EUROPEAN REGIONS OF THE RUSSIAN FEDERATION

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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Background and Aims: Familial dysbetalipoproteinemia (FD) is a highly atherogenic genetically based lipid disorder. The prevalence of FD in Russia is unknown. The aim was to investigate the prevalence of FD in one of the European regions of Russia.

Methods: 25-64 y.o. subjects (n=1858) were from the population-based cohort of the ESSE-RF study, led in the Ivanovo region. Genetic data and lipid profiles were available. The FD is defined by combined both *APOE* ε2ε2 haplotype and available for real clinical practice biochemical criteria. For this reason, the applicability of previously developed biochemical FD criteria (apoB algorithm: apoB <1.2 g/L, TG ≥1.5 mmol/L, TG/apoB <10.0 mmol/g, TC/apoB ≥6.2 mmol/g; non-HDL-C/apoB ≥3.69 mmol/g) was determined in the study cohort (for subjects without lipid-lowering therapy, n=1748). Statistical analyses were done using R 4.1.

Results: The apoB algorithm analysis showed low specificity of apoB level (11.6%) and TG/apoB ratio (0.2%) for identifying subjects without the ε2ε2 haplotype. TG level ≥1.5 mmol/l had sufficient sensitivity (78.6%) and specificity (65.4%) to identify subjects with ε2ε2 haplotype. The non-HDL-C/apoB ratio had a low specificity (1.1%) for identifying subjects without the ε2ε2 haplotype in the study population (Table 1). The prevalence of ε2ε2 haplotype was 0.8% (one in 124) (95% CI: 0.45%-1.32%). When TG ≥1.5 mmol/L criterion was added to ε2ε2 carriage, the FD was identified in 12 subjects. Thus, the prevalence of FD

was 0.6% (1 in 155) (95% CI: 0.33–1.12).

Algorithm/Criterion	Passed the algorithm for subjects with ε2ε2 haplotype, n=14	Did not pass the algorithm for subjects without the ε2ε2 haplotype, n=1734	Sensitivity, %	Specificity, %
apoB algorithm				
apoB <1.2 g/L	14	202	100	11.6
TG ≥1.5 mmol/L	11	1143	78.6	65.4
TG/apoB <10.0 mmol/g	14	3	100	0.2
TC/apoB ≥6.2 mmol/g	13	937	92.9	53.6
non-HDL-C/apoB				
non-HDL-C/apoB ≥3.69 mmol/g	14	20	100	1.1

Conclusions: A high prevalence of FD was detected in one of the European regions of Russia.

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187 / #147

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

PATIENT REFERRALS AUDIT: EVALUATION OF LOCAL CARDIOVASCULAR RISK CLINIC REFERRALS TO HELP AID PATIENT TRIAGE AND WAIT TIMES

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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Background and Aims: United Kingdom Guidance outlines when to consider Cardiovascular Risk clinic referral. However prior to referral, clinicians are advised to exclude secondary causes of dyslipidaemia. Due to the COVID-19 pandemic, there has been a reduction in elective work and waiting times have increased further. We compared Royal Alexandra (RAH), and West Ambulatory Care Hospital (WACH), Scotland clinic referrals to establish whether: national guidance was followed and secondary causes of dyslipidaemia excluded.

Methods: New patient referrals from 2018-2019 for RAH retrospectively, and, prospectively, January-June 2022 WACH referrals were reviewed. Secondary causes of dyslipidaemia were subdivided into poor glycaemic control, hypothyroidism, nephrotic syndrome, raised BMI and alcohol excess.

Results: There were 299 eligible patient referrals with two-thirds being allocated appointments. Median age was 55 years and 56% were female. Median wait time was 70 and 49 days for RAH and WACH respectively. Most common referral reasons were comparable between both sites with hypercholesterolaemia (total 45%), mixed dyslipidaemia (22%) and drug intolerance (16%). Only 40% RAH and 34% WACH referrals had excluded poor glycaemic control, hypothyroidism and nephrotic syndrome within the preceding 3 months. 9% RAH and 12% WACH had normal range BMI recorded within 6 months (48% had unknown BMI) and only 1% RAH and 5% WACH had all 5 secondary causes excluded.

Conclusions: Unsurprisingly, hypercholesterolaemia was the most common referral reason but few patients had secondary causes excluded. This raises the question if a standardised approach to clinic referrals could be adapted to improve diagnosis and management of secondary dyslipidaemia and wait time to clinic.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

188 / #571

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

A LOW-FAT, LOW-CALORIC DIET ENHANCES THE HYPOLIPIDEMIC EFFECT OF HYPOLIPIDEMIC MENTICATION IN OVERWEIGHT PATIENTS .

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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Background and Aims: INTRODUCTION: In this study, a comparative analysis between exclusive medical therapy (MT) and combined medical-dietary therapy (MDT) was conducted, in order to investigate beter results in Lipid control .

Methods: METHODS: Among patients with dyslipidemia, the ones with high body mass index (>25 kg/m^2), were selected. The allocation in the intervention group, that received MDT (100 patients), or the control group (100 patients), that received MT (mainly statins), was based upon the acceptance or the rejection respectively of the DT (energy restriction of 500-1000kcal and fat restriction up to 27-30% of total energy). The patients were finally included in the study, only if they showed good compliance for at least two consequent months and also if they did not have blood lipid levels that were extremely abnormal or uncontrolled via MT. The measurements that were collected were blood levels of triglycerides (TG), total, low-density and high-density cholesterol (T-CHOL, LDL-C, HDL-C), as well as of body mass (BM).

Results: RESULTS: Improved blood lipid levels were seen in both groups and were statistically significant. All improvements, but the TG reduction, were notably larger in the intervention group. However, these differences were not significant. There was a significant correlation, though, between the improvements of BM and those of TG.

Conclusions: CONCLUSIONS: This study brought important indications for the contribution of the DT and the consequent weight loss in the management of dyslipidemia via MT, but did not manage to prove it, mainly due to its small sample. More and larger studies are required.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

189 / #255

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

IMPACT OF SOCIO-ECONOMIC STATUS ON THE PREVALENCE OF SEVERE HYPERTRIGLYCERIDEMIA IN ARGENTINA

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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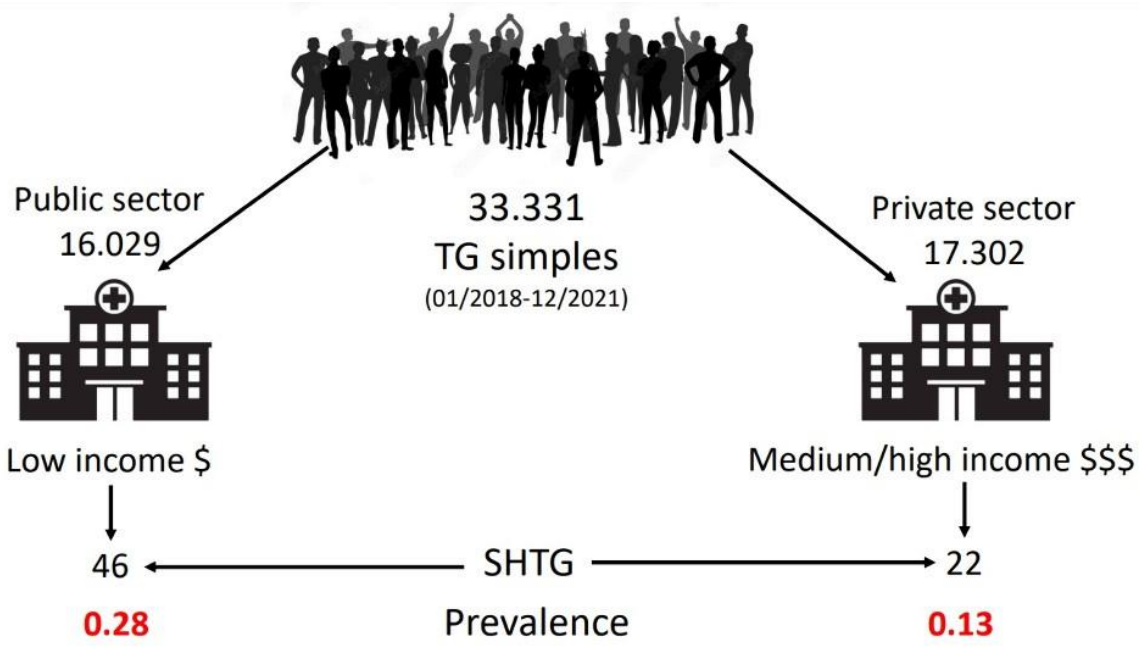
Background and Aims: Severe Hypertriglyceridemia (SHTG) is a metabolic disorder with multiple causes and management implications. The prevalence and its relationship with socioeconomic status in Argentina is unknown. The objective of this study was to estimate and compare the prevalence of SHTG in the public and private health sector.

Methods: This was a retrospective and observational analysis of electronic databases from a provincial public Hospital (low income patients) and a private Health Center (medium-high income patients) performed between January 2018 and December 2021. Both inpatients and outpatients' adults were included in the analysis when their triglycerides levels were above 885 mg/dL (10 mmol/L).

Results: 16029 samples were obtained in the public sector and 17302 in the private sector. We found that 46 patients in the public sector presented SHTG, representing a total prevalence of 0.28% and 22 participants in the private sector, representing a total prevalence of 0.13% (Figure 1). In the public sector 60.87% were men versus 86.36% (p= 0.0889) and the average age was 47.5 ±13 and 52.3±10.65, respectively (p=0.011). Median triglycerides levels were 1284.5 mg/dL (interquartile range mg/dL) p=

0.3156.



Conclusions: We report in the public sector a prevalence of SHTG that is double that of the private sector. There were probably socioeconomic factors as well as nutritional habits that have impacted on triglycerides levels and could explain this difference.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

190 / #1606

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

HIGH-FAT DIET CAUSES HEPATIC STEATOSIS, INCREASED PLASMA LOW-DENSITY LIPOPROTEIN LEVELS, AND ALTERS THE PCSK9-LDLR SYSTEM MORE PRONOUNCEDLY THAN A HIGH-CARBOHYDRATES DIET IN RATS.

POSTER ON BOARD: AS03.02 EPIDEMIOLOGY OF DYSLIPIDEMIAS

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Background and Aims: Unbalanced diet combined with excessive calorie intake increases the risk of many diseases. High-fat (HFD) and high-carbohydrates (HCD) diets are recognized as serious risk factors to obesity, dyslipidemia, liver steatosis and cardiovascular disorders. However, the effect of HFD and HCD without excessive caloric intake is obscure. We evaluated the effect of either standard, HFD or HCD diet on the liver status, plasma lipid levels and PCSK9-LDLR system in rats, with the same caloric intake.

Methods: The study was performed on 6-week-old male Sprague Dawley rats, receiving either a standard (controls, n=7), HFD (n=7) or HCD (n=7) chow. All groups received the same, daily calorie rations for 12 weeks. Histological, biochemical and molecular biology assays on tissues from sacrificed rats were performed.

Results: There was no significant difference between the groups in body weight at the end of experiment and none of the diets induced obesity in rats. HFD and HCD groups showed non-alcoholic steatohepatitis (NASH). The HFD group showed more advanced changes in liver than the HCD, including steatosis, inflammation, and fibrosis. HFD group showed significantly higher plasma LDL compare to controls and HCD. Furthermore, the HFD group had lower plasma levels of proprotein convertase subtilisin/kexin type 9 (PCSK9) and higher liver protein levels of low-density lipoprotein receptor (LDLR) than the controls or HCD group.

Conclusions: HFD and HCD cause liver steatosis and dyslipidemia without excessive caloric intake, moreover excess fat in the diet decreased plasma PCSK9 levels and increase hepatic LDLR protein levels in rats.

91ST EAS CONGRESS
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191 / #737

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

THE CONTRIBUTION OF THE LIPID AND OBESITY CLINIC IN TRIKALA GENERAL HOSPITAL TO THE LIPID CONTROL TO DIABETES PATIENTS

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: PURPOSE Although lipid control is a daily clinical practice, the goals are often difficult to achieve and maintain. Special Lipid-Obesity clinics have an important role in the primary and secondary prevention of cardiovascular diseases that are proven to be related to diabetes and lipid disorders. The assessment of the contribution of the Lipid-Obesity clinic in the management of dyslipidemic patients with or without Diabetes, based on whether lipid target values have been achieved at one-year follow-up.

Methods: MATERIAL – METHOD Dyslipidemic patients (N=105) with Diabetes II (N1=33) and without Diabetes II (N2=72) with severe dyslipidemia by ATP III were included in the study. Patients were treated with a statin ± antidiabetic drug. Smokers and patients with Chronic Kidney Disease were excluded. There was no interference with the antiplatelet and antihypertensive treatment received by the patients.

Results: RESULTS After one year of regular follow-up 15.2% of diabetic and 47.2% of non-diabetic patients had a completely normal lipid profile. 20% of diabetic and 70.3% of non-diabetic patients have achieved the target value for LDL while 37.5% of diabetics and 70.9% of non-diabetic patients have the desired total cholesterol value. Regarding triglycerides, the corresponding percentages are 22.7% and 51.6% respectively.

Conclusions: CONCLUSIONS The specialized Lipid-Obesity clinic achieves the regulation of the lipid profile of its metabolic patients. However, a statistically significant difference in the control of lipid values between diabetic and non-diabetic dyslipidemic patients is observed ($p<0.01$) which is partly justified by the pathology metabolism of diabetes.

91ST EAS CONGRESS
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192 / #1326

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

CARDIOMETABOLIC OUTCOMES OF SITAGLIPTIN-ENHANCED METFORMIN TREATMENT IN UNCONTROLLED TYPE 2 DIABETES PATIENTS WITHOUT ATHEROSCLEROTIC MANIFESTATIONS

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Type 2 diabetes mellitus (T2DM) contributes to the development and progression of subclinical diastolic dysfunction (DD) as incipient myocardial damage. This study assessed the cardio-metabolic outcomes of sitagliptin added to metformin treatment in uncontrolled T2DM patients without atherosclerotic manifestations.

Methods: This is a post-hoc comparative analysis of echocardiographic DD data, metabolic and subclinical inflammation markers at sitagliptin initiation and after 12 months.

Results: 64 consenting patients were 45.3% men, 57.88 years old, with a history of T2DM of 5.88 years, treated with metformin prior to enrolment. At baseline, 18 patients had normal diastolic function, 38 had DD (2^{nd}/3^{rd} degree in 7 cases), while DD degree was “indeterminate” in 8 cases. Mean LVEF was 66.92±9.17, IVS 11.40±1.7mm, E/A 1.12±0.47, E/e’ 6.63±2.09, EDT 191.73±40.62ms, IVRT 101.17±18.14 ms, LAVi 44.06±12.11 ml/m^2, LA 57.15±4.90 mm. The mean baseline metabolic and inflammation values were: HbA_{1c} 7.88±0.67%, glycemia 173.59±44.58 mg/dL, LDL-cholesterol 104.73±42.77 mg/dL, triglycerides 211.55±92.26 mg/dL, HOMA-IR 6.28±4.44, IL-6 3.14±2.34 pg/mL, hsCRP 8.97±10.26 mg/dL. After 12 months, 24 patients had normal diastolic function, 20 had DD (2^{nd}/3^{rd} degree in only 3 cases), and DD was “indeterminate” in 20 cases. The only statistically significant DD-relevant modification was for IVRT (105.16±18.53ms, p=0.019), while several metabolic and inflammation parameters improved substantially (HbA_{1c} 7.38±0.69% and hsCRP 5.13±4.82 mg/dL at p<0.001, HOMA-IR 4.46±3.05 and glycemia 159.44±34.22 mg/dL at p<0.05).

Conclusions: The addition of sitagliptin to metformin treatment of uncontrolled T2DM patients without atherosclerotic manifestations significantly improved the patients’ metabolic and inflammation status, while proving to be safe for cardiac function.

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193 / #414

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

PERIPHERAL ARTERY DISEASE PARTICULARITIES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: This study aimed to evaluate the particularities of peripheral artery disease (PAD) in patients with type 2 diabetes mellitus (T2DM).

Methods: The prospective study included 254 PAD patients admitted consecutively in 2nd Internal Medicine Department and Cardiology Department, Emergency Clinical Hospital “Sf. Spiridon” Iasi. This study included patients with intermittent claudication and an ankle-brachial index value <0.9, and/or previous lower extremity arterial interventions. T2DM was defined as fasting blood glucose levels ≥126 mg/dL, HbA1c values ≥6.5%, or current hypoglycemic medication used for DM control. The database included demographic, clinical and paraclinical PAD patients data.

Results: The group of PAD patients with DM presented the following particularities: urban areas (51.7%; p=0.028), obesity (48.1% vs 14%; p=0.001), fibrinogen (65.4% vs 54.2%; p=0.049), triglycerides (43.3% vs 21.3%; p=0.001), C-reactive proteine (52.6% vs 45.3%; p=0.025), cystatin C (83.7% vs 70.7%; p=0.015) and diastolic dysfunction (67.3% vs 55.3%; p=0.037). The areas under the curve for body mass index, HbA1c and triglycerides were higher than 0.7 and were highly statistically significant (p<0.05).

Conclusions: Systematic screening for peripheral arterial disease and prompt targeted treatment initiation are essential for cardiovascular secondary active prevention in patients with type 2 diabetes mellitus.

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194 / #387

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

ADVANCED GLYCATION END PRODUCTS MEASURED BY SKIN AUTOFLUORESCENCE CORRELATE WITH ARTERIAL STIFFNESS INDEPENDENT OF GLYCAEMIC STATUS AND CARDIOMETABOLIC RISK IN SINGAPORE

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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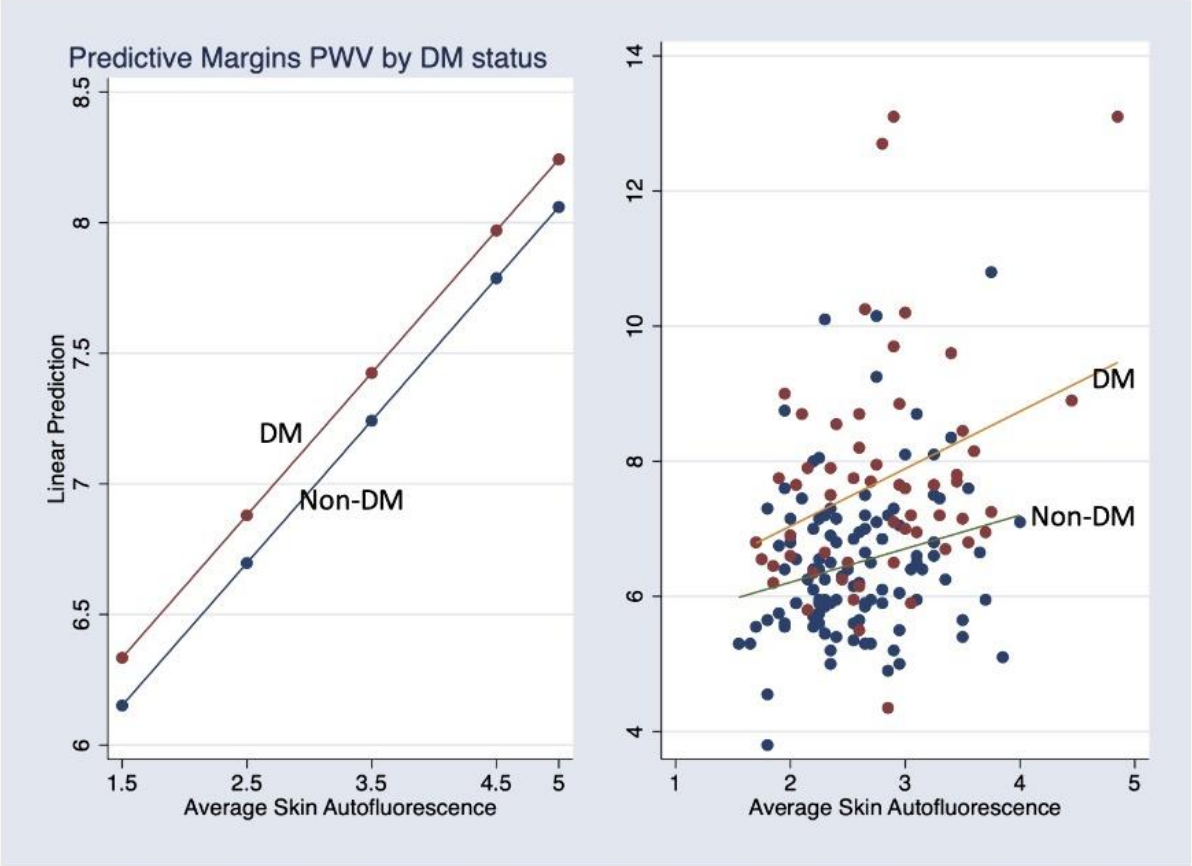
Background and Aims: Skin autofluorescence (SAF), a marker of advanced glycation end products (AGE), is impacted even before diagnosis of T2DM and correlates with arterial stiffness, but data is limited in Asia. We aim to study the correlation of SAF with arterial stiffness in patients at high risk for diabetes and recent diabetes diagnosis in Singapore's multi-ethnic population.

Methods: We recruited individuals at high risk of T2DM, n=138(70%) and those with T2DM diagnosed within past 5 years, n=58(30%). Glycaemic status was determined by the 75-gram oral glucose tolerance test. Arterial stiffness was measured as carotid femoral pulse wave velocity (cf-PWV) using Sphygmocor and SAF was measured using the AGE reader. Multivariable linear regression models were used to evaluate associations between cf-PWV and SAF adjusted for glycaemic status and other cardiometabolic risk factors. All analysis was conducted using Stata version 16.0.

Results: Patient characteristics: Mean age: 46.6 (SD:9.4) years; Male: 74 (37%). Sphygmocor-measured cf-PWV and SAF were higher in participants with T2DM when compared to non-DM; cf-PWV (m/s): non-DM: 6.5(1.1) versus T2DM: 7.7(1.7), p<0.001; SAF: Non-DM: 2.6(0.5) versus DM: 2.8(0.7), p=0.015. Multiple linear regression analysis showed that SAF is a significant predictor of arterial stiffness independent of diabetes status (beta=0.26, p<0.001). This association remains significant after adjustment for age, sex, ethnicity, BMI, and systolic blood pressure (beta=0.23, p<0.001) (Figure

1).

Figure 1: Predictive margins of PWV for SAF in the multivariable model adjusting for age, sex, ethnicity, BMI, and systolic blood pressure and scatter plot showing the associations in the DM and NonDM status



Conclusions: SAF correlates with arterial stiffness independent of glycaemic status and cardiometabolic determinants. The utility of SAF as a population based screening tool for macrovascular risk stratification needs to be evaluated longitudinally in larger cohorts.

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195 / #18

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

RELATIONSHIP BETWEEN ALBUMINURIA AND COMPENSATION OF GLYCEMIC AND LIPID PROFILES IN TYPE 2 DIABETIC PATIENTS

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Chronic kidney disease occurs in 20–40% of patients with diabetes. It can progress to end-stage renal disease and necessary dialysis or kidney transplantation. Chronic kidney disease risk progression, frequency of visits are defined according to the levels of glomerular filtration rate and albuminuria. **Aim.** To analyze the connection between albuminuria and glycated haemoglobin (HbA1c) and lipid profile in patients with type 2 diabetes mellitus (DM).

Methods: 96 patients with type 2 DM treated in the hospital in case of planned admission are included in our study. Among them 69% were men and 31% were women. They are 55.84±10.3 years old. The duration of type 2 DM was 6 years old in general. The level of total cholesterol was 5.6- 7.9 mmol/l; β-lipoproteins 69.4 units. Inclusion criteria: overweight, osteochondrosis, autoimmune thyroiditis, chronic cholecystitis and pancreatitis in remission. There was the determination of protein in urine and glomerular filtration rate by Rebergs test. Photocolorimetry was used for HbA1c assessment. The results were analyzed statistically by SPSS 21, Microsoft Excel. Pearson criterion was used for definition the relationship between albuminuria and HbA1c.

Results: The level of albuminuria was 0.05g/l, glomerular filtration rate 81.6 ml/min. HbA1c–8.6%. All patients have diabetic nephropathy connected with reduction or compensatory increase of glomerular filtration rate and presence of albumin or protein in urine. The Pearson coefficient of correlation between albuminuria and HbA1c was 0.08.

Conclusions: The positive relathionship between albuminuria with HbA1c and lipid profile in patients with type 2 DM is associated with significant role of diabetic decompensation manifested as increased HbA1c in the diabetic nephropathy progression.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

RENAL BIOCHEMICAL PROFILE OF HYPERTENSIVE DIABETIC PATIENTS WITH OVERWEIGHT

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Comorbidity is presence of several diseases, connected by the joint pathogenetic mechanism. Decompensation of diabetes mellitus type 2 (T2DM), duration of the disease, level of proteinuria, overweight and arterial hypertension (AH) play the main role in development and progress of diabetic nephropathy. Timely evaluation of biomarkers of kidneys impairment at comorbid course of T2DM may improve the stratification of the risk for development or progress of diabetic nephropathy. The present study aimed to analyze renal panel data in blood biochemical profile of type 2 diabetic patients with comorbid overweight and AH.

Methods: 579 medical records of type 2 diabetic patients, which were treated at endocrinological department in 2018-2019 years were analyzed.

Results: The analysis of renal panel data in blood biochemical profile of type 2 diabetic patients with comorbid overweight and AH found out that only serum levels of urea and uric acid were statistically different in the patients with only T2DM and comorbid course of T2DM. Herewith the maximal changes were established for serum uric acid level, which in type 2 diabetic patients with comorbid overweight exceeded by 175.9% data of only T2DM patients. Moreover, it was established a significant direct relationship between serum uric acid level and body mass index(BMI) and dyslipidemia in both type 2 diabetic patients - with comorbid overweight and with comorbid overweight and AH.

Conclusions: Our retrospective study indicates that serum uric acid level, which is an independent predictor of development and progression of chronic kidney disease, is markedly elevated and associated with BMI and dyslipidemia in type 2 diabetic patients with comorbid overweight and AH.

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197 / #1155

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

LIPID PROFILE ASSESSMENT AS A FACTOR OF DIABETIC NEPHROPATHY PROGRESSION

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Diabetes mellitus (DM) is the noninfectious epidemic nowadays. Type 2 DM is defined in 90–95% of all DM. Presence of albuminuria is the important marker of cardiovascular complications in diabetic patients. Chronic kidney disease (CKD) occurs in 20–40% of patients with diabetes. It can progress to end-stage renal disease and necessary dialysis or kidney transplantation. To analyze the levels of kidneys dysfunction such as albuminuria, filtration and the correction of them is reasonable for further reduction of CV-risk in diabetic patients. **Aim.** To analyze the connection between albuminuria and glycated haemoglobin (HbA1c) and lipid profile in patients with type 2 DM.

Methods: clinical, anthropometric, biochemical, instrumental, statistical.

Results: The level of haemoglobin was (138.27±12.8)g/l. Anemia was absent in all patients. In biochemical blood analysis the level of urea was (6.22±1.6)mmol/l; creatinine (85.92±18.5)mcmol/l; total cholesterol 5.6mmol/l; β-lipoproteins 69.4units. The level of systolic BP was (127.54±5.5)mm Hg, diastolic (83.31±3.0)mm Hg. Retinopathy, nephropathy was present in all persons. Neuropathy was defined in 90% of patients. The heart rate was (75.77±9.0)per minute. Glucose in urine was determined in 15(58%) of patients. The level of albuminuria was 0.05g/l, GFR 81.6ml/min; reabsorption (98.23±0.6)%. The range of HbA1c was 8.6%. All observed patients have diabetic nephropathy connected with compensatory increase of GFR. LV hypertrophy with diastolic dysfunction and preserved ejected fraction was observed during ultrasonography in 7(27%) patients.

Conclusions: The positive relationship between lipid profile, albuminuria, glycosuria and HbA1c in patients with type 2 DM is associated with the significant role of diabetic decompensation manifested as HbA1c increased in the diabetic nephropathy progression.

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198 / #1163

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

VISFATIN AS A POTENTIAL CARDIOMETABOLIC RISK FACTOR IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Recently, visfatin has been presented as a predictor of cardiometabolic diseases. The objective of our study was to assess the impact of visfatin on certain clinical, metabolic and atherogenic parameters in women with polycystic ovary syndrome (PCOS).

Methods: A prospective, comparative study including 29 insulin resistant and 47 non-insulin resistant women with newly diagnosed PCOS. In all the participants the following measurements and laboratory tests were performed: weight, height, waist and hip circumferences, oral glucose tolerance test (OGTT) with blood samples for glucose (GLU) and insulin (IRI) obtained 0, 60 and 120 minutes after oral 75 g glucose administration, serum levels of total cholesterol (TC), HDL-cholesterol (HDL-C), triglycerides (TG) and visfatin; systolic (SBP) and diastolic blood pressure (DBP). Body mass index (BMI), waist-to-hip ratio (WHR), homeostasis model of insulin resistance index (HOMA-IR), Matsuda index, LDL-C (Friedewald formula) and atherogenic index of plasma (AIP) were calculated. We determined a presence of IR as HOMA-IR≥2.5. Using SPSS, version 21.0 for Windows, we performed both comparative and correlation analysis.

Results: As compared to non-insulin resistant women with PCOS, those with IR showed significantly higher values of weight, BMI, waist and hip circumferences; GLU 0', 60', 120' and IRI 0', 60', 120'; TG, AIP, serum visfatin and DBP. Visfatin was found to correlate positively with DBP and negatively with HDL-C. There was an inverse relationship between visfatin and Matsuda index.

Conclusions: With our findings we want to emphasize the potential role of visfatin in the development of cardiometabolic syndrome in patients with PCOS.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

LIPID MANAGEMENT IN A SAMPLE OF PHYSICIANS INVOLVED IN TYPE 2 DIABETES CARE IN ARGENTINA

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Lipid disorders are frequent in patients with type 2 diabetes (T2D). Guidelines recommend lipid lowering treatment in different clinical scenarios. This study aimed to evaluate how physicians involved in treating patients with T2D manage their dyslipidemias.

Methods: A 24-item survey was carried out during a specific scientific meeting to evaluate the degree of agreement with different lipid-lowering indications. A descriptive analysis was performed.

Results: 302 physicians completed the survey. 60% were diabetes specialists. 49% agree to start statins independently of low-density lipoprotein cholesterol (LDL-C) values. When a LDL-C value was consider to initiate statins, 55% and 24,5% used > 100 mg/dL and > 130 mg/dL levels, respectively. In patients with high cardiovascular risk, 3% combined high dose of atrovastatin or rosuvastatin with ezetimibe. After reaching LDL-C goals, 16% stop o reduced statin dose. In patients on statins with triglyceride levels (TG) > 200 mg/dL but not reaching LDL-C goals, 53% agree with adding ezetimibe, and 47% start fibrates. 51%, 41% and 8% use an LDL-C goal of < 55, <70 and <100 mg/dL in patients on secondary preventions. 47% start treatment with fibrates with TG levels of < 500 mg/dL. When low LDL-C levels are achieved, half of the respondents reduce the statin dose because they don't consider it safe. 61% use omega 3 (not icosapent ethyl) to reduce LDL-C, TG, or cardiovascular risk.

Conclusions: We observed that in a group of physicians who attend a specific scientific meeting, there are still issues to improve knowledge concerning dyslipidemias management in patients with T2D.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

200 / #24

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

CORRELATIONS BETWEEN SERUM AFAMIN AND LIPID PARAMETERS IN OBESE TYPE 2 DIABETIC PATIENTS

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Afamin is mainly produced by hepatocytes and play a crucial role in vitamin E metabolism. Its elevated level in the bloodstream is closely associated with obesity, metabolic syndrome and type 2 diabetes. The aim of our study was to measure serum afamin level and their relationship with carbohydrate and lipid parameters in a morbid obese diabetic and non-diabetic cohort.

Methods: One-hundred non-diabetic obese (NDO) and thirty-eight age, gender and BMI matched type 2 diabetic patients (T2DM) were enrolled. We compared their data with thirty-two healthy controls. Afamin was measured with ELISA and lipoprotein subfractions were analyzed by Lipoprint® gelelectrophoresis.

Results: Afamin was significantly elevated in T2DM group compared to NDO and controls (102.4±19.7 vs. 81.1±18.8 vs. 47.6±8.5 µg/ml, p<0,001). Afamin showed positive correlations with waist circumference (p<0.001), fasting glucose (p<0.001), Hemoglobin A1c (p<0.001), HOMA-IR (p<0.001) and triglyceride levels (p<0.01). Studying LDL subfractions, large LDL and small-dense LDL subfractions showed positive correlations with afamin (p<0.001 and p<0.001, respectively); while there was a negative correlation between mean LDL size and afamin (p<0.001). A negative correlation was found between afamin and large HDL subfraction (p<0.001), while positive correlation observed between afamin and small HDL (p<0.001). All correlation was observed in overall patients (n=170), as well as in T2DM+NDO (n=138) group.

Conclusions: Afamin showed marked associations with carbohydrate parameters and lipoprotein subfractions, therefore determination of afamin level might be an excellent additional biomarker in assessing the condition of diabetic patients. Acknowledgement: This presentation was supported by NKFIH – PD124126 and K142273 projects.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

201 / #1494

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

METABOLIC ADVERSE EVENTS OF MULTITARGET KINASE INHIBITORS: A SYSTEMATIC REVIEW

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: AIM Multitargeted kinase inhibitors (MKIs) are used for the treatment of several cancers. By targeting multiple signaling pathways, MKIs have become cornerstones of the oncologic treatment. Although their use leads to important results in terms of survival, treatment with MKIs can determine important side effects the clinician must be aware of. Among those, arterial hypertension, mucositis and skin lesions are universally reported, while data about metabolic alterations are scarce. In our review, we focused on glucose and lipid alterations in MKI-treated patients.

Methods: METHODS We searched for articles, published between January 2012 and December 2022, evaluating the effects on lipid and glucose metabolism of four MKIs (Cabozantinib, Lenvatinib, Sorafenib and Vandetanib) in adult patients with cancer. We focused on drugs approved for thyroid malignancies, since a worse metabolic control may potentially impact life expectancy, due to their better overall survival rate.

Results: RESULTS As for glucose metabolism, the majority of the studies reported elevation of glucose levels (prevalence: 1-17%) with different grades of severity, including death. As for cholesterol, 12 studies reported worsening or new-onset hypercholesterolemia (prevalence: 4-40%). Finally, 19 studies reported different grades of hypertriglyceridemia (prevalence: 1-86%), sometimes leading to life-threatening events.

Conclusions: CONCLUSIONS Despite some inherent limitations, our analysis may cast light upon some of the MKIs metabolic disorders that can impact on patients' health, especially when long-term survival is expected. Future clinical trials should consider routine assessment of glucose and lipid levels, because underdetection and underreporting of alterations can lead to the overlooking of important adverse events.

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202 / #1000

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

MRC1 DEFICIENCY REWIRES BONE MARROW AND CIRCULATING IMMUNE PROFILE IN DIET-INDUCED OBESITY

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: The mannose receptor (Mrc1) is a C-type lectin receptor expressed on immune cells and sinusoidal endothelial cells (SECs) of different tissues, including the bone marrow (BM). Since obesity triggers medullary reprogramming affecting systemic immune and metabolic phenotype, aim of our study was to investigate the impact of *Mrc1* deficiency on BM response under diet-induced obesity.

Methods: *Mrc1*$^{-/-}$ and WT male mice were fed a high fat diet (HFD, 45% Kcal/diet) for 20 weeks. Weight gain and glucose and insulin tolerance were evaluated. Extensive flow cytometry profiling and histological and proteomic analyses of tissues of interest were performed.

Results: After 20 weeks of HFD feeding, *Mrc1*$^{-/-}$ mice exhibited a BM reprogramming with reduced myeloid progenitors and mature cells ($p<0.05$), paralleled with an increase in BM adipocytes ($p<0.01$) compared to controls. Concordantly, blood inflammatory myeloid cells decreased in *Mrc1*$^{-/-}$ mice compared to controls, in line with a reduced infiltration of macrophages in visceral adipose tissue ($p<0.05$) and liver ($p<0.01$). Furthermore, lack of the mannose receptor led both to decreased hepatic steatosis (*Mrc1*$^{-/-}$ 3.370%±2.610 vs WT 7.970%±1.891, mean ±SEM; $p<0.05$) and downregulation of pathways involved in liver dysfunction, assessed respectively by liver histological and untargeted proteomic analysis. This shift was confirmed by improved glucose and insulin response and reduced weight gain following HFD feeding in *Mrc1*$^{-/-}$ compared to WT mice.

Conclusions: Our data suggest that in obesity *Mrc1* deficiency leads to improved BM-release of immune cells and dampened systemic inflammatory response, in association with protection from obesity-driven dysmetabolism.

91ST EAS CONGRESS
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203 / #483

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

RISK FACTORS FOR THE DEVELOPMENT OF DIABETES AMONG PATIENTS WITH LOW TO MODERATE INTENSITY STATIN THERAPY

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Statins have been used widely due to their established benefits in cardiovascular diseases. However, a positive association between statin therapy and the risk of diabetes has been emerged, especially in patients with intensive statin therapy. The aim of this study was to estimate the incidence rate of diabetes in people with low to moderate intensity statin therapy.

Methods: We enrolled 1361(atorvastatin 10mg: 769, rousuvastatin 10mg: 300, pitavastatin 2mg: 292) patients who have taken statins for more than 2 years. We excluded the patients with initial fasting blood sugar(FBS)>110 mg/dL, diabetes, chronic renal insufficiency, prior history of statin therapy, and new onset diabetes who had been on statin for less than 2 years. We retrospectively analyzed factors affecting the development of diabetes after statin therapy. Diabetes was defined as FBS ≥126 mg/dL or HbA1c ≥ 6.5%.

Results: The mean age was 61.8 years, and the mean duration of follow-up was 4.2 years. Overt diabetes developed in 48 patients (32(4.2%) in atorvastatin 10mg, 8(2.7%) in rosuvastatin 10mg and 8 patients(2.7%) in pitavastatin 2mg). The incidence of diabetes was higher in atorvastatin 10mg group compared with other groups but there was no statistical significance(p=0.351). It is identified from logistic regression model that BMI (OR 1.129, 95% CI 1.027-1.242, p=0.012), initial FBS (OR 1.073, 95% CI 1.027-1.121, p=0.001) and TG (OR 1.004, 95% CI 1.001-0.007, p=0.005) were associated with the development of diabetes.

Conclusions: BMI, initial FBS and TG levels were positively associated with the risk of developing diabetes in patient with low to moderate intensity statin therapy.

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204 / #102

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

BIOMARKERS OF HEART FAILURE AND EPICARDIAL ADIPOSE TISSUE IN TYPE 2 DIABETES MELLITUS. EFFECT OF GLYCAEMIC CONTROL

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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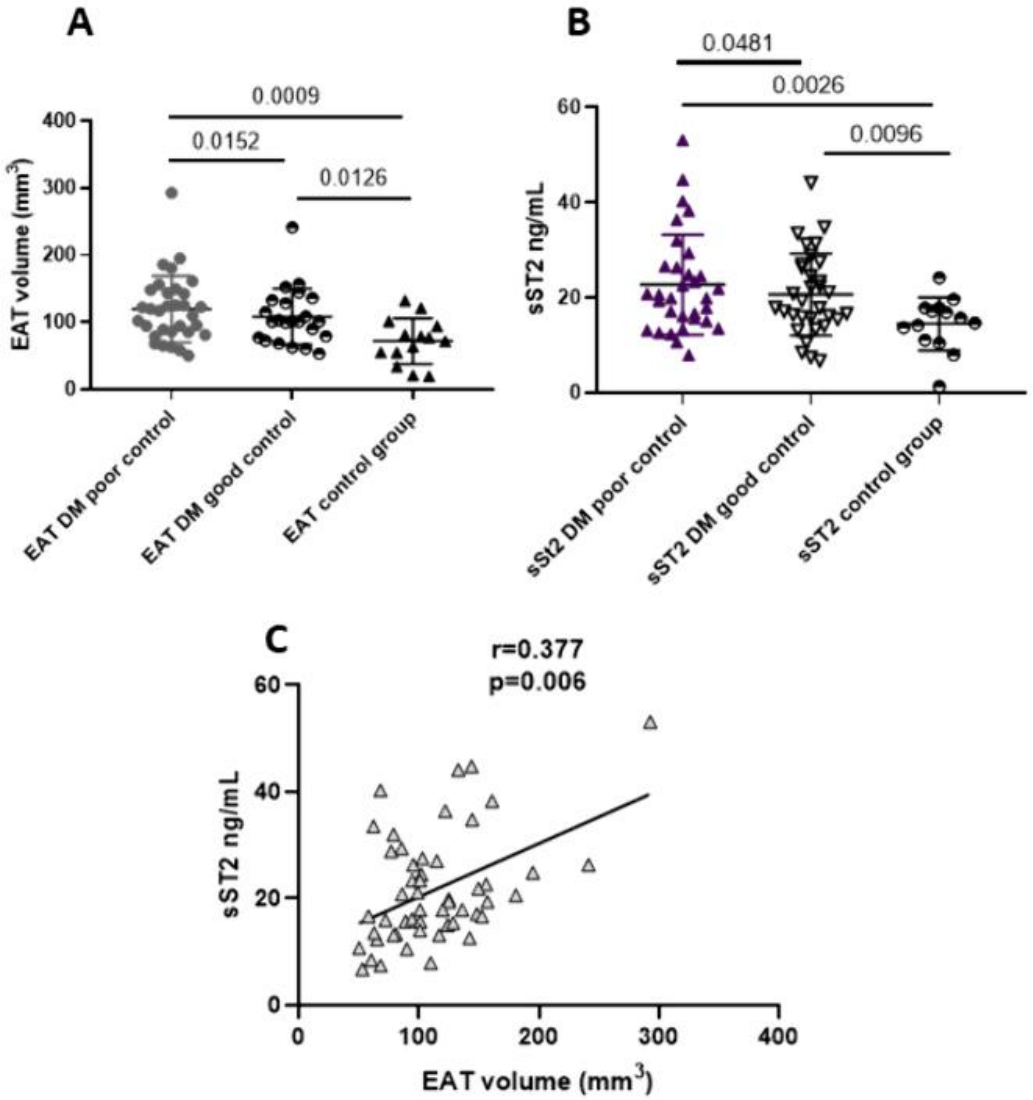
Background and Aims: Type II Diabetes mellitus (T2DM) patients accumulate excessive epicardial adipose tissue (EAT). Increased EAT volume has been associated with HF risk in these patients. EAT is quantified by image analysis such as MDCT or MRI, but there are no reliable plasma biomarkers to evaluate the accumulation of EAT. We aimed to evaluate HF-related biomarkers in T2DM patients in response to glycaemic control and its association with EAT volume, including NT-proBNP, growth differentiation factor 15 (GDF15), troponin T (TnT), galectin-3 and soluble form of the tumorigenicity suppressor factor (sST-2).

Methods: EAT volume was measured by MDCT in 32 T2DM patients, before and after glycaemic control, and 14 in healthy controls. Biomarkers were quantified by commercial methods in plasma samples. Differences between groups were tested using nonparametric tests for paired (Wilcoxon) and unpaired (U Mann-Whitney) samples. Association between parameters was tested with the Spearman test.

Results: EAT volume was higher in T2DM patients than in controls and decreased with glycaemic optimization (Figure 1A). No differences between groups were found in NT-proBNP and TnT. Galectin-3, GDF-15, and sST2 values were significantly higher in patients than in controls. Glycaemic optimization significantly decreased sST2 levels (Figure 1B). Significant correlations were found between EAT volume and GDF-15 (r=0.49, p-value=0.0003) and sST2 (r=0,377, p-value=0,006) in T2DM patients (Figure

1C).



Conclusions: Plasma sST2 and GDF-15 are increased in T2DM patients and correlate with EAT volume. After glycaemic control, sST-2 plasma levels and EAT volume decrease, suggesting that sST2 may be a biomarker to evaluate EAT volume.

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205 / #5

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

THE MICROCIRCULATORY ENDOTHELIAL FUNCTION WAS A MORE SENSITIVE METHOD IN EVALUATING THE RISK ASSESSMENT OF CORONARY ARTERY DISEASE IN SUBJECTS WITH TYPE2 DIABETES.

POSTER ON BOARD: AS03.03 DIABETES, INSULIN SENSITIVITY AND RESISTANCE

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Background and Aims: Background: Several studies demonstrated that endothelial function is impaired in patients with T2DM, but no study evaluated vascular parameters in patients with T2DM trough a combined analysis of macro and micro-endothelial function and arterial stiffness indexes. In addition, the difference in vascular parameters between T2DM patients with CAD and without CAD remains unknown. We assessed whether coronary artery disease is associated with impairment of peripheral endothelial function and arterial stiffness indexes in patients with T2DM.

Methods: We measured vascular function in 219 T2DM subjects (age 68±10 years), including 147 subjects with CAD (CAD group) and 72 subjects without CAD (control group). Flow mediated vasodilatation (FMD)indicating endothelial function in a conduit artery was measured by ultrasound using a semi-automatic device: UNEXEF18G (UNEX Co. Nagoya, Japan). Reactive hyperemia index (RHI) indicating peripheral endothelial function and Augmentation index (AI) indicating arterial stiffness were measured by peripheral arterial tonometry (EndoPAT 2000). Vascular function tests were measured on the same day.

Results: RHI and AI was significantly impaired in CAD group (RHI: 2.0±0.7 vs.1.7±0.5 P=0.012, AI: 30.2±18.1 vs.22.1±19.1 P=0.043), however FMD had no deference in the two groups. Logistic regression analysis revealed that RHI (odds ratio: 0.44, 95% confidence interval: 0.21-0.94) was an independent predictor for CAD in subjects with T2DM.

Conclusions: RHI, an acknowledged marker of microcirculatory endothelial function was a more sensitive method in evaluating the risk assessment of CAD in subjects with T2DM.

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206 / #1344

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.04 Adipose tissue homeostasis*

TREM2 MACROPHAGES IN ADIPOSE TISSUE AND CARDIOVASCULAR RISK

POSTER ON BOARD: AS03.04 ADIPOSE TISSUE HOMEOSTASIS

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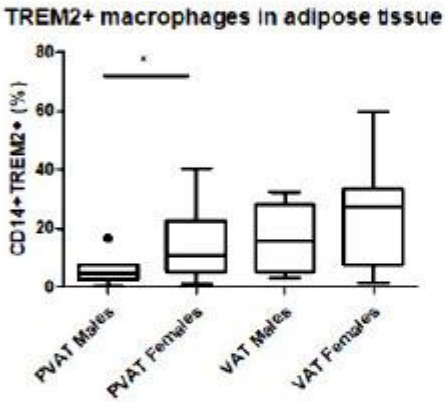
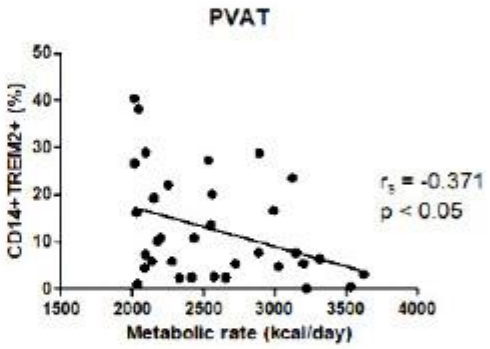
Background and Aims: Apart from brain and atherosclerotic plaques, the presence of lipid associated TREM2 macrophages was previously confirmed in obese human adipose tissue. TREM2 serves as a sensor of extracellular lipids and is involved in phagocytosis, regulation of inflammation and adipogenesis. However, data regarding the presence of TREM2 macrophages in healthy adipose tissue from different depots are scarce. Our aim was to analyze the proportions of TREM2 macrophages in adipose tissue and their relationship to the presence of cardiovascular risk factors in a relatively healthy population of living kidney donors (LKDs).

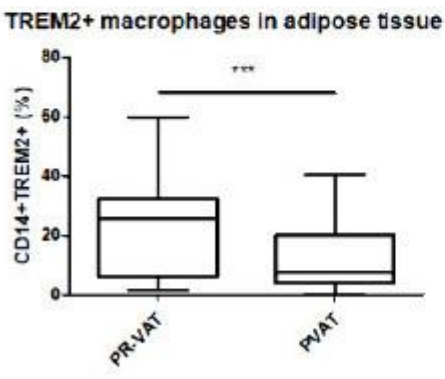
Methods: Sex, medication, BMI and age of LKDs were recorded. Lipid profile was measured in plasma. Body composition was assessed by bioelectrical impedance analysis. Macrophage proportions were analyzed by flow cytometry in visceral perirenal (PR-VAT) and perivascular (PVAT) adipose tissue.

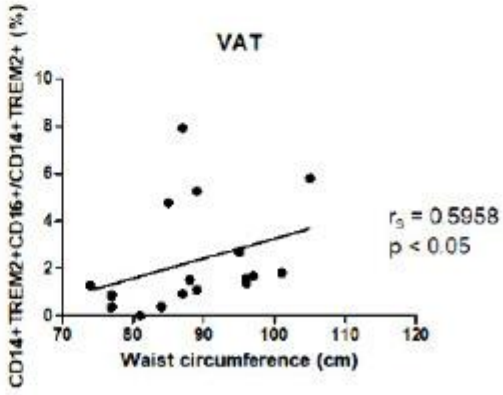
Clinical characteristics of LKDs (N = 38)?	Mean	SD
Age (years)	52,01	9,85
Waist circumference (cm)	91,74	9,92
BMI (kg/m2)	26,22	2,58
Metabolic rate (kcal/day)	2580,78	494,96
Body fat (%)	30,87	8,27
Visceral adiposity index	2,29	1,28
TC (mmol/l)	4,81	0,99
LDL-C (mmol/l)*	2,92	0,84
HDL-C (mmol/l)	1,25	0,29
TG (mmol/l)	1,55	0,66
Male sex (N; %)	14	36,84

* calculated according to Martin et al.
? N = 37 for waist circumference, metabolic rate, body fat, VAI and lipid parameters









Results: W

e included 38 LKDs in the final analysis (18 paired samples). Proportion of TREM2+ macrophages was significantly higher in women and also in PR-VAT in comparison to PVAT. Interestingly, there was a negative correlation between the proportion of TREM2 in PVAT and metabolic rate (kcal/day). The minor population of TREM2+CD16+ macrophages correlated positively with LDL-C levels in PVAT. The presence of CD16 in TREM2+ cells was positively associated with waist circumference in VAT.

Conclusions: We analyzed the proportion of TREM2+ macrophages in a relatively healthy population of LKDs. TREM2+ subpopulation was relatively prevalent. Both, adipose tissue location and sex, influenced the TREM2+ proportions. Further studies including more patients need to be done to confirm the relationship between TREM2+ macrophages and cardiovascular risk factors.

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207 / #904

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.04 Adipose tissue homeostasis*

ASSESSMENT OF THE RATIO OF BROWN AND WHITE ADIPOSE TISSUE ACCORDING TO MAGNETIC RESONANCE SPECTROSCOPY IN OBESE PATIENTS

POSTER ON BOARD: AS03.04 ADIPOSE TISSUE HOMEOSTASIS

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Background and Aims: to evaluate the ratio of white and brown adipose tissue using magnetic resonance spectroscopy (MRS) in patients with cardiovascular disease (CVD), obesity and type 2 diabetes mellitus (T2DM).

Methods: The study included 72 patients with a body mass index (BMI) of more than 30 kg/m^2 and the presence of CVD. All patients underwent MRS of adipose tissue of the supraclavicular region, liver and subcutaneous adipose tissue of the neck.

Results: In the group with T2DM (27 patients), there was a higher level of BMI (p=0.02); metabolic syndrome (p<0.001), coronary artery disease (p=0.03) and coronary artery stenting (p=0.04) were more common. Liver steatosis (hepatic triglycerides more than 5.6%) occurred in 70.4% of patients with T2DM and in 57.7% without T2DM (p=0.61). There were no statistically significant differences in the levels of adiponectin, resistin, and leptin as well as in the level of triglycerides in the adipose tissue of the supraclavicular region, liver and neck pancreas in these groups (Table 1). After dividing patients depending on the class of obesity, patients with class 3 obesity had naturally higher BMI and waist circumference (p<0.001), as well as leptin levels (46.8 [45.0;67.7] versus 20.4 [14.3;29.2] ng/ml p<0.001). There was found no statistically significant difference in triglyceride levels in the supraclavicular region, liver, and subcutaneous fat of the neck in these groups after MRS (Table 2).

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Table 1. Characteristics of patients depending on the presence or absence of type 2 diabetes

Parameters	T2DM+ n=27	T2DM– n=45	p
Age, years	57±11	51±12	0,56
Men	11 (40,8 %)	19 (42,2 %)	0,94
Weight, kg	114,4±24,0	103,9±20,2	0,16
BMI, kg/m^2	39±7,4	35,3±5,2	**0,02**
Waist circumference, cm	118,0±16,4	109,1±15,7	0,97
Smoking	7 (25,9 %)	11 (24,4 %)	0,91
Hypertension	24 (88,8 %)	36 (80 %)	0,77
Coronary heart disease	15 (55,6 %)	9 (20 %)	**0,03**
Myocardial infarction	2 (7,4 %)	3 (6,7 %)	0,91
Coronary artery bypass surgery	2 (7,4 %)	0 (0 %)	0,08
Coronary artery stenting	10 (37 %)	5 (11,1 %)	**0,04**
Atherosclerosis of the carotid arteries	11 (40,7 %)	10 (22,2 %)	0,22
Metabolic syndrome	15 (55,6 %)	2 (4,4 %)	**<0,001**
Liver steatosis	19 (70,4 %)	26 (57,7 %)	0,61
Laboratory indicators			
Adiponectin, ng/ml	4,53 [3,68;10,12]	5,32 [4,05;8,2]	0,97
Leptin, ng/ml	29,7 [18,7;44,45]	36,2 [16,07;50,16]	0,64
Resistin, ng/ml	5,6 [4,44;6,99]	5,84 [4,35;7,86]	0,62
Magnetic resonance spectroscopy			
Supraclavicular region, percentage of triglycerides	0,95±0,02	0,95±0,02	0,09
Subcutaneous fat, percentage of triglycerides	0,98±0,01	0,98±0,01	0,1
Liver, percentage of triglycerides	0,09 [0,05;0,21]	0,07 [0,04;0,12]	0,3

Notes: Data are presented as M±SD, where M is the mean; SD is the standard deviation, and n (%). T2DM – type 2 diabetes mellitus, BMI - body mass index

Table 2. Characteristics of patients depending on the degree of obesity

Parameters	Obesity (class 1) n=31	Obesity (class 3) n=19	p
Age, years	52±10	52±12	0,42
Men	12 (38,7%)	7 (36,8%)	0,93
Weight, kg	90,5±12,6	131,9±17,9	0,08
BMI, kg/m^2	31,1±2,1	45,1±4,3	**0,001**
Waist circumference, cm	101,4±13,3	127,4±14,0	**0,001**
Smoking	6 (19,4%)	6 (31,6%)	0,45
Hypertension	23 (74,2%)	18 (94,7%)	0,57
Coronary heart disease	10 (32,3%)	7 (36,8%)	0,82
Myocardial infarction	2 (6,5%)	1 (5,3%)	0,87
Bypass coronary arteries	1 (3,2%)	1 (5,3 %)	0,73
Coronary artery stenting	7 (22,6 %)	3(15,8 %)	0,63
Atherosclerosis of the carotid arteries	9 (29 %)	5 (26,3 %)	0,88
Metabolic syndrome	6 (19,4 %)	9 (47,4%)	0,13
Type 2 diabetes mellitus	12(38,7%)	11(57,9%)	0,43
Laboratory indicators			
Adiponectin, ng/ml	6,83 [4,4;9,5]	5,16 [3,7;10,7]	0,71
Leptin, ng/ml	20,4 [14,3;29,2]	46,8 [45,0;67,7]	**0,0002**
Resistin, ng/ml	5,7 [5,0;7,5]	5,7 [4,7;7,2]	0,76
Magnetic resonance spectroscopy			
Supraclavicular region, percentage of triglycerides	0,94±0,02	0,95±0,02	0,44
Subcutaneous fat, percentage of triglycerides	0,98±0,01	0,98±0,01	0,9
Liver, percentage of triglycerides	0,06 [0,04;0,13]	0,09 [0,07;0,19]	0,13

Notes: Data are presented as M±SD, where M is the mean; SD is the standard deviation, and n (%). BMI - body mass index.

Conclusions: The presence or absence of T2DM, as well as the class of obesity, does not affect the level of triglycerides in adipose tissue according to the results of MRS.

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208 / #1318

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.04 Adipose tissue homeostasis*

THE RELATIONSHIP OF EPICARDIAL ADIPOSE TISSUE AND METABOLIC SYNDROME

POSTER ON BOARD: AS03.04 ADIPOSE TISSUE HOMEOSTASIS

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Background and Aims: Visceral obesity is a key link in the metabolic syndrome and can affect the development of cardiovascular diseases. The aim of the study was to identify the clinical, laboratory and instrumental characteristics of patients with coronary artery disease, to analyze adverse cardiovascular events after coronary bypass surgery, according to the thickness of the epicardial adipose tissue (EAT).

Methods: The study included 178 patients who underwent coronary bypass surgery. The median values of the thickness of the EAT was 0.4 cm. The patients were divided into 2 groups: Group 1 — epicardial fat < 0.44 cm (n=84) and Group 2 — epicardial fat ≥0.44 cm (n=94).

Results: The frequency of metabolic syndrome in Group 1 was 59.5%, while in Group 2 — 74.5% (p=0.017). The thickness of the EAT correlated with blood glucose (r=0.28, p=0.003), BMI (r=0.27, p=0.010), waist circumference (r=0.26, p=0.001). End-diastolic volume of the left ventricle (p=0.016), stroke volume (p=0.014), thickness of the interventricular septum (p=0.010), mass of the left ventricular myocardium (MMLV) (p=0.048), left ventricular myocardial mass index (IMMLV) (p=0.035) were higher in the group with a higher content of EAT. The metabolic syndrome was a significant predictor of the EAT thickness.

Conclusions: The EAT thickness is associated with the metabolic syndrome and its components.

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209 / #428

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.04 Adipose tissue homeostasis*

ASSOCIATION OF VASPIN WITH LIPID AND GLYCEMIC PROFILES IN HYPERTENSIVE PATIENTS WITH OBESITY AGED 18-45 YEARS.

POSTER ON BOARD: AS03.04 ADIPOSE TISSUE HOMEOSTASIS

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Background and Aims: A positive correlation between hypertension (H) and obesity (OB) was demonstrated even in young people. Adipose tissue synthesizes a huge amount of hormonal substances that determine violations of metabolism with the development of endocrine and cardiovascular pathology.

Methods: To establish the association of the glycemic, lipid status and vaspin depending on the presence of OB were investigated 76 individuals 18 to 45 y.o. with H. The gr. 1 with AH - 30 patients without OB. Gr. 2 - 34 patients with overweight or OB. Gr. 3 - 12 healthy individuals.

Results: The study showed that in the group of patients with H and OB, compared with healthy individuals, BMI significantly changed by 27%, waist circumference by 31%, SBP and DBP values by 19.3% and 12%, respectively ($p < 0.05$), HOMA-IR increased 2.8 times and vaspin concentration 2.2 times ($p<0.001$). Patients of gr.2 had more severe dyslipoproteinemia - increased LDL-C ($p<0.05$) and hypertriglyceridemia and lower levels of HDL.

Conclusions: With the progression of obesity, insulin resistance, dislipidemia and arterial hypertension in patients aged 18-45 years there is an increase of proinflammatory adipokine vaspin. Most likely in obese patients there is an activation of the pro-inflammatory process and at the same time fatty tissue intensively produces this cytokine. The possibility of using vaspin as a marker for earlier prediction of possible metabolic complications in patients with arterial hypertension is suggested, in order to prevent cardiovascular events.

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210 / #195

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

IDENTIFICATION COHORT OF LYSOSOMAL ACID LIPASE DEFICIENCY PATIENTS THROUGH INFORMATION SYSTEM

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: The Dutch Criteria is widely used in hospital clinics for diagnosis Familial Hypercholesterolemia (FH). However, around one third of patients are reported mutation negative and clinical management requires lipid lowering agents. Patients with Lysosomal acid lipase deficiency (LAL-D) are commonly misdiagnosed as familial hypercholesterolemia, with extra presentation of fat accumulation in hepatocytes lead to hepatomegaly with progressive fibrosis and liver cirrhosis. The liver complication is usually not responsive to lipid lowering agents. Proper identification of these patients is important for proper clinical management. **Aim**: established a search engine to proper selection of patients with LAL-D in tertiary hospital.

Methods: Method: the hospital information system was used to extract all patients who had LDL-c above 5.5mM and with elevated liver enzymes. All patients with similar tribe/clan names were clustered. Patients were called for molecular sequencing of LIPA genes and blood blot enzyme assay of LAL.

Results: Results: electronic search identified a pattern of high LDL-c and ALT in cohort of patient sharing similar tribe/clan name. Chart review identified that they are related to one large consanguineous family with history of premature myocardial infarction, fatty liver and fibrosis in some members. DNA sequencing identified a novel mutation in LIPA. Enzyme assay confirmed lower enzyme activity in homozygous cases.

Conclusions: Conclusion: it is important to identify cases of LAL-D for proper genetic counselling for families. The use of simple search engine in hospital information system provides an easy first step for filtering patients in cardiology or lipid clinics.

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211 / #797

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

PHENOTYPE OF FAMILIAL HYPERCHOLESTEROLEMIA PATIENTS WITH ACUTE CORONARY SYNDROME - DATA FROM THE PROSPECTIVE OBSERVATIONAL REGISTRY STUDY (PRIMA-ACS)

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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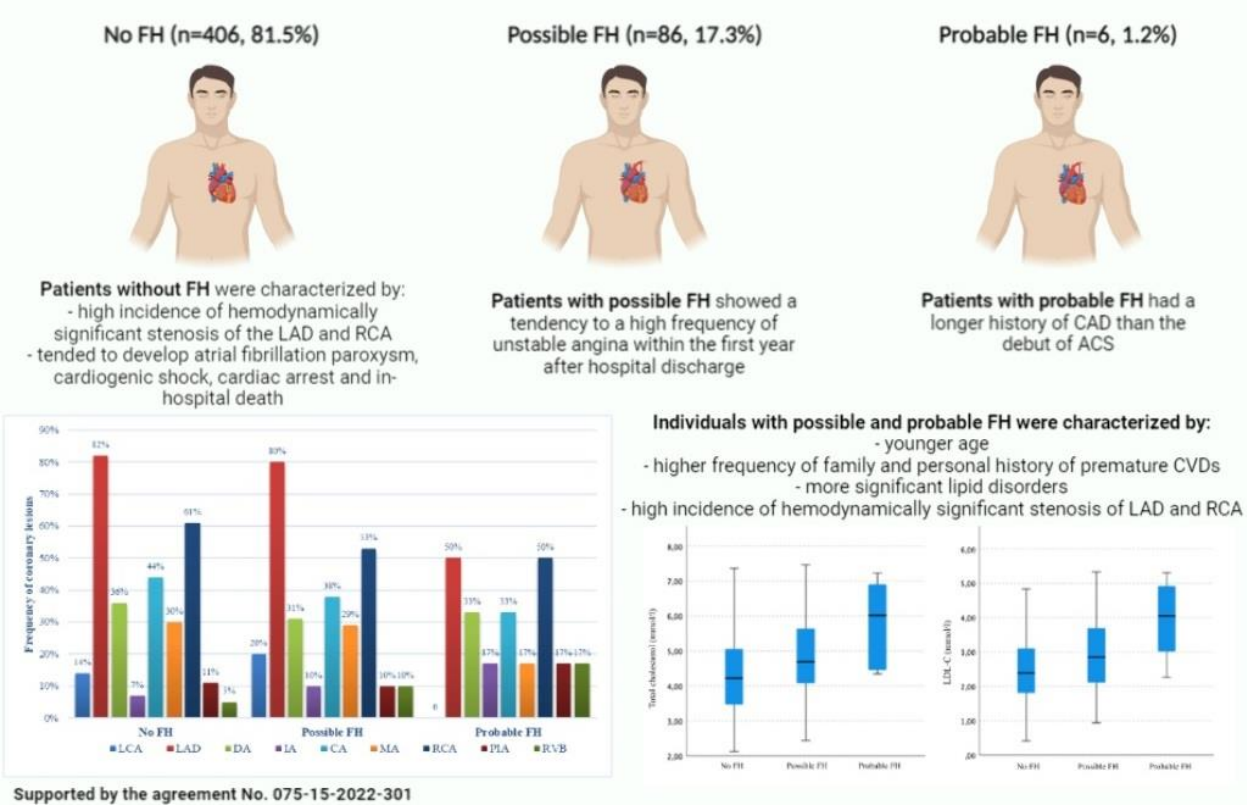
Background and Aims: There is a problem of underestimation of FH in a real clinical practice. In a significant number of patients, FH clinically debut with ACS. We aimed to analyze the prevalence and clinical parameters of patients with phenotype of FH among patients with ACS assessing the frequency of recurrent cardiovascular events.

Methods: A study included 500 patients hospitalized due to the fact of ACS (two patients were lost at the follow-up). The clinical probability of FH was assessed using the diagnostic criteria of the Dutch Lipid Clinic Network. The follow-up lasted for one year.

Results: A possible diagnosis of FH was verified in 86 (17.3%) patients, a probable diagnosis of FH - in 6 (1.2%). Patients with possible and probable FH were characterized by younger age [68.5 versus 59.5 and 50.5 years, p<0.001], a higher incidence of family history of premature CVDs [22.9% versus 77.9% and 83.3%, p<0.001] and an earlier personal history of CVDs [24.1% versus 90.7% and 100%, p<0.001] compared to patients without FH. Age-adjusted subanalysis showed that mixed type of coronary blood flow was significantly more often observed in patients with possible FH [p=0.049]. There were no significant differences in the localization of hemodynamically relevant coronary stenoses, however, the most frequent lesions were observed in the LAD and RCA. There were no significant differences in the development of cardiovascular events during hospitalization and after hospital discharge

(p>0.05).



Supported by the agreement No. 075-15-2022-301

Conclusions: A high percentage of FH among ACS patients has been determined. These results demonstrate the importance of better identification of FH patients.

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212 / #666

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA: DO WE HAVE ENOUGH THERAPY?

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Patients with Familial Hypercholesterolemia (FH) are at high cardiovascular risk in primary prevention and at very high risk in secondary prevention. The use of a high-potency statin, alone or combined with ezetimibe, is often insufficient for these patients. Authors present a case report of iPCSK9 use for treatment of dyslipidemia in a FH patient as secondary prevention.

Methods: Case report description

Results: We present a 48-year-old male, sedentary, smoker, with type 2 diabetes with albuminuria and ischemic heart disease due to an acute myocardial infarction at the age of 30. He was treated with rosuvastatin 20mg id, valsartan 80mg id, metformin/dapagliflozin 1000/5mg bid and acetylsalicylic acid 100mg id. He was referred to our Cardiovascular Risk Unit due to a cLDL >190mg/dL. It was found that more than 10 years ago, he had been diagnosed with heterozygous FH due to a deletion in an allele of the LDL receptor gene (LDLR16_18del) as well as his brother and daughter. Initially, he had total cholesterol (TC) 543mg/dL, cHDL 50mg/dL, cLDL 458mg/dL, triglycerides (TG) 116mg/dL, Lp(a) 35mg/dL. After the association of ezetimibe 10mg to rosuvastatin 20mg, he had TC 227mg/dl, cHDL 32mg/dL, cLDL 164mg/dL and TG 155mg/dL. As cLDL was persistently above target, evolocumab was started. A month after iPCSK9 therapy, the patient had CT 123mg/dL, cHDL 34mg/dL, cLDL 53mg/dL, TG 100mg/dL – meeting his recommended target.

Conclusions: Authors demonstrate that triple therapy allows a significant reduction in cLDL (>65%) thus in the cardiovascular risk in patients with heterozygous FH allowing them to reach the recommended targets.

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213 / #1058

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

GENETIC BACKGROUND OF FH: VARIANTS OF UNCERTAIN CLINICAL SIGNIFICANCE IN SEVERE FH PHENOTYPE.

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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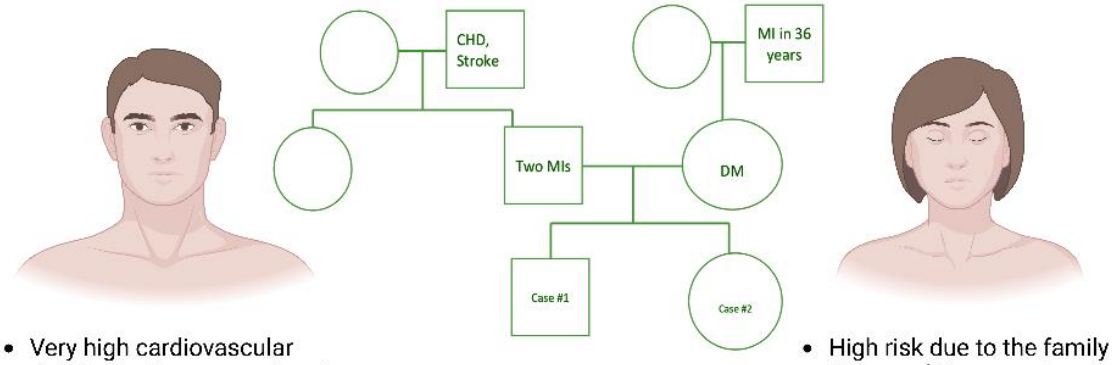
Background and Aims: The clinical interpretation of variants of uncertain clinical significance (VUS) detected by genetic testing of familial hypercholesterolemia (FH) is a real dilemma for geneticists and clinicians alike. Aim: to identify genetic background, including new VUS, responsible for the severe FH phenotype.

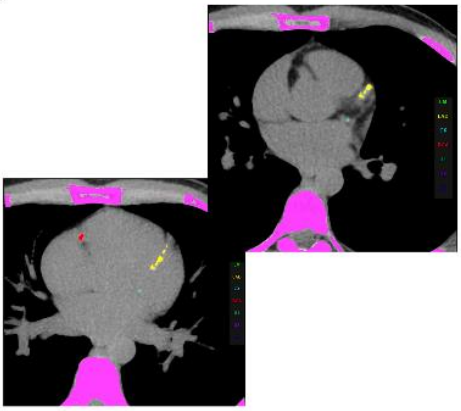
Methods: 107 patients with a severe FH phenotype (6 or more points on the DLCN score criteria) were enrolled. Blood testing, subclinical atherosclerosis methods were used (coronary artery calcium – CAC score, carotid artery duplex scan) as well as genetic testing were performed.

Results: Positive results of FH were detected in 31 (39.2%) patients, VUS variants were detected in 24 (30.4%) patients. 7 new VUS variants are found out in patients with severe FH phenotype (in the LDLR gene: c.*653G>A, c.1053 A>G, c.1968C>A, c.2474A>T; in the apoB gene: c.-547C>T; in the PCSK9 gene: c.1180+24G>A; in the LDLRAP1 gene: c.*737G>T). The severe clinical phenotype in these patients was due to the presence of clinical signs of FH (tendon xanthomas), high LDL-C [362.7±131.8, mg/dL], while the impact of lp(a) increase and polygenic score was excluded. Of a particular interest is the identified VUS in the PCSK9 gene in heterozygote, whose owners are a 29-year-old and 31-year-old

siblings.



- Very high cardiovascular risk due to the personal and family history of the premature cardiovascular disease.
- High levels of LDL-C.
- High score of the coronary artery calcium.
- Coronary angiography data brought him to myocardial revascularization.



- High risk due to the family history of the premature cardiovascular disease.
- High levels of LDL-C.
- High score of the coronary artery calcium.

Conclusions: The identified VUS in patients with a severe clinical phenotype of FH may add to the knowledge of a genetic background of FH. Further studies are needed in order to consider a probability of its likely pathogenicity. This work was financially supported by the grant No. 075-15-2022-301.

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214 / #1334

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

ANXIETY AND DEPRESSION IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Background: The levels of anxiety and depression are important factors that may influence treatment adherence, that is especially important in patients with familial hypercholesterolemia (FH). **Aim**: To analyze the levels of anxiety and depression in patients with FH before and after cardiological preventive counseling.

Methods: In total 163 patients (41,7% male, 45,5 ± 13,95 years old) with FH diagnosis (≥6 points on Dutch Lipid Clinic Network Score) were included in the analysis. The level of anxiety and depression was measured with the Hospital Anxiety and Depression Scale (HADS) initially at visit 1. At the same visit the cardiologist's consultation was conducted, including pharmacological treatment and advanced nonpharmacological preventive counseling. In 1-3 month patients again completed the HADS questionnaire before the visit 2.

Results: Results: Initially the level of anxiety in patients with FH was 6,50 ± 3,70 points, that is considered to be in normal range but close to subclinical anxiety; the level of depression was 4,56 ± 2,90 points. At visit 2 the level of anxiety became 5,88 ± 3,51 and the level of depression – 4,55 ± 3,05 points. Statistical analysis showed that the level of anxiety became lower at visit 2 comparing with visit 1 (p=0,0017), and the level of depression hadn’t changed (p=0,92).

Conclusions: Conclusions: Patients with FH have upper-normal level of anxiety. Cardiological counseling with advanced preventive component may help to reduce anxiety level in such patients. There was no effect of the cardiological preventive counseling on depression level.

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215 / #1015

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

CAROTID AND FEMORAL PLAQUES IN PATIENTS WITH FAMILIAL DYSBETALIPOPROTEINEMIA, FAMILIAL HYPERCHOLESTEROLEMIA, POLYGENIC AND SEVERE HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: To compare severity of carotid and femoral atherosclerosis in patients with severe hypercholesterolemia with different etiology.

Methods: Patients with median age 54 (47-61) with familial dysbetalipoproteinemia (FD) (*APOE* ε2ε2 haplotype and TG ≥1.5 mmol/L; n=26), familial hypercholesterolemia (FH) (pathogenic or probably pathogenic variants in *LDLR*, *APOB* or *PCSK9* and DLCN criteria ≥9 points; n=61), polygenic hypercholesterolemia (LDL-C polygenic score >80th percentile and LDL-C >4.9 mmol/L, without tendons xanthomas; n=49) or severe hypercholesterolemia (LDL-C polygenic score <50th percentile and LDL-C >4.9 mmol/L, without tendons xanthomas; n=41). Logistic regression (adjusted for age, sex, BMI, arterial hypertension, diabetes, smoking and statin treatment duration) and Holm–Bonferroni method were used. Carotid and femoral arteries were analyzed for plaque number (total number of plaques) using Samsung Medison MySono U6 and Philips iU22.

Results: Patients with FH had a higher carotid plaque number (MED 4 (1-5)) compared with patients with FD (MED 2 (1-3)), polygenic (MED 2 (1-4)) or severe (MED 2 (1-3)) hypercholesterolemia (p=0,018). The patients with FD, polygenic or severe hypercholesterolemia were comparable in carotid plaque number. Femoral plaque number in patients with FH (MED 3 (0-5)), FD (MED 2 (0-3.8)), polygenic (MED 1 (0-3)) or severe (MED 1 (0-2)) hypercholesterolemia did not differ.

Conclusions: When the severity of carotid and femoral atherosclerosis in patients with FH, FD, polygenic or severe hypercholesterolemia was compared, differences were obtained only for patients with FH who had a significantly higher number of carotid plaques.

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216 / #505

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

REFINEMENT OF THE DIAGNOSTIC TOOL FOR THE DIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLEMIA IN CHILDREN AND ADOLESCENTS: EVIDENCE FROM THE LIPIGEN STUDY

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: The identification of familial hypercholesterolemia (FH) in childhood poses several issues. We aimed to identify limits of one of the most applied algorithms (Dutch Lipid Clinic Network (DLCN) criteria), and compare its application in genetically-confirmed FH adult and pediatric patients, proposing additional parameters to support diagnosis at young age.

Methods: From the LIPIGEN study, we selected 1188 (≥18years) and 708 (<18years) heterozygous FH patients, with no missing DLCN parameters about physical examination and clinical history, and untreated LDL-C available. The main FH features were compared between the two groups, and data about premature CHD in second-degree family members were integrated in a paediatric sub-group.

Results: The lower prevalence of FH characteristics in children/adolescents vs adults was confirmed: tendon xanthoma 2.1%vs13.1%, arcus cornealis 1.6%vs11.2%, respectively. No children presented clinical history of premature CHD or cerebral/peripheral vascular disease (in adults 8.8% and 5.6%, respectively) while the presence of tendon xanthoma and/or corneal arcus as well as hypercholesterolemia in first-degree relatives were comparable (18.7%vs20.0% and 92.9%vs93.5%, respectively). The premature CHD prevalence in first-degree relatives was significantly higher in adults compared to subjects <18 years (38.9%vs19.7%). The pediatric sub-group with data about second-degree relatives was representative of the whole paediatric cohort. While a premature CHD events in parents was reported in 63 of 374 subjects, the percentage increased from 16.8% to 54.0% extending the evaluation also in second-degree relatives.

Conclusions: DLCN parameters in children are clearly less informative than in adults, suggesting that a specific refinement of the diagnostic approach with a tailored data collection is requested.

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217 / #250

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

A PATIENT WITH SEVERE MULTIFACTORIAL CHYLOMICRONEMIA SYNDROME TREATED WITH VOLANESORSEN, ARE THESE PECULIAR CASES NEGLECTED AND UNDERTREATED?

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Chylomicronemia can be either monogenic (FCS) or multifactorial (MCS). FCS is mainly characterized by a severe clinical phenotype, whereas MCS is usually asymptomatic. However, there is a grey zone between the two conditions. Our goal was to detect new cases of FCS and patients with MCS with a severe clinical phenotype.

Methods: We extracted data from a wide laboratory database. Data from patients with triglycerides>885 mg/dl were collected in order to rule out secondary non-metabolic conditions causing hypertriglyceridemia. Moulin and Lipigen scores were subsequently filled out. Willing patients were subjected to a salivary genetic test for known genes for FCS.

Results: From a database of 563765 samples for triglycerides, 12 patients were selected. 6 were subjected to the genetic test. We detected a new diagnosis of FCS in a young subject with a history of recurrent pancreatitis, resulted compound heterozygous for 2 LPL variants. We report two different cases of MCS: One patient single heterozygous for a variant of LPL gene, with drug-resistant, asymptomatic severe hypertriglyceridemia. One patient double heterozygous for variants of LPL and APOA5 genes, with a history of drug-resistant hypertriglyceridemia and recurrent pancreatitis. Since the beginning of a treatment with volanesorsen, triglycerides have been in range and no pancreatitis events have occurred.

Conclusions: We detected a new case of FCS. Under the definition of MCS a broad spectrum of conditions are included. Some of them have a severe clinical phenotype, similar to FCS. Other are asymptomatic but have severe, drug-resistant hypertriglyceridemia. It is probably time to expand indications for volanesorsen.

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218 / #276

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

ANALYSIS OF ROUTINE MOLECULAR GENETIC DIAGNOSTICS OF FAMILIAL HYPERCHOLESTEROLEMIA AT TERTIARY CARE LIPID CLINICS IN VIENNA

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

Moritz Ferch[1], Lukas Galli[2], Paul Fellinger[1], Harald Esterbauer[3], Sabina Baumgartner-Parzer[1], Walter Speidl[2], Alexandra Kautzky-Willer[1], Yvonne Winhofer-Stöckl[1]
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Background and Aims: Familial Hypercholesterolemia (FH) is an autosomal dominant genetic disease causing dyslipidemia and premature ASCVD, with ~40,000 people thought to be affected in Austria. Aim of this study was to analyze the current yield of routine molecular genetic diagnostics for FH and the spectrum of mutations in two specialist lipid clinics in Vienna.

Methods: We investigated all genetic testings performed for FH in our clinics over a 4-year period. Reports of causative mutations in the main FH-causing genes including *LDLR, APOB, PCSK9* were collected. Variants were classified based on HGVS nomenclature using the mutation database ClinVar. For clinical classification, the Dutch Lipid Clinic Network Score (DLCNS) was used.

Results: Of 450 patients tested, 102 (22.4%) had a causative mutation (*LDLR*=84%, *APOB*=9%, *PCSK9*=5%), 3 of which were novel. 14 further previously unreported variants of unknown significance were identified. The detection rate was 64% in patients with clinically definite FH i.e. DLCNS >8 (10.6% of the cohort), 30% in those with DLCNS 6-8 (20.2%), 16% in DLCNS 3-5 (47.8%) and 4% in DLCNS <3 (21.4%). Median DLCNS at testing was 4, in positively tested 6. Mean off-treatment LDL-C levels were significantly higher in positively compared to negatively tested (264±71 mg/dl vs 196±60 mg/dl; p<0.001), and in those with DLCNS ≥6 compared to <6 (285±70 mg/dl vs 189±53 mg/dl p<0.001).

Conclusions: To our knowledge, this is the first comprehensive report on diagnostic yield of genetic testings for FH in Austrian adults in clinical routine, presenting an update on the mutation spectrum.

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219 / #1296

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

FUNCTIONAL STUDIES OF APOB VARIANTS – THE EXPERIENCE OF THE PORTUGUESE FAMILIAL HYPERCHOLESTEROLEMIA STUDY

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

Maria Ferreira[1], Joana Chora[1,2], Ana Medeiros[1,2], Mafalda Bourbon[1,2], Ana Catarina Alves[1,2]
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Background and Aims: Familial hypercholesterolemia (FH) is clinically characterized by increased levels of circulating LDL cholesterol leading to premature coronary heart disease. It can be caused by variants in *LDLR*, *APOB*, and *PCSK9* genes. *APOB* variants are responsible for 5-10% of the FH cases, p.(Arg3527Gln) being the most common. Only recently the whole gene has been sequenced due to Next Generation Sequencing, increasing the variant spectrum of *APOB* and with it the number of variants that need to be functionally assessed. We aimed to characterize novel *APOB* variants identified in patients included in the Portuguese FH Study to confirm if they are the genetic cause of hypercholesterolemia.

Methods: To better analyze these variants, we also create a database with all *APOB* rare variants found up to date in the Portuguese FH Study. The functional study of 5 variants is ongoing. To access if these variants affect apoB:LDL receptor binding, LDL from index cases and relatives with the variants was separated using sequential ultracentrifugation, and proliferation assays were performed with U937 cells. These cells do not synthesize cholesterol but need it to grow, they depend on apoB:LDL receptor binding.

Results: We have identified 110 rare variants, of which only 6% had functional characterization. Preliminary results for p.(Ile3347Thr) and p.(Asp2213del) variants showed that they do not seem to affect apoB:LDL receptor binding.

Conclusions: Functional studies are crucial to increase the scientific knowledge about the effect of the variants in protein function, being one of the most important criteria to be able to classify variants as pathogenic.

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MANNHEIM GERMANY | MAY 21-24, 2023

220 / #1254

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

CHARACTERISTICS AND MANAGEMENT OF INDIVIDUALS WITH FAMILIAL HYPERCHOLESTEROLEMIA IN AUSTRIA – DATA FROM THE NATIONAL FH-REGISTRY.

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: To identify, characterize and evaluate individuals with familial hypercholesterolemia (FH).

Methods: Patients were enrolled at 14 clinical centres across Austria following signed informed consent based on Dutch Lipid Clinic Network scores (≥6), modified Simon-Broome criteria, or results from cascade screening. The study was approved by local research ethics committees.

Results: A total of 1158 individuals enrolled since inception in 2015, with 21% of participants <18 years. In total, 20% were identified through cascade screening. Genetic and clinical diagnosis of FH was available for 44%, while 25% were included based solely on clinical diagnosis, and 13% had a genetic diagnosis without the clinical features of FH. For 18% complete data were still missing. Two percent had homozygous FH. Among adult and paediatric participants, the mean age (± SD) at diagnosis was 45 ± 17 and 7 ± 4 years, respectively. Sixteen percent had already experienced a myocardial infarction. At baseline, 77% of adults and 30% of the paediatric population were on lipid-lowering medication (LLM). Overall, 40% were on combination therapy, with statins and ezetimibe being the most prevalent

combination (40%), followed by statins, ezetimibe plus PCSK9 inhibitors (23%). At inclusion, 11% of adults attained LDL-Cholesterol levels <70 mg/dl, while 34% of 10- to 17-year-old participants reached their goal (<130 mg/dl). Follow-up visits were available for 138 participants, in which 15% of adults attained target LDL-Cholesterol.

Conclusions: Compared to recent global data, a higher proportion of Austrian FH patients takes combination LLM, and more individuals achieve LDL-Cholesterol targets. However, FH remains underdiagnosed and undertreated.

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221 / #1179

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

ACHIEVING TARGET LIPID LEVELS IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLAEMIA IN CLINICAL PRACTICE

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Background: Familial hypercholesterolemia (FH) is a severe inherited disease associated with very high LDL cholesterol (LDL-C) concentrations. This leads to early atherosclerotic cardiovascular complications. The cause of FH is most commonly a mutation in the LDL receptor (LDLR) or Apolipoprotein B (APOB) gene. Achieving target LDL-C levels with intensive hypolipidemic therapy is essential for the prevention of cardiovascular events. This is often impossible in patients with FH. Aims: To determine what percentage of long-term treated patients with FH achieved target levels of LDL-C and other lipids, depending on the mutation detected, the type of therapy and the risk of fatal cardiovascular event.

Methods: Using unpaired t-test, we analysed data from 179 patients with FH undergoing long-term treatment at the specialised centre of St. Anne's University Hospital in Brno.

Results: 61% of patients had high-intensity statin therapy (HIT), 19% had PCSK9 inhibitors (BIO) and 13% had a combination of BIO+HIT. Patients with LDLR mutation had significantly higher baseline total cholesterol (TC), LDL-C, Non-HDL-C and Apo B values compared to the APOB mutation group. Treatment achieved a mean reduction of 40.2% in TC, 51.1% in LDL-C, 49.1% in Non-HDL-C and 38.3% in Apo B. Target LDL-C was achieved by 53% of patients (61% with LDLR mutation and 31% with APOB mutation), 56% of patients treated with HIT and 82% of patients treated with PCSK9-i, 53% of patients in high and 54% in very high cardiovascular risk.

Conclusions: We achieved the target LDL-C value in more than half of the patients with FH.

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222 / #1484

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

IDENTIFICATION OF A NOVEL NONSENSE MUTATION IN THE APOB GENE BY NEXT GENERATION SEQUENCING

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Familial hypobetalipoproteinemia (FHBL) is an autosomal codominant disorder of lipoprotein metabolism characterized by low plasma levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and apolipoprotein B (apoB). It may be due to loss-of-function mutations in APOB or, less frequently, in PCSK9 genes. The 50% of FHBL-1 cases is caused by mutations in APOB gene which result in assembly defects and secretion of lipoproteins containing apoB. Most of the FHBL-1 subjects are heterozygous carriers of nonsense pathogenetic variants and frameshift of the APOB gene which interfere with the complete translation of the mRNA coding the apoB protein, determining the formation of truncated forms of apoB. FHBL heterozygotes are generally asymptomatic but often develop fatty liver.

Methods: We designed a custom panel for Next Generation Sequencing (NGS) in order to analyze known genes involved in FHBL by Ion Torrent GeneStudio S5 Plus. We sequenced the FHBL candidate genes in 10 patients presenting LDL-C and ApoB levels below the 5th percentile.

Results: In the majority of subjects no functionally relevant mutations in candidate genes were detected. Two unrelated patients was found to be carrier of a novel heterozygous nonsense mutation in the exon 26 of the APOB gene (c.10324C>T, p.Gln3442Ter). The mutation lead to the formation of a premature stop codon and an apoB truncated protein of an expected size of 75.8% of wild type apoB (apoB-75.8).

Conclusions: In this work we describe a novel nonsense mutation of the APOB gene responsible for FHBL identified by a Next generation sequencing approach.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

METABOLIC SYNDROME AND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN NON-DIABETIC ADULT PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA: DATA FROM THE HELLAS-FH REGISTRY

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: We investigated the association of Familial Hypercholesterolemia (FH) with the Metabolic Syndrome (MetSyn) in a population of adult non-diabetic patients with heterozygous FH.

Methods: Adult non-diabetic patients from the HELLAS FH registry were evaluated. The NCEP ATPIII criteria were used for the definition of the MetSyn. Patients were classified into 2 groups: with and without MetSyn. Demographic data, lipid profile and cardiovascular profile of the 2 groups were compared.

Results: A total of 748 patients were evaluated, 41.1% of of whom had MetSyn. These patients were older (54±13 vs 46±14 years,p<0.001), had more often hypertension (34.8% vs 6.3%, p<0.001), abdominal obesity (70.8% vs 21.6%,p<0.001), impaired fasting glucose (39.8% vs 10.4%,p<0.001), and increased body mass index (77.6% vs 54.8%,p<0.001) as compared with patients without MetSyn. Lipid profile before hypolipidemic therapy was characterized by higher TG and lower HDL-C levels (150 vs 112 mg/dL; p<0.001 and 52 vs 57 mg/dL, p<0.001, respectively). Patients with MetSyn had more frequently established ASCVD (20.8% vs 11.7%; p<0.001), association that remained significant after adjustment for major ASCVD risk factors. Lipid profile on hypolipidemic therapy was characterized by higher TG and lower HDL-C levels (142 vs 93 mg/dL,p<0.001 and 50 vs 56 mg/dL,p<0.001, respectively). Hypolipidemic

treatment did not differ between the 2 groups. The LDL-C goal achievement was numerically lower in the MetSyn group (2.1% vs 3.8%,p=NS).

Conclusions: A total of 4 out of 10 non-diabetic patients with FH have the MetSyn. These patients have a more atherogenic lipid profile and an increased prevalence of ASCVD compared with non-MetSyn FH patients.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

TRIGLYCERIDES AND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN ADULT PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA: DATA FROM THE HELLAS-FH REGISTRY

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

Christos Rizos[1], George Liamis[1], Ioannis Skoumas[2], Anastasia Garoufi[3], Loukianos Rallidis[4], Genovefa Kolovou[5], Konstantinos Tziomalos[6], Emmanouil Skalidis[7], George Sfikas[8], Vasileios Kotsis[9], Michalis Doumas[10], Panagiotis Anagnostis[11], Vaia Lambadiari[12], Eleni Bilianou[13], Ermioni Petkou[1], Iosif Koutagiar[2], Achilleas Attilakos[14], Estela Kiouri[4], Vana Kolovou[5], Evangelos Zacharis[7], Charalambos Koumaras[8], Christina Antza[9], Chrysoula Boutari[10], Evangelos Liberopoulos[15]
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Background and Aims: Patients with familial hypercholesterolemia (FH) have increased risk of atherosclerotic cardiovascular disease (ASCVD) associated with inherently elevated LDL cholesterol (LDL-C) levels. Elevated triglyceride (TG) levels represent an additional ASCVD risk factor. We investigated the association of TG levels with the presence of ASCVD in a population of adult patients with heterozygous FH.

Methods: Adult patients from the HELLAS FH registry were evaluated. Depending on the pre-treatment fasting TG levels, patients were classified into 3 groups: group 1 (G1; TG<100 mg/dL), group 2 (G2; TG 100-150 mg/dL) and group 3 (G3; TG >150 mg/dL).

Results: Results: A total of 1772 patients (51.2% male, 51±15 years) were included. Patients in the G3 group had more often hypertension, type 2 diabetes and smoking compared with the other 2 groups. Regarding pre-treatment lipid profile, the G3 group had higher levels of TCHOL and ApoB, but lower levels of HDL-C. On treatment, the G3 group had higher levels of ApoB and TG. Attainment of LDL-C goal was similar in the 3 groups. The unadjusted prevalence of coronary artery disease differed significantly between groups: G1 15.4%, G2 24.8% and G3 25.8% (p<0.001 among groups). Patients with

established ASCVD had higher TG levels (p<0.001). However, after adjustment for the presence of other major ASCVD risk factors, TG levels were not associated with the presence of ASCVD.

Conclusions: In patients with FH, elevated TG levels (>150 mg/dL) were associated with prevalent ASCVD. However, after adjustment for major ASCVD risk factors, TG levels were not associated with the presence of ASCVD.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

CASCADE TESTING OF ELEVATED LP(A) IN CHILDREN AND ADOLESCENTS VIA THE FAMILIAL HYPERCHOLESTEROLEMIA SCREENING PROGRAM

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: *Background:* Elevated plasma lipoprotein(a) [Lp(a)] is a common inherited condition independently associated with atherosclerotic cardiovascular disease (ASCVD). Early detection and management of elevated Lp(a) in affected children and adolescents are important to prevent the development of cardiovascular complications. Recent expert recommendations suggest opportunistically testing for elevated Lp(a) during cascade testing for familial hypercholesterolaemia (FH). *Aim:* This study investigated the effectiveness of detecting elevated Lp(a) in children and adolescents participating in an FH cascade screening program.

Methods: *Methods:* 103 children and adolescents (≤18 years old) who were first-degree relatives of FH adult probands were tested for elevated Lp(a) via an established FH cascade screening program. Elevated Lp(a) in probands was defined as ≥50 mg/dL. The detection yield of elevated Lp(a) at cut-off levels of ≥30 mg/dL and ≥50 mg/dL in children and adolescents was assessed.

Results: *Results:* Of the 66 FH probands, 24.2% had elevated Lp(a). Cascade testing from FH probands with elevated Lp(a) identified 1 case of Lp(a) ≥30 mg/dL for every 2.0 children or adolescents screened and 1 case of Lp(a) ≥50 mg/dL for every 2.8 children or adolescents screened. In contrast, the corresponding yield of detection was lower in those FH probands with normal Lp(a) levels (n=50), demonstrating 1 in 7.5 for Lp(a) ≥30 mg/dL and 1 in 15 for Lp(a) ≥50 mg/dL among children or adolescents tested.

Conclusions: *Conclusion:* Cascade testing for elevated Lp(a) from FH probands with elevated Lp(a) is effective in identifying new cases of elevated Lp(a) in children and adolescents.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

ELEVATED SPHINGOSINE 1-PHOSPHATE LEVEL IN FAMILIAL HYPERCHOLESTEROLEMIC PATIENTS

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Sphingosine-1-phosphate (S1P) plays important roles in cardiovascular diseases and its plasma concentrations have been associated with coronary and peripheral artery disease and myocardial infarction. However, alteration of S1P level in familial hypercholesterolemia is not fully clarified.

Methods: We enrolled 81 newly diagnosed FH patients and 32 healthy controls. Serum S1P concentrations was determined by ELISA. Lipoprotein subfractions were detected by gel electrophoresis (Lipoprint). Dutch Lipid Clinic Network criteria was used for diagnosing FH.

Results: We detected significantly higher serum S1P level in FH patients compared to healthy controls (7.73 ± 2.07 vs. 6.79 ± 2.09 ng/mL, $p<0.05$). Significantly higher proportions and levels of large- and small-density LDL subfractions, while significantly lower mean LDL size were found in FH patients compared to controls. Furthermore, we detected a lower percentage and concentration of large and intermediate HDL subfractions. Moreover, a higher percentage and concentration of small HDL subfractions, were found in FH patients compared to controls. S1P negatively correlated with large HDL and positively with small HDL subfractions in FH patients.

Conclusions: Elevated small HDL-associated S1P level may contribute to improved HDL functions, such as the maintenance of endothelial homeostasis, arterial vasodilation, and cardioprotection in FH patients. Our results highlight the potential importance of studying HDL function and the regulatory role of S1P in FH.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

IDENTIFICATION OF APOB VARIANTS IN SAMPLES FROM THE BRAZILIAN POPULATION WITH HYPERCHOLESTEROLEMIC PHENOTYPE

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Apolipoprotein B plays a crucial role in regulating plasma cholesterol by mediating the interaction of low-density lipoprotein (LDL) with LDL receptors in the liver. Inherited mutations in this gene may increase the risk of developing premature atherosclerotic cardiovascular disease, especially in individuals with familial hypercholesterolemia type 2 (FH2). The aim of this study is to identify *APOB* variants that may indicate pathogenicity in a sample of the Brazilian population using a data bank exome sequencing study by NGS in a Brazilian population phenotypically diagnosed by clinical and laboratory profile. This finding is going to improve genetic hypercholesteremia diagnosis.

Methods: High-quality DNA samples (n=300) were sequenced using an exon-targeted gene sequencing (ETGS) strategy to identify variants in FH-related genes. Pathogenicity classification was based on criteria established by the American College of Medical Genetics and Genomics (ACMG), also using information from ClinVar and pathogenicity scores from previous association studies.

Results: A total of 121 variants were identified in *APOB*, of which four are novel variants missense (p.Thr626Asn, p.Ile2750Thr, p.Gln2078Lys and p.Met4184Arg). After curating pathogenicity scores, variants were classified according to the ACMG criteria. Among them four as pathogenic or likely pathogenic (p.Pro2739Leu, p.His1923Arg, p.Pro994Leu and p.Pro877Leu), and 21 variants had uncertain significance. Additionally, 92 previously known variants with uncertain significance were classified as benign or likely benign. The results were submitted to Clinvar for actualization of pathogenicity.

Conclusions: These results improve the molecular diagnosis associating *APOB* variants with the clinical phenotype of hypercholesterolemia

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

CARDIOVASCULAR DISEASE RISK MODIFIERS IN PATIENTS WITH HETEROZYGOUS FAMILIAL HYPERCHOLESTEREMIA

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: EAS/ESC guidance identifies factors which may modify cardiovascular (CVD) risk. The presence of established CVD or one other major risk modifier encompass the criteria guiding the stratification of hFH patients into the high or very-high-risk categories with treatment intensity, including the addition of PCSK9 inhibitors, directed accordingly. We aimed to assess the frequency of these modifiers in a hFH cohort.

Methods: An ethically approved retrospective chart review was performed of consecutive adult patients attending a specialist lipid clinic over a six-month period in 2021. Patient data recorded included demographics, clinical characteristics, treatment received and biochemical profiles.

Results: 370 patients were included. 70 patients (19%) had a genetically confirmed diagnosis of hFH. These patients were predominantly female (60%) with mean age 41.4±13.5 years. Established CVD was noted in 16% [coronary artery disease (16%), percutaneous coronary intervention (9%), carotid stenosis (4%), myocardial infarction (3%), coronary artery bypass graft (3%), valvular disease (3%)]. Co-morbidities included type 2 diabetes (7%), hypertension (15%), major psychiatric disorder (10%), non-alcoholic fatty liver disease (9%) and inflammatory diseases (6%). Additional risk modifiers included a family history of CVD (84%), a family history of premature CVD (61%), elevated BMI [overweight (30%), obese (26%)], smoking status [current smoker (14%), ex-smoker (21%)], elevated coronary artery calcium scores (16%) and elevated lipoprotein(a) (30%). Physical activity data suggested at least 9% were sedentary.

Conclusions: This study reports the frequency of risk modifiers in a hFH cohort. Modifiers beyond established CVD warrant due consideration to differentiate between high and very-high-risk hFH patients to guide treatment intensity accordingly.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

A RETROSPECTIVE STUDY OF SUBJECTS WITH FAMILIAL HYPERCHOLESTEROLEMIA IN A BELGIAN LIPID CLINIC

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Familial hypercholesterolemia (FH) is a genetic disease characterized by hypercholesterolemia and premature cardiovascular events. Early diagnosis and appropriate treatment can strongly reduce the cardiovascular burden. We aim to describe the characteristics of patients with heterozygous FH followed in the lipid clinic in Leuven, Belgium.

Methods: We retrospectively studied a cross-sectional cohort of 321 patients with genetically confirmed heterozygous FH followed at the department of endocrinology in the University Hospitals of Leuven between 1/1/2016 and 31/12/2020. Sociodemographic, clinical, and biochemical data were collected and analyzed. Data are represented as mean ±SD.

Results:

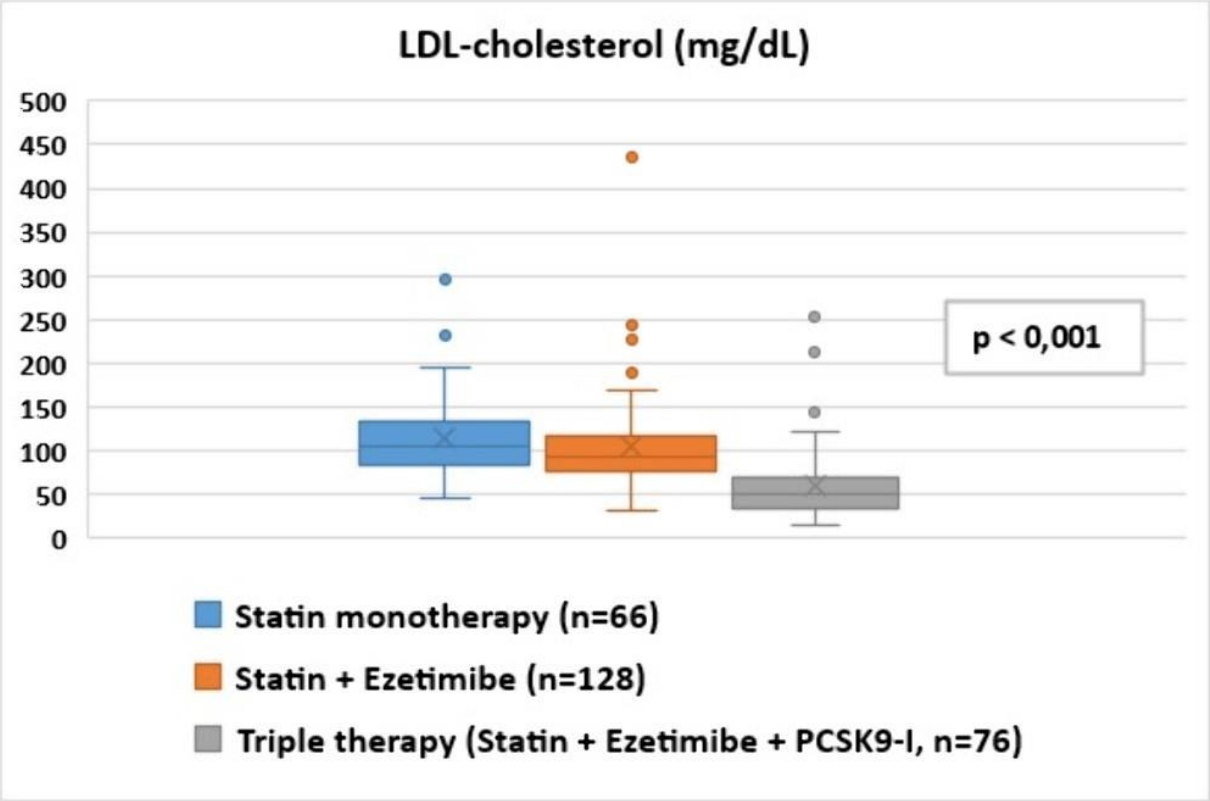

Figure 1. Boxplot of LDL-cholesterol in 3 treatment groups.

The mean ±SD age of the study population at time of diagnosis of FH was 39 ±18 years old. Patients in secondary prevention had a higher age (p<0.001), were more often male (p<0.001) and smokers (=0.007), had a higher body mass index (p<0.001), had more often (pre)diabetes (p<0.001) and hypertension (p<0.001) and had higher low-density lipoprotein-cholesterol levels (LDL-C) (p<0.001) compared to subjects in primary prevention. The average LDL-C in both primary (109 ±53 mg/dL) and secondary (81 ±63 mg/dL) prevention didn't meet the targets of LDL-C as proposed by the 2019 ESC/EAS guidelines for the management of dyslipidemias. However, LDL-C levels in the subgroup of patients treated with PCSK9-inhibition therapy, and especially in the triple therapy group (combination of statin, ezetimibe and PCSK9-inhibitor), were markedly lower (p<0.001, figure 1).

Conclusions: In this Belgian cohort, patients with heterozygous FH were undertreated. Meeting treatment targets in FH is possible, although this requires combination treatment (with PCSK9-inhibitors) in most patients.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

230 / #540

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

PEDIATRIC PATIENT WITH HETEROZYGOUS FAMILIAL HYPOBETALIPOPROTEINEMIA DUE TO A NOVEL APOB VARIANT

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Familial hypobetalipoproteinemia (FHBL) is an autosomal codominant disorder usually caused by variants in the *APOB* gene that frequently interfere with protein length. Truncated apoB can form varying sizes and densities of lipoprotein particles depending on the length of truncation. Symptoms include malabsorption, non-alcoholic fatty liver, low levels of lipid-soluble vitamins, and neurological, endocrine, and hematological dysfunction. We report a pediatric case with diagnosed FHBL at the age of 10.

Methods: DNA was isolated from peripheral blood of the proband, his brother and parents. Next generation sequencing was performed. A panel of seven genes associated with hypocholesterolemia (*CCT5, ANGPTL3, PANK2, SAR1B, APOC3, APOA5, APOB*) was used to filter changes. The identified change in the APOB gene was confirmed by Sanger sequencing. Moreover, in the systematic review, we present 66 patients with variants in the *APOB* gene associated with FHBL.

Results: Genetic investigation revealed the presence of novel heterozygous variant in the *APOB* (NM_000384.3) gene c.6624dup[=], which changes the open reading frame and leads to early termination of translation into the p.Leu2209IlefsTer5 protein (NP_000375.3). The identified variant was not previously reported.

Conclusions: We have identified a novel pathogenic variant in *APOB* gene causing FHBL in a pediatric patient. We also confirmed the change in the subject's mother. We introduced a therapy that includes limiting fat in the diet and adding lipid-soluble vitamins E, A, K and D and calcium carbonate. In our case, we were the first to associate the detected change with the diagnosis of FHBL.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

231 / #1591

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

USE OF LIPID-LOWERING DRUGS WITHIN A MULTICENTER GENETIC CASCADE SCREENING PROGRAM FOR FAMILIAL HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Once an index case has been diagnosed with a pathogenic variant for familial hypercholesterolemia (FH), genetic cascade screening of relatives is recommended. However, evidence for the effectiveness of such family screening remains scarce. In a genetic cascade screening program for FH, we compared the control of cardiovascular risk factors between positive index cases and positive relatives.

Methods: We conducted a nationwide multicenter genetic cascade screening program for FH in Switzerland. Adults older than 16 years were genetically tested, and those with pathogenic variant in the *LDLR*, *APOB* or *PCSK9* gene were defined as positive index case. A genetic cascade screening of relatives was performed using indirect contact methods according to Swiss medical ethics rules.

Results: Between November 2020 and February 2023, the program identified 88 positive index cases and 59 positive relatives with a pathogenic variant for FH, mostly in the *LDLR* gene. The mean age was 45.8 years, 55.8% were female and 27.6% were current smokers. Compared to positive index cases, positive relatives were younger (40.3 vs 49.6 years old) and had lower untreated LDL-cholesterol levels (5.4 vs 7.7 mmol/l). The use of lipid-lowering drugs was lower among positive relatives compared to positive index cases (47.1% vs 77.1%, $p<0.001$). These differences in lipid-lowering drug use were observed for statins ($p =0.009$), ezetimibe ($p =0.001$), and PCSK9 inhibitors ($p =0.008$).

Conclusions: Despite elevated LDL-c levels caused by a pathogenic variant for FH, positive relatives identified within a multicenter genetic cascade screening program used less frequently lipid-lowering drugs than positive index cases.

91ST EAS CONGRESS
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232 / #335

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

SCREENING FOR LYSOSOMAL ACID LIPASE DEFICIENCY IN JAPANESE PATIENTS WITH SUSPECTED FAMILIAL HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Lysosomal acid lipase deficiency (LALD) is an autosomal recessive disease caused by loss-of-function mutations in the *LIPA* gene, resulting in high LDL cholesterol (LDL-C) levels and liver dysfunction. Familial hypercholesterolemia (FH) and LALD have similarities in terms of high LDL-C and premature atherosclerotic cardiovascular disease. In Europe, the prevalence of LALD is reported to be 1 in 9000 to 170000 persons, but less than 10 patients have been diagnosed in Japan. Therefore, we thought we were overlooking LALD among patients we were treating for suspected FH. Accordingly, we aimed to find LALD in our patients with high LDL-C levels.

Methods: We measured LAL activity using dried blood spots in 553 consecutive dyslipidemic patients who visited our outpatient clinic.

Results: No patient had LAL activity below the mean value for patient controls (0.005 ± 0.044 μmol/hr/L). However, an 18-year-old female patient with statin-resistant markedly high LDL-C levels and unexplained liver dysfunction had a relatively low LAL activity of 0.255 μmol/hr/L (14.6% activity of normal average). Genetic testing revealed two novel missense mutations, and the patient was diagnosed as compound heterozygous LALD and started on enzyme replacement therapy.

Conclusions: Although the proportion of LALD in this study was less than 0.2% (1/553), much smaller than that reported in Europe, a method of screening for LALD from patients with suspected FH may be useful for early diagnosis and early treatment. It was also found that combined use with genetic testing can diagnose LALD patients with relatively preserved LAL activity.

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233 / #1569

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

SCREENING FOR FAMILIAL HYPERCHOLESTEROLEMIA AMONG PATIENTS WITH INTERNAL CAROTID ARTERY STENOSIS

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Familial hypercholesterolemia (FH) is a disease manifested by accelerated atherosclerosis and consequently, increased morbidity and mortality from cardiovascular(CV) and cerebrovascular diseases(CVA). Unfortunately, the disease is still unrecognized, and many patients are not adequately treated. Among FH patients focus is mainly on CV complications, consequently screening for FH in patients with acute coronary syndrome was performed at our hospital. We decided to screen for FH in patients with internal carotid artery (ICA) stenosis and a stent placement (CAS). The aim of this study was to screen for patients with FH among patients with ICA stenosis and an CAS.

Methods: A retrospective study was conducted among patients under the age of 60 who were treated at the Neurology Department from 2019-2022 for ACI stenosis and placement of CAS. Dutch Lipid Clinic Network (DLCN) criteria was used to evaluate the patients for the FH diagnosis .

Results: The research included 52 patients (39 men, 13 women). According to the DLCN, a total of 11 patients (21.15%) have a possible diagnosis of FH. 19 patients (36.53%) previously had stroke or myocardial infarction. 21 patients (40.38%) had a statin included before CAS placement, while 33 patients (63.46%) had a statin introduced after the procedure, of which only 15 patients (28.84%) had a highly potent statin at discharge.

Conclusions: Conclusion: According to screening data, there are patients who may have FH. It is also important to emphasize that the vast majority of patients had a previous cardiovascular or cerebrovascular event, and were not adequately treated, prior to the CAS implantation nor post procedurally.

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234 / #159

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

UPDATED ANALYSIS OF THE EGYPTIAN FAMILIAL HYPERCHOLESTEROLEMIA RESEARCH FORUM REGISTRY

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

Ashraf Reda[1], Atef Elbahry[2], Samir Rafla[3], Ihab Daood[4], Sameh Emil[5], Mouhamed Sobhy[6], Ghada Kazamel[7], Yasir Huzayen[8], Hazem Khamis[9], Mouhamed Bendary[10], Ahmed Bendary[11]
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Background and Aims: The aim of the familial hypercholesterolemia research forum (FHRF) is to collect date about the clinical and laboratory phenotypes of the Egyptian patients with FH. We present an updated analysis of the Egyptian registry.

Methods: An online electronic case report form (e-CRF) was prepared to collect data matching the protocol of the familial hypercholesterolemia Studies Collaboration (FHSC) of the European Atherosclerosis Society (EAS).

Results: From August 2017 to November 2022, 257 cases with FH (48% males, mean age 47 ±15 years) were enrolled. The median time from diagnosis to enrolment was 7 (range 0.5-22) years. Dutch Lipid Network criteria was used in all patients, with 15.6%, 10.1% and 74.3% in the definite, probable, and possible categories respectively. Mean baseline level for total cholesterol was 324±99 mg/dl, for triglycerides was 188 (range 29-1400) mg/dl, for LDL-C was 217.0 (range 73-706) mg/dl and for HDL-C was 47±14 mg/dl. Nearly all patients (99.6%) received lipid-lowering therapy (42.6% monotherapy with statins and 57.4% combination with Ezetimibe). Statin intolerance was reported in 7.5% of patients. PCSK-9 inhibitors were used in 4.3% of patients. Fibrates were added in 7% of cases. Only 2 patients received lipoprotein apheresis.

Conclusions: This updated analysis showed that phenotype of enrolled Egyptian FH cases showed very high lipoprotein levels, adequate utilization of statins (± Ezetimibe), but with inadequate usage of advanced non-statin lipid lowering therapies.

91ST EAS CONGRESS
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235 / #1233

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

EFFECTS OF NUTRITIONAL INTERVENTION - LESSONS FROM A KINDRED WITH FAMILIAL HYPOBETALIPOPROTEINEMIA

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Familial hypobetalipoproteinemia (FHBL) is a rare genetic disorder characterized by decreased plasma levels of apolipoprotein B (apoB) containing lipoproteins. The likelihood of developing a fatty liver is significantly increased. Currently, there is no treatment available besides dietary intervention.

Methods: We investigated the effects of dietary intervention on 5 afflicted members of an FHBL kindred and compared them to the other 2 non-afflicted kindred members. Plasma lipoprotein and apolipoprotein as well as liver enzyme analysis, liver function tests, and apoB gene sequence were performed. The presence of fatty liver was assessed by ultrasound scans including fibroscans.

Results: After dietary intervention, the liver enzymes of the FHBL patients dropped to the level of their non-afflicted relatives. Liver fibroscans revealed a regression of liver steatosis as well as fibrosis.

Conclusions: We provide further evidence for the effectiveness of dietary intervention in FHBL. Since FHBL can lead to fatal liver cirrhosis, it is essential to identify affected patients early and to treat them appropriately. Diagnostic and dietary guidelines should be implemented to improve the treatment of patients suffering from this rare disease.

91ST EAS CONGRESS
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236 / #75

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA IN THE CLINICAL MANAGEMENT

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Heterozygous familial hypercholesterolemia (HeFH) is a common genetic disorder with extremely elevated plasma low density lipoprotein cholesterol and risk of premature atherosclerotic cardiovascular disease (ACVD). However, in Vietnam, there is likely a limit on diagnosis and treatment for HeFH. The objective of this study was to characterize patients with genetic diagnosed HeFH.

Methods: Here, we collected HeFH patients from the Vietnam FH Registry. Patients were eligible if they had a genetic diagnosis of HeFH based on a pathogenic or likely pathogenic mutation or for novel variant that were bio-informatically predicted to be loss-of-function in LDLR (Low density lipoprotein receptor), APOB (Apolipoprotein B) or PCSK9 (Proprotein convertase subtilisin/kexin type 9) gene.

Results: In the overall group of 35 HeFH, there was 85.7% had LDLR mutation and 14.3% had APOB mutation. Rate of coronary artery disease, atherosclerotic carotid artery and lower extremity arterial disease were 54.3%, 14.3% and 8.6%, but not statistically different between LDLR and APOB mutant group. Most of HeFH were used a moderate-low intensity statin or no statin (57.1%).

Conclusions: In conclusion, HeFH patients tended a severe ACVD, and under-treatment with lipid lowering therapy.

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237 / #771

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

LOMITAPIDE BUT NOT EVOLOCUMAB REDUCES LDL-CHOLESTEROL TO GOAL IN HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA – 2 CASE REPORTS

POSTER ON BOARD: AS03.05 INHERITED DYSLIPIDEMIAS

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Background and Aims: Lomitapide lowers LDL-cholesterol (LDL-C) by inhibiting the microsomal transfer protein independently of LDL-C-receptors. This is the only available oral treatment option for patients with homozygous familial hypercholesterolemia (hoFH). Evolocumab, a monoclonal antibody addressing PCSK9, is approved at high dose in hoFH. However, effectivity is limited, the extend depending on the underlying mutation.

Methods: Two patients with proven hoFH and established ASCVD undergoing regular lipoprotein-apheresis received Lomitapide additionally to Rosuvastatin 40 mg and Ezetimibe 10 mg in a clinical setting (named patient program). Afterwards both were switched to Evolocumab 420 mg biweekly. Effects on LDL-C (before lipoprotein-apheresis) were compared (mean).

Results: Both patients were fully adherent to diet instructions and no safety concerns arose. Patient 1: LDL-C 252mg/dl was lowered to 68mg/dl (minimum 46mg/dl) with Lomitapide 20 mg and increased to 176mg/dl with Evolocumab. Reimbursement for Lomitapide allowed back-switch to Lomitapide. LDL-C is at goal (52mg/dl, range 28-68) and Lipoprotein-apheresis was discontinued. Patient 2: LDL-C 236mg/dl dropped to 71mg/dl (minimum 54mg/dl) with Lomitapide 30 mg despite reduced apheresis-frequency and increased to 214mg/dl with Evolocumab. Decision for reimbursement for back-switch to Lomitapide is pending.

Conclusions: A medium dose of Lomitapide reduced LDL-C in both cases markedly. Evolocumab was less effective. Patient 1 with regular Lomitapide treatment could stop apheresis, which might also be possible for patient 2, if reimbursement is permitted. For the first time an oral treatment lowers LDL-C in hoFH profoundly. Data regarding long term safety and reduction of cardiovascular events remain to be seen.

91ST EAS CONGRESS
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238 / #1021

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

RISKS ASSOCIATED WITH USE OF STATINS AND OTHER LIPID-MODIFYING AGENTS ACROSS PREGNANCY – A NATIONWIDE DRUG SAFETY STUDY IN NORWAY IN 2005-2018

POSTER ON BOARD: AS03.06 GENDER AND CARDIOVASCULAR RISK

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Background and Aims: Statins have traditionally been contraindicated during pregnancy; however, the risks associated with exposure to statins and other lipid-modifying agents (LMAs) in human pregnancies remain unclear. We aimed to examine the associations between exposure to LMAs across pregnancy and health outcomes in mother and offspring.

Methods: We linked registry data for all pregnant women in Norway in 2005-2018 from national registries in Norway. Exposures were pregnancy-related (before, during or after pregnancy) prescription fillings of any LMA, any statin- or non-statin LMA, or subgroups of these. Primary outcomes were major congenital malformations and miscarriage, and secondary outcomes were offspring growth and preeclampsia.

Results: In 2005-2018, 34778 pregnancies in Norway resulted in an offspring with a congenital malformation (4.3% of all 805368 pregnancies, omitting multiple births and chromosomal abnormalities). For pregnancies exposed to any type of LMA during first trimester, 22/340 exposed pregnancies developed a malformation (6.5%). For second and third trimester exposure, 3/78 (3.8%) and 2/56 (3.6%) developed a malformation, respectively. For pregnancies exposed 6-12 and 0-6 months before conception, 82/1228 (6.7%) and 70/1217 (5.6%) developed a malformation, respectively; also, for pregnancies exposed 0-6 and 6-12 months after birth, 58/772 (7.5%) and 84/1275 (6.6%) developed a malformation, respectively.

Conclusions: In crude analyses, the prevalence of malformations seemed to be numerically higher for pregnancies exposed to LMAs across pregnancy, although confounding is likely, for example by diabetes mellitus. Drug safety analyses for all outcomes are ongoing and will be presented at the congress, including multivariable models and sensitivity analyses.

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239 / #569

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

RELATIONSHIP BETWEEN LIPID PROFILE AND SEVERITY OF ANGIOGENIC IMBALANCE IN HYPERTENSIVE DISORDERS DURING PREGNANCY

POSTER ON BOARD: AS03.06 GENDER AND CARDIOVASCULAR RISK

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Background and Aims: Several studies confirmed changes in lipid panel (total cholesterol (TL), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides (TG)) in women with hypertensive disorders during pregnancy (HDP). However, there is just few studies examining relationship between lipid profile and angiogenic imbalance (AI) severity, which occurs in preeclampsia. The aim is to study the relationship of serum lipid panel and severity of angiogenic imbalance in hypertensive disorders during pregnancy.

Methods: A cross-sectional study was done on 24 pregnant women with HDP treated in the Vilnius University Hospital Santaros Clinics in Vilnius, Lithuania, from December 2021 to October 2022. The average age of the participants was (33,1 ± 4,8) years. All the taken blood samples were examined for lipid profile, soluble fms-like tyrosine kinase-1 (sFlt-1), placental growth factor (PlGF) and their ratio (sFlt-1/PlGF). Patients were divided into 3 groups based on their degree of AI, evaluated by the sFlt-1/PlGF ratio: no AI (≤38), mild AI (>38-<85), and severe AI (≥85).

Results: The results showed no statistically significant differences in lipid profile. After adjusting these results for atherosclerosis risk factors and divided patients into groups: early onset preeclampsia (<34 pregnancy week) and late onset preeclampsia (≥34 pregnancy week), were found statistically significant differences in women with late onset preeclampsia older that 40 years and TL (p=0,018), LDL (p=0,020).

Conclusions: Findings shows that lipid profile seems to be poor marker of early preeclampsia grading, but quite meaningful in late onset preeclampsia.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

240 / #1140

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

THE GERMAN CARE HIGH REGISTRY FOR FAMILIAL HYPERCHOLESTEROLEMIA –SEX DIFFERENCES, TREATMENT STRATEGIES, AND TARGET VALUE ATTAINMENT

POSTER ON BOARD: AS03.06 GENDER AND CARDIOVASCULAR RISK

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Background and Aims: Familial hypercholesterolemia (FH) is among the most common genetic disorders in primary care. However, only 15% or less of patients are diagnosed, and few achieve the

goals for low-density lipoprotein cholesterol (LDL-C). In this analysis of the German Cascade Screening and Registry for High Cholesterol (CaRe High), we examined the status of lipid management, treatment strategies, and LDL-C goal attainment according to the ESC/EAS dyslipidemia guidelines.

Methods: We evaluated consolidated datasets from 1501 FH patients diagnosed clinically and seen either by lipid specialists or general practitioners and internists. We conducted a questionnaire survey of both the recruiting physicians and patients.

Results: Among the 1501 patients, 86% regularly received lipid-lowering drugs. LDL-C goals were achieved by 26% and 10% of patients with atherosclerotic cardiovascular disease (ASCVD) according to the 2016 and 2019 ESC/EAS dyslipidemia guidelines, respectively. Lipid-lowering drugs were prescribed more often to patients with ASCVD. Males received lipid-lowering drugs more often than females. Treatment was more intense in patients with a genetic diagnosis of FH.

Conclusions: FH is under-treated in Germany compared to guideline recommendations. Male gender, genetic proof of FH, treatment by a specialist, and presence of ASCVD appear to be associated with increased treatment intensity. Achieving the LDL-C reduction goals of the 2019 ESC/EAS dyslipidemia guidelines remains challenging if pre-treatment LDL-C is very high.

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241 / #986

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

GENDER DIFFERENCES IN ATTAINMENT OF LDL-C GOALS INDEPENDENTLY OF TREATMENT INTENSITY

POSTER ON BOARD: AS03.06 GENDER AND CARDIOVASCULAR RISK

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Background and Aims: This study aims to assess the role of gender in attaining LDL-C goals, controlling for Lipid-Lowering Therapy (LLT) intensity, cardiovascular (CV) risk category, and socio-economic context.

Methods: We performed a retrospective cohort study of patients aged 40-85, followed in 1 hospital and 14 primary care centers in Portugal, using electronic health records from 1/1/2012-31/12/2020. The analysis considered an episode-based design, where exposure refers to any moment when LLT started or changed intensity. The likelihood of reaching LDL-C goal according to the contemporanean ESC/EAS guidelines was modelled with adjusted cox regression. The outcome of interest was the probability of reaching the LDL-C target at 180 days. Patients were censored for outcome of interest or death. The main analysis was repeated at 30 day follow-up intervals up to 360 days and also stratified by CV risk.

Results: We identified 40,032 changes in LLT therapy in 30,323 distinct patients. Factors associated with better LDL-C control were male gender, age > 50, lower risk category and higher LLT intensity (Figure 1) . The model shows that men have a 29% higher likelihood of reaching LDL-C goal (HR=1.29, CI:1.21, 1.37) than women, independently of age, LLT intensity, analysed time point, risk category, social or mental health status (Figure
2).

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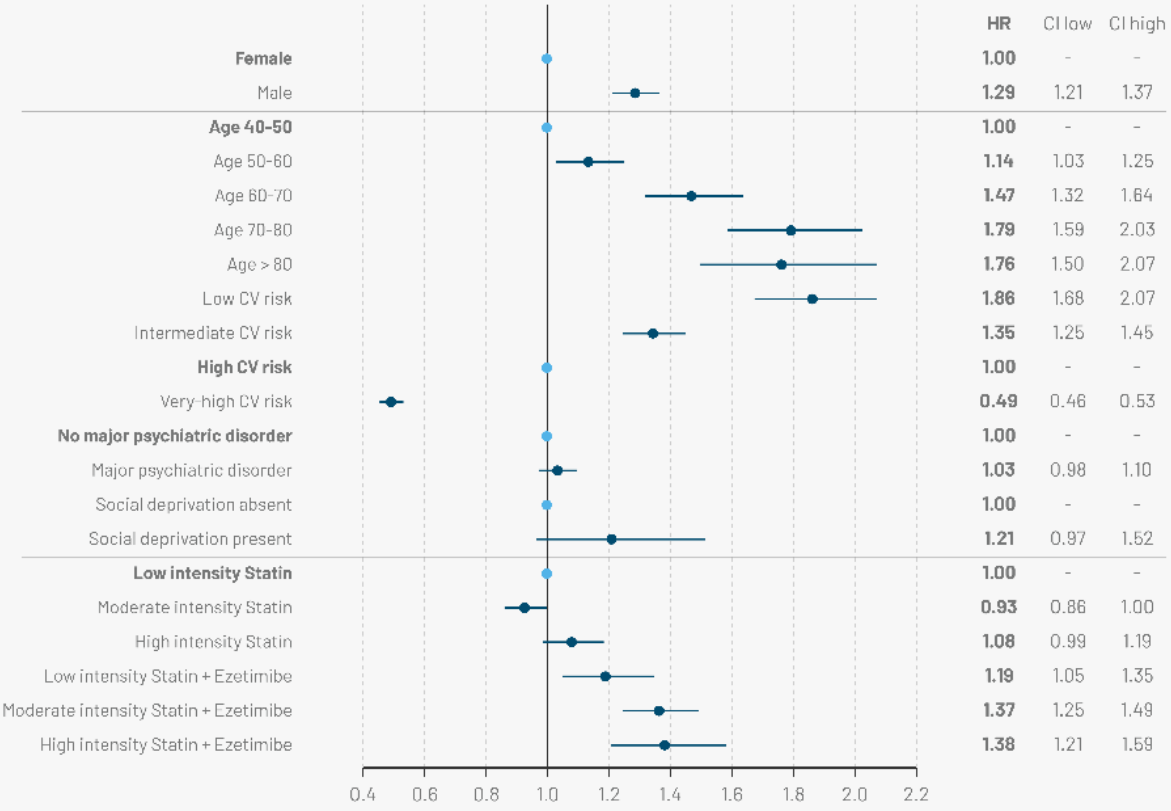
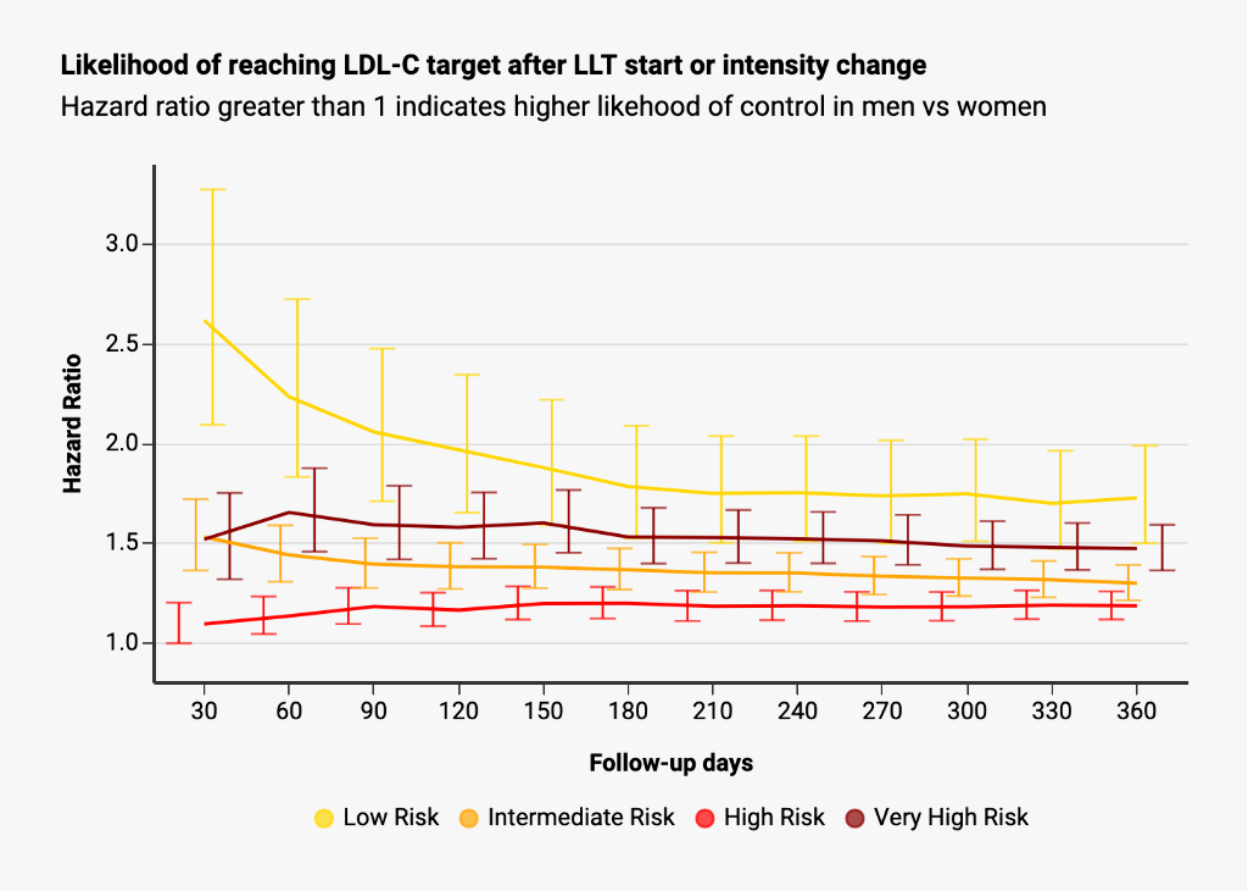
Likelihood of reaching LDL-C target 180 days after LLT start or intensity change

Values presented as hazard ratios with 95% CI.For each variable, reference category is presented in bold and light blue



	HR	CI low	CI high
Female	**1.00**	-	-
Male	**1.29**	1.21	1.37
Age 40-50	**1.00**	-	-
Age 50-60	**1.14**	1.03	1.25
Age 60-70	**1.47**	1.32	1.64
Age 70-80	**1.79**	1.59	2.03
Age > 80	**1.76**	1.50	2.07
Low CV risk	**1.86**	1.68	2.07
Intermediate CV risk	**1.35**	1.25	1.45
High CV risk	**1.00**	-	-
Very-high CV risk	**0.49**	0.46	0.53
No major psychiatric disorder	**1.00**	-	-
Major psychiatric disorder	**1.03**	0.98	1.10
Social deprivation absent	**1.00**	-	-
Social deprivation present	**1.21**	0.97	1.52
Low intensity Statin	**1.00**	-	-
Moderate intensity Statin	**0.93**	0.86	1.00
High intensity Statin	**1.08**	0.99	1.19
Low intensity Statin + Ezetimibe	**1.19**	1.05	1.35
Moderate intensity Statin + Ezetimibe	**1.37**	1.25	1.49
High intensity Statin + Ezetimibe	**1.38**	1.21	1.59



Conclusions: Men have a higher likelihood of attaining LDL-C goals than women after adjustment for LLT intensity, age or risk category. This finding underscores the need for tailoring LLT management strategies by gender.

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242 / #946

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

THE TIMING OF THE STATIN TREATMENT AFTER OVARIECTOMY IN RAT MODEL OF PREDIABETES: CARDIOVASCULAR AND METABOLIC EFFECTS.

POSTER ON BOARD: AS03.06 GENDER AND CARDIOVASCULAR RISK

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Background and Aims: The timing of hormone replacement therapy in the prevention of cardiovascular disease after menopause is intensively investigated. In this respect, no data are available regarding the effect of statins**.**

Methods: To determine the effect early vs. late statin treatment after ovariectomy we have investigated model of prediabetes, hereditary hypertriglyceridemic rat females, including control group and 3 groups started on atorvastatin (5 mg/kg) at 2nd, 8th and 14th week after ovariectomy. After 25 weeks we analyzed strain (percentage change in the arterial diameter) of the abdominal aorta and of right carotid artery by ultrasound, and metabolic and inflammatory markers with potential impact on cardiovascular disease. Results were analyzed using methods of descriptive statistics in R studio.

Results: One-way ANOVA revealed that there was not a statistically significant difference between groups neither for the strain of the abdominal aorta (F(3,36) = [2.852], p = [0.508]) nor for the strain of the the right carotid artery (F(3,36) = [0.4251], p = [0.736]). We have found no significat difference for the expression of connexin 37 in aorta (F(3,18) = [0.987], p = [0.421]), mass of left ventricle (F(3,36) = [2.013], p = [0.130]) and myocardial triglyceride concentration (F(3,18) = [2.837], p = [0.067]). However there was a significant difference for the serum concentration of IL-6 (F(3,20) = [5.042], p = [0.009]) and MCP-1 (F(3,36) = [6.535], p =[0.001]).

Conclusions: The timing had different vascular and myocardial effects and based on our preliminary results we cannot reliably determine the therapeutic window suitable for starting statin therapy after menopause.

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243 / #1059

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

INFLUENCE OF SEX ON THE RESPONSE TO ANTI-INFLAMMATORY TREATMENT AND ON SURVIVAL IN A MURINE MODEL OF DIET-INDUCED CORONARY ARTERY DISEASE

POSTER ON BOARD: AS03.06 GENDER AND CARDIOVASCULAR RISK

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Background and Aims: Cardiovascular risk considerably increases in women after menopause, even surpassing that of men, suggesting an effect of age and sex (1-3). We proposed to study sex-dependent differences on survival, systemic inflammation and monocyte population and its response to anti-inflammatory treatment in young male and female mice, using a diet-induced model of atherosclerosis.

Methods: Male and female SRB1 KO/apoEhypomorphic mice, aged 2-3 months, were randomly assigned to 2 groups: Control (HFD-Control) and minocycline (HFD-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. Systemic inflammation and monocyte populations were compared by Mann–Whitney U test and PCA analysis.

Results: Female mice have a slightly better survival than male mice when fed an atherogenic diet (P=0.12). Minocycline improved survival in male by 35% (P=0.006) and 33% in female mice (P=0.01). Minocycline significantly reduced IL-6 levels (P=0.04) and Ly-6Chigh subset (P= 0.006) and increased Ly6Clow subset (P= 0.006) in male mice without affecting total blood monocytes (P= 0.3). Male and female fed with HFD clustered in different groups; however, after minocycline intervention, were indistinguishable.

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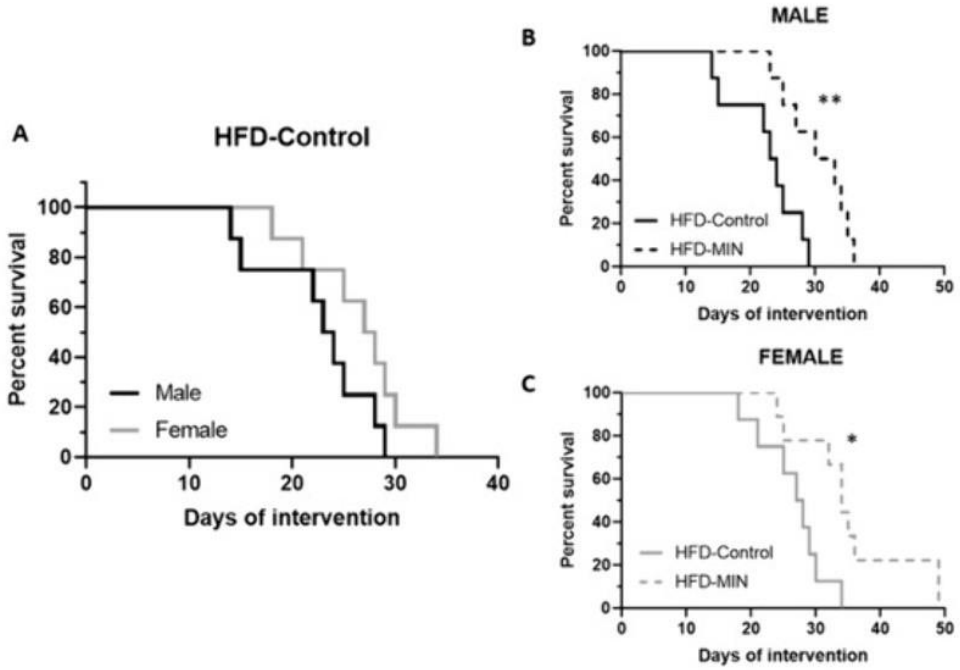

Figure 1. Effect of Minocycline on survival of male and female SRB1 KO/apoE-hypomorphic mice fed atherogenic diet. Kaplan–Meier survival curves of (A) Male (n= 8) and Female (n= 8) HFD-Control groups after fed with an atherogenic diet, (B) Male: HFD-Control (n= 8), HFD-MIN (n= 8) and (C) Female: HFD-Control (n= 8), HFD-MIN (n= 9). *P<0.05 and **P<0.005

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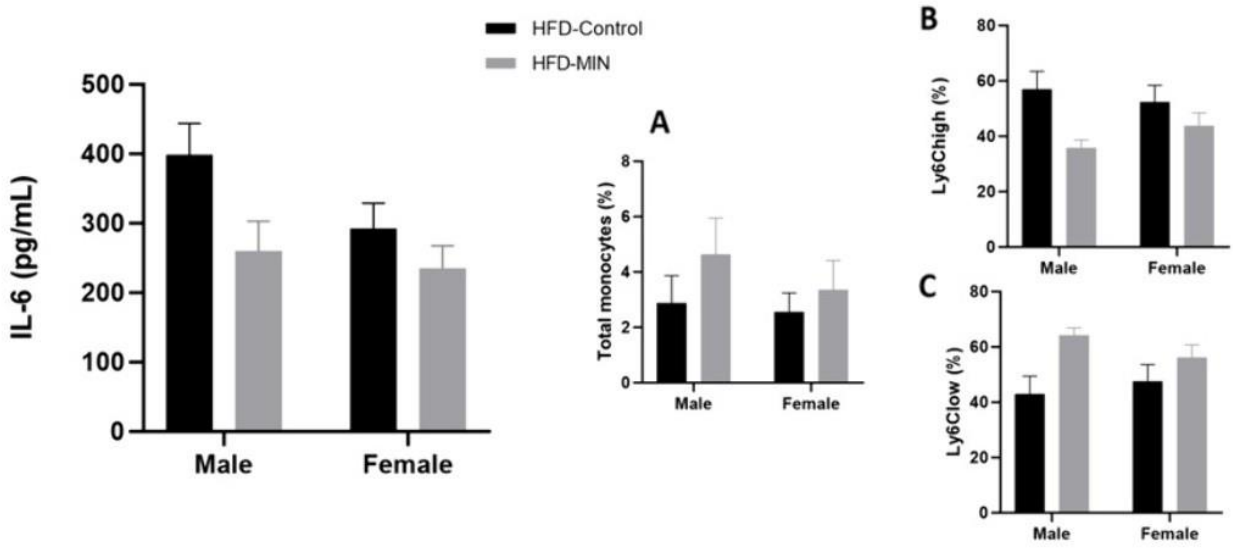

Figure 2. Effect of Minocycline on plasma IL-6 levels and Blood Monocyte content and Subsets in diet-fed female and male SRB1 KO/apoE-hypomorphic mice. IL-6 levels in male: HFD-Control (n=9), HFD-MIN (n=9) and female: HFD-Control (n=10), HFD-MIN (n=13) after 21 days of feeding HFD and minocycline administration. **(A)** Flow cytometric quantification of % monocytes in the sample **(B)** Flow cytometric quantification of Ly6Chigh and **(C)** Ly6Clow monocyte subsets expressed as percentage of cells over total monocytes. Male: HFD-Control (n= 9), HFD-MIN (n= 10) and female: HFD-Control (n= 9), HFD-MIN (n= 10). Data were represented as mean ± SEM. *P<0.05

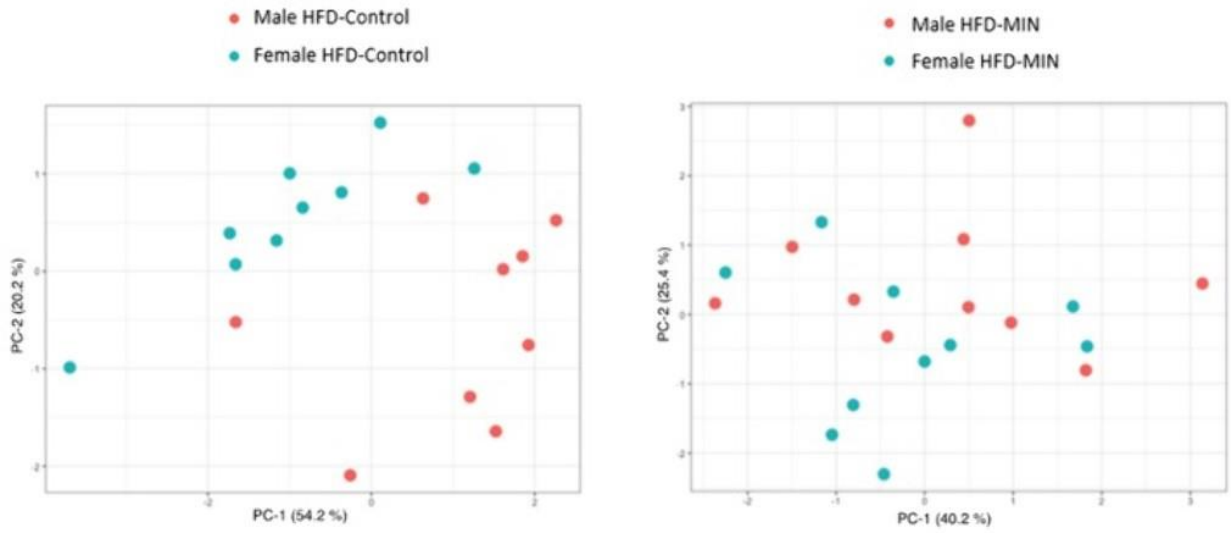

Figure 3. Simultaneous analysis of all inflammatory parameters by PCA Subsets in male and female SRB1 KO/apoE-hypomorphic mice after 21 days of feeding HFD and minocycline administration.

Conclusions: High fat diet decreased the survival and caused early death in this model; however, female have a slightly better survival than male mice. Minocycline improved survival in both, however it had a higher impact on systemic inflammation in male mice by reducing plasma IL-6 levels and shifting toward a more “reparative” phenotype on circulating monocyte subsets.

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244 / #73

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

WOMEN LIVING WITH FAMILIAL HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS03.06 GENDER AND CARDIOVASCULAR RISK

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Background and Aims: Familial hypercholesterolemia (FH) is an important risk factor for atherosclerotic cardiovascular disease. It exsits some hypothesis about disparities of care for FH between genders, but current data is uncompleted. This study aims to access gender differences regarding clinical signs, status of atherosclerosis, lipid profile and treatment intensity in FH.

Methods: We designed a cross-sectional study that collected clinical profile of 95 FH adults from the Vietnam Familial Hypercholesterolemia (VINAFH) registry.

Results: Among these patients, 44 (46.3%) were female. Women as compared with men received FH diagnosis at a later age (57.5±11.3 vs 48.9±13.5 years, p=0.001). Also, men had higher smoking prevalence (76.5% vs 0%, p<0.001). No significant differences were noted regarding hypertension, diabetes, obesity, tendinous xanthomata and arcus cornealis prevalence between men and women. There were not significant differences in baseline level of plasma LDL-C between men and women. A trend for more frequent use of high-intensity statins was noted in men (41.2% vs 15.9%, p=0.007).

Conclusions: In conclusion, FH seems to be diagnosed later in women, whiles male FH patients smoke more frequently and have markedly increased prevalence of coronary artery disease. Treatment intensity was more common in men comparing to women.

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245 / #648

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.07 Environmental risk factors*

MECHANISMS OF NLRP3 INFLAMMASOME ACTIVATION IN MACROPHAGES BY AIR POLLUTION FINE PARTICULATE MATTER (PM2.5)

POSTER ON BOARD: AS03.07 ENVIRONMENTAL RISK FACTORS

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Background and Aims: Exposure to air pollution fine particulate matter ($PM_{2.5}$) aggravates cardiorespiratory diseases by inflammatory cytokine secretion from alveolar macrophages (AMs). We aim to study the mechanisms leading to NLRP3 inflammasome activation and IL-1β release in this process.

Methods: THP1-ASC-GFP cells were incubated with 0, 1, 10, or 100 µg/mL of a $PM_{2.5}$ surrogate (ROFA, Residual Oil Fly Ash). Bone marrow derived macrophages (BMDMs) and AMs from C57BL/6 wild type, transgenic, and knockout mice were also used.

Results: After incubation with ROFA, NLRP3 priming and specks formation was detected by flow cytometry and confirmed by imaging BMDMs from ASC-Citrine mice. Increased IL-1β was detected in cell culture supernatants of ROFA-exposed BMDMs and AMs from wild type mice, but not from *Nlrp3*$^{-/-}$ or *Casp1*$^{-/-}$ mice, or after pre-incubation with the NLRP3-specific inhibitor MCC950. Upregulation of *Tnf* expression and increased TNF-α level in cell culture supernatants were observed. Pre-incubation with an anti-TNF-α antibody decreased IL-1β release from ROFA-exposed AMs. Mechanistically, increased mitochondrial $O_2^{\bullet-}$ production was found in ROFA-exposed BMDMs, together with decreased maximal respiration rate. Inhibition of mitochondrial complex I site responsible for $O_2^{\bullet-}$ production resulted in decreased IL-1β levels. K^+ efflux contribution on NLRP3 activation was evident in ROFA-exposed BMDMs incubated with increasing concentrations of KCl. Lysosomal leakage was also observed after ROFA exposure.

Conclusions: $PM_{2.5}$ induces NLRP3 inflammasome priming and activation in macrophages, leading to IL-1β release. TNF-α, mitochondrial $O_2^{\bullet-}$, K^+ efflux, and lysosomal disruption drive inflammasome engagement by $PM_{2.5}$. These findings unravel the mechanisms by which $PM_{2.5}$ promotes cardiorespiratory inflammation and disease.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.07 Environmental risk factors*

FRUCTOSE CONSUMPTION DURING PREGNANCY INCREASES INTESTINAL CHOLESTEROL ABSORPTION IN RAT MALE DESCENDANTS TREATED WITH A HIGH-FRUCTOSE HIGH-CHOLESTEROL DIET

POSTER ON BOARD: AS03.07 ENVIRONMENTAL RISK FACTORS

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Background and Aims: The epidemic rise in MetS and CVD has been correlated with fructose intake from added sugars. It has been suggested that maternal fructose consumption causes metabolic disorders in offspring. However, it is acceptable to drink beverages with fructose when pregnant. Another well-known CVD risk factor is cholesterol intake. The effects of maternal fructose on the offspring receiving a Western diet combining fructose and cholesterol should be thoroughly investigated.

Methods: Rat offspring from control and fructose-fed mothers were given a high-cholesterol (2%) diet along with liquid fructose (10%) as an example of a Western diet. Plasma, fecal, and tissular parameters of cholesterol metabolism were evaluated along with gene expression.

Results: Male offspring from control mothers ingested more liquid fructose and cholesterol-rich food than those from fructose-fed dams. Furthermore, male descendants of fructose-fed mothers who were given a Western diet presented higher levels of cholesterol both in bile and feces than male descendants of control mothers. However, despite these mitigating factors to create a proatherogenic profile, similar hypercholesterolemia and severity of steatosis were detected in descendants fed a Western diet, independently of maternal intake. Interestingly, males from fructose-fed dams who consumed a Western diet showed in ileum increased absorption, synthesis, esterification, and assembly in lipoproteins of cholesterol.

Conclusions: Maternal fructose induced fetal programming that provoked the Western diet to be considerably more detrimental in their descendants than in the progeny of control mothers. This work was supported by funds from MCIN: SAF2017-89537-R/MCIN/AEI/10.13039/501100011033/FEDER and PID2020-118054RB-I00/MCIN/AEI /10.13039/501100011033. EF had a FPU fellowship from MCIN.

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MANNHEIM GERMANY | MAY 21-24, 2023

247 / #1614

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.07 Environmental risk factors*

DIETARY PATTERN OF ELDERLY PEOPLE LIVING IN THE RURAL AREA OF MORTUGABA (BA), BRAZIL

POSTER ON BOARD: AS03.07 ENVIRONMENTAL RISK FACTORS

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Background and Aims: Introduction: Globally, chronic diseases account for 71% of deaths and are the leading cause of morbimortality in elderly population. **Aim:** Access the metabolic condition and the dietary profile in the studied population.

Methods: Methods: Cross-sectional study conducted in 64 women and 16 men aged > 60 years, in the rural area of Mortugaba (BA). Food frequency questionnaire previously validated in Brazilian population was applied. Anthropometric measurements were evaluated; laboratorial data and the presence of chronic diseases were accessed in the medical record.

Results: Results: The population studied consisted of elderly people (60-88 years), mainly females (80%). Among participants, 84% presented excess weight, of these 52,5% were obese; 35% had Type 2 Diabetes and 54% hypertension. Plasma cholesterol concentration was elevated (221±65 mg/dL), as well as LDL-c (149±16 mg/dL) and triglycerides (157±67 mg/dL); fasting glucose plasma concentration was also high (119,5±38,0 mg/dL). Waist circumference was altered on 32,5% of participants, presenting a positive association with LDL-c. Participants had a regular to high intake of grains, fruit, vegetables, as well as a regular to high intake of sweet beverages and cookies. High frequency of meal replacement with fast-food and pizza were observed, specially at dinner.

Conclusions: Conclusion: The studied population had an elevated prevalence of obesity, type 2 Diabetes, and hypertension, even with an adequate intake of grains, fruit and vegetables. However, the intake of sweet beverages and cookies (ultra-processed foods), fast-foods and pizza were also elevated, increasing the amount of fat, sugar, and calories, predisposing to weight gain and chronic disease development.

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248 / #1251

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.07 Environmental risk factors*

ASSESSMENT OF MEDITERRANEAN DIET ADHERENCE CHANGES OVER TIME IN THE GENERAL POPULATION

POSTER ON BOARD: AS03.07 ENVIRONMENTAL RISK FACTORS

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Background and Aims: Dietary guidelines for cardiovascular disease prevention suggest increasing adherence to Mediterranean-based dietary patterns (MedDiet). We aimed at describing any MedDiet adherence pattern over time and evaluating changes determinants.

Methods: Clinical information on 711 healthy subjects (mean age 68±10 years; 42% males), enrolled in presence and Progresson of Intimal atherosclerotic Lesions in Carotid arteries (PLIC) study, were collected during two visits conducted on average after 4.5 years. MedDiet adherence was assessed both at basal and follow-up visits via the PREDIMED score (14 items), and absolute change in the score was calculated (ΔPREDIMED). Then, subjects were evaluated according to whether their score had worsened or improved.

Results: At the basal visit, the mean PREDIMED score was 8.72±1.82. Overall, 34% subjects improved (ΔPREDIMED:1.87±1.13) and 48% subjects worsened their MedDiet adherence (ΔPREDIMED:-2.02±1.14). Subjects who improved versus worsened their score showed higher presence of obesity and higher blood pressure at basal visit, and a trend toward lower Intima-Media Thickness mean increase from basal to follow-up visits (4.7% versus 6.2%, p=0.11). Food items that contributed to increased PREDIMED score were: olive oil (+66%), legumes (+58%) and fish consumption (+55%) and use of dishes seasoned with sofrito (+177%). Instead, those that contributed to worsening of the score over time were: fruit (-85%), legumes (-77%), fish (-74%) and nuts (-64%) consumption.

Conclusions: The presence of cardiometabolic risk factors at baseline seemed to be associated with an improvement of MedDiet adherence over time.

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249 / #555

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.07 Environmental risk factors*

ASSOCIATIONS BETWEEN CHOLESTEROL LEVELS, BODY MASS INDEX, AND OVERWEIGHT/OBESITY STATUS IN PRESCHOOL CHILDREN

POSTER ON BOARD: AS03.07 ENVIRONMENTAL RISK FACTORS

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Background and Aims: As global health concerns, overweight and obesity have substantial effects on all major organ systems, including the development of high blood pressure, impaired glucose tolerance, dyslipidemia, metabolic syndrome, and cardiovascular disease (CVD) risk factors. Familial hypercholesterolemia (FH), and environmental factors can both contribute to childhood dyslipidemia.

Methods: To ascertain the relationship between cholesterol levels, BMI SDS, and overweight/obesity status, a cohort of 15, 000 children from two populations were analyzed. As part of routine medical examinations of preschool children (aged 2-6 years), information on body mass index (BMI), height, and LDL-C (low-density lipoprotein cholesterol)/TC (total cholesterol) values were gathered.

Results: A weakly positive statistically significant ($p<0.01$) association between LDL-C/TC levels and BMI SDS was found ($R = 0.04$ and $R = 0.05$, respectively). A statistically significant difference in LDL-C levels was seen for the underweight children with all other BMI SDS categories ($p<0.05$), between normal and severely obese children ($p<0.01$), and between overweight and severely obese children ($p<0.05$), when children were categorized by their BMI-SDS (Figure 1C). Additionally, this tendency was not seen when TC was measured, which could be related to obese people having lower levels of high-density lipoprotein cholesterol.

Conclusions: Elevated LDL-C levels were statistically significantly related to higher BMI SDS at the population level but tended to be clinically irrelevant at the individual level. These findings suggest that in preschool children genetic factors have a considerably stronger influence on an individual's cholesterol levels than environmental influences. Therefore, this may be the best age for population-wide screening for inherited hypercholesterolemia.

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250 / #1135

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.07 Environmental risk factors*

THE SOCIO-ECOLOGICAL VIEW ON THE STRATEGIES OF TOBACCO CONTROL FOR CORONARY ARTERY DISEASE PREVENTION

POSTER ON BOARD: AS03.07 ENVIRONMENTAL RISK FACTORS

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Background and Aims: Coronary artery disease (CAD) is an epidemic health problem and becoming more prevalent. Tobacco-smoking is one of the major causes of CAD that contributes to one of every four deaths due to CAD. Tobacco-smoking leads to various cardiovascular problems such as increasing triglycerides, lowering high-density lipoprotein, damaging cells in blood vessels. Since tobacco use is the top significant risk factor for CAD, the aim of this study is to explore the strategies of tobacco-smoking behaviour based on socio-ecological view.

Methods: A systematic review was adopted in this study. Literature related to the topic was searched using the following databases: PubMed, ProQuest, Medline, Cinahl and Embase. Results were retrieved and analysed based on socio-ecological view.

Results: Socio-ecological influences impacted tobacco control behaviour. The personal level influences of beliefs and attitudes were the major barriers on tobacco control behaviours. Strategies focusing on positive reinforcement regulating the beliefs and attitudes on the importance of tobacco control were suggested. At the socio-cultural level, the influences from spouses and children were significantly impacting smokers' decision on whether to quit smoking or not. At the information environmental level, face-to-face counselling and telephone counselling showed positive impact on decreasing the incident of tobacco-smoking. Thus, implementing counselling sessions in tobacco cessation intervention programmes could be considered.

Conclusions: With strong evidences supporting tobacco use leading to CAD, efforts are needed in minimizing tobacco use. The present study reviewed the strategies in tobacco control behaviour based on the socio-ecological view. Intervention programmes should consider applying the strategies for tobacco control intervention and education.

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251 / #1164

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

REDUCTION OF ATHEROGENICITY IN A MODEL OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Patients with focal segmental glomerulosclerosis (FSGS) have an augmented risk of developing cardiovascular disease and a higher prevalence of cardiovascular burden than the general population. The mechanism of Atherogenicity in FSGS is unclear and the role of enhanced podocyte survival by trehalose on Atherogenicity is not investigated. This study aims to investigate atherogenic markers in a mouse model of FSGS and study the effect of trehalose.

Methods: FSGS was induced in male balb/c mice via adriamycin. Mice were monitored weekly for proteinuria and disease development. After six weeks of treatment with trehalose and sucrose as a control, serum and urine samples were collected and kidney tissue was harvested for further analysis.

Results: Kidney damage was confirmed by proteinuria and immunohistological analysis. Mice that received trehalose had significantly less proteinuria and less histological damage with better podocyte morphology on electron microscopy. There was no difference seen in inflammatory markers between study groups. Current work aims to measure plasma levels of LDL-C, HDL-C, sICAM-1, and sVCAM-1 as atherosclerotic plaque instability and lipid markers.

Conclusions: FSGS was induced in mice and ongoing work aims to determine plasma levels of atherogenic markers in the induced model.

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252 / #306

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

TELOMERASE ACTIVITY IN PATIENTS WITH CEREBRAL ATHEROSCLEROSIS AND DIABETES MELLITUS

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: The aim of our study is to determine the relationship between telomerase activity and lipid spectrum, structural and functional state of the heart and cerebral vessels and heart rate variability, as well as with telomere length in patients with stage 1–3 cerebral atherosclerosis (CA) and type 2 diabetes (T2D).

Methods: The clinical and instrumental study: 161 patients with CA. Patients were divided into 2 groups: I - with CA of the 1st-2nd degree, II - after ischemic stroke. Mean age = 65.1±10.5 and 65.4±9.1 years.

Results: To identify factors influencing telomerase activity, we used the method of constructing logistic regression models. When building models, the following categories were used: lower telomerase activity — T/S < 3.16 (low and medium tertiles); higher telomerase activity - T/S above 3.16. One-way regression analysis revealed one statistically significant (p=0.02) relationship between telomerase activity and male gender. To select a set of significant risk factors, the method of stepwise inclusion/exclusion of signs was used. Based on the identified significant risk factors, a multivariate logistic regression model was built. A statistically significant positive relationship was established between telomerase activity and the HRV index, as well as a negative relationship with the atherogenicity index.

Conclusions: Based on multivariate regression analysis, there was a correlation between telomerase activity and the atherogenicity index and the index of the total tension of the autonomic regulation of the heart rhythm in patients at different stages of CA, including those with type 2 diabetes (AUC=0.73 (95% CI 0.63–0.83).

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253 / #714

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

AMYLOIDOSIS-RELATED ORTHOPEDIC EVENTS, LOW PLASMA TRANSTHYRETIN, AND RISK OF CARDIAC EVENTS

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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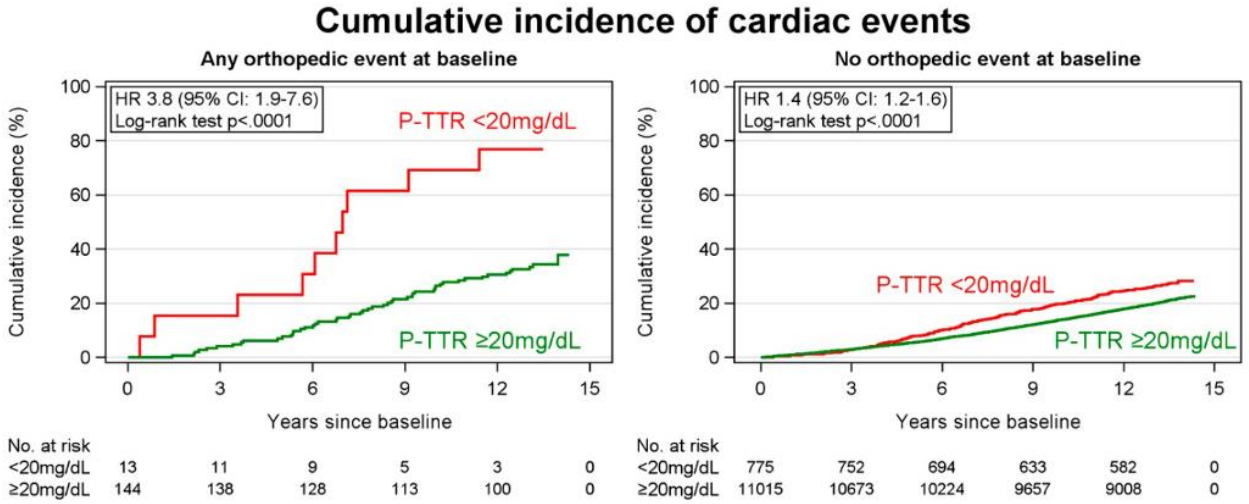
Background and Aims: Carpal tunnel syndrome, spinal stenosis, and biceps tendon rupture may precede cardiac transthyretin amyloidosis (ATTR-CA). We tested the hypothesis that amyloidosis-related orthopedic events herald amyloidosis and cardiac events consistent with ATTR-CA through transthyretin destabilization.

Methods: In observational analysis in the Copenhagen General Population Study (CGPS; n=93,637), we first tested whether amyloidosis-related orthopedic events at baseline were associated with amyloidosis and incident cardiac events consistent with ATTR-CA (heart failure, atrial fibrillation, myocardial infarction, or death), and whether a low plasma transthyretin was associated with a higher risk. In genetic analysis, in CGPS and the Copenhagen City Heart Study(CCHS) combined (n=102,496), we tested whether TTR genotypes associated with stepwise lower plasma transthyretin, marking lower transthyretin tetramer stability and higher amyloidogenic potential, was associated with both orthopedic and incident cardiac events, implying a common mechanistic background through transthyretin destabilization.

Results: In individuals with versus without orthopedic events at baseline, hazard ratios (HRs) were 10.7 (95% CI: 3.9-29.3) for amyloidosis, and 1.3(1.1-1.4) for cardiac events. Furthermore, in individuals with orthopedic events at baseline, HRs for cardiac events were 3.8(1.9-7.6) in those with transthyretin <20 mg/dL versus ≥20 mg/dL (Figure). Finally, HRs as a function of TTR genotype increased with lower transthyretin and lower transthyretin tetramer stability up to 3.0(1.4-6.6) for orthopedic events and 1.6(95% CI: 1.0-2.6) for cardiac events.

Conclusions: Amyloidosis-related orthopedic events are associated with increased risk of incident cardiac events, with the highest risk in those with low transthyretin levels. Orthopedic and cardiac events are linked through transthyretin tetramer

destabilization.



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254 / #336

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

LDL-C/APOB RATIO PREDICTS FUTURE CARDIOVASCULAR EVENTS IN CARDIOVASCULAR DISEASE PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE AS WELL AS IN THOSE WITHOUT NONALCOHOLIC FATTY LIVER DISEASE

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: A low LDL-C / apoB ratio reflects small LDL particle size and is associated with insulin resistance. Non-alcoholic fatty liver disease (NALFD) is an important feature of the insulin resistance syndrome and confers an increased cardiovascular risk. The impact of the LDL-C / apoB ratio on the risk of cardiovascular events in patients with NAFLD is unclear and is addressed in the present study.

Methods: We enrolled a large high risk cohohort of 1515 patients with established cardiovascular disease (1272 patients with angiographically proven stable CAD and 243 patients with sonographically proven peripheral artery disease). NAFLD was diagnosed using the validated fatty liver index. Prospectively, cardiovascular events were recorded over a mean follow-up period of 7.6±4.9 years.

Results: At baseline, the LDL-C / apoB ratio was significantly lower in patients with NAFLD (n=709) than in subjects who did not have NAFLD (1.34±0.29 vs. 1.39±0.26 mg/dl; p=0.001). During follow-up, 755 patients suffered cardiovascular events. The event rate was higher in patients with than in those without NAFLD (53.6 vs. 47.6%; p=0.020). The LDL-C/ApoB ratio significantly predicted cardiovascular events in the total study cohort, with a standardized adjusted hazard ratio (HR) of 0.86 [0.80-0.94]; p<0.001 and both in patients with NAFLD (HR 0.87 [0.78-0.97]; p=0.013) and in subjects who did not have NAFLD (HR 0.87 [0.77-0.97]; p=0.013, respectively).

Conclusions: We conclude that in subjects with established cardiovascular disease the LDL-C / apoB ratio predicts cardiovascular events both among patients with NAFLD and in those who do not have NAFLD.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

RISK ASSESSMENT OF CARDIOVASCULAR EVENTS USING ULTRASONOGRAPHIC ACHILLES TENDON THICKNESS AND SOFTNESS AND INTIMA MEDIA THICKNESS IN FAMILIAL HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Familial hypercholesterolemia (FH) is a genetic disorder characterized by high LDL-C, tendon xanthomas and atherosclerotic cardiovascular diseases. Japanese FH criteria have adopted Achilles tendon (AT) thickness (ATT) measured by XP and/or ultrasonography. This study aimed to determine the cutoff values for major adverse cardiovascular events (MACE) in patients with heterozygous FH (HeFH) for ATT, AT softness and intima-media thickness of carotid artery (C-IMT).

Methods: This was a retrospective cohort study of 391 HeFH patients. We measured AT thickness and softness and C-IMT by ultrasonography. We classified the subjects according to the cut-off values of AT thickness and softness and C-IMT, and assessed risks for MACE.

Results: The median observation period was 1239 days (700-1827 days). Twenty-one subjects (5%) had MACE during the observation period. The cutoff values of MACE for ATT were 9.9 mm in male and 7.1 mm in female; and C-IMT were 1.6 mm in male and 1.5 mm in female. The cutoff values for EI as AT softness were 3.9 in male and 4.4 in female. Subjects were divided into two groups according to the cutoff values, we compared the rate of MACE. The MACE rates were significantly increased in groups of AT thickening, softening and C-IMT thickening ($P<0.001$).

Conclusions: We indicated the cutoff values of AT and C-IMT for MACE in HeFH patients. Since ATT is useful not only for the diagnosis but also for risk assessment in FH, we consider it is necessary to controvert of measurement of ATT in addition to the presence of xanthoma.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

IDENTIFICATION OF BLOOD MODULAR GENOME-WIDE GENE EXPRESSION BIOMARKERS OF CARDIOVASCULAR HEALTH AND DEPRESSION IN THE YOUNG FINNS STUDY

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: We aimed at identifying the shared gene co-expression modules underlying cardiovascular health (CVH) and depression.

Methods: We analysed blood genome-wide expression data to identify gene co-expression modules shared by cardiovascular health (CVH) metrics and Beck's depression score, markers of cardiovascular health and depression respectively. CVH metrics were defined according to the American Heart Association's criteria using seven metrices based on smoking, diet, physical activity, body mass index (BMI), blood pressure, total cholesterol, and fasting glucose. Beck's depression scores were derived from Beck's depression inventory, a 21-item self-report inventory that measures characteristics and symptoms of depression. Joint association of the modules, identified with weighted co-expression analysis, with the markers of CVH and depression was tested with multivariate analysis of variance (MANOVA) .

Results: We identified a gene module with 256 genes significantly correlated with both CVH metrics ($r=-0.13$, $p=6 \times 10^{-5}$) and Beck's depression score ($r=0.09$, $p=0.009$). Based on MANOVA test results adjusted for age and sex, the gene module was jointly associated with both CVH and depression markers with $p=2.4 \times 10^{-6}$. The three most significant member genes from the significant modules were YOD1, RBX1, and LEPR with Bonferroni adjusted p-value ($p.adj < 1.3 \times 10^{-7}$). Genes in the modules were enriched with biological pathways involved in several diseases such as non-alcoholic fatty liver disease and brain diseases including Alzheimer's, Parkinson's and Huntington's disease with $p.adj < 0.05$.

Conclusions: The identified gene module and its most significant member genes can provide new joint biomarkers for CVH and depression .

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

INFLUENCE OF PCSK9 INHIBITION ON BIOMARKERS OF ATHEROSCLEROTIC PLAQUE DESTABILIZATION RELEASE IN PATIENT WITH DYSLIPIDEMIA

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Other plasma factors play an important role in the pathogenesis of atherosclerosis, in addition to elevated cholesterol levels. These factors may be responsible for the stabilization of atherosclerotic plaque and include osteopontin (OPN), osteoprotegerin (OPG), and metalloproteinases (MMPs). The purpose of this study was to evaluate the impact of modern lipid-lowering therapy utilizing proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors on the levels of these factors.

Methods: Participants in the study had dyslipidemia and were candidates for alirocumab therapy. In this group, the concentrations of OPN, OPG, and MMPs were measured prior to and three months following the initiation of therapy.

Results: In the study, the concentrations of OPN, OPG (p0.001), and metalloproteinase 2 (MMP-2) ($p<0.05$) decreased significantly following the administration of therapy. In addition, we observed that the concentrations of these factors were higher in the patient group prior to treatment initiation compared to the control group ($p<0.001$).

Conclusions: The findings of our study indicate that therapy with PCSK-9 inhibitors significantly reduces the concentration of factors that increase the vulnerability of atherosclerotic plaques, which may explain their important role in reducing cardiovascular risk in patients undergoing this therapy.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

HIGH CHOLESTEROL ABSORPTION, A POTENTIAL RISK FACTOR FOR ATHEROSCLEROSIS. A POSSIBLE PROATHEROGENIC MECHANISM IN A COHORT STUDY.

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Approximately 30% of individuals have high cholesterol absorption efficiency, which originates from genetic variabilities in the small intestinal sterol transporters. In these individuals, the absorption of cholesterol and the ASCVD risk are increased compared with those with low cholesterol absorption. Serum lipid concentrations do not explain the increased risk, and the mechanism(s) remains unresolved. We evaluated the link between cholesterol absorption and proatherogenic functions of LDL in a cohort of 90 individuals.

Methods: Mildly to moderately hypercholesterolemic office employees, 56 females and 34 males, with a median age of 52 years and without lipid lowering therapy or ASCVD were divided into low (n=45) and high (n=45) cholesterol absorbers by the median value of serum cholestanol to cholesterol ratio, a validated biomarker of cholesterol absorption efficiency. LDL aggregation susceptibility was analysed by inducing aggregation of isolated LDL and following the aggregate formation. LDL lipidome was determined by mass spectrometry. Serum cholesterol and noncholesterol sterols were analysed with gas-liquid chromatography.

Results: Age, diets, and serum lipid levels were similar between the groups. LDL aggregation susceptibility was higher in the high vs low cholesterol absorbers. The mean aggregate size after 2 hour incubation was 1650 nm vs 1360 nm in the high vs low absorbers ($P<0.04$). Of LDL surface lipids, sphingomyelin 16:0, lysophosphatidylcholine 18:0, and especially phosphatidylcholines 32:0, 32:1, and 32:2 were significantly higher in the high vs low cholesterol absorbers ($P<0.011$).

Conclusions: Increased LDL aggregation and more aggregation-prone LDL surface lipidome were present in high cholesterol absorbers.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

CIRCULATING OBESITY-INDUCED MCP-1 AFFECTS GRAY-SCALE MEDIAN (GSM) SCORING IN PATIENTS UNDERGOING CAROTID ENDARTERECTOMY.

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Monocyte chemoattractant protein-1 (MCP-1) is one of risk factors initiating atherosclerosis process. The infuence of obesity on atherosclerotic disease in the carotid district is still unclear. The purpose of our study was to evaluate the role of obesity in MCP-1 production and destabilization of carotid plaques in patients undergoing carotid endarterectomy (CEA).

Methods: A total of 77 consecutive patients undergoing CEA were enrolled in the study group. The control group consisted of 15 patients without symptoms of atherosclerosis undergoing abdominal aortic aneurysm repair. The patients were divided into three subgroups, according to their body mass index (BMI): BMI<25, BMI 25-30 and BMI>30. The stability of carotid plaques was assessed ultrasonifically, using GSM scoring system. Serum MCP-1 levels were determined using commercial ELISA kit.

Results: Serum MCP-1 levels increased along with BMI values, and were higher in subgroup with overweight (BMI 25-30) and in group with obesity (BMI>30) compared to controls (p=0.015 and p=0.007; respectively). There was also the difference in MCP-1 level between patients with normal body weight (BMI<25) and patients with obesity (p=0.048). In contrary, GSM scale, which reflects carotid plaque stability, was the highest in patients with BMI<25, and decreased gradually in overweight and obesity groups. The inverse relationship was observed between MCP-1 and GSM scale (R= -0.240, p=0.036) in the whole group of patients.

Conclusions: Results from our study showed that overweight/obesity can participate in carotid plaque destabilization by mechanism dependent on the intensification of MCP-1 production in population of patients undergoing carotid endarterectomy.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

PLASMA LEVELS OF PROPROTEIN CONVERTASE SUBTILISIN/KEXINTYPE 9 ARE INVERSELY ASSOCIATED WITH N-TERMINAL PRO B-TYPE NATRIURETIC PEPTIDE IN OLDER POPULATION

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Cardiac natriuretic peptides (NPs) exert several effects on lipid metabolism. In vitro studies, NPs have been found to modulate low-density lipoprotein receptor (LDLR) trafficking by preventing proprotein convertase subtilisin/kexin type 9 (PCSK9) overexpression. Aim: to investigate an association between plasma PCSK9 levels and N-terminal pro B-type natriuretic peptide (NT-proBNP) in vivo.

Methods: We performed a cross-sectional study on 160 consecutive older patients. Patients taking lipid-lowering drugs or with acute heart failure were excluded. Fasting blood samples were collected in stable health condition.

Results: Mean age was 87.8±6.4 years with a female prevalence (62.5%). The median NT-proBNP was 2340 (814–5397) pg/mL. The mean plasma PCSK9 was 275.2±113.2 ng/mL. We found an inverse correlation between plasma PCSK9 and NT-proBNP (r = −0.280; p=0.001). This association was confirmed after taking into account NT-proBNP tertiles (plasma PCSK9 levels: 317.4±123.6 ng/mL in the first tertile, 283.3 ± 101.8 ng/mL in the second tertile, 231.3±99.0 ng/mL in the third tertile, p=0.001) and even after an adjustment for confounding factors (beta = −0.361, p=0.001 for ln(NT-proBNP); beta = −0.330, p=0.001 for NT-proBNP tertiles).The strength of the correlation between plasma PCSK9 and NT-proBNP was likely greater in patients affected by type 2 diabetes mellitus (r = −0.483; p=0.006) and in male patients (r = −0.431, p=0.001).

Conclusions: The inverse association found between PCSK9 and NT-proBNP plasma levels in our real-life clinical study supports the hypothesis that NPs may play a role in cholesterol metabolism, possibly through an inhibitory action on circulating PCSK9 concentrations, thus increasing the availability of LDLR.

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MANNHEIM GERMANY | MAY 21-24, 2023

261 / #761

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

EFFECTS OF AEROBIC TRAINING ON OXIDATIVE STRESS PARAMETERS AND METABOLIC ENZYMES ACTIVITIES IN LIVER IN RATS WITH EXPERIMENTALLY INDUCED HYPERHOMOCYSTEINEMIA

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Data from literature indicate that hyperhomocysteinemia causes significant effects on digestive and cardiovascular system. The aim of this study was to investigate the effects of experimentally induced hyperhomocysteinemia under the condition of aerobic training on oxidative stress parameters and metabolic enzymes activities in rat liver.

Methods: Male *Wistar albino* rats were separated into four groups (n = 10, per group): C: 0.9% NaCl 0.2 mL/day subcutaneous injection (s.c.); H: homocysteine 0.45 µmol/g b.w./day s.c.; CPA saline (0.9% NaCl 0.2 mL/day s.c.) and a program of aerobic treadmill training; and HPA homocysteine (0.45 µmol/g b.w./day s.c.) and a program of aerobic treadmill training. Substances were applied during two weeks, while aerobic training was performed during four weeks.

Results: Activity of catalase was decreased in HPA group (0.26 ± 0.12 U/mg protein) compared to C group (0.54 ± 0.24 U/mg protein), $p < 0.05$. Concentration of malondialdehyde was increased in HPA group (0.94 ± 0.42 µmol/mg protein) compared to C (0.47 ± 0.21 µmol/mg protein), $p < 0.01$ and CPA (0.60 ± 0.27 µmol/mg protein) group, $p < 0.01$. Total activity of lactate dehydrogenase was increased in HPA group (6.63 ± 0.36 U/mg protein) compared to C (4.64 ± 1.01 U/mg protein), $p < 0.01$, H (4.58 ± 0.43 U/mg protein), $p < 0.01$, and CPA (5.12 ± 0.27 U/mg protein) group, $p < 0.01$.

Conclusions: Hyperhomocysteinemia under the condition of aerobic training causes increase lipid peroxidation (higher MDA level), and increase of lactate dehydrogenase activity in rat liver.

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MANNHEIM GERMANY | MAY 21-24, 2023

262 / #715

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

EFFECTS OF VITAMIN B6 ON CARDIOVASCULAR BIOMARKERS IN SERA, OXIDATIVE STRESS PARAMETERS, AND METABOLIC ENZYMES ACTIVITIES IN CARDIAC TISSUE OF RATS WITH EXPERIMENTALLY INDUCED HYPERHOMOCYSTEINEMIA

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: The aim of this study was to examine the effects of vitamin B6 in hyperhomocysteinemic conditions on cardiovascular biomarkers in sera, oxidative stress parameters, and metabolic enzymes activities in cardiac tissue of rats.

Methods: Male *Wistar albino* rats were divided into four groups (n = 10, per group): C: 0.9% NaCl 0.2 mL/day s.c. + 0,9% NaCl 0.5 mL i.p; H: homocysteine 0.45 µmol/g b.w./day s.c. + 0.9% NaCl 0.5 mL i.p; C-B6: saline (0.9% NaCl 0.2 mL/day s.c.) + vitamin B6 (7 mg/kg b.w. i.p.); and H-B6: homocysteine (0.45 µmol/g b.w./day s.c.) + vitamin B6 (7 mg/kg b.w. i.p.). Substances were applied s.c. for 2 weeks and i.p for 4 weeks.

Results: Level of homocysteine was significantly higher in H group (21.03 ± 4.40 µmol/L) compared to C group (12.95 ± 1.44 µmol/L), $p < 0.01$. Application of vitamin B6 in hyperhomocysteinemic conditions led to significant decrease in homocysteine levels (11.61 ± 3.08 µmol/L) compared to H group, $p < 0.01$. Levels of troponin T, lactate dehydrogenase, total cholesterol, HDL, LDL, triglycerides and folate did not differ significantly between groups. Activity of superoxide dismutase was increased in H group (18.05 ± 2.40 U/mg protein), compared to C group (7.11 ± 2.19 U/mg protein), $p < 0.01$, and H-B6 group (8.73 ± 0.68 U/mg protein), $p < 0.01$.

Conclusions: Hyperhomocysteinemia can lead to increased oxidative stress and cause increasing of superoxide dismutase activity, but parallel application of vitamin B6 can lower levels of homocysteine and oxidative stress.

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263 / #980

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

PCSK9: COULD THEIR PLASMA LEVELS AND CD34+CPCS PREDICT PWV IMPROVEMENT IN OPTIMIZED LIPID LOWERING STRATEGY?

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: In the era of innovative therapies, non-statin lipid lowering treatments are gaining increasing attention. Research currently also focuses on the identification of novel biomarkers in atherosclerosis, with pulse wave velocity (PWV), circulating CD34+ progenitor cells (CD34+CPCs) and PCSK9 plasma levels looking like promising markers. Our study aimed to evaluate the effects of LDL-C lowering on PWV, the correlation of PCSK9 plasma levels and CD34+CPCs with PWV, and their changes with PCSK9 inhibitors (PCSK9-i).

Methods: One-hundred-one patients with genetically confirmed heterozygous familial hypercholesterolemia (HeFH) not reaching the lipid goals despite high-intensity statin with/without ezetimibe were enrolled from the Lipid Centers of the University Hospital of Messina and Catania, Italy, between September 2017 and May 2019. Therapy was intensified every six months (with ezetimibe or PCSK9i, respectively); lipid panels and PWV measurement were obtained at each time-point (T0,T1,T2). Fifty-six patients receiving add-on ezetimibe (T1) and then PCSK9i (T2) were selected to determine PCSK9 plasma levels (26 patients) or CD34+CPCs (30 patients). PWV was also evaluated at each time-point. Non-parametric statistics were applied.

Results: 77.3% of patients achieved their lipid goal on the triple-combination-therapy. PWV values decreased in the whole study population at each stage of therapy optimization, being the decrease more marked in PCSK9i group. PCSK9 levels increased after statin/ezetimibe optimization(T1), yet significantly decreased after PCSK9i treatment(T2). CD34+CPCs were widely distributed ad T1, while their counts neared to controls' values at T2.

Conclusions: PWV decrease correlated to LDL-C lowering, but also with PCSK9 levels/change at the steady-state therapy and to CD34+CPCs change.

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264 / #1287

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

THROMBOCYTOPENIA AND KIDNEY DISEASE, TWO POSSIBLE HALLMARK OF FCS PHENOTYPE: PRELIMINARY EVIDENCE FROM A COHORT STUDY

POSTER ON BOARD: AS03.08 NOVEL RISK FACTORS AND BIOMARKERS

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Background and Aims: Familial Chylomicronemia Syndrome (FCS) is a rare monogenic autosomal recessive disorder of lipid metabolism determining severe hypertriglyceridemia (HTG).As the use of Volanesorsen, a novel FCS treating drug, has been associated with thrombocytopenia, the relationship between FCS and low platelets counts should be firmly established.It has been reported also kidney complication in FCS.To this aim, we have retrospectively evaluated the spontaneous variation of platelet counts and Kidney impairment in a cohort of patients with FCS.

Methods: This study enrolled 20 FCS patients.The occurrence of thrombocytopenia was defined as mild, moderate, or severe if platelet count (PLTs) were below 140000, 100000 or 50000, respectively.Kidney impairment has been defined as a composite of hyperfiltration, proteinuria and eGFR<90 ml/min.

Results: During follow-up, 8 (44.4%) patients experienced at least one episode of mild and 1of moderate thrombocytopenia.Mean triglycerides do not significantly predict mean platelet values.However,when considering a multivariate model including mean triglycerides, sex, the presence of hepatic steatosis and age we found that male sex and the presence of ultrasound estimated hepatic steatosis were associated with significantly lower platelet.Median eGFR was significantly associated with history of hypertension.Proteinuria occurred in 5 patients, and it did not associate with hypertension, diabetes, age, sex nor triglyceride levels.Four patients meet the criteria of hyperfiltration whereas 3 were exhibiting an eGFR below 90 ml/min.Overall, the impairment in kidney function was independent from age, diabetes, hypertension, median TGs, AP, sex.

Conclusions: The present analysis confirmed that thrombocytopenia and kidney impairment might be a clinical characteristics of FCS phenotype.Further studies in larger cohort are needed.

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265 / #1153

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.09 Epidemiology of socioeconomic and psychosocial risk factors*

PSCYHOEMOTIONAL STATUS ASSESSMENT IN PATIENTS WITH HIGH CARDIOVASCULAR RISK

POSTER ON BOARD: AS03.09 EPIDEMIOLOGY OF SOCIOECONOMIC AND PSYCHOSOCIAL RISK FACTORS

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Background and Aims: Under the influence of complex action of risk factors there are significant changes in the psycho-emotional state that cause hypertension. With the progression of hypertension there are more profound changes in the personality of the patient, which is accompanied by the accumulation of personal anxiety, which can lead to a depressive state of neurotic genesis.
Aim: to study pscyhoemotional status in patients with high cardiovascular risk.

Methods: clinical, laboratory, instrumental, inquire.

Results: By the method of Holmes and Rage, high level of stress resistance was found only in patients with 2 stage hypertension (163.8±11.28). In patients with 3 stage hypertension the level corresponds to threshold level of stress-resistance. Using the Taylor anxiety measurement technique, it was an average level of anxiety with a tendency to high (23.8±1.22) already in I group($p<0.05$), the level of anxiety in 2nd and 3rd groups can be considered as high 39.9±2.31 and very high 43.7±1.90($p<0.001$ with control), which significantly exceeded the control and I group($p<0.001$).
The highest level of reactive anxiety was in I group (54.1±0.97) against the background of the lowest personal anxiety of 40.7±0.68 points, compared with control (46.7±1.32,$p<0.01$) and (46.1±2.09,$p<0.05$). There is a significant increase in personal anxiety (as a persistent human's characteristic) as hypertension is progressing: in the II group 51.2±1.03 points, in the third group 53.9±0.74 points, compared with the control group 46.1±2.09 points ($p<0.05$) and ($p<0.01$), respectively.

Conclusions: The effect of stress on the occurrence of a syndrome of psychoemotional stress is shown, which leads to a steady increase in blood pressure.

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266 / #953

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.10 Coagulation*

IMPACT OF PCSK9 INHIBITORS ON HEMOSTASIS IN PATIENTS WITH HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS03.10 COAGULATION

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Background and Aims: In addition to lowering plasma lipid levels, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors may have multiple pleiotropic effects unrelated to lipids. This study aimed to evaluate the efficacy of PCSK9 inhibitors in patients with isolated hypercholesterolemia.

Methods: The trial enrolled 21 individuals with isolated hypercholesterolemia and atherosclerosis who received alirocumab for 90 days (150 mg every two weeks) (150 mg every two weeks). Plasma levels of lipids, glucose homeostasis factors, and hemostatic markers were measured at baseline and following treatment.

Results: The PCSK9 inhibitor administered to these patients reduced plasma levels/activity of fibrinogen (from 3.6 ± 0.5 to 2.9 ± 0.4 g/l, $p < 0.01$), factor VII (from 143.8 ± 16.7 to 114.5 ± 14.1 %, $p < 0.01$) and plasminogen activator inhibitor-1 (PAI-1) (from 74.9 ± 13.9 to 52.8 ± 9.1 ng/ml, $p<0.001$) without a significant reduction in von Willebrand factor levels, and it tended to prolong the partial thromboplastin and prothrombin times.

Conclusions: Our results suggest that treatment with PCSK9 inhibitors has a multipotential effect on fibrinolysis and coagulation in patients with isolated hypercholesterolemia and that this medication may have future benefits for patients who are statin-intolerant or contraindicated for statin use.

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267 / #512

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.11 Gut microbiome*

MULTI-OMICS APPROACH TO INVESTIGATE GUT DYSBIOSIS IMPLICATIONS IN LYSOSOMAL ACID LIPASE DEFICIENT MICE

POSTER ON BOARD: AS03.11 GUT MICROBIOME

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Background and Aims: One of the major symptoms of lysosomal acid lipase (LAL)-deficient patients is lipid malabsorption that usually leads to death. In particular, we recently discovered that the intestinal phenotype seen in LAL KO mice is due to macrophage infiltration which results in disruption of whole-body homeostasis. Since intestinal disturbances are often a consequence of microbiome dysbiosis, we aim to investigate gut microbiome and metabolome functionality and relation to host physiology through untargeted proteomics.

Methods: Cecum content of WT and LAL KO mice was used to perform 16S sequencing and NMR analysis to identify differenttialy abundant bacteria and metabolites, respectively. Small intestine from WT and LAL KO mice were processed for proteomics analysis on Orbitrap Fusion Tribrid Mass Spectrometer, equipped with a nano-ESI ion source.

Results: The microbiome and metabolome composition of LAL KO mice was strikingly different when compared to WT mice. For example, we found a 50-fold increase in the abundance of Rikenellaceae, normally associated with elevated plasma lipids, and a 1.6-fold decrease in the presence of propionate and acetate, usually linked to a healthy gut status. WIth our proteomics analysis, we identified 779 statisticaaly significant proteins, of which 418 were upregulated and 239 downregulated.

Conclusions: Our work suggests that a remarkable dysbiosis in LAL KO mice is occurring and this might have an impact on the phenotype of the mice. Whether this microbial signature has an effect on intestinal homeostasis is under investigation through untargeted proteomics pathway analysis.

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268 / #149

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.13 Genomics, GWAS and population genetics; Mendelian randomization*

RARE VARIANT ANALYSIS IN CAD RELATED LOCI IN PATIENTS WITH PREMATURE CAD REVEALS POSSIBLE TARGETS FOR FURTHER FUNCTIONAL STUDIES

POSTER ON BOARD: AS03.13 GENOMICS, GWAS AND POPULATION GENETICS; MENDELIAN RANDOMIZATION

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Background and Aims: Genetic susceptibility and lifesytle factors lead to atherosclerotic cardiovascular disease.The genetic basis of coronary artery disease (CAD) is highly complex where both monogenic forms and rare variants contribute to the disease. The aim of this study was to detect rare variants in numerous disease-related genes and their possible association with the disease.

Methods: We included patients with premature CAD with mean age of 50.4 from a CAD cohort and performed whole exome sequencing (WES). To determine rare variants in disease relevant genes/loci, a bunch of CAD-associated loci from different GWAS were analyzed. Missense, nonsense and splice variants with minimum alelle frequency (MAF<0.01) were filtered for analysis.

Results: We have identified 132 rare variants in total in 42 of 48 people in CAD related loci. Variants were detected in a bunch of disease-associated GWAS loci and along with the genes related to monogenic conditions associated with CAD such as familial dyslipidemias and metabolic syndrome.

Conclusions: Variants found in genes related to monogenic conditions associated with CAD were mostly variant of unknown significance (VUS) and candidates for further family and functional studies except for a *LDLR* variant which was classified as pathogenic. An intriguing outcome of the study was detection of same rare variants (MAF<0.01) in more than person in a relatively small cohort. Thus, these variants might be polymorphic in the Turkish population or functionally be related to CAD. Consequently, having revealed rare variants which could be targets for further functional research, this study contributes to our understanding of complex genetic architecture of CAD.

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269 / #657

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.13 Genomics, GWAS and population genetics; Mendelian randomization*

TRIGLYCERIDES, POLYMORPHISMS AND THE RISK OF ACUTE CORONARY SYNDROME IN THE CZECH POPULATION

POSTER ON BOARD: AS03.13 GENOMICS, GWAS AND POPULATION GENETICS; MENDELIAN RANDOMIZATION

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Background and Aims: Elevated levels of plasma triglycerides (TG) have been identified as a risk factor for the development of cardiovascular disease, including acute coronary syndrome (ACS). Increased values of plasma TG have a significant genetic background. We have screened SNPs within 17 different genes, associated with TG values, and examined their potential association with increased risk of ACS.

Methods: The variants within *APOA5, GCKR, MAP3K1, CTF1, CYP26A1, LRP1, CILP2, LIPC, APOE, GALNT2, LPL, CAPN3, FRMD5, CETP, NAT2, HLA* and *TRIB1* genes were genotyped in total 929 patients with ACS and 936 healthy controls (post-MONICA study). Only adult men under the age of 65 were included.

Results: Plasma TG levels did not differ significantly between patients and controls (1.96 ± 1.30 mmol/L vs. 2.06 ± 1.47 mmol/L). Individually, only *CYP26A1* AA homozygosity (rs2068888) was associated (P<0.05; OR; 95% CI – 1.37; 1.05 – 1.77) with ACS. SNPs within *APOA5, CTF1, CYP26A1, CILP2, LIPC, APOE, LPL, CAPN3, FRMD5, NAT2,* and *TRIB1* (reached OR for ACS risk above 1.15) were used to calculate the genetic risk score. Subjects with a score of 15 or more vs. less than 10 occurred more frequently among patients with ACS than among controls (P<0.001; OR; 95% CI – 1.85; 1.30 – 2.62).

Conclusions: Genetic risk score calculated from eleven genetic variants associated with plasma TG levels is a significant predictor of ACS in Czech Caucasian males. *Supported by Ministry of Health,Czech Republic-conceptual development of research organization 64165,General University Hospital in Prague,Czech Republic;and by the Charles University,project Cooperatio,research area "Metabolic Diseases" No.207037.*

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270 / #432

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.14 Epigenetics and microRNA*

SYNERGETIC EFFECT BETWEEN NFKB1A AND MICRORNAS GENETIC VARIATIONS IN METABOLIC SYNDROME PATIENTS

POSTER ON BOARD: AS03.14 EPIGENETICS AND MICRORNA

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Background and Aims: Metabolic syndrome (MetS) is a common multifactorial disorder that involves abdominal obesity, dyslipidemia, hypertension, and hyperglycemia. Although the nuclear factor-kappaB (NF-κB) is involved in the various metabolisms, the pathogenesis of MetS is still well unknown. MicroRNA (miR)-146a, miR-155 and miR-499 have been shown to play an important role in the regulation of NFKB expression and found to be differentially expressed in DM. The aim of this study was to investigate the association of MetS with NFKB1, NFKB1A and miRNAs polymorphisms as well as the analysis of their single and combined effects on its susceptibility in a Korean population.

Methods: We analysed the distribution of NFKB1-94 ins/del ATTG (rs28362491), NFKBIA (rs696), miR-146a (rs2910164), miR-155 (rs767649) and miR-499 (rs3746444) genetic polymorphisms using PCR-RFLP assay in 236 MetS patients and 247 healthy controls.

Results: The data revealed no significant differences in the distribution of the genotypes and alleles of NFKB1 rs28362491, NFKB1A rs696, miR-146, miR-155 and miR-499 polymorphisms between the both groups. Whereas significant differences were found between MetS patients and control subjects, concerning combined genotypes and allele combinations composed of five polymorphisms.

Conclusions: These findings indicate that combined effects of NFKB1, NFKB1A and miRs polymorphisms may represent novel markers of MetS susceptibility.

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271 / #495

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.14 Epigenetics and microRNA*

REGULATION OF NC886 RNAS IS ASSOCIATED WITH CARDIOMETABOLIC RISK FACTORS, DEATH AND STROKE

POSTER ON BOARD: AS03.14 EPIGENETICS AND MICRORNA

Sonja Rajić[1], Saara Marttila[1], Nina Hutri-Kähönen[1], Mika Kähönen[1], Terho Lehtimäki[1], Leo-Pekka Lyytikäinen[1], Pashupati Mishra[1], Nina Mononen[1], Olli Raitakari[2], Melanie Waldenberger[3], Thomas Delerue[3], Winfried März[4], Marcus Kleber[4], Emily Harville[5], Ruiyuan Zhang[5], Emma Raitoharju[1]
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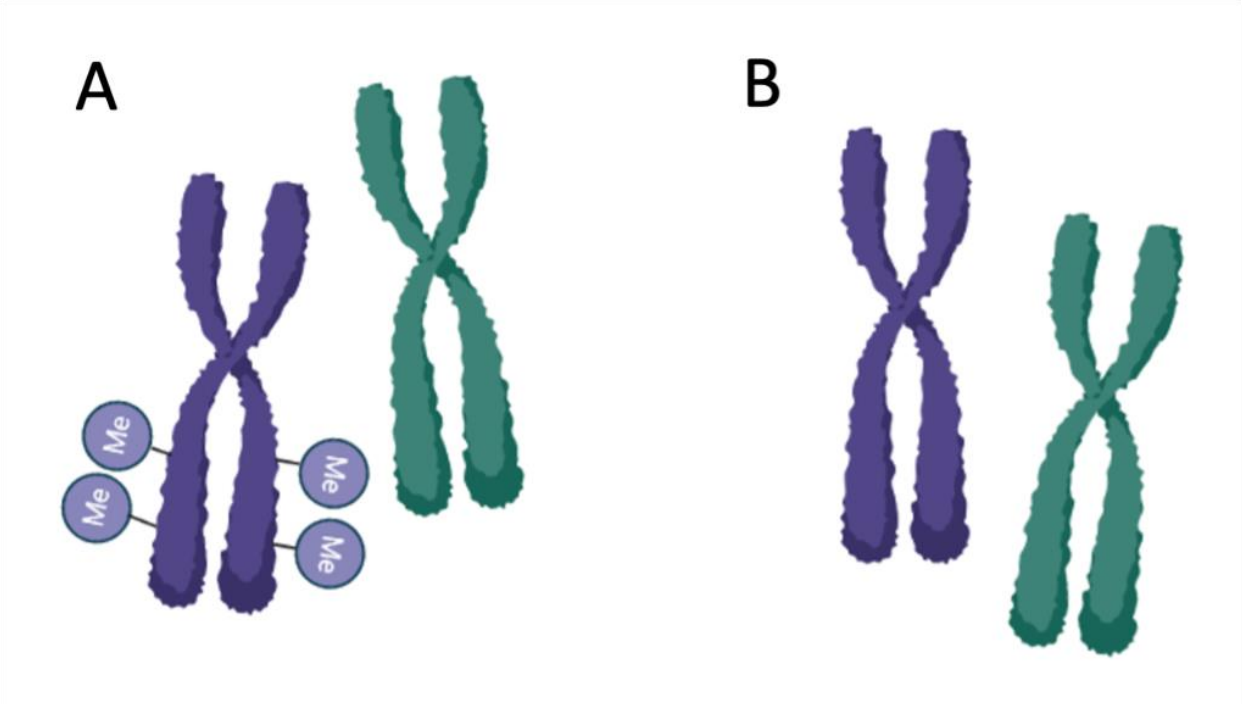
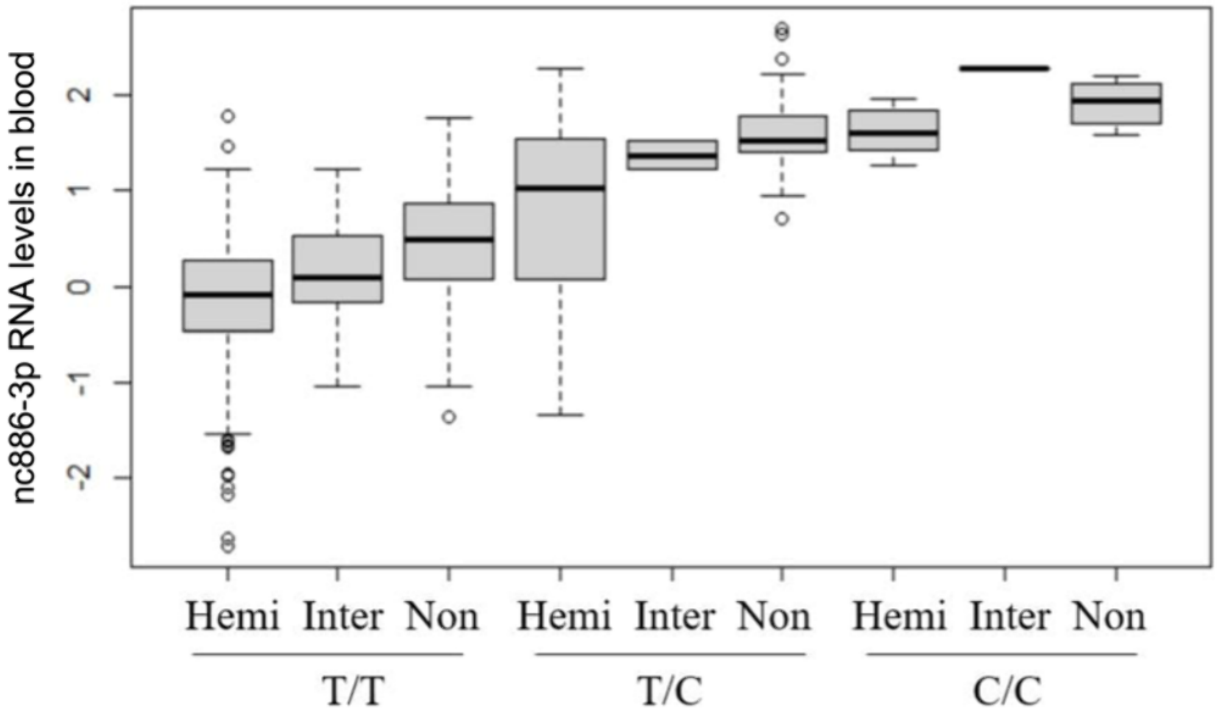
Background and Aims: Non-coding *886* is a unique polymorphically imprinted gene (Figure1). Its methylation status has been suggested to mediate DOHaD/Barker's hypothesis. We have previously shown that both *nc886* methylation status and genetics have an independent effect on nc886 RNA levels. Here we have combined this information to predict lifelong nc886 RNA levels and study their association to cardiometabolic diseases (CMDs)

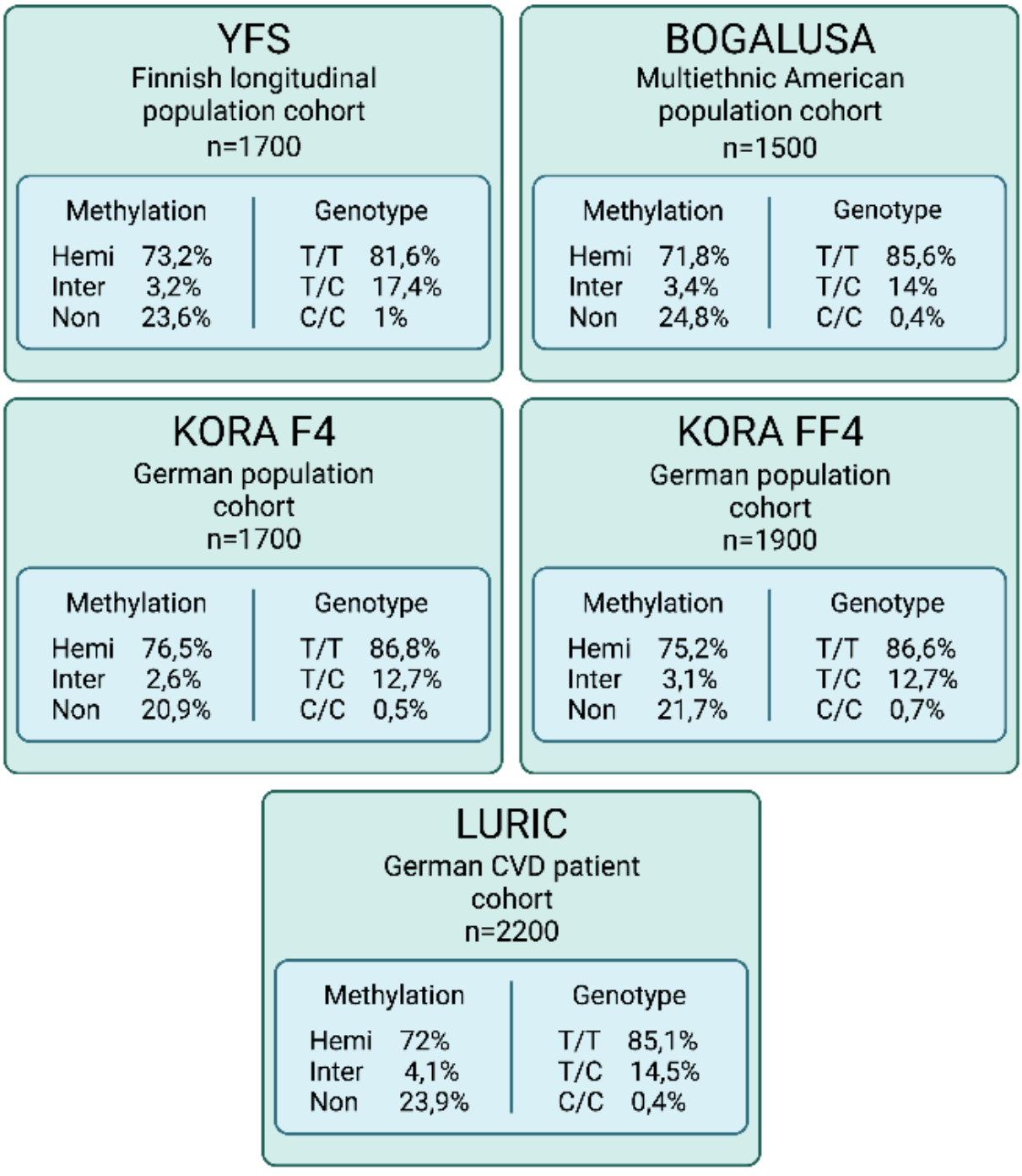


Methods: We studied the imprinting pattern of *nc886*, as well as the association of the predicted levels of RNAs it codes, to cardiometabolic diseases across 5 cohorts from both Europe and America, utilizing a total of >7600 individuals. We have combined two known regulatory elements of RNA expression – the *nc886* methylation status and genotypes of the lead SNP (Figure2), to investigate their proportions between cohorts and study their associations to CMD phenotypes using logistic regression.



Results: The imprinting pattern of *nc886* is stable across multinational cohorts, as are the SNP allele frequencies (Figure3). Elevated predicted nc886 RNA levels are associated with glucose, cholesterol levels and blood pressure across multiple cohorts. In a CMD patient cohort LURIC, individuals presenting with elevated nc886 RNA levels have increased incidence of stroke and

death.


YFS
Finnish longitudinal population cohort
n=1700
Methylation
Hemi 73,2%
Inter 3,2%
Non 23,6%
Genotype
T/T 81,6%
T/C 17,4%
C/C 1%
BOGALUSA
Multiethnic American population cohort
n=1500
Methylation
Hemi 71,8%
Inter 3,4%
Non 24,8%
Genotype
T/T 85,6%
T/C 14%
C/C 0,4%
KORA F4
German population cohort
n=1700
Methylation
Hemi 76,5%
Inter 2,6%
Non 20,9%
Genotype
T/T 86,8%
T/C 12,7%
C/C 0,5%
KORA FF4
German population cohort
n=1900
Methylation
Hemi 75,2%
Inter 3,1%
Non 21,7%
Genotype
T/T 86,6%
T/C 12,7%
C/C 0,7%
LURIC
German CVD patient cohort
n=2200
Methylation
Hemi 72%
Inter 4,1%
Non 23,9%
Genotype
T/T 85,1%
T/C 14,5%
C/C 0,4%

Conclusions: Our results show that stable regulation of nc886 RNAs is associated with CMD phenotypes. As the methylation pattern of *nc886* is established before birth, the associations here further validate *nc886* as a mediator of DOHaD. The stable regulation of *nc886* would provide genetics-independent metabolic variation to the population. Combined, these findings can help us understand and advance health throughout one's lifespan.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.15 Gene-Environment interactions*

ASSOCIATION BETWEEN LONG NON-CODING RNA ANRIL GENE POLYMORPHISMS AND RISK OF DIABETES MELLITUS

POSTER ON BOARD: AS03.15 GENE-ENVIRONMENT INTERACTIONS

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Background and Aims: Diabetes mellitus (DM) posting one of the most common chronic diseases develops generally in individuals with insulin resistance in insulin target tissues and impaired insulin secretion from pancreatic β-cells in the presence of appropriate genetic and environmental factors. Various mutations in long non-coding RNA (lncRNA) were associated with pathogenesis of many diseases including cancers and vascular diseases. This study aims to elucidate correlation to lncRNA ANRIL gene polymorphisms (rs4977574, rs133048 and rs496892) in patients with DM.

Methods: Two hundred thirty-eight patients with DM and 300 healthy subjects were enrolled in this study. LncRNA ANRIL gene polymorphisms were analysed by polymerase chain reaction-restriction fragment length polymorphism.

Results: Among three polymorphisms, no SNP was associated with risk of DM. Whereas several combined genotypes and haplotypes composed of rs4977574, rs133048 and rs496892 polymorphisms showed significant differences between patients with DM and control subjects. In addition, rs133048 polymorphism revealed association with triglyceride and systolic blood pressure levels by stratified and ANOVA analyses.

Conclusions: These observations suggest that combined effects of lncRNA ANRIL rs4977574, rs133048 and rs496892 polymorphisms were associated with the susceptibility to DM in Koreans.

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273 / #725

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.16 Cardiometabolic factors implicated in the development of heat failure with preserved ejection fraction*

ASSOCIATION OF BRANCHED-CHAIN AMINO ACIDS WITH MORTALITY RISK IN THE LUDWIGSHAFEN RISK AND CARDIOVASCULAR HEALTH (LURIC) STUDY

POSTER ON BOARD: AS03.16 CARDIOMETABOLIC FACTORS IMPLICATED IN THE DEVELOPMENT OF HEAT FAILURE WITH PRESERVED EJECTION FRACTION

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Background and Aims: Branched-chain amino acids (BCAAs, i.e. sum of leucine, isoleucine and valine) are biomarkers and effectors of metabolic diseases, but their impact on mortality is largely unknown. We aimed to evaluate whether serum BCAA concentrations are associated with cardiometabolic risk factors and mortality in a cohort of patients referred to coronary angiography.

Methods: We investigated 2,236 participants (mean age 62.5 ± 10.8 years; 29.9 % women; 37.7 % diabetes mellitus type 2) of the Ludwigshafen Risk and Cardiovascular Health (LURIC) study with available serum BCAA concentration measurements.

Results: In multivariate linear regression analyses adiponectin (β = -0.27), hemoglobin (Hb; β = 0.25), C-peptide (β= -0.17), HbA_{1c} (β= 0.16), and homoarginine (β= 0.13; P< 0.001 for all) showed the strongest association with serum BCAA concentration. During a median follow-up of 10.5 years, a total of 715 participants died, including 450 cardiovascular deaths. Serum BCAA concentrations were inversely associated with all-cause and cardiovascular mortality HR 0.75 (95 % CI 0.69 - 0.82), p< 0.001, and HR 0.72 (95 % CI 0.65 - 0.80), p < 0.001, respectively after adjustment for potential confounders. Addition of BCAAs to established risk factors for mortality significantly improved discrimination and reclassification for all-cause and cardiovascular death.

Conclusions: Higher concentrations of BCAAs are associated with cardiometabolic risk but inversely with mortality in persons with intermediate to high cardiovascular risk. Further studies are warranted to evaluate diagnostic and therapeutic utility of BCAA in the context of cardiovascular diseases.

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274 / #527

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.16 Cardiometabolic factors implicated in the development of heat failure with preserved ejection fraction*

THE EXERCISE CAPACITY IN PATIENTS WITH METABOLIC SYNDROME, VISCERAL OBESITY AND RIGHT AND LEFT VENTRICULAR HYPERTROPHY

POSTER ON BOARD: AS03.16 CARDIOMETABOLIC FACTORS IMPLICATED IN THE DEVELOPMENT OF HEAT FAILURE WITH PRESERVED EJECTION FRACTION

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Background and Aims: Exercise intolerance in patients with metabolic syndrome (MS) is well known and influences cardiovascular mortality. It appears due to multiple factors such as insulin resistance, visceral obesity, heart remodeling etc. The aim of our study was to evaluate the role of visceral adiposity [intraabdominal fat thickness (IFT), epicardial fat thickness (EFT), abdominal wall fat index (AWFI)] and right (RV) and left ventricular (LV) hypertrophy in exercise tolerance in patients with MS.

Methods: Our study included 93 patients with MS, and 93 controls. For MS we used ≥3 criteria of IDF, AHA/NHLBI. Using 2D echocardiography we assessed LVmass/$h^{2.7}$, RV free wall thickness (FWT), EFT. By abdominal sonography we assessed IFT, AWFI. All participants underwent exercise ECG stress test and the exercise capacity was determined by exercise duration (ED) and metabolic equivalents (METs).

Results: Statistical analysis showed that IFT, AWFI, EFT, LVmass/$h^{2.7}$ and RVFWT were significantly higher in MS group (all P<0.01). Patients with MS showed lower ED and METs (P<0.001). In bivariate analysis we found that METs and ED were negatively associated to LVmass/$h^{2.7}$ (r=-0.399, P<0.001; r=-0.367, P<0.001), RVFWT (r=-0.501, P<0.001; r=-0.226, P=0.020), EFT (r=-0.646, P<0.05; r=-0.538, P<0.001), IFT (r=-0.208, P=0.033; r=-0.367, P<0.001), AWFI (r =-0.423, P<0.001; r=-0.618, P<0.001) in MS group. Multivariate regression analysis showed that EFT, AWFI, LV and RV hypertrophy were independently associated with ED in patients with MS (P<0.05).

Conclusions: Our findings support that LV and RV hypertrophy, EFT, AWFI have an impact on exercise capacity in patients with MS.

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275 / #124

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

PREDICTORS OF ADHERENCE TO LIPID-LOWERING MEDICATIONS AMONG ADULT OMANI PATIENTS WITH HYPERLIPIDEMIA

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: Background: Dyslipidemia is recognized as a significant risk factor for cardiovascular diseases. Its treatment has shown a decrease in cardiovascular disease morbidity and mortality. However, non-adherence prevalence among patients with dyslipidemia was reported to be high. Poor adherence to medications can negatively impact health outcomes.
Aim: The study aimed to identify factors contributing to lipid-lowering medication adherence among patients with hyperlipidemia in Oman.

Methods: A descriptive cross-sectional survey design study was conducted to identify factors (socioeconomic, patient-related, and treatment-related) contributing to lipid-lowering medication adherence among patients with hyperlipidemia in Oman. A sample of 228 both male and female Omani hyperlipidemia patients was recruited from an outpatient lipid clinic and LDL-Apheresis Day care unit at Sultan Qaboos University Hospital (SQUH). Multiple linear regression was performed to identify the predictor factors for non-adherence to lipid-lowering medication.

Results: The mean age of the patients was 49.2 years (SD = 14.08, range = 18-85). The majority were male (54.8%), married (74.1%), and higher education (57%). Joint ache (51.8%) and muscle pain (51.4%) were the most common and frequent side effects of the lipid-lowering medication. MARS-5 adherence 68.5% of patients adhered to lipid-lowering medication. Five variables (barriers, age, knowledge, sex and level of education) predict adherence significantly affected medication adherence.

Conclusions: Conclusion: The study outcome may guide future interventional studies to improve lipid-lowering medication adherence among patients with hyperlipidemia in Oman. The results of study open a window to investigate the factors associated with heart disease among the Omani population.

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276 / #516

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

HIGH-INTENSITY THERAPY CHOICES TO MANAGE HYPERCHOLESTEROLAEMIA: PATIENT AND PHYSICIAN PERSPECTIVES

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: High-intensity lipid-lowering therapies (HI-LLTs) are used less often than recommended by guidelines. We examined prescriber and patient perspectives regarding intensifying LLTs to identify corresponding barriers.

Methods: 450 healthcare professionals (HCPs) and 456 patients were recruited from Germany, Italy and UK. Participants responded to a very-high cardiovascular risk case study to explore treatment preferences and barriers. The case involved a 55-year-old male with first-line (statin) treatment failure who experienced a myocardial infarction 6 months ago**.** Treatment preferences were categorised as conservative (wait and watch or switch to alternative statin) or intensified (add-on or switch to alternative HI-LLT). Data were analysed using descriptive statistics and differences explored using independent t-tests and McNemar/chi-square tests, where appropriate.

Results: Contrary to guidelines recommendation to intensify treatment for very-high risk patients, 38.4% of HCPs chose a conservative approach. These HCPs had doubts about the necessity of guidelines (p=0.01), greater concerns about their application (p=<0.001) and held more negative views of guidelines in general (p=<0.001). They were more likely to be primary care physicians than specialists (73.0%:50.0%, p=<0.001). When cost and access restrictions were theoretically removed, 29.2% of HCPs continued with a conservative approach (p=<0.001). Patients were more sceptical than HCPs about intensifying treatment with 49.6% preferring the conservative treatment option.

Conclusions: One-third of clinicians chose conservative treatment in a very-high-risk patient scenario where guidelines recommend treatment escalation . Approximately half of patients were reluctant to consider intensifying treatments. This highlights the need for further support to optimise the use of evidence-based treatment for hypercholesterolaemia.

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277 / #985

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

IDENTIFYING UNMET NEEDS IN PATIENTS WITH HYPERCHOLESTEROLAEMIA: ARE CLINICIAN AND PATIENT VIEWS SIMILAR?

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: Patients' treatment perceptions and preferences are important determinants of adherence, and are often not revealed in consultations, creating a disconnect between clinician and patient perceptions. We describe patient preferences for the management of hypercholesterolaemia and quantify this disconnect based on a quantitative survey.

Methods: 456 patients (mean age 57 years) with hypercholesterolaemia and 450 HCPs (224 primary care and 226 specialist physicians) from Germany, Italy and the UK responded to the survey. Patients provided responses to validated questionnaires assessing hypercholesterolaemia treatment preferences, experiences and beliefs (necessity and concerns). HCPs provided estimates of patient responses.

Results: HCPs correctly predicted patient preferences for involvement in decisions, satisfaction with cholesterol testing and preferences for tablets over injections. However, HCPs underestimated patients' information needs about their hypercholesterolaemia (74.6% patients wanted more information; HCP estimated 32.2%) and the number of patients willing to take an additional treatment if their current therapy was ineffective (82% patients, 55% HCP). HCPs underestimated the proportion of patients who have doubts about the need for cholesterol-lowering medication (64% patients; 40% HCP) and those who reported any treatment concerns (78.7% patients; 40% HCP).

Conclusions: Our findings show that many patients have information needs, treatment preferences and beliefs that clinicians are not aware of. In particular, clinicians underestimated the proportion of patients who have doubts and/or concerns about their LLT. This pattern of beliefs is known to predict non-adherence. Addressing this disconnection could help to improve treatment adherence and outcomes.

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278 / #1006

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

HYPERTRIGLYCERIDEMIC CRISIS ASSOCIATED WITH SEVERE ACUTE PANCREATITIS – CASE SERIES

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: Hypertriacylglyceridemia has significant influence on the development of severe acute pancreatitis (HTG-AP). We present case reports from consequtive cases with the aim to discuss the individualized and most efficient therapeutic approach including use of plasmapheresis.

Methods: Methods: We analyzed the clinical data of patients treated for severe HTG-AP at the ICU at our workplace:

Patient	1
Age(years)/sex	38/Female
Initial TAG (mmol/l)	65.65
Final TAG (mmol/l)	6.06
Uses of plasmapheresis	No
Length of hospital stay	215
Complications	Yes
Hypolipidemic therapy	Atorvastatin 20mg, Fenofibrate 145mg

TAG - triglycerides

Results: All patients (age 34.4 ± 5.9 years) were hospitalized. Initial TAG were 77.77 ± 13.84 mmol/l. After therapy TAG decreased to 4.48 ± 2.49 mmol/l. Two patients had severe complications (repeated surgery, drainage of abdominal cavity, intraabdominal bleeding). Plasmapheresis was used in three cases, but dit not influence the lenght of hospital stay nor occurence of complications. Genetic cause of hypertriglyceridemia was not known at the time of analysis.

Conclusions: HTG causes the most severe pancreatitis from among the different etiologies. Literature data suggest that early removal of TAGs from the blood could be beneficial; further studies should be designed to provide the evidence for or against early intervention in HTG-AP.

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279 / #969

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

CORRELATION BETWEEN NEW ATHEROSCLEROTIC PLAQUE VULNERABILITY MARKERS AND THE CAROTID MAGNETIC RESONANCE IMAGES IN HYPERLIPIDEMIC PATIENTS TREATED WITH PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 INHIBITORS.

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: Atherosclerosis is a multifactorial, progressive, chronic inflammatory disease. The most accurate predictors of atherosclerotic plaque destabilization are imaging techniques, specifically ultrasonography and magnetic resonance imaging (MRI). Cytokines such as osteopontin, osteoprotegerin, and metalloproteinase 9 could be used as the most recent markers to identify and monitor the efficacy of anti-atherosclerotic therapy.

Methods: Patients (n=16) with ultrasonography (USG) and MRI evidence of unstable atherosclerotic plaque were included in the study. Before and after 90 days of proprotein convertase subtilisin/kexin type 9 (PCKS9) inhibitor (alirocumab) treatment, the concentrations of biomarkers were determined and compared. In addition, there was a correlation between pre-treatment concentrations and carotid MRI images.

Results: After treatment with alirocumab, concentrations of metalloproteinase 9 (MMP-9) and osteopontin (OPN) and osteoprotegerin (OPG) decreased significantly (p 0.05). Also, the results of OPN, OPG, and MMP 9 varied significantly depending on the type of atherosclerotic plaque in the MRI assay. In atherosclerotic plaques deemed more stable, the concentrations of OPN and OPG were greater (p 0.01), whereas the concentration of MMP-9 correlated with the instability of the plaque (p 0.05).

Conclusions: We demonstrated, probably for the first time, that alirocumab therapy significantly decreased the serum concentration of atherosclerotic plaque markers. Also, we showed the correlation between atherosclerotic plaque type as assessed by carotid MRI and the concentration of these markers.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

NOVEL MISSENSE VARIANTS IN THE LMF1 GENE: IDENTIFICATION BY NEXT GENERATION SEQUENCING AND FUNCTIONAL CHARACTERIZATION

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: Hypertriglyceridemia (HTG) is a common form of dyslipidemia associated with an increased risk of cardiovascular disease and pancreatitis. The severe forms are characterized by very high plasma levels of triglycerides (TG) (> 1000 mg/dL -11.2 mmol/l). Monogenic autosomal recessive forms are characterized by homozygous or compound heterozygous loss-of-function mutations of genes involved in the intravascular lipolysis of the triglyceride-rich lipoproteins, namely lipoprotein lipase (LPL), apolipoprotein C2 (APOC2), apolipoprotein A5 (APOA5), glycophosphatidylinositol (GPI)-anchored high-density lipoprotein-binding protein 1 (GPIHBP1), lipase maturation factor 1 (LMF1), and glycerol-3-phosphate dehydrogenase 1 (GPD1). LMF1 has been shown to be essential for the maturation of both LPL and hepatic lipase (HL) to their fully functional forms.

Methods: We performed Next Generation Sequencing (NGS) analysis on Ion GeneStudio S5 Plus to study the coding exons and intron/exon boundaries of genes affecting the main pathways of triglyceride synthesis and metabolism.

Results: In the majority of subjects no functionally relevant mutations in the LPL, APOC2, APOA5, GPIHBP1 genes were detected. Four patients were found to be carriers of unknown missense variants in LMF1 gene: a) one compound heterozygous carrier for c.787C>T (p.His263Tyr) and c.1381C>T (p.Arg461Cys); b) one homozygous carrier for c.874 G>A (p.Gly292Arg). The other two were heterozygous carriers for c.1351 C/T (p.Arg451Trp) and c.428 C/T (p.Thr143Met) respectively. A functional analysis was carried out to assay LMF1 activity, protein expression and specific activity.

Conclusions: The results showed that the Arg461Cys and Gly292Arg dramatically impair LMF1 function, the Arg451Trp does not have an impact, whereas His263Tyr and Thr143Met exhibit moderate effects.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

THE EFFECT CHANGE OF PHARMACOTHERAPY OF DYSLIPIDEMIA FROM FREE TO FIXED COMBINATION, EFFECT TO ADHERENCE OF THE PHARMACOTHERAPY

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: The effect change of pharmacotherapy of dyslipidemia from free to fixed combination, effect to adherence of the pharmacotherapy Aim: The main purpose of this study is to describe the different success rates in achieving the target values of LDL cholesterol by using a fixed combination of statins with ezetimibe compared to patients on a free combination and prove the importance of patient compliance in the case of using a smaller amount of equally effective drugs.

Methods: A descriptive, non-interventional, retrospective cohort study of 282 patients from the Center of Preventive Cardiology 3rd Department of Internal medicine 1st Faculty of Medicine and General Teaching Hospital in Prague, with elevated LDL-C, was conducted. A database included 97 patients with a combination of Rosuvastatin with Ezetimibe (130 patients on 40 mg Rosuvastatin and 10 mg Ezetimibe, 30 patients on 20 mg Rosuvastatin and 10 mg Ezetimibe), and 185 patients with a combination of Atorvastatin with Ezetimibe (61 patients 40 mg Atorvastatin and 10mg Ezetimibe, 24 patients 20 mg Atorvastatin and 10 mg Ezetimibe). All patients started on a free combination, which was subsequently switched to a fixed combination.

Results: based on this retrospective study showed that patients experienced a decrease in LDL after switching from the free combination to the fixed combination.

Conclusions: Based on this study, we indirectly expect an increase in patient adherence to pharmacotherapy.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

ASSESSMENT OF HYPERTRIGLYCERIDEMIA ASSOCIATED RESIDUAL CARDIOVASCULAR RISK IN SECONDARY PREVENTION PATIENTS

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: Hypertriglyceridemia (HTG) is accepted as a cause of residual cardiovascular risk. We investigated the frequency of HTG in secondary prevention patients.

Methods: In-hospital and 1-year follow-up data of patients hospitalized with diagnosis of acute coronary syndrome were collected. Discharge and 1-year follow-up lipid lowering therapies, achieved lowest LDL-c and TG levels were analyzed. HTG was defined as fasting triglyceride level ≥150 mg/dL. Statin adherence was defined as ≥ 9 statin refills/year.

Results: Median TG level during hospitalization was 153[109-220] and 31% of the cases had TG ≥200 mg/dL and 51% of the cases had TG ≥150 mg/dL (Table 1). Eighty-eight percent of the cases were discharged with statin therapy, but only 48% were found to be statin adherent during follow-up. In total, fibrate therapy was used in 182 cases (6%). LDL-C < 70 mg/dL and LDL-C decrease ≥ 50% from baseline targets could not be achieved in 67% and 61% of the cases. In 788 cases (28%), TG levels were found ≥ 150 mg/dL during follow-up. In these patients, 431 (54%) were statin nonadherent, 590 (75%) had LDL-C ≥ 70 mg/dL and 579 (73%) did not achieve LDL-C decrease ≥ 50% from baseline. Only in 164 (21%) cases, both LDL-C targets were achieved in whom TG lowering medications were indicated according to guidelines. This corresponds to 5.9% of the study

population.

Table 1. The demographic, clinical, laboratory characteristics of the study population.

Variables	All (n=2772)	STEMI (n=612)	NSTEMI (n=2160)	P value
Age, years	61.5±12.3	59.1±11.8	62.2±12.4	<0.01
Male gender, n (%)	1943 (70)	484 (79)	1459 (67)	<0.01
Diabetes mellitus n (%)	1010 (36)	170 (27)	840 (39)	<0.01
Hypertension, n (%)	1639 (59)	277 (45)	1362 (63)	<0.01
Active Smoker, n (%)	1098 (39)	328 (53)	770 (36)	<0.01
Prior myocardial infarction, n (%)	767 (27)	115 (19)	652 (30)	<0.01
Follow-up medication				
Statin at discharge, n (%)	2446 (88)	587 (96)	1859 (86)	<0.01
High intensity statin at discharge, n (%)	1521 (55)	472 (77)	1049 (48)	<0.01
*Statin adherent group, n (%)	1337 (48)	362 (59)	975 (45)	<0.01
Fibrates at discharge + during follow-up, n (%)	182 (6)	24 (4)	158 (7)	<0.01
Laboratory parameters, in-hospital				
Total cholesterol, mg/dL	187±46	181±44	188±47	<0.01
LDL-C, mg/dL	117±39	116±39	117±39	0.497
Triglyceride level, mg/dL	153[109-220]	137 [97-192]	158[115-1228]	<0.01
Triglyceride level ≥ 200mg/dL, n (%)	874 (31)	145 (24)	729 (33)	<0.01
Triglyceride level ≥150 mg/dL, n (%)	1429 (51)	254 (41)	1175 (54)	<0.01
Laboratory parameters, follow-up				
LDL-C md/dL	91±36	87±37	92±36	<0.01
LDL-C ≥ 70 mg/dL, n (%)	1877 (67)	381 (62)	1496 (69)	<0.01
LDL-C decrease <50% from baseline, n (%)	1727 (61)	356 (57)	1373 (62)	0.032
Triglyceride level, mg/dL	114[87-157]	110 [84-159]	115 [87-157]	0.18
Triglyceride level ≥200 mg/dL, n (%)	348 (12)	64 (10)	284 (13)	0.08
Triglyceride level ≥150 mg/dL, n (%)	788 (28)	175 (28)	613 (28)	0.91

Abbreviations: LDL, low density lipoprotein; MI, myocardial infarction; NSTEMI, nonST segment elevation myocardial infarction, STEMI, ST segment elevation myocardial infarction

* Parametric variables are depicted as mean ± standard deviation and nonparametric variables are depicted as median [25th-75th percentile]; Statin adherence is defined as statin refills ≥ 80% during follow-up period.

Conclusions: Even though, hypertriglyceridemia is common during hospitalization and follow-up of patients with ACS, it is mostly associated with inadequate use of LDL-C lowering therapies and low LDL-C target attainment rates.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

283 / #220

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

THE EFFECT OF PCSK9 MONOCLONAL ANTIBODIES ON CIRCULATING ENDOTHELIAL PROGENITOR CELLS IN PATIENTS WITH CARDIOVASCULAR DISEASE

POSTER ON BOARD: AS03.17 OTHER

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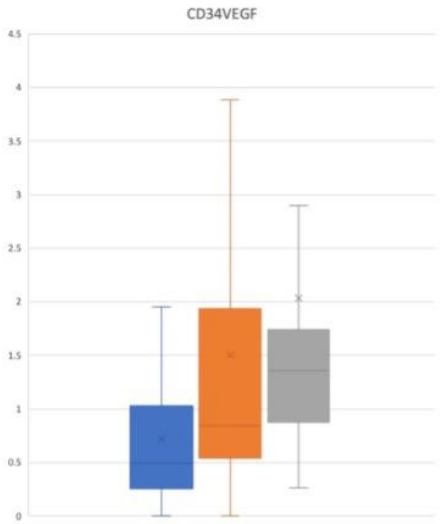
Cardiology, Rabin Medical Center, Petah-Tikva, Israel

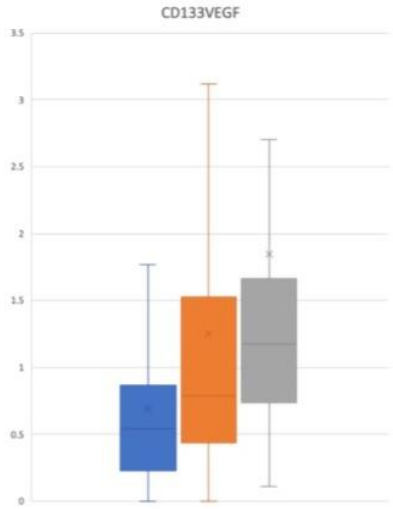
Background and Aims: Circulating endothelial progenitor cells (cEPCs) are vital to vascular repair by reendothelialization. We aimed to examine the effect of proprotein convertase subtilisin kexin type 9 monoclonal antibodies (PCSK9 mAB) on cEPCs with the hypothesis there might be a class pleiotropic effect.

Methods: Patients with cardiovascular disease (CVD) were sampled for cEPCs at baseline, 1 month and 3 months following the initiation of PCSK9 mAB. cEPCs were assessed using flow cytometry by the expression of $CD34^{(+)}/CD133^{(+)}$, expression of vascular endothelial growth factor receptor (VEGFR)-$2^{(+)}$, and formation of colony forming units (CFUs).

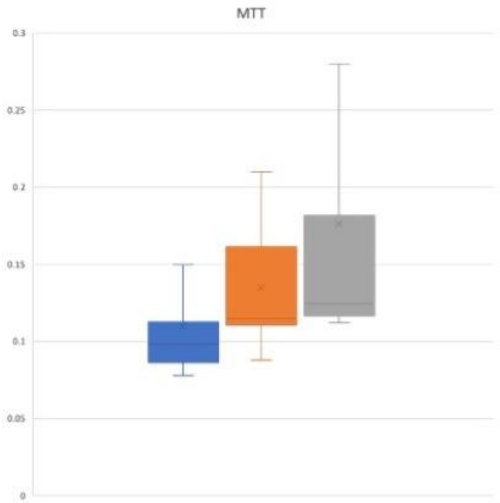
Results: Included were 51 patients (median age 67 (IQR 63, 74) years; 63% male). Following 3-month of treatment with PCSK9 mAB, LDL-C levels significantly decreased (125 (IQR 102, 165) to 52 (IQR 28, 75) mg/dL), p<0.001). There was an increase in $CD34^{(+)}/CD133^{(+)}$ and VEGFR-$2^{(+)}$ cell levels (0.50% (IQR 0.30, 1.04) to 1.36% (IQR 0.89, 1.73), p<0.001 and 0.57% (IQR 0.25, 0.88) to 1.18% (IQR 0.74, 1.66), p<0.001, respectively; Figure 1). Functionally, increase in EPCs-CFUs was microscopically evident (0.5 CFUs (IQR 0.0, 1.0) to 2.0 (IQR 1.5, 2.5), p<0.001) with concomitant increase in EPC's viability as demonstrated by MTT assay (0.11 (IQR 0.09, 0.15) to 0.17 (IQR 0.12, 0.21), p<0.001; Figure 2). Stratifying by type of PCSK9 mAB (Evolocumab 22 patients, Alirocumab 29 patients), treatment with both agents was associated with an increase in EPCs level and function.

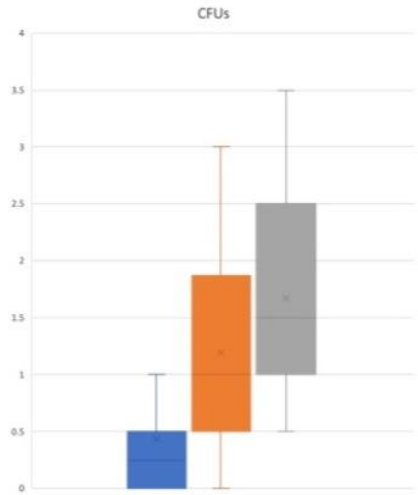


Baseline to 1-month, p<0.001
Baseline to 3-months, p<0.001



Baseline to 1-month, p<0.001
Baseline to 3-months, p<0.001





Baseline to 1-month, p<0.001
Baseline to 3-months, p<0.001

Baseline to 1-month, p<0.001
Baseline to 3-months, p<0.001

Conclusions: In patients with CVD treated with evolocumab or alirocumab, there was an increase in EPCs levels and function, suggesting a class pleiotropic effect of PCSK9 mAB.

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284 / #592

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

CELL-FREE DNA AS AN POTENTIAL MARKER OF STATIN INDUCED MUSCLE INJURY

POSTER ON BOARD: AS03.17 OTHER

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Background and Aims: The most commonly reported undesirable side effects of statin treatment are myalgia and myopathy. Short DNA fragments freely present in plasma (cfDNA) and potentially released from stressed and damaged muscle tissue could be important marker of such complications.

Methods: Using quantitative PCR we analyzed cfDNA concentrations (two assays, gene IDs - 79068 and 3569) in a total of 14 men (age 35-65 years), non-diabetic, treated two months with 10mg rosuvastatin. Two samples were available before initiation of statin treatment, three during treatment and one sample after short-term discontinuation of treatment.

Results: Muscle discomfort and weakness were subjectively reported in two subjects. In these subjects, unadjusted cfDNA concentrations were nonsignificantly elevated. CfDNA concentrations did not significantly correlated with statin treatment.

Conclusions: The pilot study did not demonstrate a significant increase of cfDNA concentrations in subjects treated with low-dose statins. A larger number of individuals, especially those with statin-induced muscle discomfort, should be analyzed to (dis)prove an association between muscle weakness and statin treatment. "Supported by Ministry of Health of the Czech Republic, grant nr. NU21-01-00146. All rights reserved."

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

285 / #482

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

THE REAL-WORLD EFFICACY OF PEMAFIBRATE ON METABOLIC-ASSOCIATED FATTY LIVER DISEASE (MAFLD): A ONE-YEAR RETROSPECTIVE STUDY

POSTER ON BOARD: AS03.17 OTHER

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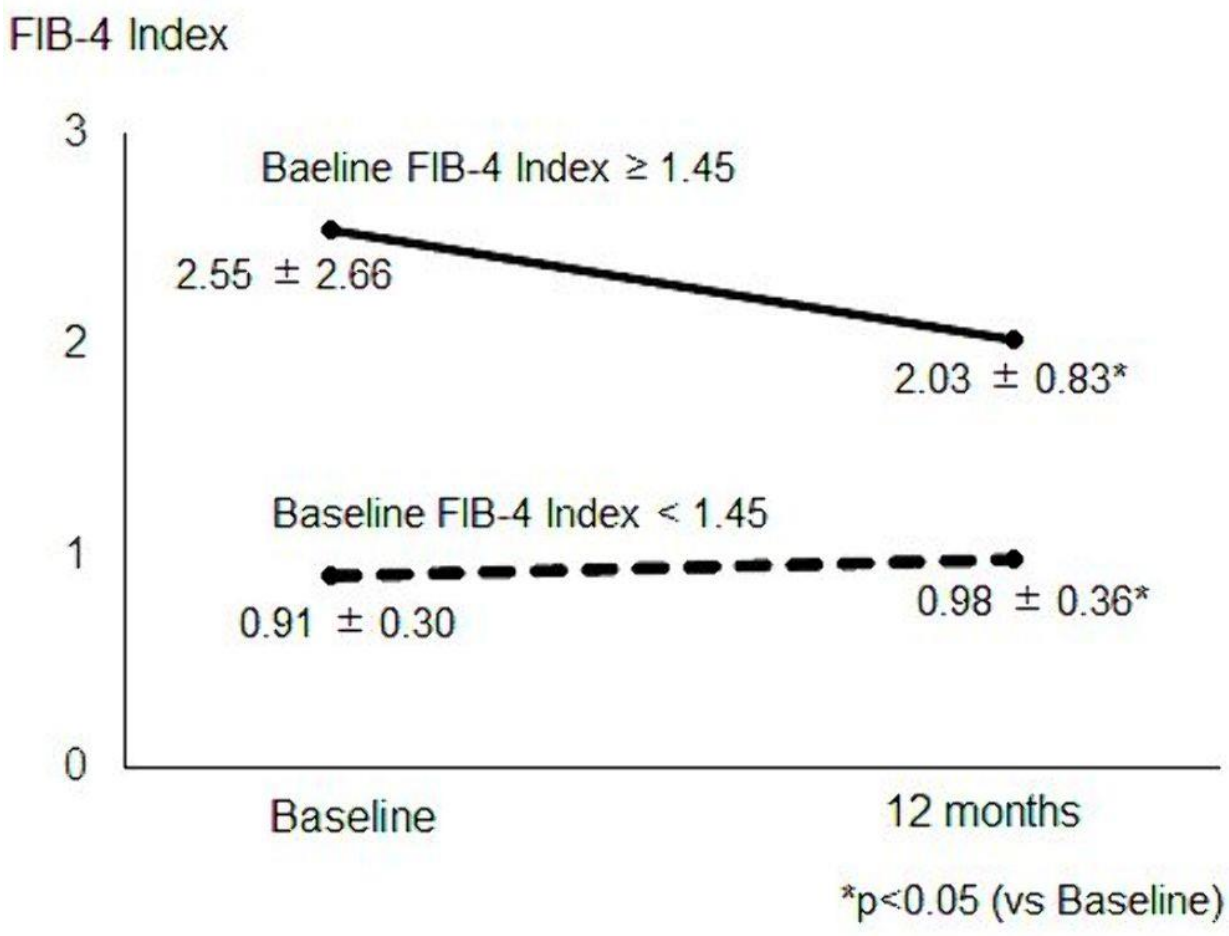
Background and Aims: Metabolic-associated fatty liver disease (MAFLD) was associated with an elevated risk of cardiovascular events as well as the progression to fibrosis/cirrhosis and hepatocellular carcinoma. Pemafibrate, a novel selective peroxisome proliferator-activated receptor α modulator, was reported to improve liver dysfunction in patients with dyslipidemia. This study aims to evaluate the real-world efficacy of pemefibrate on the progression of MAFLD.

Methods: We retrospectively selected the patients with hypertriglycemia who had newly received pemafibrate and continued for over 12 months between June 2018 and August 2021. We compared the data of anthropometric measurements and blood tests before and after the 12-month pemafibrate treatment.

Results: 134 patients (mean age 59.8 years, female 52, BMI 27.6) were enrolled in this study. Significant reductions were observed in serum ALT, γGTP, total cholesterol, triglyceride and Non-HDL-Cholesterol levels during the 12-month pemafibrate treatment, whereas serum albumin, HDL-cholesterol levels, and platelet count increased. Despite a significant decrease in the hepatic steatosis index (HSI) during the pemafibrate treatment, no change was observed in FIB-4 index. A subanalysis revealed that FIB-4 index decreased significantly only in patients with a high value of baseline FIB-4 index (≥ 1.45). The correlations between the change of FIB-4 index during the pemafibrate treatment were correlated inversely with the baseline FIB-4

index.



Conclusions: Our real-world study demonstrated that pemafibrate could attenuate hepatic steatosis in patients with hypertriglycemia, and ameliorate fibrosis in the liver in high-risk patients for hepatic fibrosis.

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286 / #809

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

NEW METHOD OF CALCULATING LOW DENSITY LIPOPROTEIN CHOLESTEROL USING KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (KNHANES) AND ITS VALIDATION

POSTER ON BOARD: AS03.17 OTHER

Sang-Hyun Kim[1], Ju-Eon Lee[1], Ho-Hyun Lee[1], Hyanglim Lee[2]
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Background and Aims: Although Friedewald formula is the most representative for calculating low density lipoprotein cholesterol (LDL-C), its limitation was already suggested with hypertriglyceridemia. Martin/Hopkins method suggested variables for 180 subgroups and improved the accuracy. We calculated variables with 105 cells and derived new method for calculating LDL-C using Korean data.

Methods: Data of 16,101 people of Korea National Health and Nutrition Examination Survey (KNHANES) in 2009~2017 who has directly measured LDL-C with triglyceride < 400 mg/dL were analyzed. Medians of TG/VLDLC ratio were explored in 105 subgroups to derive KNHANES method.. We validated new method with directly measured LDL-C with KNAHENS and Boramae hospital data (n = 326,181).

Results: Overall concordance rate of Friedewald formula was the lowest (74.2%) among 3 methods, especially in group with LDL-C < 70 mg/dL (60.8%). KNHANES method (105 cell) showed better concordance than Friedewald formula in all subgroups, and comparable concordance with Martin/Hopkins. Concordance rate in group with LDL-C < 70 mg/dL were 60.8% (58.3 ~ 63.3) with Friedewald, 84.5% (82.1 ~ 86.9) with KNHANES, 82.7% (80.4 ~ 85.0). ($p<0.05$) with Martin/Hopkin.

Conclusions: KNHANES method is more accurate than Friedewald formula, and comparable to Martin/Hopkins method for calculating LDL-C level, especially in patients with LDL-C < 70 mg/dL.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

287 / #584

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

MACHINE LEARNING TO INFORM CHOLESTEROL-LOWERING PHARMACOTHERAPY: PROOF-OF-CONCEPT IN UK PRIMARY CARE

POSTER ON BOARD: AS03.17 OTHER

Andrew Krentz
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Background and Aims: Machine learning technology has potential to improve the management of lipid disorders; we explored the utility of machine learning in a primary care setting.

Methods: Machine learning algorithms were created based on current lipid management guidelines for England (National Institute for Health and Care Excellence CG181) that reproduced the guidance with >95% accuracy. Natural language processing and therapy identification algorithms were applied to anonymised electronic records from South London primary care general practices (n=6) to extract medication information from free text fields.

Results: Of 48,226 patients, a subset of 5,630 (mean + SD age 67 + 13 years; M:F 55:45%) with a history of lipid-lowering therapy were identified. Of these, 4,290 (76%) and 1,349 (24%) were in primary and secondary cardiovascular disease prevention cohorts, respectively. Statin monotherapy was the most common current medication (82%, n=4,632). For patients receiving statin monotherapy, 71% (n=3,269) were on high-intensity therapy aligned with NICE guidance with rates being similar for the primary and secondary prevention cohorts. In the combined cohort, 46% (1,211/2640) patients who had been prescribed lipid-lowering therapy in the previous 12 months failed to achieve the NICE treatment target of >40% reduction in non-HDL cholesterol from baseline. The algorithm recommended increasing the statin dose in 46% of patients and addition of other medications or obtaining a specialist opinion in the remainder.

Conclusions: Machine learning can be of value in (a) quantifying suboptimal lipid-lowering prescribing patterns (b) identifying patients who could benefit from more intensive therapy and (c) suggesting evidence-based therapeutic options.

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MANNHEIM GERMANY | MAY 21-24, 2023

288 / #830

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

THE TENDENCY OF STATIN USE IN OCTOGENARIANS

POSTER ON BOARD: AS03.17 OTHER

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Cardiology, Beypazarı State Hospital, Ankara, Turkey

Background and Aims: Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients.However older patients are defined in guidelines as patients older than 70 years old. There are limited datas about statin use for secondary prevention in octogenarians.The aim of this study is to present current status of statin use and percentage of patients with achieved LDL-cholesterol in octogenarians.

Methods: All of the octogenarian patients with atherosclerotic cardiovascular diseases, who admitted my hospital between January 2022 and November 2022 were enrolled. Datas were obtained from hospital electronic database.

Results: A total of 104 patients were enrolled. Mean age of the population was 84.5±2.4 years and 45.1%(n=47) of them were male. Coronary artery disease was present in 81(77.8%) cases, lower extremity peripheral artery disease was present in 28(26.9%) cases and carotid artery disease was present in 14(13.4%) cases. Only 24(23.0%) patients were under treatment with statins and mean LDL-C level was 113.1±30.5 mg/dL. LDL-C level was below 55 mg/dL in only 7(6.7%) patients and below 100 mg/dL in 35(33.6%) cases. Causes of not using statins were as follows; previous statin related adverse events(20%), patient refusal to use statins(45%) and not recommended or stopped by the healthcare provider(35%).

Conclusions: Although guidelines recommends lipid lowering treatment in older patients in the same way as younger patietns, results of this study demonstrates that it is difficult to achive target cholesterol levels in these cases. However, statins should be administered at tolerated doses in order to lower LDL-C levels even target levels does'nt achieved.

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MANNHEIM GERMANY | MAY 21-24, 2023

289 / #1490

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

THE IMPORTANCE OF CASCADE SCREENING OF FAMILIAL HYPERCHOLESTEROLEMIA IN ROUTINE CLINICAL PRACTICE

POSTER ON BOARD: AS03.17 OTHER

Soreiia Urazgildeeva[1,2], Kseniia Dracheva[3], Valentina Miroshnikova[3]
[1]Clinical, Science And Education Center “cardioilogy", Saint Petersburg State University, Saint Petersburg, Russian Federation, [2]Center For Atherosclerosis And Lipid Disorders, Northwest District Scientific and Clinical Center named after L.G. Sokolov, Saint Petersburg, Russian Federation, [3]Laboratory Of Medical Genetics, Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation

Background and Aims: The problem of late diagnosis of familial hypercholesterolemia (FH) is common in routine clinical practice. Cascade screening within the family is necessary to ensure early diagnosis of FH for timely initiation of treatment. We report a three-generation pedigree where 7 cases of FH were identified.

Methods: FH was documented by DLCN criteria. Mutation was identified by targeted NGS sequencing for the proband and subsequently by Sanger sequencing in family members.

Results: The proband was a female with FH diagnosed at the age of 33. She has a tendon xanthomas and atherosclerotic lesions of carotids. Maximal level of total cholesterol (TC) was 16 mmol/l. In her twin sons high level of TC (10,5 and 12,0 mmol/l) was detected at the age of 3. The proband’s mother and elder sister of 37 years have TC level 9,0 and 13,0 mmol/l respectively. Two of the three children of the sib (the girl of 12 years and boy of 3 years) also have elevated level of TC: 8,77 and 6,89 mmol/l. The mother of the proband has a history of acute ischemic insult at the age of 53. Pathogenic variant of LDLR: rs121908038 c.1202T>A p.(Leu401His), was detected in the proband, her sib and their affected siblings. Combined lipid lowering therapy was initiated in the proband and her sib. The siblings with FH are supervised by pediatrist and lipidologist.

Conclusions: The cascade screening of FH provides the necessary ensures for early diagnosis and timely initiation of treatment to prevent the cardiovascular events.

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290 / #1337

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

DETERMINANTS OF CORONARY ARTERY CALCIUM SCORE IN PATIENTS WITH MULTIFACTORIAL CHYLOMICRONEMIA SYNDROME

POSTER ON BOARD: AS03.17 OTHER

Carla Vullien[1], Elisa Dybal[1], Mathilde Di Filippo[2,3], Oriane Marmontel[3,4], Delphine Collin-Chavagnac[2,3], Myriam Moret[1], Laure Groisne[1], Philippe Moulin[1,3], Sybil Charrière[1,3]
[1]Fédération D'endocrinologie, Maladies Métaboliques, Diabète Et Nutrition, Ghe, Hospices Civils de Lyon, Bron, France, [2]Biochemistry And Molecular Biology, Hospices Civils de Lyon, BRON, France, [3]Carmen Laboratory, Inserm U1060, Inra U1397, Université Claude Bernard Lyon 1, Insa Lyon, Univ-Lyon, Villeurbanne, France, [4]Biochemistry And Molecular Biology, Hospices Civils de Lyon, Bron, France

Background and Aims: Coronary artery calcium score (CAC) improves cardiovascular (CV) risk prediction and is validated in many high risk populations such as type 1/type 2 diabetes and familial hypercholesterolemia. We aimed to characterize CAC distribution and determinants in patients with multifactorial hyperchylomicronemia syndrome (MCS) in primary CV prevention.

Methods: Retrospective monocentric study, 164 MCS patients in primary prevention with a CAC assessment from 01/01/2011 to 31/08/2022.

Results: The cohort had 79.3% of men. Mean age was 51.1±10.9 years. 48.2% of patients had type 2 diabetes, 45.1% hypertension (HTA), 34.7% had a history of acute pancreatitis. CAC median value was 1.0 (IQT 165) with the following distribution: CAC=0 47.1%, CAC 1- 100 23.2%, CAC 101-300 11.0% and CAC >300 18.9%. 48.2% of patients had CAC below the 25th percentile for age and sex and 34.1 % over the 75th. In univariate analysis, age, HTA, diabetes and smoking were significantly associated with a CAC >300 vs CAC=0 and with CAC >75th percentile vs <25th percentile. Sex and lipid parameters at the time of CAC assessment were not associated with the CAC score. In multivariate analysis (binary logistic regression), age, HTA, diabetes and smoking, remained significantly associated with CAC >300 vs CAC=0 and age, HTA, and smoking with CAC >75th percentile vs < 25th percentile.

Conclusions: Traditional CV rick factors such as age, diabetes, HTA and smoking are the major determinants of CAC score. CAC may contribute to identify a subgroup of MCS patients at very high cardiovascular risk which might benefit for treatment intensification with new therapies.

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MANNHEIM GERMANY | MAY 21-24, 2023

291 / #654

Topic: *AS04 Clinical Vascular Disease / AS04.01 Coagulation and Thrombosis*

THE ROLE OF VON WILLEBRAND FACTOR IN THROMBOTIC POST-TRANSPLANTATION COMPLICATIONS

POSTER ON BOARD: AS04.01 COAGULATION AND THROMBOSIS

Parnian Alavi[1], Sayed Himmat,[2], Max Buchko[2], Nader Aboelnazar[2], Jayan Nagendran[2], Nadia Jahroudi[1]
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Background and Aims: Von Willebrand factor (VWF) is an endothelial-specific pro-coagulant glycoprotein. External stimuli, including hypoxia upregulate VWF. Increased VWF levels, is a significant risk factor for thrombus formation. Since during organ-transplantation donor organs are under hypoxic conditions, we investigated whether transplantation could alter the expression pattern of VWF, and whether modification of the procedure to reduce hypoxic exposure could prevent such alterations. Toward this goal, we used pig's lung transplantation model.

Methods: Procured pig's lungs that were maintained in static cold storage "SCS" or exposed to ex vivo lung perfusion (before and after perfusion) were used. Lung tissue biopsies were obtained immediately after organ harvest, 12 hours post cold storage, or post warm perfusion. VWF RNA and protein expression levels were analyzed using RT-PCR and western blot. To determine whether SCS preservation also alters the proportion of pig's lung vascular endothelial cells that exhibit VWF expression we performed double stained immunofluorescence (IF) analyses using CD31 (endothelial cell marker) and VWF antibodies on samples of lungs that were preserved and transplanted.

Results: VWF mRNA and protein levels are reduced in lungs, which were perfused under ex vivo lung perfusion "EVLP" for 12 hours compared to control. IF analysis demonstrated that preservation of lungs under SCS conditions but not warm perfusion, prior to transplantation alters VWF expression patterns leading to an increasing number of microvascular (indicated by CD31 staining) endothelial cells that express VWF.

Conclusions: Reduction of VWF expression through ex vivo normothermic perfusion may have a significant effect in reducing potential thrombogenic complications.

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292 / #1020

Topic: *AS04 Clinical Vascular Disease / AS04.01 Coagulation and Thrombosis*

EVALUATION OF THE EFFICACY AND SAFETY OF RIVAROXABAN COMPARED TO WARFARIN IN PATIENTS WITH LEFT VENTRICULAR APICAL THROMBUS: A RANDOMIZED CLINICAL TRIAL

POSTER ON BOARD: AS04.01 COAGULATION AND THROMBOSIS

Mohammad Mansouri[1], Pejman Mansouri[2], Zahra Azamian Jazi[1]
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Background and Aims: Our study is one of the first randomized clinical trials (RCT) to evaluate the efficacy and safety of rivaroxaban in the management of LVT in patients with the acute coronary syndrome (ACS).

Methods: This is a randomized, controlled, interventional, open-label study. The patients were randomly divided into warfarin and rivaroxaban groups. Transthoracic echocardiography was performed on admission and three months later. The area of thrombus was calculated in mm^2. The morphology of the thrombus was categorized into mural and round, and the mobility was classified into immobile, semi-mobile and hypermobile. Adverse effects like bleeding, systemic embolic events, rehospitalization and major adverse cardiac events (MACE) were also evaluated.

Results: Fifty-two patients were included in the intention-to-treat analysis (26 in the rivaroxaban group and 26 in the warfarin group). The average follow-up period was three months. The thrombus resolution rate in rivaroxaban (76.9%) and warfarin (69.2%) groups and also the thrombus size reduction did not reach a statistical significance between groups. All semi or hypermobile thrombi transformed into immobile and all of the round LVTs changed into a mural in both rivaroxaban and warfarin groups. No significant difference was observed in bleeding complications and rehospitalization between the two groups.

Conclusions: In conclusion, in this randomized controlled trial, we showed that rivaroxaban was non-inferior to Warfarin in thrombus resolution rate, thrombus size improvement, risk of bleeding, and rehospitalization rate. These results demonstrate that rivaroxaban may be an alternative option to Warfarin for the treatment of LV thrombus.

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293 / #781

Topic: *AS04 Clinical Vascular Disease / AS04.01 Coagulation and Thrombosis*

MOLECULAR MRI OF MPO ACTIVITY DETECTS RUPTURED HUMAN ATHEROSCLEROTIC PLAQUES AND PREDICTS ATHEROTHROMBOSIS IN AN ANIMAL MODEL

POSTER ON BOARD: AS04.01 COAGULATION AND THROMBOSIS

James Nadel *[1,2,3], Xiaoying Wang *[4], Prakash Saha[5], André Bongers[6], Sergey Tumanov[1,7], Nicola Giannotti[8], Weiyu Chen[1], Andrew Jabbour[2,3], Mohammed Chowdhury[9], Gastao Lima Da Cruz[10], Carlos Velasco Jimeno[4], Claudia Prieto Vasquez[4,11], René Botnar[4,11,12], Roland Stocker †[1], Alkystis Phinikaridou †[4,13]

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Background and Aims: Intraplaque MPO activity is associated with unstable atherosclerosis and elevated following acute cardiovascular events. MPO activity can be imaged non-invasively with MRI probes like MPO-Gd. As the predictive utility of MPO activity in plaque rupture has not been examined, we tested its utility in ruptured human atheroma and a pre-clinical model of atherothrombosis.

Methods: Following pre-surgical *in vivo* MRI of plaque characterisation, carotid endarterectomy specimens (CEA) were imaged *ex vivo* using MPO-Gd, and MPO-Gd retention correlated with AHA plaque grading by histology, *in vivo* MRI, and MPO activity quantified by a liquid chromatography mass spectrometry (LC-MS/MS). A rabbit model of triggered atherothrombosis was used, and thrombosis related to arterial MPO activity determined pre-trigger by MPO-Gd enhanced MRI.

Results: *Ex vivo* MPO-Gd retention in CEA was greater in histologically and *in vivo* MRI-graded ruptured and destabilised AHA type VI compared with types III-V plaques. This association was confirmed by comparing histological AHA grade plaques with MPO activity determined by LC-MS/MS. In the rabbit model, MPO activity was higher in aortic segments with plaque causing trigger-induced atherothrombosis

(R1 = 2.2 ± 0.2 s^{-1}) compared with plaque resistant to trigger-induced atherothrombosis (R1 = 1.6 ± 0.2 s^{-}

Figure 1

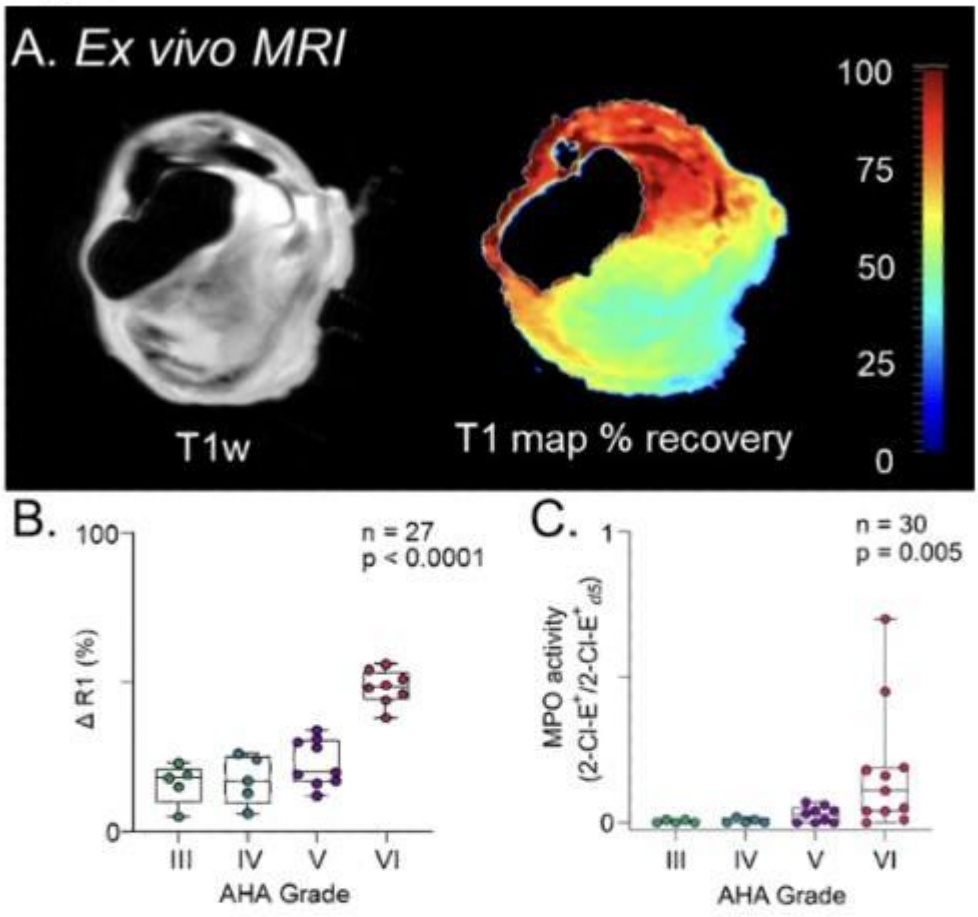
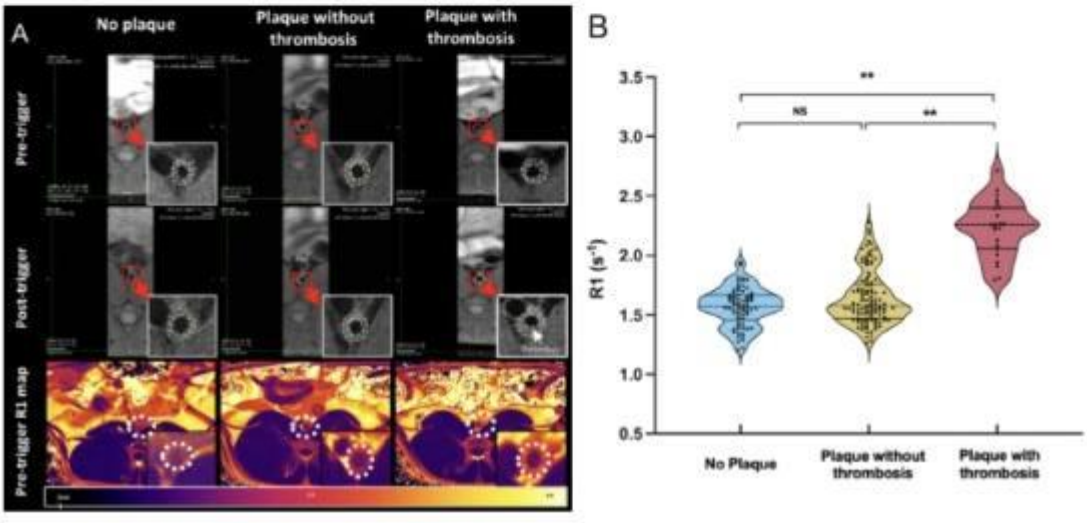


Figure 2



[1]).

Conclusions: MPO activity determined by MPO-Gd and compared with histology is increased in ruptured human plaques and predictive of atherothrombosis in a pre-clinical model, highlighting the potential utility of MPO activity as a molecular target to detect vulnerable atherosclerosis. *Equal contribution; †Co-corresponding authors.

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294 / #733

Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

INVESTIGATION OF FLOW-MEDIATED DILATATION, CAROTID ARTERY INTIMA-MEDIA THICKNESS AND ARTERIAL STIFFNESS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

POSTER ON BOARD: AS04.02 ENDOTHELIAL DYSFUNCTION; CLINICAL ASSESSMENT

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Background and Aims: Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder that predominately affects women and associated with an increased atherosclerotic and cardiovascular risk**.** Although several vascular imaging and other non-invasive diagnostic tests have been studied in SLE previously, the complex assessment of these vascular diagnostic tests has not been reported.

Methods: We enrolled 51 clinically active SLE patients and 41 age- and gender-matched control subjects to the study. Common carotid intima-media thickness (CMT) and brachial artery flow-mediated dilatation (FMD) were detected by ultrasonography. Arterial stiffness indicated by augmentation index (AIx) and pulse wave velocity (PWV) was measured by arteriography. SLE disease activity was assessed using SLEDAI score.

Results: We found significantly higher AIx in SLE patients compared to controls. However, there were no significant differences in CMT, FMD and PWV between SLE patients and controls. 43 patients had mildly or moderately active SLE (SLEDAI score 1-10), while 8 patients had high or very high disease activity (SLEDAI score ≥11). Higher CMT was found in patients with high and very high disease activity.

Conclusions: Elevated AIx may indicate an early vascular damage in all active SLE patients, while patients with high and very high disease activity are characterized by elevated CMT values indicating enhanced atherogenesis. Our findings highlight the role of non-invasive vascular diagnostic tests in early recognition of vascular complications and their targeted management in SLE.

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Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

ENDOTHELIAL FUNCTION AND ARTERIAL STIFFNESS OF PATIENTS WITH CARDIOVASCULAR DISEASES HOSPITALIZED DUE TO COVID-19

POSTER ON BOARD: AS04.02 ENDOTHELIAL DYSFUNCTION; CLINICAL ASSESSMENT

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Background and Aims: Background: The novel coronavirus disease (COVID-19) may cause vascular (e.g., prothrombotic, endothelial dysfunction, and arterial stiffness), cardiac and systemic inflammatory response via direct viral attack, hypoxia-induced injury, or immunological dysregulation, especially in those patients with pre-existing cardiovascular diseases (CVD). No study showed prevalence of endothelial function and arterial stiffness in patients with previous CVD hospitalized due to acute COVID-19. **Aim:** This study aimed to assess the prevalence of endothelial dysfunction, and arterial stiffness in patients with CVD hospitalized due to COVID-19.

Methods: This cross-sectional study was conducted from July 2020 to February 2021. Included male and female adult patients aged 40 to 60 years with previous CVD and diagnosed with COVID-19. Anthropometric data, comorbidities, and blood tests were analyzed. Endothelial function and arterial stiffness were assessed using peripheral arterial tonometry (PAT), and the statistical significance was set at 5%.

Results: Fourteen (51.8%) patients presented endothelial dysfunction (reactive hyperemia index = 1.2 ± 0.3). There was a high prevalence of endothelial dysfunction, especially in patients with chronic heart failure (10 (71.4%)). Patients with preserved endothelial function showed a high augmentation index normalized to a heart rate of 75 bpm ($p < 0.01$), suggesting arterial stiffness.

Conclusions: Patients with CVD hospitalized due to COVID-19 presented endothelial dysfunction assessed using PAT, which could be used as a biomarker for arterial stiffness. The possibility of detecting vascular during acute phase of COVID-19 may help to prevent possible long-term complications.

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Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

FLOW-MEDIATED DILATION AFTER TREATMENTS OF FIXED DOSE COMBINATION OF SIMVASTATIN AND FENOFIBRATE VERSUS HIGH DOSE ROSUVASTATIN IN HYPERTRIGLYCERIDEMIA

POSTER ON BOARD: AS04.02 ENDOTHELIAL DYSFUNCTION; CLINICAL ASSESSMENT

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Background and Aims: Hypertriglyceridemia (triglycerides>200mg/dl) is a major cardiovascular risk factor. We want to compare between combination of simvastatin and fenofibrate and high intensity rosuvastatin (20mg) in treatment of hypertriglyceridemia.

Methods: This is a non-randomized prospective observation study. One hundred fifty four hypertriglyceridemia patients were assigned 3 groups (Group A ; rosuvastatin 20mg, B ; simvastatin 20mg + fenofibrate 145mg, C ; simvastatin 40mg + fenofibrate 145mg). The brand name of fixed dose combination is Cholib. There were significant differences of age, blood glucose, BMI and ABI between 3 groups. We checked baseline and follow up lipid profile, flow medicated dilation (FMD), pulse wave velocity (PWV), carotid intima media thickness (cIMT) and augmentation index (AIx). After 1yr, we checked above parameters again.

Results: After treatment, significant decrease in triglyceride and total cholesterol in all groups. Compared with Group A (rosuvastatin 20mg), B (simvastatin 20mg + fenofibrate) and C (simvastatin 40mg + fenofibrate) showed better reduction in triglyceride ($p=0.044$, 0.001 respectively). And, compared with Group A, Group B and C showed improvements in HDL cholesterol ($p<0.001$, 0.017 respectively). In contrast, Group A is better than B and C in LDL cholesterol reduction ($p=0.025$) There was no difference in changes of PWV and AIx between 3 groups except ABI of Group B and C ($p=0.03$). However, the difference of 2 groups was very small (0.0±0.1 vs 0.1±0.1). There was no difference in changes of IMT and FMD.

Conclusions: Combination treatment of simvastatin and fenofibrate was better than high intensity rosuvastatin in control of hypertriglyceridemia and improvement of HDL cholesterol.

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Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

CARDIOVASCULAR DISEASE RISK FACTORS AND THEIR ASSOCIATION WITH PERIPHERAL AND CENTRAL BLOOD PRESSURES IN CHILDREN AND ADOLESCENTS

POSTER ON BOARD: AS04.02 ENDOTHELIAL DYSFUNCTION; CLINICAL ASSESSMENT

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Background and Aims: There is evidence that central blood pressure (cBP) may improve risk profiling and that risk factors for cBP may be distinct from those for peripheral brachial blood pressure (pBP). Blood pressure tracks strongly from childhood into adulthood, but there is limited evidence regarding risk factors for cBP in children and adolescents. Accordingly, we sought to compare the association between early life anthropometric risk factors with cBP and pBP in children and adolescents.

Methods: 97 healthy children and adolescents aged 2 to 20 years were prospectively recruited (mean age 11.2 years [SD 5.1]; stratified into five sex-balanced age groups). Hemodynamic measures were obtained using an appropriately-sized brachial cuff and cBP was measured at the carotid artery using applanation tonometry (SphygmoCor XCEL, AtCor Medical, Australia).

Results: In univariate analysis, systolic cBP and pBP increased significantly with age ($P < 0.0001$) but there was no association with sex. In multivariable analysis, BMI z-score was associated with both higher cBP (3.5 mmHg per 1 kg/m^2 [95% CI: 1.0, 5.9], $P = 0.005$) and pBP (2.4 mmHg per 1 kg/m^2 [95% CI: 0.1, 4.7], $P = 0.04$), adjusted for age and sex. There was weak evidence that these associations were stronger in older children (cBP older: 5.2 mm Hg per 1 kg/m^2 [95% CI 1.6, 8.7]; cBP younger: 1.1 mm Hg per 1 kg/m^2 [95% CI -2.3, 4.5]; $P_{HETEROGENEITY} = 0.09$). These associations were independent of height z-score.

Conclusions: BMI is independently associated with systolic cBP in childhood and adolescence. This association may become stronger with age during childhood.

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Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

THE CORRELATION BETWEEN EPICARDIAL FAT PAD AND CORONARY ARTERY DISEASE

POSTER ON BOARD: AS04.02 ENDOTHELIAL DYSFUNCTION; CLINICAL ASSESSMENT

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Background and Aims: The pathogenesis of coronary artery disease is multifactorial. The epicardial fat pad is a localized fat depot lying between the myocardium and the visceral layer of the pericardium. The mechanisms through which epicardial fat pad can cause atherosclerosis are complex. The epicardial fat pad can surround the coronary arteries and contributes to the development and progression of coronary artery disease. The epicardial fat pad provides a novel horizon on the pathophysiology of cardiovascular diseases.e. Further investigations are needed to determine whether medical treatment can reduce the mass of epicardial fat pad and can help to improve atherosclerosis.

Methods: we selected 50 patients who underwent coronary artery angiography for the evaluation of coronary artery disease that results were positive for coronary artery disease. All patients underwent an echocardiographic examination after coronary angiography to measure of epicardial fat pad thickness. The epicardial fat pad was defined as an echo-free space between the myocardium's outer wall and the pericardium's visceral layer.

Results: The epicardial fat pad was measured on the RV Apex in 46 patients. Sixty- five percent of the studied patients were male. The most common vessel with stenosis was LAD. A significant correlation was observed between epicardial fat pad thickness and the severity of coronary artery disease.

Conclusions: The epicardial fat pad measurement could be used as an indicator of coronary arteries' atherosclerosis. Therefore, thickness measurement of the epicardial fat pad in the clinical practice could be of assistance in identifying patients at risk and if required, undergoing supplementary diagnosis with coronary angiography.

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Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

BASELINE PREDICTORS OF VASCULAR AND ENDOTHELIAL OUTCOMES AT 18-MONTH FOLLOW-UP IN PEOPLE LIVING WITH HIV: RESULTS FROM THE ENDOAFRICA STUDY.

POSTER ON BOARD: AS04.02 ENDOTHELIAL DYSFUNCTION; CLINICAL ASSESSMENT

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Background and Aims: People living with HIV (PLWH) have a 2-fold greater cardiovascular disease (CVD) risk vs. general population. We investigated whether HIV-related immunovirological and cardiometabolic variables are associated with vascular/endothelial outcomes at 18-months follow-up.

Methods: Longitudinal study (baseline and 18-months) of PLWH and HIV-free participants. Health, immunovirological and cardiometabolic data were collected. Vascular endpoints included: flow-mediated dilatation (FMD), retinal microvessel calibers (central retinal arteriolar and venular equivalent; CRAE and CRVE), and carotid intima-media thickness (c-IMT). Mixed-model ANOVA and best subsets regression were applied (Statistica™,Version 14).

Results: HIV+ participants were subdivided into ART-experienced at baseline (HIV+ART+): N=156 and ART-naive at baseline (ART commencement before 18-month follow-up) (HIV+ART-/+): N=47. The population was young (~39 years), predominantly female (~74%) and ~63% were smokers. There was a high hypertension prevalence. Mixed model ANOVA revealed group:time interactions (baseline→18-months) for FMD ($p=0.08$) and CRVE ($p<0.01$). In HIV+ART+, systolic bloodpressure (SBP) (β:-0.21), eGFR (β:0.13) and LDL-Cholesterol (β:-0.14) were top baseline predictors of 18-month FMD, whereas CRAE was predicted by urine albumin-creatinine ratio (urine ACR)(β:-0.17) and eGFR (β:0.23), and CRVE by high-sensitivity CRP (β:0.19), ART duration (β:-0.16) and viral load (β:0.15). In HIV+ART-/+, c-IMT was best predicted by haemoglobin (β:-0.37), SBP (β:1.03) and γ-GT (β:0.28).

Conclusions: FMD and retinal microvessels showed group:time interactions over 18 months in PLWH. Prominent baseline predictors of vascular/endothelial outcomes in HIV+ participants included SBP, eGFR, hsCRP, urine ACR, ART duration, viral load and haemoglobin. This study highlights the importance of assessing temporal vascular changes in PLWH, and identifies potential novel early predictors of vascular endothelial risk in PLWH.

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Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

ENDOTHELIAL FUNCTIONAL STATUS IN PATIENTS WITH ATHEROSCLEROTIC CORONARY ARTERY DISEASE AND TYPE 2 DIABETES MELLITUS AFTER COVID-19

POSTER ON BOARD: AS04.02 ENDOTHELIAL DYSFUNCTION; CLINICAL ASSESSMENT

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Background and Aims: Aim of the study was to estimate endothelial functional status in patients with atherosclerotic coronary artery disease (ASCAD) and type 2 diabetes mellitus (T2DM) who underwent Covid-19.

Methods: 65 patients with ASCAD and T2DM after coronavirus infection (Group I) and 65 patients with ASCAD and T2DM without any history of Covid-19 (Group II) were enrolled in this study. Group I patients aged 45-73 years, mean age 61.3±11.8 years; male=48% and Group II patients aged 41-76 years, mean age 62.5±13.8 years; male=46%. Endothelial functional status was assessed by flow-mediated vasodilation of brachial artery (FMD). All statistical analysis were performed by STATA software.

Results: FMD of brachial artery was significantly decreased in patients with ASCAD and T2DM after Covid-19 than those patients without Covid-19 (P<0.01). There were a correlation between Covid-19 and reduced FMD in Group I (r=0.7, CI 95%, P=0.032). When we assessed systolic function of the left ventricle, there were a positive correlation between reduced FMD and low ejection fraction (r=0.6, CI 95%, P=0.028), however this correlation were more pronounced in Group I (P=0.001). Multivariate analysis revealed that reduced flow-mediated vasodilation of brachial artery was independent predictor of poor systolic function of patients with ASCAD and T2DM especially in those after Covid-19 (odds ratio [OR] 1.52, P = 0.026). When we separately analyzed between men and women there were not any statistical significant changes between male and female (P>0.05).

Conclusions: Patients with atherosclerotic coronary artery disease and T2DM after Covid-19 had impaired FMD of brachial artery.

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Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

EFFECTS OF HIGH-DOSE ROSUVASTATIN AND ATORVASTATIN ON CYSTATIN C-ORIENTED CONTRAST- INDUCED NEPHROPHY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION (RACCOON-AMI)

POSTER ON BOARD: AS04.04 CHRONIC KIDNEY DISEASE AND NEPHROPATHIES

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Background and Aims: There are several studies for comparing the incidence of creatinine-based contrast-induced nephropathy(Cr-CIN) of rosuvastatin and atorvastatin in percutaneous coronary intervention(PCI). Serum cystatin C can help early detection of CIN because it rises earlier after contrast exposure than serum creatinine. We evaluated the incidence of Cystatin C-based CIN(Cys-CIN) of high-dose rosuvastatin and atorvastatin after coronary angiography(CAG) with and without PCI in AMI patients.

Methods: This multicenter registry included 431 patients with AMI undergoing CAG and/or PCI(Rosuvastatin 20mg: n=231, Atorvastatin 40mg: n=200). The primary endpoint was Cys-CIN within 48 hours after contrast exposure and secondary endpoints were Cr-CIN within 72 hours and adverse events at post 30 days.

Results: The incidence of Cys-CIN in Rosuvastatin and Atorvastatin groups was 7.4% and 12.1%, respectively(p=0.10). The incidence of Cr-CIN in Rosuvastatin and Atorvastatin groups was each 4.4% and 6.7%(p=0.30). In the multivariable logistic regression analysis adjusted for known CIN risk variables and the variables with univariate relationships(p<0.05), rosuvastatin did not increase the risk of Cys-CIN compared to atorvastatin(OR[95% CI], 0.46[0.20, 1.06], p=0.069). However, atorvastatin in the statin-naive subgroup significantly increased the risk of Cys-CIN compared to rosuvastatin(0.30[0.11, 0.81], p=0.017). At post 30 days, adverse events including elevated liver and muscle enzymes, persistent renal damage, and clinical cardiovascular events were very low without any difference between the two groups.

Conclusions: This findings showed that there was no significant difference in Cys-CIN incidence between rosuvastatin and atorvastatin in AMI patients and Cystatin C was more sensitive to the early detection of CIN than creatinine.

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Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

CHRONIC KIDNEY DISEASE, TYPE 2 DIABETES AND THE RISK OF MAJOR CARDIOVASCULAR EVENTS IN CORONARY ARTERY DISEASE VERSUS PERIPHERAL ARTERY DISEASE PATIENTS

POSTER ON BOARD: AS04.04 CHRONIC KIDNEY DISEASE AND NEPHROPATHIES

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Background and Aims: Chronic kidney disease (CKD) is a paramount indicator of cardiovascular risk and is highly prevalent in patients with established cardiovascular disease, especially among those with type 2 diabetes (T2DM). Peripheral artery disease (PAD) confers an even higher risk than coronary artery disease (CAD). How cardiovascular risk compares between PAD and CAD patients when analyses are stratified by the presence of CKD is still unclear.

Methods: We prospectively recorded major cardiovascular events (MACE) over 10.0±4.7 years in 1356 patients who had stable CAD, of whom 18.4% had CKD, and in 382 patients with PAD, of whom 20.9% had CKD. Four groups were analyzed: CAD patients without CKD (CAD/CKD-; n=1106), CAD patients with CKD (CAD/CKD+; n=250), PAD patients without CKD (PAD/CKD-; n=316) and PAD patients with CKD (PAD/CKD+; n=66).

Results: The incidence of MACE was lowest in CAD/CKD- patients (27.2%) and significantly higher in CAD/CKD+ patients (49.6%; p<0.001), in PAD/CKD- patients (40.9%; p<0.001), and in PAD/CKD+ patients (56.9%; p<0.001), who in turn were at a higher risk than CAD/CKD+ or PAD/CKD- patients (p=0.015 and p<0.001, respectively). The risk of MACE did not differ significantly between CAD/CKD+ and PAD/CKD- patients (p=0.063). In Cox regression analysis after multivariate adjustment including gender, age, BMI, hypertension, history of smoking, LDL-C, and HDL-C the presence of PAD versus CAD (HR=1.51 [1.25-1.84]; p<0.001), CKD (HR=1.85 [1.51- 2.26]; p<0.001) and T2DM (HR=1.53 [1.29-1.83; p<0.001) were mutually independent predictors of MACE.

Conclusions: We conclude that CKD, T2DM and the presence of PAD versus CAD are mutually independent predictors of MACE.

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Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

INCREASED SERUM PEDF LEVELS AND ALTERED LIPID PROFILE AFTER RENAL TRANSPLANTATION IN PATIENTS WITH END-STAGE RENAL DISEASE

POSTER ON BOARD: AS04.04 CHRONIC KIDNEY DISEASE AND NEPHROPATHIES

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Background and Aims: Pigment epithelium-derived factor (PEDF) is a multifunctional protein with anti-angiogenic and anti-inflammatory properties. Transplant recipients have markedly higher cardiovascular risk compared to the general population. To date, the serum level of PEDF and lipid parameters are not fully clarified in renal transplanted (TX) patients.

Methods: We enrolled 70 TX patients and 34 healthy controls into the study. We examined the serum creatinine, C-reactive protein, fasting glucose and lipid parameters right before, then 1 and 6 months after TX. Lipoprotein subfractions were determined by gel electrophoresis (Lipoprint). Oxidized low-density lipoprotein (oxLDL) and PEDF levels were measured by ELISA.

Results: Patients had a significantly higher PEDF level compared to control subjects before transplantation (23.88 ± 4.2 µg/ml versus 14.68 ± 3.7 µg/ml; $p < 0.001$). One month after transplantation, their PEDF level decreased significantly, and this lower level was maintained during the 6 months follow-up period as well. We found significantly higher initial oxLDL level in the patient group compared to controls. Significant positive correlations were found between PEDF and total cholesterol, low-density lipoprotein (LDL)-cholesterol, triglyceride, oxLDL and small HDL subfraction, while negative correlations were found between PEDF and mean LDL size and large HDL subfraction during the entire follow-up period.

Conclusions: Our data suggest that PEDF may be a therapeutic target for alleviating ox-LDL–induced vascular endothelial cell damages after renal transplantation. The pathophysiological role of changes in PEDF levels after transplantation needs to be further studied.

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Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

LIPOPROTEIN GLOMERULOPATHY: A FIRST CASE OF LAS VEGAS IN THE NETHERLANDS

POSTER ON BOARD: AS04.04 CHRONIC KIDNEY DISEASE AND NEPHROPATHIES

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Background and Aims: A rare cause of nephrotic syndrome and end-stage kidney disease is lipoprotein glomerulopathy, which is due to germline mutations in the *APOE* gene. Hitherto, worldwide 274 cases with *APOE* germline mutations have been reported. We aim to describe the first Dutch case, which also confirms the pathogenicity of the Las Vegas mutation.

Methods: A 63-year-old man presented with nephrotic syndrome. Based on kidney biopsy, membranous glomerulopathy was the most likely diagnosis and treatment was started. Unfortunately, no treatments, including rituximab and tacrolimus, had effect. Therefore, the kidney biopsy was reexamined showing dilated glomerular capillaries with amorph material on light microscopy. Electronic microscopy showed compatibility with lipoprotein thrombi, a characteristic of lipoprotein glomerulopathy. Consequently, the patient was referred to our outpatient clinic for further investigation.

Results: Additional diagnostics, being lipoprotein ultracentrifugation and agarose gel electrophoresis, were performed showing increased remnant- and decreased LDL-lipoproteins. Therefore, we expected the patient to have a *APOE2/E2* genotype conform dysbetalipoproteinemia. However, *a APOE3/E4* genotype was found. Gene sequencing of *APOE* was performed showing a C to A change at DNA-position 509, resulting in substitution of alanine for aspartic acid at amino acid-position 170 (NM_000041.4[APOE]:c.509C>A[p.Ala170Asp]). In 2010, the first case with this variant named "*APOE* Las Vegas" was described in a patient with lipoprotein glomerulopathy. Our findings corroborate the pathogenicity of this mutation. Following diagnosis, our patient started lipid-lowering drugs.

Conclusions: Lipoprotein glomerulopathy is likely to be underdiagnosed due to non-specific clinical manifestations. Timely diagnosis is important for instituting effective treatment since conventional immunosuppressive therapy for nephrotic syndrome is unsuccessful.

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Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

REDUCTION OF CIRCULATING LEVELS OF METHYLGLYOXAL BY A MEDITERRANEAN DIET IS ASSOCIATED WITH PRESERVED KIDNEY FUNCTION IN TYPE 2 DIABETES PATIENTS WITH CORONARY HEART DISEASE

POSTER ON BOARD: AS04.04 CHRONIC KIDNEY DISEASE AND NEPHROPATHIES

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Background and Aims: Advanced glycation end products (AGEs) are involved in kidney disease pathogenesis in type 2 diabetes. Our aim was to analyze whether AGE reduction and the consequent modulation of AGE metabolism, after consumption of two healthy diets, could be involved in delaying the impairment of kidney function in coronary heart disease (CHD) patients and type 2 diabetes.

Methods: Type 2 diabetes patients (540 out of 1002 patients from the CORDIOPREV study) were classified into three categories according to serum creatinine-based estimated glomerular filtration rate (eGFR) at baseline: normal eGFR (≥90 mL/min/1.73m^2), mildly-impaired eGFR (60-<90 mL/min/1.73m^2) and severely-impaired eGFR (<60 mL/min/1.73m^2). Serum AGE levels (methylglyoxal-MG) and N-carboximethyllysine-CML) and gene expression related to AGE metabolism (*AGER1*, *RAGE*, and *GloxI m*RNA) were measured before and after 5-years of dietary intervention [Mediterranean diet (35% fat, 22% MUFA, <50% carbohydrates) or a low-fat diet (28% fat, 12% MUFA, >55% carbohydrates)].

Results: Mediterranean diet produced a lower declined of eGFR compared to the low-fat diet, both in total population and in mildly-impaired eGFR patients (p = 0.035). Moreover, Mediterranean diet was able to decrease MG levels and increase *GloxI* expression in normal and mildly-impaired eGFR patients (all p<0.05). An increment of a SD of MG levels, after dietary intervention, determined 5.5-fold (95% CI 0.053–0.633) more the probability of declining eGFR.

Conclusions: These findings reinforce the clinical benefits of the Mediterranean diet in the context of secondary cardiovascular disease prevention providing a dietary strategy for the reduction of AGEs that could reduce CKD complications.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

306 / #679

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

PREVALENCE OF DISTAL SENSORY PERIPHERAL NEUROPATHY AND ALBUMINURIA IN INDIVIDUALS WITH PREDIABETES

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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Background and Aims: To investigate the prevalence of distal sensory peripheral neuropathy and albuminuria in individuals with prediabetes.

Methods: A cross-sectional study in patients with prediabetes at a University Hospital Clinic. Secondary causes of distal sensory peripheral neuropathy (DSPN) were excluded. DSPN was diagnosed by: Neuropathy Symptom Score (NSS) ≥5 + Neuropathy Disability Score (NDS) ≥3 or NDS ≥6 or abnormal vibration perception threshold (VTP) + NSS ≥3 + NDS ≥3. Albuminuria was diagnosed in the case of albumin-creatinine ratio (ACR) = 30 mg/g. Ankle-brachial index (ABI) and arterial stiffness assessed with aortic pulse wave velocity (PWV) were also measured.

Results: Individuals with prediabetes were included (n=137, median age 63 years, 56.2% males). Of the participants, n=25 (18.2%) had DSPN and 21 (15.3%) had albuminuria. Patients with DSPN had higher age and PWV compared with those without DSPN (Table 1). Patients with albuminuria had higher age, fasting plasma glucose, and PWV compared with those without albuminuria (Table

Table 1. Baseline characteristics of individuals with or without DSPN

	Individuals with DSPN N= 25	Individuals without DSPN N=112
Gender, male, N (%)	15 (60)	57 (55)
Age, years	70 (61-74) *	63 (55-70)
Height, cm	171 (163-177)	166 (160-173)
Body mass Index, kg/m^2	30.3 ± 4.3	29.8 ± 6.3
Fasting plasma glucose, mg/dL	106 (102-110)	104 (100-111)
2 hour 75-g Oral Glucose Tolerance Test, mg/dL	130 (105-174)	122 (95-146)
Impaired glucose tolerance, N (%)	11 (44)	26 (23)
Insulin, µIU/Ml	10.3 (7.6-13.6)	10.3 (6.6-12.7)
Homeostatic Model Assesment for Insulin Resistance index	2.7 (2.0-4.1)	2.6 (1.5-3.4)
Hemoglobin A1c, %	6.3 ± 2.2	6.3 ± 3.2
Creatinine, mg/dL	0.91 (0.83-1.02)	0.90 (0.80-1.00)
eGFR, mL/min/1.73 m^2	79 (74-91)	82 (60-90)
Total cholesterol, mg/dL	174 ± 41	174 ± 41
Triglycerides, mg/dL	104 (73-122)	100 (75-148)
High-intensity lipoprotein cholesterol, mg/dL	52 ± 10	52 ± 10
Low-intensity lipoprotein cholesterol, mg/dL	101 ± 36	94 ± 31
Apolipoprotein B-100, mg/dL	72.4 ± 27	82.1 ± 69.2
Lipoprotein(a), mg/dL	8.5 (2.6-18.3)	12.3 (4.3-31.3)
Vitamin D <20 ng/mL, N (%)	16 (64)	50 (45)
Microalbuminuria, N (%)	6 (24)	14 (16)
Albumin-creatinine ratio, mg/g	13.4 (6.3-37.4)	9.0 (5.6-16.0)
Pulse wave velocity, m/s	8.6 (7.6-10.3) *	8.1 (7.4-9.0)
Ankle-branchial index	1.24 (0.8-1.3)	1.19 (1.05-1.29)
Vibration perception threshold, V	26 ± 10	19 ± 8

*p <0.05 for comparison versus study group without DSPN

2).

Table 2. Baseline characteristics of individuals with or without albuminuria

	Individuals with albuminuria N=21	Individuals without albuminuria N=116
Gender, male, N (%)	15 (71)	54 (47)
Age, years	71 (68-76) ^	63 (56-70)
Height, cm	166 (162-173)	168 (160-174)
Body mass Index, kg/m^2	29.4 (26.6-30.3)	28.6 (26.9-31.8)
Fasting plasma glucose, mg/dL	108 (106-114) ^	105 (100-110)
2 hour 75-g Oral Glucose Tolerance Test, mg/dL	137 (114-172)	124 (96-150)
Impaired glucose tolerance, N (%)	8 (38)	29 (25)
Insulin, µIU/Ml	11.3 (7.5-18.3)	9.6 (6.5-12.5)
Homeostatic Model Assessment for Insulin Resistance index	2.9 (2.0-4.8)	2.4 (1.5-3.3)
Hemoglobin A1c, %	6.0 ± 0.4	6.3 ± 2.3
Creatinine, mg/dL	1.0 (0.8-1.1)	0.9 (0.8-1)
Estimated glomerular filtration rate, mL/min/1.73 m^2	74 (70-89)	82 (70-91)
Total cholesterol, mg/dL	158 ± 32	174 ± 42
Triglycerides, mg/dL	94 (75-153)	100 (73-137)
High-intensity lipoprotein cholesterol, mg/dL	50 ± 11	50 ± 12
Low-intensity lipoprotein cholesterol, mg/dL	83 ± 24	97 ± 33
Apolipoprotein B-100, mg/dL	73.0 ±18.2	81.4 ± 69.5
Lipoprotein(a), mg/dL	8.7 (2.6-30.0)	10.3 (3.2 -24.8)
Vitamin D < 20 ng/mL, N (%)	13 (62)	55 (47)
Pulse wave velocity, m/s	9.0 (8.3-11.1)	8.2 (7.3-9.0)
Ankle-branchial index	1.2 (1.1-1.3) ^	1.2 (1.1-1.3)
Distal sensory peripheral neuropathy, N (%)	6 (29)	19 (16)
Vibration perception threshold, V	22 ± 10	20 ± 9

^p <0.05 for comparison versus study group without microalbuminuria.

Conclusions: Nearly 1 of 5 individuals with prediabetes present with DSPN and/or albuminuria.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

307 / #345

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

ADVANCED GLYCATION END PRODUCTS CORRELATES WITH CAROTID ARTERY INTIMA-MEDIA THICKNESS IN NORMOGLYCEMIC, PREDIABETES AND DIABETES INDIVIDUALS.

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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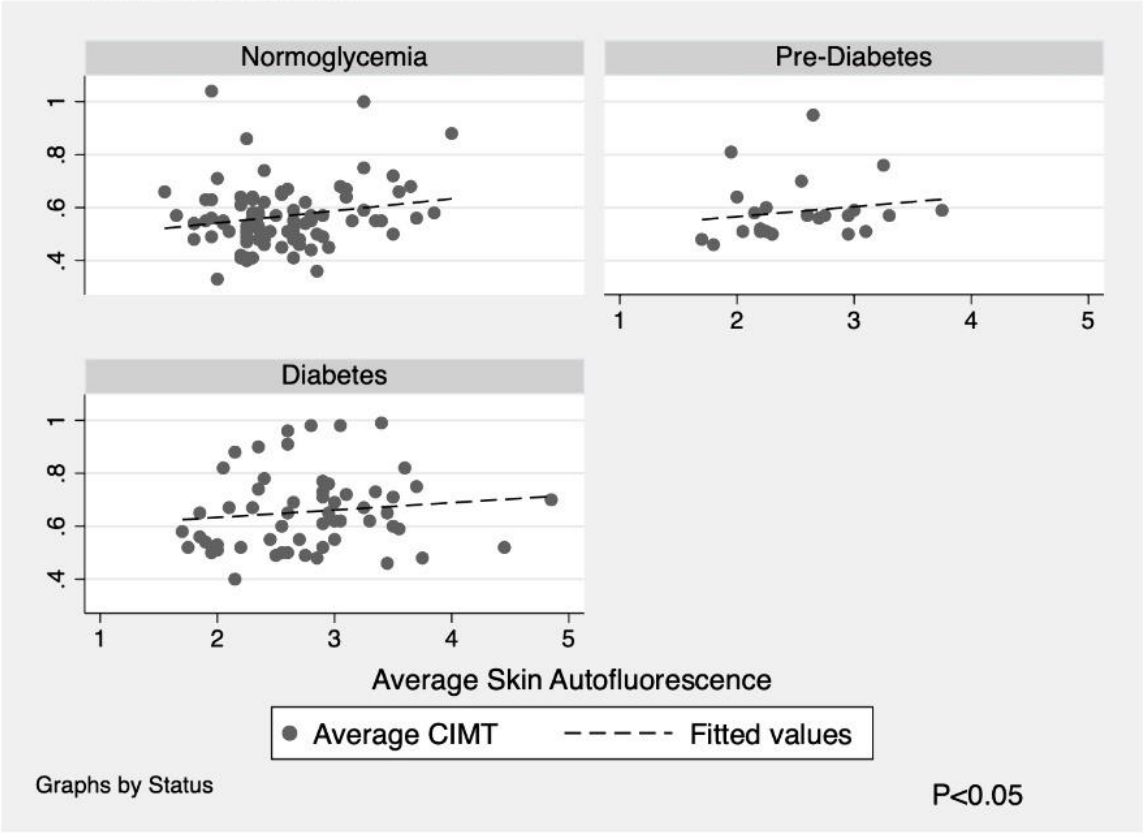
Background and Aims: Skin autofluorescence (SAF), a non-invasive and validated marker of advanced glycation end-product (AGE), is associated with vascular complications in diabetes mellitus (DM). However, the associations between SAF and subclinical carotid atherosclerosis in normoglycemia and prediabetes are unclear. We aimed to study the associations between SA and SAF in various glycaemic strata.

Methods: Three groups of individuals were recruited: normoglycemic but at risk of DM, n=106(53%); prediabetes, n=32(16%) ; recent diagnosis of T2DM, n=58(29%). Glycaemic status was determined by the 75gm oral glucose tolerance test. Carotid intima-media thickness (CIMT) and SAF were measured by carotid ultrasonography (Mannheim consensus) and AGE reader respectively (1). The average of CIMT measurement at three sites (proximal, mid and distal) on the right and left common carotid artery was calculated as CIMTavg. Multivariable regression model was used to evaluate associations between CIMT and AGE adjusted for glycaemic status. All analysis was done using Stata version 16.0.

Results: Patient characteristics: Mean Age 46.6 years (SD:9.4); Male-74 (37%). Both CIMTavg and SAF were higher in T2DM when compared to normoglycemic/pre-diabetes status (Normoglycemia : SAF: Mean: 2.57; CIMTavg: Mean: 0.57mm; Pre-diabetes: SAF: 2.52; CIMT: 0.58mm; Diabetes: SAF: 2.79; CIMT: 0.66mm, $p<0.05$). Multivariable analysis showed that SAF is a significant predictor of CIMT after

adjustment for glycaemic status (adjusted beta coeff:0.16; p=0.039). (See Figure 1).

Figure 1: Scatterplot and linear regression model showing association between skin autofluorescence derived AGE and CIMTavg in participants with normoglycemia, pre-diabetes and diabetes.



Conclusions: SAF is associated with CIMT irrespective of glycaemic status. The utility of SAF as a population based screening tool for SA needs to be evaluated longitudinally in larger cohorts.

91ST EAS CONGRESS
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308 / #997

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

ASSOCIATION OF HBA1C WITH SEVERITY OF CORONARY ARTERY DISEASE IN PATIENTS PRESENTING AS NON-DIABETIC ACUTE CORONARY SYNDROME

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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Background and Aims: Acute coronary syndrome (ACS) indicates the serious clinical manifestation of coronary artery disease (CAD) . This study was aimed to study the relation of HbA1c with the severity of CAD in patients presenting as non-diabetic ACS. Diabetic status of the patients was assessed with fasting blood sugar (FBS) and HbA1c levels, and coronary artery disease burden was assessed by coronary angiography.

Methods: This prospective observational cross-sectional study was conducted in our department . Inclusion criteria Patients presenting as non-diabetic acute coronary syndrome Exclusion criteria Patients who known diabetics, patients with known coronary artery disease

Results: Out of 300 patients, 75% were males, and 25% were females; 80% of cases had STEMI, 20% had NSTEMI, .According to HbA1c, 41.8% were diabetic, 39.4% were pre-diabetic, and 18.8% were nondiabetic. A significant positive correlation was found between HbA1c and Gensini score and between HbA1c and the number of vessels involved

Conclusions: This study emphasises the importance of evaluating the presence of diabetes in patients presenting as non-diabetic acute coronary syndrome. Acute coronary syndrome may be considered as one of the presentations of diabetes mellitus.

91ST EAS CONGRESS
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309 / #1568

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

METABOLIC CHARACTERISTICS FOR DIFFERENT GENDERS WITH DIABETES, A RETROSPECTIVE EPIDEMIOLOGICAL STUDY

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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Background and Aims: Genders are known to have different metabolic characteristics as have been repeatedly demonstrated in different studies. We decided to study if these differences are the same in a Diabetic Egyptian Cohort.

Methods: We retrospectively collected data for 500 patients attending our Diabetes clinic and analyzed multiple metabolic characteristics for correlations.

Results: Population studied was 500(M/F 275/225), with Mean age 49/50.8, DM duration of 10.1/10 years, The female population had significantly higher BMI, HDL, LDL, LPa. Males had significantly higher

HbA1c, TG, eGFR. Both groups had similar BP and Total Cholesterol.

Gender	Male	Female	Probability
Number	275	225	0.02
Age	48	52	0.15
BMI	30.3	35	**<0.001**
Sys BP	138	136	0.24
HbA1c	8.9	8.3	**0.008**
Duration	8	8	0.8
Chol	182	189	0.199
TG	165	147	**0.013**
HDL	45.4	54.4	**<0.001**
LDL	100	108.5	**0.038**
LPa	21.5	34.5	**0.019**
eGFR	97	90	**0.006**

Conclusions: This cohort shows that Egyptian females with diabetes tend to have higher BMI, higher lipid profile and LPa. than Egyptian males with diabetes, while Males have poor glycemic control and higher TG.

91ST EAS CONGRESS
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310 / #1043

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

LYSINE-SPECIFIC HISTONE DEMETHYLASE 1A MEDIATES THE UP-REGULATION OF NADPH OXIDASE EXPRESSION IN THE KIDNEY OF DIABETIC MICE

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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Background and Aims: Epigenetic alterations have been increasingly connected to the pathology of diabetic kidney disease (DKD), a degenerative disorder leading to kidney failure that is characterized by structural-functional alterations of the glomerular microvascular system. NADPH oxidase (Nox) represents a major source of oxidative stress in DKD. We aimed at elucidating the potential implication of lysine-specific histone demethylase 1A (LSD1) in the up-regulation of Nox expression in diabetic kidney.

Methods: Male non-diabetic and streptozotocin-induced diabetic C57BL/6J mice (n=10/group) were treated with 5 mg/kg GSK2879552, a specific LSD1 inhibitor, or its vehicle, for 4 weeks. Human endothelial cells (EA.hy926, EC) were exposed to normal (5 mM) or high (25 mM) concentrations of glucose in the absence/presence of 5 μM GSK2879552, or subjected to transient transfection. Fluorescence microscopy, real-time PCR and Western blot techniques were used.

Results: Significant increases in LSD1 mRNA and protein levels correlated with elevated Nox subunit mRNA/protein expression were detected in the kidney of diabetic mice, 4 weeks after installation of hyperglycemia. A marked immunostaining of LSD1 was detected in the glomeruli of diabetic mice. Pharmacological inhibition of LSD1 suppressed the up-regulation of Nox subunit (Nox1, Nox2, Nox4, p22phox) mRNA/protein levels in the kidney of diabetic mice. LSD1 blockade significantly reduced the up-regulation of Nox subtype expression levels in high glucose-exposed EC. Overexpression of LSD1 increased the mRNA levels of Nox subunits in cultured EC.

Conclusions: LSD1-oriented pharmacological inhibitors could become important therapeutic tools to prevent epigenetic instability and oxidative stress in DKD. **Acknowledgements:** Work supported by UEFISCDI (PN-III-P1-1.1-TE-2021-0180, PN-III-P4-ID-PCE-2020-1898).

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MANNHEIM GERMANY | MAY 21-24, 2023

311 / #425

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

TRANSCRIPTOMIC AND PHYSIOLOGICAL ANALYSES REVEAL TEMPORAL CHANGES CONTRIBUTING TO THE DELAYED HEALING RESPONSE TO ARTERIAL INJURY IN DIABETIC RATS

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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Background and Aims: Atherosclerosis is a major complication of diabetes and a leading cause of mortality in diabetic patients. Vascular interventions in diabetic patients can lead to complications attributed to defective vascular remodeling and impaired healing response. In this study, we aim to elucidate the physiological and molecular differences in vascular healing response using a rat model of arterial injury applied to healthy and diabetic conditions.

Methods: Wistar and Goto-Kakizaki (GK) rats (n = 40 per strain) were subjected to left common carotid artery (CCA) balloon injury and euthanized at different timepoints: 0, 24 hours, 5 days, 2, 4 and 6 weeks. Non-invasive morphological and physiological assessment of the CCA was performed with Ultrasound Biomicroscopy (US). Total RNA was isolated from the injured CCA at each timepoint and microarray profiling was performed (n=3 rats per timepoint). Bioinformatic analyses were conducted using R software, DAVID bioinformatic tool, online STRING database and Cytoscape software.

Results: Significant increase in neointimal thickness ($p<0.01$; 2-way ANOVA) was observed after 2 weeks of injury in GK compared to heathy rats, which was confirmed by histology. Bioinformatic analyses showed that expression of SMC and coagulation genes were increased in diabetic rats and dysregulation of immune pathways. TF-PPI analysis provided mechanistic evidence wherein an array of transcription factors was dysregulated in diabetic rats specifically from 2 weeks after injury.

Conclusions: In this study, we have demonstrated that diabetic rats exhibit impaired arterial remodeling characterized by a delayed healing response. These results further provide molecular insights into the mechanisms contributing to impaired arterial healing in diabetes.

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312 / #1160

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

DIABETES IN PATIENTS WITH GENETICALLY VERIFIED FAMILIAL HYPERCHOLESTEROLEMIA

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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Background and Aims: Both diabetes and familial hypercholesterolemia (FH) can lead to increased risk of cardiovascular disease (CVD). We study the risk of CVD in patients who have both FH and diabetes and compare their risk with age and sex adjusted controls. A second aim is to study if long time high dose statin treatment in genetically verified FH is associated with prevalence of diabetes in FH patients with very long high dose statin treatment.

Methods: We performed a prospective matched cohort study of 5,635 subjects with genetically verified FH and 112,589 age and sex matched controls. We used National Norwegian Health registers to identify patients registered with the ICD10-codes E10-E14 (diabetes type 1, type 2, malnutrition-related diabetes, other specified diabetes mellitus and unspecified diabetes mellitus), as well as the incidence of I00-99 (CVD) during 2008-2019.

Results: Follow-up time was from 2008 or start of follow-up until death or end of follow-up in 2019, whichever occurred first. In the FH population, 2119 patients were registered as having CVD compared to 25591 in age and sex adjusted controls without FH. Further, 370 subjects having FH were registered with diabetes (E10-E14) compared to 5637 registered with diabetes among the controls.

Conclusions: Hazard Ratios comparing risk of CVD in subjects with both FH and diabetes versus controls will be presented at the congress using Cox proportional hazards regression with stratification on matched case-set. The prevalence of diabetes (ICD10 codes E10-14) in the FH population was 6.6% versus 5.0% in age and sex adjusted controls.

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313 / #1165

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

ARTERIAL STIFFNESS AND VASCULAR AND HEMODYNAMIC PARAMETERS IN ADOLESCENTS AND YOUNG PEOPLE WITH TYPE 1 DIABETES MELLITUS: FIVE-YEAR FOLLOW-UP DATA

POSTER ON BOARD: AS04.05 DIABETES; MACRO- AND MICROANGIOPATHIES

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Background and Aims: Background: Type 1 diabetes mellitus (DM1) patients present important risk factors for cardiovascular events. **Objective**: To analyze arterial stiffness and cardiovascular parameters in a cohort of patients with DM1.

Methods: Methods: Longitudinal study involving 32 patients with DM1, with two visits carried out within a 5-year interval. Arterial stiffness indices, peripheral and central systolic and diastolic blood pressures (SBPp, SBPc, DBPp, DBPc), hemodynamic parameters, quality of life, and glycated hemoglobin (HbA1c) were evaluated. To compare baseline and follow-up measurements, the Student's t test for paired samples or the Wilcoxon test was used. Spearman's or Pearson's correlation coefficients were used to verify associations between variables. The established significance level was $p<0.05$.

Results: Results: The five-year follow-up sample consisted of 32 patients from Brazil (16.68±4 years, 9.16 years of disease), 59.4% of whom were female. Pulse wave velocity increased significantly and augmentation index (AIx@75) did not change five years after (4.79±0.42m/s, 28.86±10.26%) the first measurement (4.42±0.33m/s, 34.33±10.49%). SBPp, SBPc, DBPp, DBPc increased significantly in the second measurement (119,01±11,59, 106.3±11.59, 74.18±10.48, 76.05±10.52mmHg) compared to first measurement (107.90±10.66, 96.82±10.08, 64.83±9.40, 66.16±9.40mmHg). Cardiac output increased and cardiac index decreased at the five-year follow-up. HbA1c was positively associated with the impact domain of disease ($r=0.4099$, $p=0.0220$) and the total score ($r=0.3562$, $p=0.0492$) of the quality of life questionnaire.

Conclusions: Conclusion: At the five-year follow-up, patients with DM1 increased vascular pressures and worsened the arterial stiffness indices and hemodynamic parameters. This study shows the importance of cardiovascular assessment in addition to conventional control of children and adolescents with DM1.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

314 / #430

Topic: *AS04 Clinical Vascular Disease / AS04.06 Aneurysms and other non-atherosclerotic arteriopathies*

LIPIDOMICS PLASMA ANALYSIS SUPPORTS A DIFFERENTIAL THORACIC AORTIC ANEURYSM DIAGNOSIS FOR BICUSPID OR TRICUSPID AORTIC VALVE PATIENTS

POSTER ON BOARD: AS04.06 ANEURYSMS AND OTHER NON-ATHEROSCLEROTIC ARTERIOPATHIES

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Background and Aims: Thoracic aortic aneurysm (TAA) is potentially fatal with a chance diagnosis. Its prevalence is significantly higher in subjects with bicuspid aortic valve (BAV) for unknown reasons. Here we aimed to identify plasma lipid alterations as diagnostic markers of aortic dilatation in idiopathic TAA valve-associated.

Methods: Plasma samples from 17 idiopathic TAA patients and 16 subjects without aortic dilatation (control, C) were collected and classified according to aortic valve type (BAV or tricuspid aortic valve, TAV). Untargeted lipidomics was carried out by LC-MS/MS and enrichment analysis was performed to reveal main biological processes. Significant variation in lipid abundance and metabolism were considered if p value <0.05 by Mann-Whitney or GSEA, respectively.

Results: Principal component and partial least square analyses classified TAA and C groups both globally and valve-associated. The main lipids contributing to TAA development were lysophospholipids in BAV patients, whereas phospholipids were in TAV. Lysophosphatidylethanolamines, lysophosphatidylcholines and lysophosphatidic acid correlate with the aortic diameter in BAV patients. Phosphatidylethanolamines and phosphatidylcholines negatively correlate to aortic diameter in TAV patients. Oxidative stress was revealed as a key hallmark in both TAA-associated valves. Vitamin D3 and tyrosine metabolisms, and androgen and estrogen biosynthesis were evidenced as trigger mechanisms of TAA development in BAV patients. Energy imbalance involving fatty acids and sugars was the main altered process in TAV.

Conclusions: TAA development is differentially reflected in plasma from BAV or TAV patients, supporting and individualized diagnosis valve-dependent. Specific lipid classes and metabolisms are also shown as potential targets of novel therapies.

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315 / #242

Topic: *AS04 Clinical Vascular Disease / AS04.06 Aneurysms and other non-atherosclerotic arteriopathies*

IN-DEPTH ANALYSIS OF HUMAN VASCULAR SMOOTH MUSCLE CELLS FROM IDIOPATHIC THORACIC AORTIC ANEURYSM PATIENTS EVIDENCES THE MECHANISMS PREDISPOSING TO AORTIC DILATATION IN BICUSPID AORTIC VALVE

POSTER ON BOARD: AS04.06 ANEURYSMS AND OTHER NON-ATHEROSCLEROTIC ARTERIOPATHIES

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Background and Aims: To identify the hallmarks that difference the aortic dilatation associated to bicuspid (BAV) and tricuspid aortic valve (TAV) patients

Methods: A total of 91 patients with idiopathic thoracic aortic aneurysm (TAA) or without aortic dilatation (control) were recruited and classified according to valve type as having BAV or TAV. To identify in tissue changes VSMCs were isolated from TAA aortas, and protein levels and protein coordinated behavior were differentially analyzed in BAV-TAA *versus* TAV-TAA by high throughput proteomics. To identify diagnostic markers, plasma quantification of TAA secreted proteins was performed compared to control patients for each valve type by ELISA and correlated with aortic diameter

Results: VSMC contractile and proliferative phenotypes did not differ significantly between BAV and TAV patients. However, BAV-TAA patients exhibited a stress phenotype affecting protein homeostasis and featuring DNA damage and poor DNA repair, together with increased signal transduction mediated by G proteins. Vascular remodeling in BAV was reflected in diminished focal adhesions, weakened extracellular matrix interactions, and cell death, resulting in a defective arterial wall with poor adaptive capacity to external mechanical forces. Two individual diagnostic marker panels valve-associated were identified. Correlations with aortic diameter were found for C1QTNF5, LAMA2, and SPARC in BAV patients and for CP and FAP in TAV patients

Conclusions: The molecular pathways here identified in the human aorta evidence differences in TAA of BAV or TAV patients that support differential therapeutic approaches

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316 / #1039

Topic: *AS04 Clinical Vascular Disease / AS04.06 Aneurysms and other non-atherosclerotic arteriopathies*

INHIBITION OF CD40-TRAF6 SIGNALING REDUCES AAA PROGRESSION

POSTER ON BOARD: AS04.06 ANEURYSMS AND OTHER NON-ATHEROSCLEROTIC ARTERIOPATHIES

Miriam Ommer-Bläsius[1], Christin Elster[1], Tanja Vajen[1], Sarah Verheyen[1], Susanne Pfeiler[1], Malte Kelm[1], Esther Lutgens[2], Norbert Gerdes[1]
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Background and Aims: Abdominal aortic aneurysm (AAA) is a complex, multifactorial disease. A common hallmark is inflammation, which leads to the progressive degeneration of the aortic wall. The CD40/CD40L dyad regulates inflammatory responses such as immune cell activation, differentiation and cytokine production contributing to AAA progression. Therefore, we investigate whether inhibition of CD40 signaling via its adaptor molecule TNF receptor protein (TRAF)-6 by a small molecule inhibitor (TRAF-STOP) protects from AAA progression.

Methods: The porcine pancreatic elastase perfusion model was used to induce experimental AAA in C57BL/6J mice. Mice were treated with either the small molecule inhibitor, TRAF-STOP, or solvent control. AAA progression was monitored weekly via non-invasive ultrasound imaging. Immune cell infiltration was examined by flow cytometry and cytokine concentrations were quantified by a multiplex immune assay. Further, spatial transcriptomics technology was used to analyze gene expression levels in aneurysmal tissue.

Results: TRAF-STOP treatment reduced aortic dilation and AAA incidence. Flow cytometric analysis of aneurysmal tissue at day 7 and 28 after AAA induction indicated no changes in immune cell distribution upon treatment. However, multiplex immune assay and spatial transcriptomics technology revealed a reduction of inflammatory markers in aneurysmal tissue 7 and 14 days after AAA induction.

Conclusions: Using TRAF-STOP as pharmacological inhibitor of CD40-TRAF6 signaling reduces AAA progression and incidence in experimental AAA. TRAF-STOP modulates the production of effector molecules released from immune cells in the aneurysmal tissue during the intermediate phase of AAA formation (7 to 14 days after AAA induction) thereby stabilizing AAA progression.

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317 / #825

Topic: *AS04 Clinical Vascular Disease / AS04.06 Aneurysms and other non-atherosclerotic arteriopathies*

TYPE B INTERRUPTED AORTIC ARCH WITH A HUGE RIGHT SUBCLAVIAN ARTERY ANEURYSM IN AN ADULT

POSTER ON BOARD: AS04.06 ANEURYSMS AND OTHER NON-ATHEROSCLEROTIC ARTERIOPATHIES

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Background and Aims: Interruption of the aortic arch and right subclavian artery aneurysm is a rare congenital malformation. Survival in adults depends on the formation of collaterals to supply the descending aorta. The interruption of the aortic arch must be taken into account, particularly in patients with hypertension and weak pulses in the lower extremities.

Methods: A 66-year-old woman with the main complaint of exertion dyspnea for a period of six months. She had a history of hypertension for several years and had been treated with Captopril. On physical examination, her arterial blood pressure was 160/90 mmHg in the right upper extremity and 110/60 mmHg in the left upper extremity. Chest radiography showed a huge intrathoracic mass in the upper lobe of the right lung. Computed tomography angiography (CTA) showed an interruption of the aortic arch between the left subclavian artery and the left common carotid artery and profuse collateral circulation and a saccular aneurysm in the subclavian artery. The aneurysm measured 76 × 64 mm with atherosclerosis change and mural calcification.

Results: The patient was scheduled for surgical correction but refused surgery due to a COVID-19 infection. She underwent conservative therapy with medications to reduce hypertension. Her condition has been stable for 12 months of follow-up.

Conclusions: Hypertension is an important public health issue. Appropriate diagnosis is important in reducing complications related to hypertension. A careful physical examination plays a central role in the diagnosis of hypertension. This case report highlights the importance of considering IAA in the etiology of hypertension.

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318 / #294

Topic: *AS04 Clinical Vascular Disease / AS04.07 Nutrition, nutraceuticals*

ASSOCIATIONS OF CAROTENOIDS, VITAMIN A AND MORTALITY: THE LUDWIGSHAFEN RISK AND CARDIOVASCULAR HEALTH (LURIC) STUDY

POSTER ON BOARD: AS04.07 NUTRITION, NUTRACEUTICALS

Angela Moissl[1,2,3], Graciela Delgado[2], Marcus Kleber[2], Winfried März[2,4,5], Bernhard Krämer[2], Stefan Pilz[6], Hubert Scharnagl[5], Rüdiger Siekmeier[7], Günther Silbernagel[8], Andreas Tomaschitz[9], Brigitte Winklhofer-Roob[10], Stefan Lorkowski[1,3]
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Background and Aims: Retinol and carotenoids are nutrients that are essential for several physiological functions. Since vitamin A is controversially discussed and both beneficial and harmful effects on cardiovascular health have been proposed, we examined the association of retinol and carotenoids with overall and cardiovascular mortality in the Ludwigshafen Risk and Cardiovascular Health (LURIC) study

Methods: The LURIC study consists of 3,316 patients that were referred for coronary angiography at a tertiary care centre in Southwest Germany. Patients were followed up for a median of 9.9 years. Association of carotenoids (α-carotene, β-carotene, lycopene, luteine-zeaxanthin, β-cryptoxanthine and retinol) with all-cause and cardiovascular mortality was analysed using Cox proportional hazard regression.

Results: The risk of all-cause and cardiovascular mortality increases steadily with increasing concentrations for all carotenoids [HR 0.93 (95 % CI 0.87-1.00) and 0.93 (95 % CI 0.86-1.02)], respectively); except retinol, which shows a U-shaped relationship without adjustment. For example, α-carotene concentrations were associated with the risk of overall mortality [HR 0.73 (95 % CI 0.65 - 0.82) and cardiovascular mortality (HR 0.66 (95 % CI 0.56-0.77)]; β-carotene concentrations were associated with the risk of overall mortality [HR 0.88 (95 % CI 0.81 - 0.95) and cardiovascular mortality 0.92 (95 % CI 0.83-1.01)]) without adjustment. These results were robust against adjustment for age, gender, and conventional cardiovascular risk factors.

Conclusions: Carotenoid concentrations show clear associations with mortality risk. Since carotenoids show relatively low serum concentrations, further studies should be conducted to determine a controlled dose-dependent relationship more accurately.

91ST EAS CONGRESS
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319 / #295

Topic: *AS04 Clinical Vascular Disease / AS04.07 Nutrition, nutraceuticals*

DEFICIENCY OF MICRONUTRIENTS AND KIDNEY FUNCTION: THE LUDWIGSHAFEN RISK AND CARDIOVASCULAR HEALTH (LURIC) STUDY

POSTER ON BOARD: AS04.07 NUTRITION, NUTRACEUTICALS

Angela Moissl[1,2,3], Graciela Delgado[2], Marcus Kleber[2,3,4], Bernhard Krämer[2], Winfried März[2,3,5,6], Stefan Lorkowski[3]
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Background and Aims: The contribution of micronutrients to all-cause and cardiovascular mortality is discussed controversially. Due to the association of cardiovascular diseases and renal function, we analysed serum concentrations of micronutrients and their relationship to renal disease in a patient population at high cardiovascular risk.

Methods: Our study comprised 3,307 patients (mean age 62.7 ± 10.6 years) from the Ludwigshafen Risk and Cardiovascular Health (LURIC) study with serum measurements of micronutrients stratified for three different estimated glomerular filtration rate (eGFR) categories, i.e. <60, 60-90 and >90 ml/min/1.73 m², according to KDIGO2022. We evaluated the association of micronutrient concentrations with renal function and overall and cardiovascular mortality.

Results: Our analyses revealed that high zinc concentrations of 75.71 µmol/L correlate with reduced all-cause mortality and concentrations >77.78 µmol/L with reduced cardiovascular mortality. Copper concentrations >102 µg/dl are associated with increased overall and cardiovascular mortality risk in all renal function groups. Analyses of micronutrients by kidney function groups revealed that the optimal range of micronutrients in serum is strongly related to kidney constitution (Figure

1).

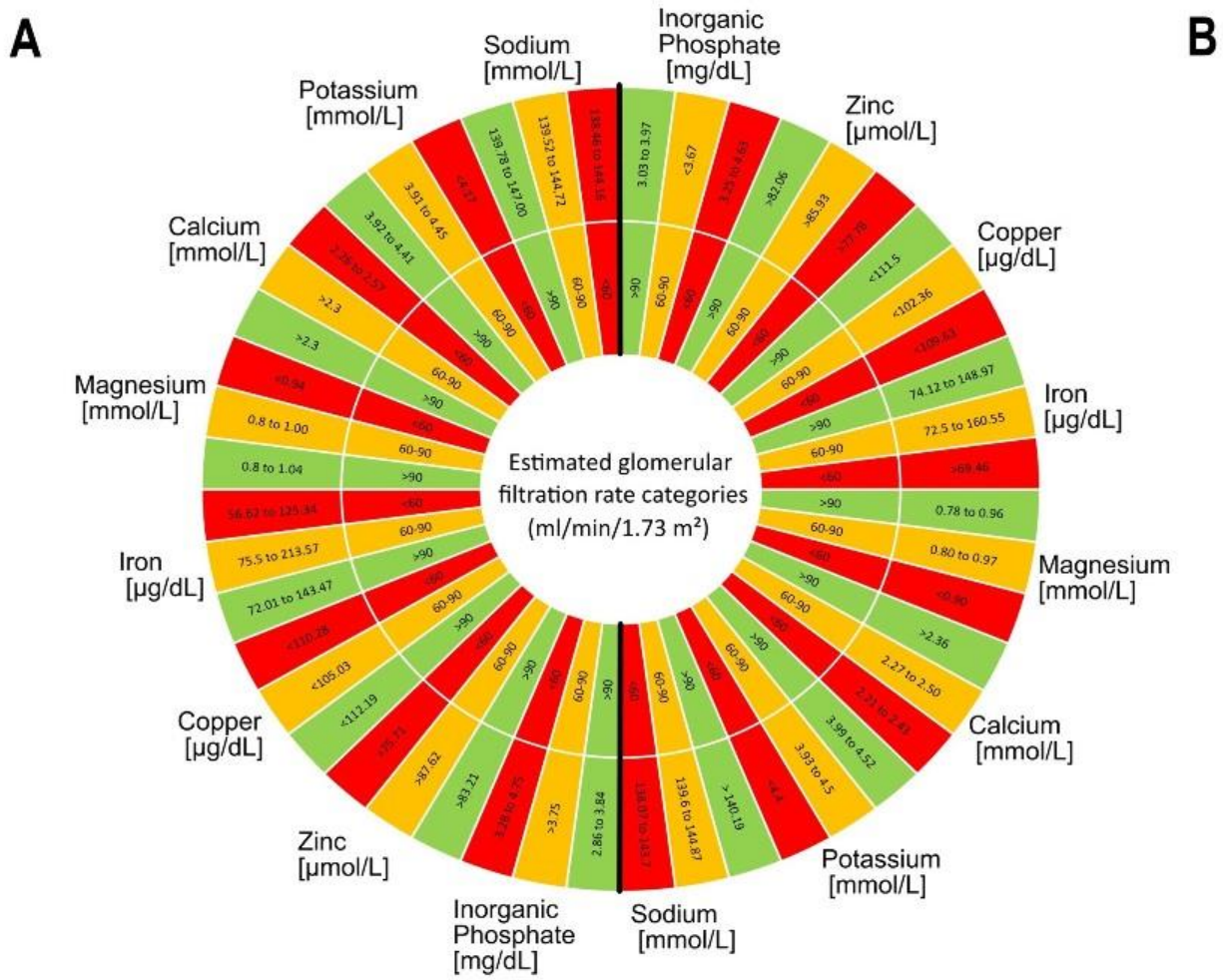

Figure 1: Optimal micronutrient concentration rate according to estimated glomerular filtration rate categories (eGFR, <60, 60-90 and >90 ml/min/1.73m²), A) All cause mortality and B) Cardiovascular mortality

Conclusions: We found that high zinc serum concentrations are associated with lower mortality risk and high copper serum concentrations with increased mortality risk. Serum micronutrient concentrations might be an important indicator of poor renal function and are associated with mortality. Therefore, micronutrient concentrations and renal function of patients should be monitored. Serum electrolyte concentrations appear to be rather inadequate in poor renal function, so attention should be paid to adequate micronutrient supplementation in patients.

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320 / #1230

Topic: *AS04 Clinical Vascular Disease / AS04.07 Nutrition, nutraceuticals*

INFLUENCE OF LOW GLYCEMIC INDEX DIET ON INFLAMMATORY STATE AND LIPID PARAMETERS IN PATIENTS WITH ATHEROSCLEROTIC CORONARY ARTERY DISEASE

POSTER ON BOARD: AS04.07 NUTRITION, NUTRACEUTICALS

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Background and Aims: Purpose of the study was to evaluate influence of low glycemic index diet (LGID) on blood inflammation state and lipid parameters in patients with atherosclerotic coronary artery disease (ASCAD).

Methods: 160 with ASCAD (confirmed by coronary angiography) entered as 12 week dietary intervention either with LGID (n=80) or routine diet (RD; n=80) along with standard treatment from 2016 to 2019 (male=48%). Laboratory (including neutrophil, platelet, lymphocyte counts, hs-CRP, pro-inflammatory interleukins, IL-1β, IL-6, TNF-α, lipid parameters TC, TG, LDL-Cholesterol, HDL-Cholesterol) with evaluation of the systemic immune inflammatory index (SII) and instrumental data were obtained at baseline and in 12 weeks of the intervention.

Results: LGID 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 8.1 pg/mL to 4.7 pg/mL, P<0.005) than RD. 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). Group 1 had more pronounced influence on SII and reduced significantly than group 2 in patients with ASCAD (14% vs. 9%, P<0.05).

Conclusions: LGID demonstrated superiority to routine diet to improve inflammatory state including systemic immune inflammatory index and lipid parameters in patients with ASCAD.

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321 / #1532

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

PSCK9 INHIBITORS (PCSK9I) (MONOCLONAL ANTIBODIES AND INCLISIRAN) IN CLINICAL PRACTICE. 5 YEARS' EXPERIENCE OF LONDON TERTIARY LIPID CENTRE.

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: Background: In United Kingdom, Proprotein convertase subtilisin kexin-9 inhibitor (PCSK9i) antibodies (MAb) are approved for secondary prevention (LDL-C>3.5-4.0mmol/L) and primary prevention in familial hypercholesterolemia (FH) (LDL-C>5mmol/L). Inclisiran is approved for secondary prevention with LDL-C>2.6mmol/L. **Aims:** To review the outcomes of PSCK9i therapy.

Methods: Methods: A retrospective study of patients attending a secondary/tertiary care centre. Demographics, qualifying characteristics, clinical and biochemical data were gathered. The primary endpoints were absolute and percentage change in LDL-C.

Results: Results: A)MAbs were taken by 242 patients. FH was found in 50%; 10% smoked and 10% had diabetes and 72% were statin intolerant. Coronary heart disease (CHD) was present in 41%; multivascular disease in 16%. Statins were contraindicated in 24%. Statins were taken by 40% and ezetimibe by 45%. TC, LDL-C, apolipoprotein (Apo)-B and Lipoprotein (Lp)(a) were reduced by 34%, 49%, 39% and 33% respectively (table1). The effects were similar in FH and non-FH patients. 19 patients (8%) stopped mostly due to myalgia. 2 patients died of non-CVD causes; none have had CVD events (2018-22). B)Inclisiran was taken by 30 patients. CHD was present in 70%; carotid stenosis in 18% and stroke in 13%. FH was present in 23%, smoking in 20% and diabetes in 7%. Statin therapy was taken by 27% and ezetimibe by 43%. Previously 9 patients switched from MAbs (2 were intolerant, 7 for convenience). LDL-C was reduced by 31% (average 1.5 injections) in 18 patients. One patient has proved intolerant.

Table 1: Pre-and post-treatment effects of PCSK9 MAB compared with t- test. * P-values are significant

Biochemical parameter	pre-treatment data (N)	pre-mean	pre-SD or 25%IQ& 75%IQ	post-treatment data (N)	post mean	post-SD or 25%IQ& 75%IQ	P value
TC (mmol/L)	238	7.27	2	217	4.65	1.44	<0.0001*
HDL (mmol/L)	227	1.44	0.49	205	1.51	0.5	0.108
LDL(mmol/L)	232	4.83	1.71	209	2.35	1.33	<0.0001*
LPL (a)(nmol/L)	178	77.55	IQ 25%=20,IQ75% 232	99	102	IQ 25%=20,IQ75%180	<0.008*
ALT (IUI/L)	205	27.12	16.8	79	26.98	16.12	0.9
CK(IUI/L)	192	153	IQ 25%=79,IQ75% 174	141	175.97	IQ 25%=83,IQ75%207	0.187
HbA1c (mmol/mol)	145	42.1	13.6	122	45.5	34.2	0.2864
ApoA	152	1.58	0.04	93	1.6	0.38	0.4677
ApoB	152	1.57	0.43	92	0.97	0.41	<0.001

Conclusions: Conclusion: PCSK9is deliver similar effects in real world as in clinical trials.

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322 / #604

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

FIRST CLINICAL EXPERIENCES WITH INCLISIRAN IN REAL WORLD SETTING

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: Inclisiran is the first-in-class small interfering RNA (siRNA) PCSK9 inhibitor. In clinical trials, inclisiran showed effective and sustained LDL-C reduction. However, data about the efficacy and safety in clinical setting are not available yet. We aim to investigate this in high-risk patients with FH and or ASCVD in clinical practice.

Methods: Registry of all consecutive patients who started with siRNA at a lipid clinic of a university hospital. Patients were eligible either if they started with Inclisiran as first line PCSK9 inhibitor (group 1) or if they switched from PCSK9 monoclonal antibody (mAbs) to inclisiran (group 2). LDL-C levels were measured 3 months after administration of inclisiran initiation. Median change of LDL-C levels was calculated on an individual and group level.

Results: We analyzed 31 patients (18 women, 23 patients with FH), median age of 64 [55; 68] years. Patients in group 1 showed a LDL-C decrease of 38% [-49; -33]. However, patients in group 2 had an increase in LDL-C of +38% [+4; +81]). Most patients (90%) experienced mild burning during administration. During follow-up 3 (9.7%) patients reported side-effects; nausea, dizziness and injection site reactions in the first days after administration. No patients stopped treatment because of side

effects.

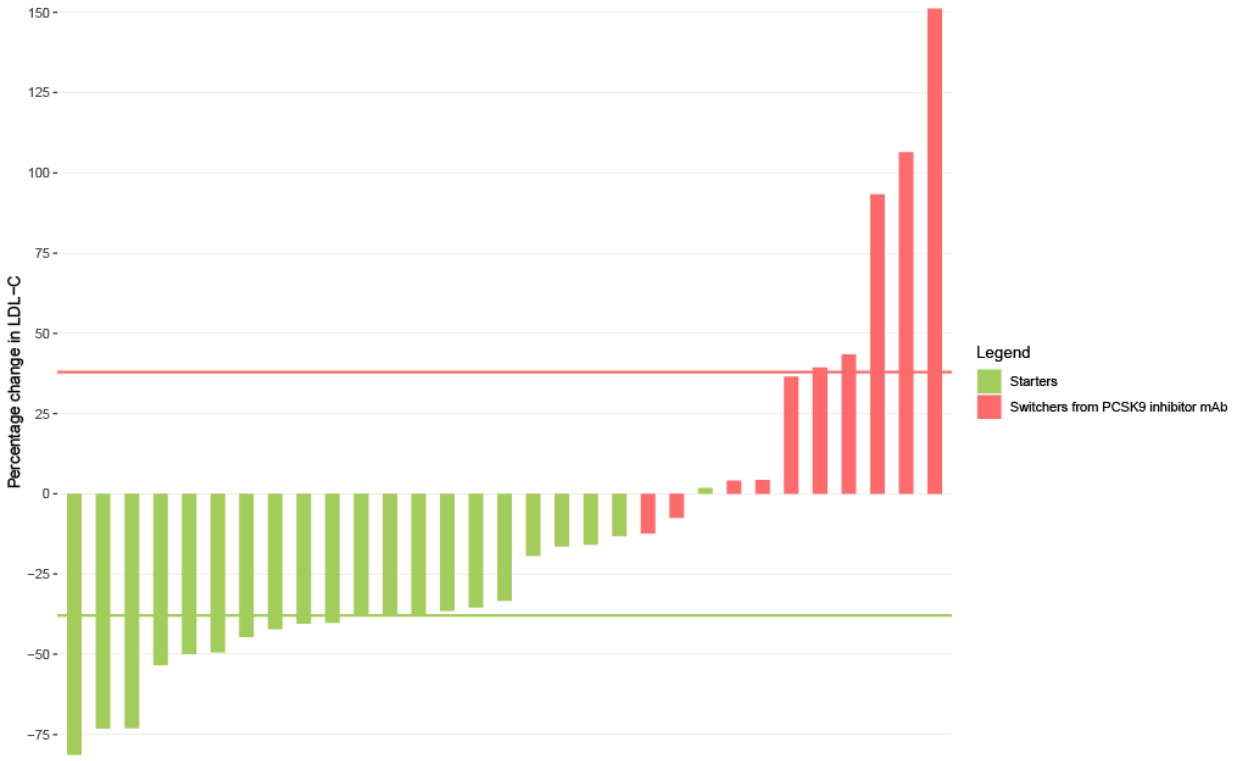

Figure 1 Waterfall plot of percentage LDL−C change at 3 months follow−up after start of PCSK9 siRNA inhibitor

Conclusions: Our initial experience of inclisiran in a clinical setting showed less reduction in LDL-C levels compared to clinical trials but a similar safety profile. Moreover, patients who switched from PCSK9 mAbs to inclisiran showed an increase in LDL-C levels implying that inclisiran is less potent in LDL-C reduction compared to PCSk9 mAbs.

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323 / #1515

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

MACHINE LEARNING PREDICTION MODELS OF CORONARY PLAQUE PROGRESSION AFTER ONE-YEAR OF HIGH-INTENSITY ROSUVASTATIN THERAPY FROM INTRAVASCULAR ULTRASOUND IMAGES

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

Hector Garcia-Garcia[1], Carlos Bulant[2], Ronald Bass[3], Gustavo Boroni[2], Alejandro Clausse[2], Pedro Lemos[4], Pablo Blanco[5], Sylvain Losdat[6], Lorenz Räber[7]
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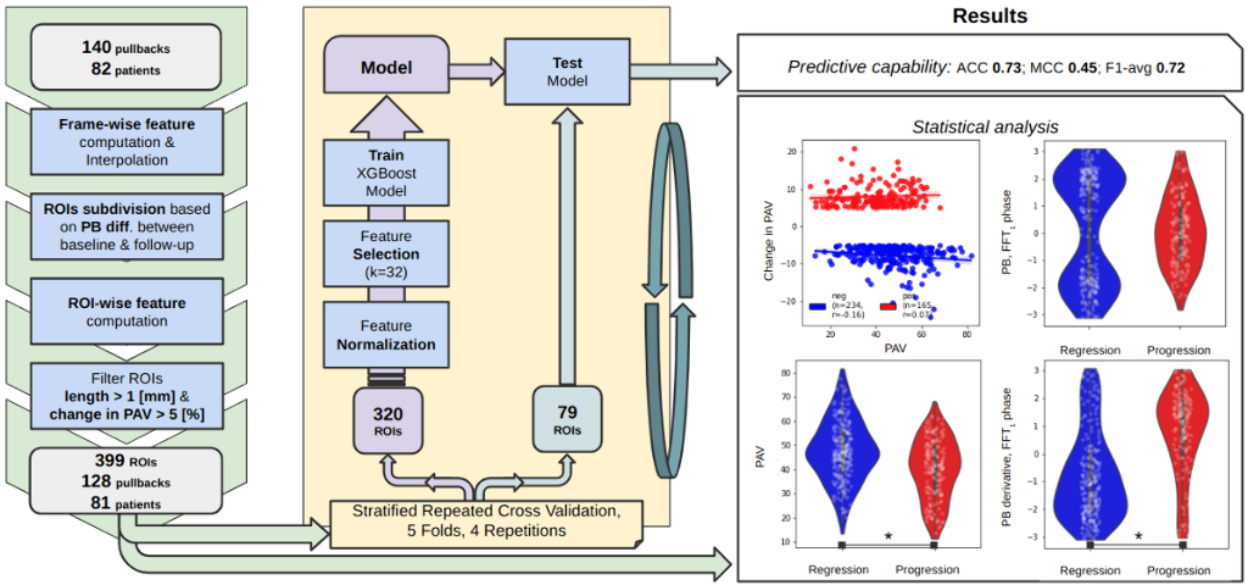
Background and Aims: The IBIS-4 showed an association between plaque regression and high-intensity rosuvastatin therapy over a 13-month period. However, it has not been possible to predict if a patient would respond favorably to such treatment. We aim to develop a machine learning model that predicts future (FUP) percent atheroma volume (PAV) changes in arterial regions using baseline (BL) geometric features from IVUS frames.

Methods: This is a post-hoc analysis of the IBIS-4 study. We performed computational analysis over delineated lumen and vessel contours of 140 IVUS pullbacks to compute frame-wise features (area, plaque burden, eccentricity, circularity, and curvature). Each pullback was divided into regions of interest (ROI) such that the difference of plaque burden (>5%) between the BL and FUP pullbacks was homogeneously positive (progression) or negative (regression). A stratified 5-fold cross validation strategy trained 20 XGBoost models on different subsamples.

Results: The PAV difference between FUP minus BL over all ROIs was -1.31 (8.35). When subgrouping BL ROIs by regression (234) and progression (165), the PAV was 47.75 (12.91) and 40.03 (12.64) respectively. For predictive capabilities, each XGBoost model was tested on 79 unseen ROIs. The results are [mean (std)]: 0.73 (0.04) Accuracy; 0.45 (0.08) Matthews Correlation Coefficient; 0.67 (0.05) progression F1-Score; 0.77 (0.04) regression F1-Score, 0.72 (0.04) averaged F1-

Score.



Conclusions: This the first ever machine learning algorithm to identify geometrical coronary plaque features that informed plaque progression changes despite intensive treatment with statins. This automated IVUS analysis may help to stratify patients at risk of plaque progression.

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324 / #203

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

EVALUATION OF THE IMPACT OF THE MANAGEMENT OF HYPERCHOLESTEROLEMIA USING A PRE-ESTABLISHED REGIMEN IN PATIENTS WITH VERY HIGH CARDIOVASCULAR RISK

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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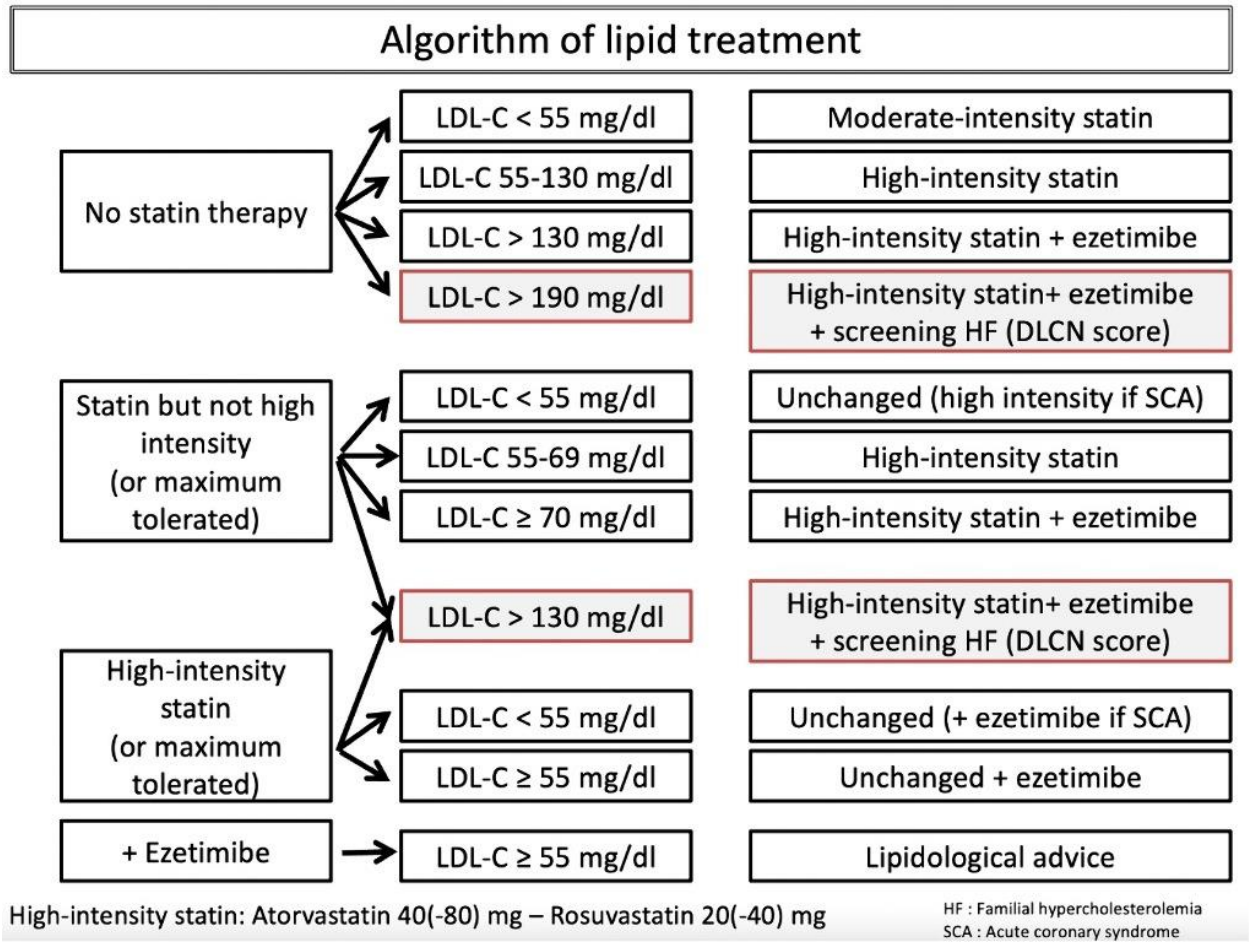
Background and Aims: Recent data from European studies (EUROASPIRE V, DA VINCI, SANTORINI) show that the LDL-C target in patients at very high cardiovascular risk is rarely reached and that the use of dual therapy (statin and ezetimibe) remains infrequent. Aims: Single-center evaluation of the use of a pre-established lipid treatment algorithm at the end of hospitalization of patients at very high cardiovascular risk (cardiovascular risk at 10 years > 10% according to the SCORE table (primary prevention) or in secondary prevention) on the achievement of the LDL-C target 1-month post hospitalization.

Methods: In our center, an algorithm for adjusting lipid-lowering treatments has been established based on the expected effectiveness of the treatments and data from the literature. Depending on the level of LDL on admission and prior treatment, an adjustment is proposed at discharge. Intolerant patients (statin and/or ezetimibe) are excluded. A phone call is performed 4 to 6 weeks after the hospitalization as well as a lipid

assessment.



Results: 87 patients were included (6 primary prevention and 81 secondary prevention) with a mean LDL-C of 118,1 +- 40.54 mg/dL. Following the algorithm, 32 received a high-intensity statin and 55 a combination of high-intensity statin and ezetimibe. At follow-up, 74/87 patients (85.06%) are adherent, with a mean LDL-C of 53,95 +- 17.3 mg/dL. LDL-C target (< 55mg/dL) is reached in 40/74 (54%).

Conclusions: One month after hospitalization, we observe a good adhesion to the hypolipidemic treatment proposed by the algorithm, with good tolerance. Just over half of the adherent patients achieved the LDL-C target (<55mg/dL).

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325 / #328

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

STATIN THERAPY IN INDIVIDUALS WITH INTERMEDIATE CARDIOVASCULAR RISK

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: LDL-C target for individuals with moderate cardiovascular risk of <100 mg/dL in the current European guidelines is based on a previous meta-analysis. We aimed to analyze outcomes of statin therapy and identify an optimal LDL-C level in these people.

Methods: This study used the database of the National Health Insurance Service of Korea. In individuals who underwent health examination and follow-up, 27,793 with moderate risk with new statin therapy were enrolled. Moderate risk was defined LDL-C 100-189 mg/dL and the presence of ≥2 of following conditions: 1) males >45 years or females >55 years, 2) history of premature coronary disease, 3) hypertension, 4) smoking, 5) HDL-C <40 mg/dL. Composite events (myocardial infarction, coronary revascularization, and ischemic stroke) and total mortality were compared between those who achieved following LDL-C levels: ≥140, 120-139, 100-119, <100 mg/dL.

Results: During the mean follow-up of 7.2 years, adjusted hazard ratios (HRs) of events and total mortality in the groups ranged down to 0.78 (p=0.0001) and 0.87 (nonsignificant), respectively. HRs of composite events were lower in the groups who achieved LDL-C <120 mg/dL compared to those who did not. However, HR (0.78) in the group with LDL-C <100 mg/dL did not show additive HR reduction. HRs of each event ranged down to 0.60, 0.71, and 0.79, respectively, in these groups.

Conclusions: The current study showed clinical benefit associated with LDL-C <120 mg/dL in Korean individuals with moderate cardiovascular risk. These results provide evidence on appropriate LDL-C target in this population.

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MANNHEIM GERMANY | MAY 21-24, 2023

326 / #204

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

PCSK9 INHIBITORS PREFERENCES AND SHARED DECISION MAKING

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: High risk patients who do not reach LDL-C target currently have three options: 1) addition of PCSK9 monoclonal antibody (mAb), 2) addition of a PCSK9 siRNA, or 3) no additional medication. Shared decision making is considered important in contemporary patient care. The first step is to gain insight in the preferences of patients and healthcare providers, which is the aim of our study.

Methods: We performed a mixed methods study. High risk patients who qualified for reimbursement for add-on lipid lowering therapy (PCSK9 mAb/siRNA) were asked about their preferences. In addition, healthcare professionals filled in an online questionnaire about their personal preferences and their opinion on patient preferences.

Results: We interviewed 22 patients (median age 58 [min. 26; max.75] years, 59% women, 68% FH, 59% CVD, 59% statin comedication) who were categorized into 4 groups (table 1). Most patients (77%) would prefer shared decision making. The majority (73%) chose efficacy as most important attribute of add-on LLT (table 1).
Of the 54 healthcare professionals (table 2), only 24% indicated that patient preference would be leading for the type of PCSK9-inhibitor which they would prescribe. Healthcare professionals indicated different preferences for different PCSK9-inhibitor types for various patient categories (figure 1).

Table 1 Patient interviews

	Total **N = 22**	mAb n = 6	siRNA n = 10	Not decided yet n = 3	No add-on medication n = 3
Examples findings interview					
1) *Who should decide on additional LLT:*					
Healthcare professional	**4 (18%)**	2 (33%)	2 (20%)	0 (0%)	0 (0%)
Shared (physician + patient)	**17 (77%)**	4 (67%)	8 (80%)	3 (100%)	2 (67%)
Patient	**1 (5%)**	0 (0%)	0 (0%)	0 (0%)	1 (33%)
2) *Most important in decision (ranking 1-3):*					
Efficacy as most important	**16 (73%)**	3 (50%)	7 (70%)	3 (100%)	3 (100%)
Side-effects as most important	**4 (18%)**	2 (33%)	2 (20%)	0 (0%)	0 (0%)
Ease of use as most important	**2 (9%)**	1 (17%)	1 (10%)	0 (0%)	0 (0%)

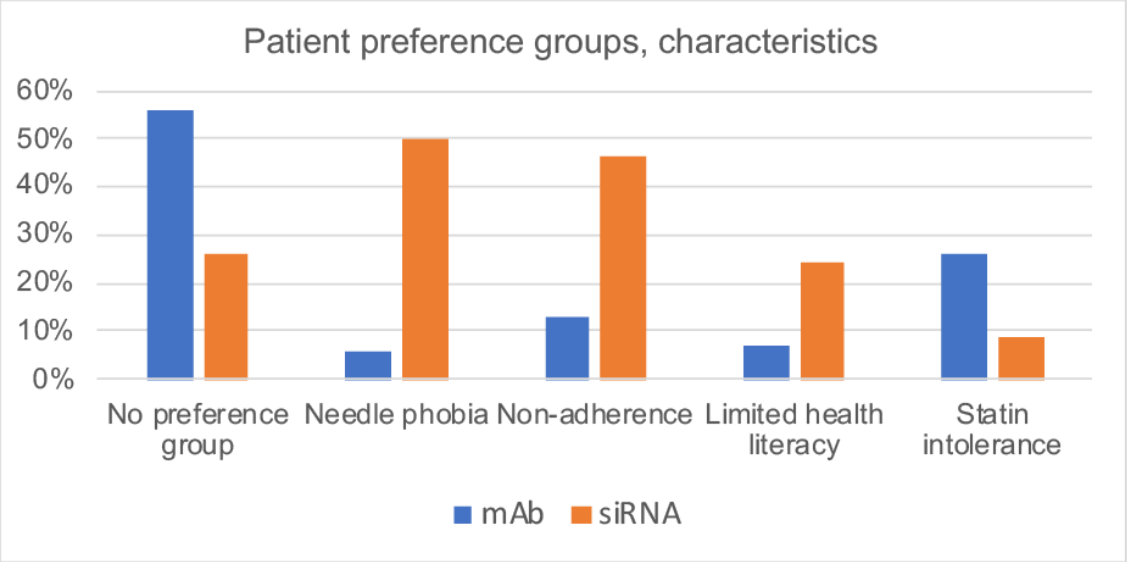
Data are shown in count (%). mAb = monoclonal antibody; siRNA = small-interfering RNA; FH = familial hypercholesterolemia; CVD = cardiovascular disease; LLT = lipid-lowering therapy.
Four subgroups were identified: patients on mAbs, on siRNA, with indication and wish to start a PCSK9-inhibitor, and with indication and no wish to start additional therapy.

Table 2 Online survey of healthcare professionals

	Total **N = 54**	Internal medicine n = 38	Cardiology n = 12	Other* n = 4
Characteristics				
Women	**25 (46%)**	19 (50%)	4 (33%)	2 (50%)
Age, in years	**44 [26; 64]**	41 [26; 64]	50 [36; 62]	44 [29; 49]
Medical specialist	**39 (72%)**	29 (76%)	10 (83%)	0 (0%)
PCSK9-inhibitor prescriber	**45 (83%)**	34 (89%)	11 (92%)	0 (0%)
University hospital	**20 (37%)**	15 (39%)	4 (33%)	1 (25%)
Results				
Current preference for prescribing:				
mAb	**33 (61%)**	25 (66%)	8 (67%)	0 (0%)
siRNA	**3 (6%)**	0 (0%)	0 (0%)	3 (75%)
mAb = siRNA (no preference)	**4 (8%)**	2 (5%)	1 (8%)	1 (25%)
Depends on patient preference	**13 (24%)**	11 (29%)	2 (17%)	0 (0%)
Other	**1 (2%)**	0 (0%)	1 (8%)	0 (0%)

Data are shown in count (%) or median [minimum; maximum]. PCSK9 = proprotein convertase subtilisin/kexin type 9; mAb = monoclonal antibody; siRNA = small-interfering RNA.
*Other includes: family medicine, immunology, neurology, anticoagulation care

Figure 1 Most chosen preference groups per type of PCSK9-inhibitor according to healthcare professionals



Conclusions: Patients show a strong preference for shared decision making in starting add-on LLT, whereas only a minority of healthcare professionals consider patient preferences. Our study seems to underline the need for a decision tool to assist patients and healthcare professionals to make the most optimal choice for add-on LLT, which requires further research.

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327 / #1528

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

TARGET LDL CHOLESTEROL LEVEL IN PATIENTS WITH ACUTE CORONARY SYNDROMES UNDERGOING PERCUTANEOUS CORONARY INTERVENTION: THE JET-LDL REGISTRY

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: We aimed to investigate levels of low-density lipoprotein cholesterol (LDL-C) obtained in a cohort of patients with acute coronary syndromes (ACS) and reporting treatment with different lipid lowering therapies (LLTs).

Methods: The JET-LDL registry is a multicenter, prospective, real-world data collection carried out during a 3-month period including consecutive patients with ACS undergoing percutaneous coronary intervention at 36 hospitals. Follow-up visits were performed at 1 and 3 months. Primary endpoint was LDL-C reduction >50% from baseline or LDL-C level <1.4 mmol/L (55 mg/dL) at 1 month.

Results: A total of 1095 patients were included: median age was 67 (58-75) years; 35% were already on LLT. Baseline LDL-C levels were 105 (76.5-137) mg/dL. At hospital discharge, 442 patients (40%) received high-dose statin, 547 (50%) statin plus ezetimibe and 93 a PCSK9i (8.5%). At 1-month, LDL-C levels significantly dropped to 53 (38-70) mg/dL ($p<0.001$ vs baseline). Primary endpoint was achieved in 62% of the cases. At 1 month, LDL-C was at recommended target levels in 55.5% of patients, but PCSK9i prescription was not increased. At 3 months, LDL-C levels further decreased to 50 (38-65) mg/dL ($p<0.001$ vs both baseline and 1 month), 58.5% of patients were at target of LDL-C and a PCSK9i was added in 7 patients.

Conclusions: In this real-world registry, recommended LDL-C levels were obtained in 58.5% of ACS patients, but PCSK9i prescription was limited (10% of the cases). An approach of early optimization of LLTs treatment at discharge after ACS, also including PCSK9i when indicated, needs to be improved.

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328 / #391

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

EFFECTS OF HIGH INTENSITY STATIN THERAPY ON RENAL OUTCOMES

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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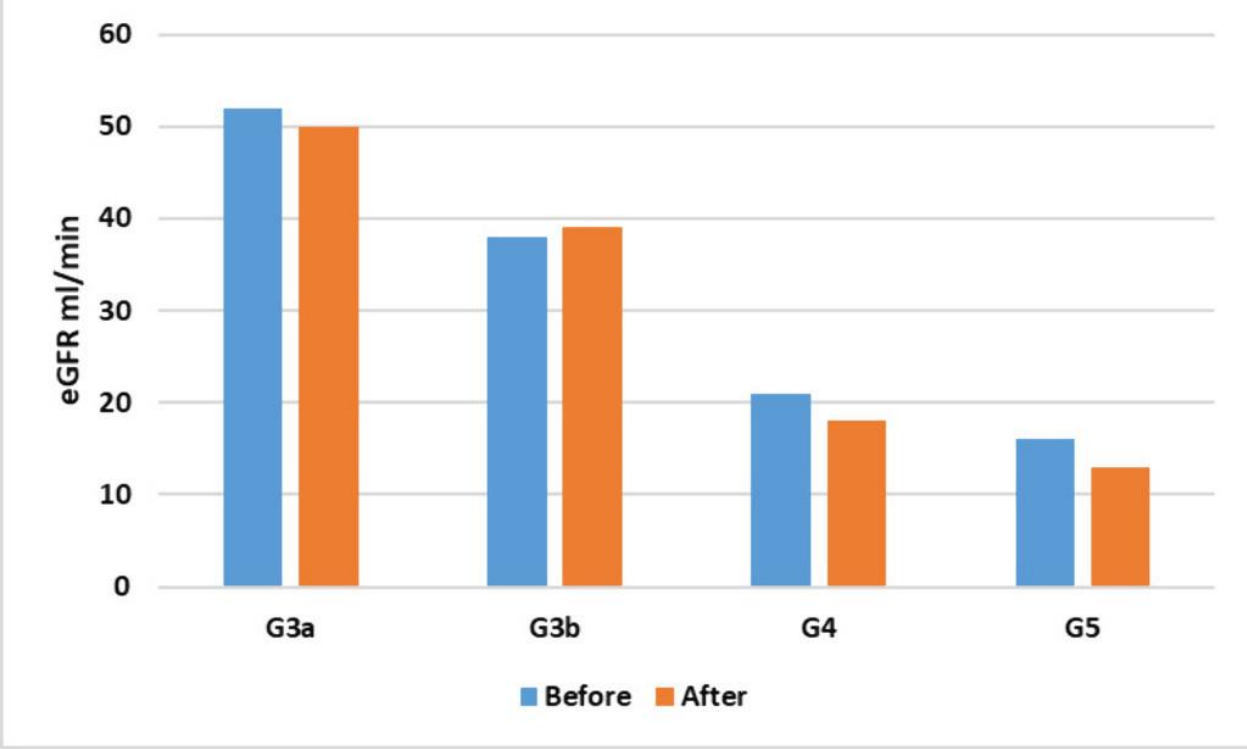
Background and Aims: Statins are the cornerstones of lipid lowering therapies in patients with cardiovascular disease (CVD). ESC/EAS guidelines on CVD prevention recommend high dose statin in secondary prevention patients. However, there are some concerns regarding high dose statin use in chronic kidney disease (CKD) patients. We aimed to investigate whether high dose statin use had any effects on renal outcomes.

Methods: We prospectively evaluated CKD patients who were on high dose atorvastatin (40 or 80 mg) therapy and admitted with acute coronary syndrome. We assessed baseline and three-month control estimated glomerular filtration rate (eGFR) of the patients and the association of decline in eGFR with statin use.

Results: The study included a total of 34 patients. The mean age was 70.7±9.1. The patient population was divided into four subgroups according to their GFRs. Of the patients 9, 12, 6, and 7 were categorized into mildly to moderately decreased (G3a), moderately to severely decreased (G3b), severely decreased (G4), and renal failure (G5) stages respectively. There was no statistically significant decrease in patients' eGFR in three months follow-up 34.1±15.1 vs 32.9±17.0 p=0.756 compared to baseline. The changes in eGFR according to renal failure stages were given in Figure. G3a 52.3±5.2 vs 50.4±9.4 p=0.613, G3b 37.9±3.7 vs 39.1±11.3 p=0.720, G4 20.7±5.2 vs 17.8±3.1 p=0,269, G5 16.1±8.9 vs 12.9±2.0 p=0.375

baseline and three-month follow-up respectively.



Conclusions: High intensity statin therapy was not associated with progression of renal failure in secondary prevention patients with CKD. High dose atorvastatin should be used in high cardiovascular risk patients regardless of renal functions.

91ST EAS CONGRESS
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329 / #404

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

REDUCTION IN LDL-C FOLLOWING TREATMENT WITH INCLISIRAN AT 2 MONTHS IN A SINGLE CENTRE LIPID CLINIC COHORT

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: Inclisiran is a new first in class small interfering RNA (siRNA) lipid lowering drug that has been shown to be effective in reducing low-density lipoprotein cholesterol (LDL-c) in randomised controlled trials. However, real-world data of its use is currently lacking. We aimed to analyse the early effects of this drug in a tertiary centre lipid clinic.

Methods: In this retrospective analysis, a total of 80 patients received a single dose of inclisiran at our lipid clinic at Hammersmith Hospital, London between December 1st 2021 and September 1st 2022. Data including patient demographics, past medical history and current lipid lowering medications were obtained from electronic healthcare records. Baseline blood tests were taken prior to the start of treatment and at routine 2 month follow up for comparison. Incidences of adverse reactions and discontinuation were also recorded.

Results: At 2 months mean baseline LDL-c fell by 48.6% from 135.3 ±42.5 mg/dL to 69.6 ±38.7 mg/dL and total cholesterol fell by 33.3% from 220.4mg/dL to 147 ±42.5 mg/dL (both $p<0.0001$). Median triglycerides fell by 31.3% to 97.4 mg/dL (interquartile range 79.7– 177.1) and mean HDL-c rose by 7.7% to 54.1 ±15.5 mg/dL ($p=0.02$). Thirty-seven patients achieved ≥50% reduction in baseline LDL-c. Adverse reactions occurred in 3 patients and included injection site reaction, headache and fatigue with all resolving by time of follow up.

Conclusions: Significant reduction in baseline LDL-c was achieved at 2 months following a single dose of inclisiran. Incidence of adverse reactions were similar to those reported in clinical trials.

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330 / #319

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

NATIONAL TRENDS IN THE USE OF STATE-REIMBURSED ORAL LIPID-LOWERING MEDICATIONS IN LATVIA (2012-2021)

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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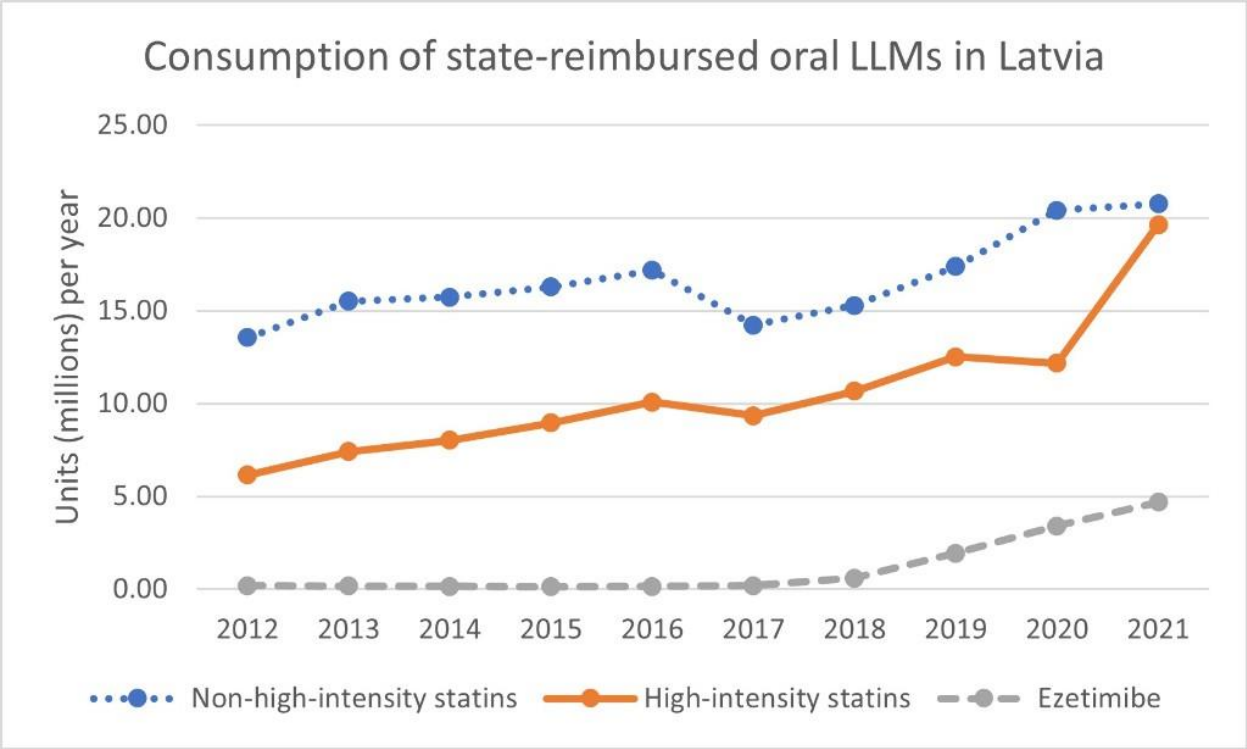
Background and Aims: The patterns of statin use in Latvia have not been examined in any prior research. We aimed to assess trends of state-reimbursed lipid-lowering medication (LLM) use over a ten-year period in Latvia.

Methods: The National Health Service database of all the state-reimbursed prescriptions dispensed from 2012 to 2021 in Latvia was used to extract information for a retrospective analysis on all LLM-containing drugs. Based on the quantity of tablets or capsules per package for each dose of the LLM, the annual number of all dispensed units was computed. High-intensity statin therapy was defined as atorvastatin 40–80 mg or rosuvastatin 20–40 mg. Version 22 of IBM SPSS Statistics was used to analyze the data.

Results: Number of statin units grew twice over a ten-year period, from 19.720 million units in 2012 to 40.419 million units in 2021. The use of high-intensity statins rose from 31.25% in 2012 to 48.61% in 2021. As opposed to atorvastatin 20mg, atorvastatin 10mg, and atorvastatin 40mg (7.398, 4.051, and 3.352 million units, respectively) in 2012, the most popular statins in 2021 were rosuvastatin 20mg, atorvastatin 20mg, and rosuvastatin 40mg (12.248, 10.583, and 5.011 million units, respectively). From 184.744 thousand units in 2012 to 4.685 million units in 2021, ezetimibe 10mg usage grew by a factor of

25.



Conclusions: Over the past ten years, Latvia has seen a considerable growth in the use of statins and ezetimibe that is covered by the state.

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331 / #753

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

CAN THE EFFECTIVENESS OF LIPID-LOWERING THERAPY BE IMPROVED IN VERY HIGH-RISK PATIENTS? RESULTS OF THE 3T-FIGHT STUDY

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: A prospective, observational study was conducted to improve the current management of dyslipidemia in very high cardiovascular risk patients in Hungary. The study protocol was prepared and approved even before the publication of the 2019 ESC/EAS recommendation. The main objective of the study was to achieve the LDL-C target value using high-intensity rosuvastatin or rosuvastatin-ezetimibe combination during the 6 months.

Methods: In our study, we analyzed the results of 3017 patients (female: 1405 (47%); age: 65+/-10 years). At the baseline 8% of the patients were statin naive and 56% on high-intensity statin monotherapy, 55.5% suffered from CAD, 35.6% from stroke, 20.4% from PAD, 2.9% from CKD, 86.1% from hypertension, 43.4% from diabetes. We calculated LDL-C by using the Martin/Hopkins estimation. After 6 months, we analyzed how many patients achieved the 1.8 or 1.4 mmol/L target LDL-C values and least a 50% reduction.

Results: At the end of the study, 20.5% of the patients were treated with high-intensity rosuvastatin monotherapy and 79.5% rosuvastatin-ezetimibe combination (63.7% fix combination). The initial LDL-C level of 3.64+/-1.05 decreased to 2.03+/-0.79 mmol/L (-42%) at 6 month. 48% of patients reached the LDL-C target value of 1.8 and 19% the 1.4 mmol/L, and for rosuvastatin-ezetimibe 20/10 fix combination the target value achievement was: 55.2 and 23.4%, respectively. The LDL-C reduction of at least 50% was achieved in 41% of the patients.

Conclusions: In this East-Central European real-world study, it was possible to significantly increase the prescription of the more effective rosuvastatin-ezetimibe combination in secondary prevention.

91ST EAS CONGRESS
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332 / #670

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

POTENTIAL THERAPEUTIC COMPOUNDS AGAINST HYPERCHOLESTEROLEMIA: AN IN-SILICO ANALYSIS

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: Statins and ezetimibe, the two most prescribed drugs for hypercholesterolemia are associated with adverse effects like myalgia, gastrointestinal disturbances, fatigue, and increased liver enzymes. The efficiency of these drugs is also influenced by genetic polymorphisms particularly in the solute carrier organic transporter 1B1 (SLCO1B1) gene that help internalize statins, also identified in Pakistani population. We employed an in-silico analysis to identify molecules which can bind to the drug target of statins; 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA reductase), with the potential to be used against hypercholesterolemia.

Methods: Molecular docking of the eight compounds (25-Hydroxycholesterol, TAK-715, flufenamic acid, piceatannol, retinol, nortriptyline hydrochloride, losmapimod and AG555 (tyrphostinb46) predicted by the online software Datasets2Tools, was performed against HMG-CoA reductase using PatchDock and Fire Dock while the ADMET analysis was done by SwissADME and admetSAR. The in-silico drug-likeness and bioactivity were determined by the Molinspiration server.

Results: The in-silico docking analysis revealed that all the compounds effectively bind with the target HMG-CoA reductase by forming ligand- receptor interactions. ADMET analysis predicted satisfactory results for the pharmacokinetic properties of these compounds such as blood-brain barrier (BBB), CYP2D6 binding, intestinal absorption, and Caco2 permeability. In drug-likeness analysis, all eight compounds had the highest score binding affinity and satisfied the “rule of 5” with a good bioavailability score which shows that they can be absorbed by oral route.

Conclusions: The findings revealed that these compounds could be used as therapeutic agents for hypercholesterolemia, however further studies are required to elucidate the therapeutic efficacy of these in biological systems.

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333 / #510

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

POSITIVITY OF STATIN-ASSOCIATED MUSCLE SYMPTOMS – CLINICAL INDEX IN A HYPERTENSIVE POPULATION CANDIDATED TO LIPID-LOWERING THERAPY BUT NOT TAKING STATINS

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: Statin use has been claimed to be associated with muscle-related symptoms, called SAMS (Statin-Associated Muscle Symptoms). The SAMS-Clinical Index (SAMS-CI) is an approved questionnaire to assess the probability that muscle symptoms are related to statin. Aim: evaluate the difference in prevalence and characteristics of muscle symptoms between hypertensive patients taking statins and hypertensive patients candidates for statins.

Methods: Cross-sectional observational study on 390 outpatients referred to our Hypertension Centre: 250 patients were already on statin therapy and 140 who took at least one other drug different from statins. Patients underwent a modified version of SAMS-CI (rechallenge not included).

Results: Mean age: 60.5±13.6 years. Male prevalence: 53.8%. Patient-reported episodes of muscle symptoms was reported by 50.8% of patients in the group taking statins and by 44.3% in the group not taking them (p=0.217). Within patients with reported episodes of muscle symptoms, a slightly higher score at SAMS-CI emerged in the statin group (3.6±2.4 vs 2.8±1.6 points, p=0.004). Regarding SAMS-CI items, no significant difference emerged in the localization of muscle pain (p=0.170) and timing of symptoms onset in relation to drug (p=0.067). A slightly higher score in the item “resolution timing of muscle symptoms after drug/statin withdrawal” was showed in the statin group (p=0.002).

Conclusions: This finding is in line with the growing evidence that most subjective muscle-related adverse effects are misattributed to statins and occurring because of the nocebo/drucebo effect or due to other common conditions.

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334 / #655

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

NO ASSOCIATION BETWEEN CHANGES IN LIPID PARAMETERS AND TOTAL PCSK9 IN CORONARY ARTERY DISEASE PATIENTS TREATED WITH PCSK9 INHIBITORS

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: Increased concentration of lipoprotein(a) (Lp(a)) is an independent risk factor for coronary heart disease regardless of LDL cholesterol levels. Treatment with PCSK9 inhibitors reduces the incidence of cardiovascular events not only via lowering LDL cholesterol but also via reducing Lp(a) levels. The purpose of our study was to determine whether the decrease in Lp(a) concentration is associated with a change in the concentration of total PCSK9 after treatment with PCSK9 inhibitors in post-myocardial infarction patients treated with the highest tolerated dose of statin, and increased Lp(a) concentration.

Methods: One hundred patients after myocardial infarction before the age of 55 years and with high Lp(a) concentration were randomised to lipid-lowering therapies in three groups, first without PCSK9 inhibitors (control; N=31), second, with alirocumab 150 mg SC (N=35), and third with evolocumab 140 mg SC (N=34), every 2 weeks. The concentrations of Lp(a), lipids and total PCSK9 were measured before and 6 months after treatment.

Results: There were no changes in the measured parameters in the placebo group. Treatment with PCSK9 inhibitors reduced Lp(a) from 1538±627 to 1232±543 mg/l (p=0.035), total cholesterol from 4.2±0.8 to 2.8 1.0 mmol/l and LDL cholesterol from 2.3±07 to 0.9±0.8 mmol/l (p< 0.001 for all). Total PCSK9 increased from 308±132 to 2647±07 ng/ml (p< 0.001). Associations between changes in Lp(a), total and LDL cholesterol were not statistically significant.

Conclusions: Our results suggest that in patients treated with the highest tolerated dose of statins, changes in lipid parameters are not associated with changes in total PCSK9 concentrations after PCSK9 inhibitors treatment.

91ST EAS CONGRESS
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335 / #1350

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

STATINS, BUT NOT PCSK9 INHIBITORS, REDUCE THE ADIPOKINE CHEMERIN IN FAMILIAL HYPERCHOLESTEROLEMIA: FOCUS ON LIPOPROTEIN SUBFRACTIONS.

POSTER ON BOARD: AS04.09 LIPID-LOWERING THERAPIES

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Background and Aims: Familial hypercholesterolemia (FH) is characterized by severe elevations in circulating LDL-c, and an increase in the risk of dyslipidemia-related CVD. Chemerin, as a newly identified adipokine, is considered as an additional risk factor for CVD. Here we investigated whether it can be modified by cholesterol-lowering therapy.

Methods: Lipoprotein subfractions were isolated by density gradient ultracentrifugation. Lipids and chemerin concentrations were determined both before and after cholesterol lowering with either a statin or a PCSK9 inhibitor (PCSK9i). *In vitro*, *HepG2 cells* were used for investigating chemerin secretion by pravastatin or evolocumab, and *THP-1 differentiated* cells were used for chemerin challenge on cholesterol efflux ability.

Results: At baseline, chemerin and lipids levels were not different between two groups. Both statins and PCSK9i reduced LDL-c (by 41 and 62%, P<0.0001), TG (by 13 and 19%, P<0.01), and increased HDL-c (by 8 and 23%, P<0.01), but only statins reduced chemerin (by 35%, P<0.005). The lipoprotein profile revealed that chemerin accumulated particularly in the HDL. Statins reduced HDL3-c and HDL3-TG, and the chemerin level bound to all subfractions. PCSK9i reduced HDL3-c but did not affect HDL3-TG or the level of chemerin bound to HDL. *In vitro,* pravastatin, not evolocumab, inhibited chemerin secretion in HepG2 cells. Moreover, chemerin broken-down cholesterol efflux in THP-1 cells, while pravastatin attenuated this effect.

Conclusions: Circulating chemerin occurs in different lipoprotein subfractions, accumulating in the HDL3 fraction. Statins, but not PCSK9i, lowers chemerin, possibly by interfering with its levels across lipoprotein subfractions and hepatic secretion. This may represent a novel cardiovascular protective function of statins.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

336 / #1211

Topic: *AS04 Clinical Vascular Disease / AS04.10 Anti-thrombotic therapies*

EFFICACY OF TICAGRELOL IN PATIENTS WITH CHRONIC CORONARY SYNDROME AND TYPE 2 DIABETES MELLITUS AFTER PERCUTANEOUS CORONARY INTERVENTIONS

POSTER ON BOARD: AS04.10 ANTI-THROMBOTIC THERAPIES

Daler Orziev[1], Akbar Abdullaev[1], Bakhromkhon Alyavi[2], Jamol Uzokov[2]
[1]Internal Medicine, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan, [2]Interventional Cardiology, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Background and Aims: Aim of the study was to evaluate the efficacy of ticagrelol in patients with chronic coronary syndrome (CCS) and type 2 diabetes mellitus (T2DM) after elective percutaneous coronary interventions (PCI).

Methods: 112 patients with CCS and T2DM who admitted for the elective PCI were enrolled in the study from 2018 to 2022. Patients were divided into two groups by 56. Group I patients were assigned ticagrelol 90 mg BID whereas Group II were assigned clopidogrel along with aspirin for 1 year. 20 µmoll ADP induced platelet aggregation was assessed at baseline and after 12 hours of administering loading dose of antiplatelet. Efficacy and safely were assessed during the follow up in both group of patients.

Results: Inhibition of platelet aggregation with 20 µmoll ADP at 12 hours was significantly higher in ticagrelol group than clopidogrel group (71.65±14.25% vs. 42.74±18.25%, P<0.001). Besides, it was significantly higher in ticagrelol group than clopidogrel group (68.12±13.27% vs. 45.82±17.54%, P<0.001) during the maintenance dose at 48 hours. PCI bleeding complications were similar in each group (P>0.05). During the follow-up ticagrelol group tended to have higher bleeding (log-rank test; 0.752), lesser MACE than clopidogrel group, (Mantel–Cox test; P=0.045). 56 ticagrelol treated patients showed that MACE negatively associated with post PCI bleeding complications (P=0.048).

Conclusions: Dual antiplatelet therapy with ticagrelol and aspirin is superior than clopidogrel plus aspirin to prevent MACE in patients with CCS and T2DM after elective PCI. However, ticagrelol should be used cautiously in patients with gastrointestinal ulcers due to its PCI related bleeding risks.

91ST EAS CONGRESS
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337 / #1229

Topic: *AS04 Clinical Vascular Disease / AS04.10 Anti-thrombotic therapies*

RELATIONSHIP BETWEEN BLOOD INFLAMMATION STATE AND PLATELET AGGREGATION RATE IN PATIENTS WITH ATHEROSCLEROTIC CORONARY ARTERY DISEASE AFTER PERCUTANEOUS CORONARY INTERVENTIONS

POSTER ON BOARD: AS04.10 ANTI-THROMBOTIC THERAPIES

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Interventional Cardiology, Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Background and Aims: Aim of the study was to investigate the possible links between blood inflammation state parameters and platelet aggregation rate in patients with atherosclerotic coronary artery disease after percutaneous coronary interventions.

Methods: 110 patients who were diagnosed with atherosclerotic coronary artery disease and planned for elective PCI were enrolled in this study from 2017 to 2021 years (mean age 59.8±8.06 years, male= 86%). Interleukin-1 (IL-1), IL4, IL-6, IL-10, high sensitive C reactive protein (hsCRP) and systemic immune inflammatory index (SII) were assessed for the assessment of inflammation state. Platelet aggregation rate was analyzed with 5 µmoll ADP on aggregometer before PCI. Pearsons's correlation was used to analyze possible links between inflammatory state and platelet aggregation rate with 5 µmoll ADP.

Results: There were a positive correlation between IL-1 and 5 µmoll ADP induced platelet aggregation rate (PAR) (%) (r=0.38, CI 95%, P<0.05) as well as IL-4 and 5 µmoll ADP induced PAR (%) (0.45, CI 95%, P<0.05). Even though, there was positive correlation between IL-6 and 5 µmoll ADP induced PAR (0.25, CI 95%, P>0.05), this correlation were not statistically significant. When we analyzed IL-10 and 5 µmoll ADP induced PAR, there was negative correlation between them (r=-0.61, CI 95%, P<0.0001). Regarding the hsCRP there was a slight statistically insignificant positive correlation with 5 µmoll ADP induced PAR (r=0.27, P>0.05). SII positively correlated with 5 µmoll ADP induced PAR (r=0.51, CI 95%, P<0.05).

Conclusions: Inflammation state is over activated in atherosclerotic coronary artery disease patients with increased platelet aggregation rate.

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339 / #397

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE RELIABILITY OF CORONARY ARTERY CALCIUM SCORE IN SYMPTOMATIC PATIENTS: QUESTIONING THE "POWER OF ZERO"

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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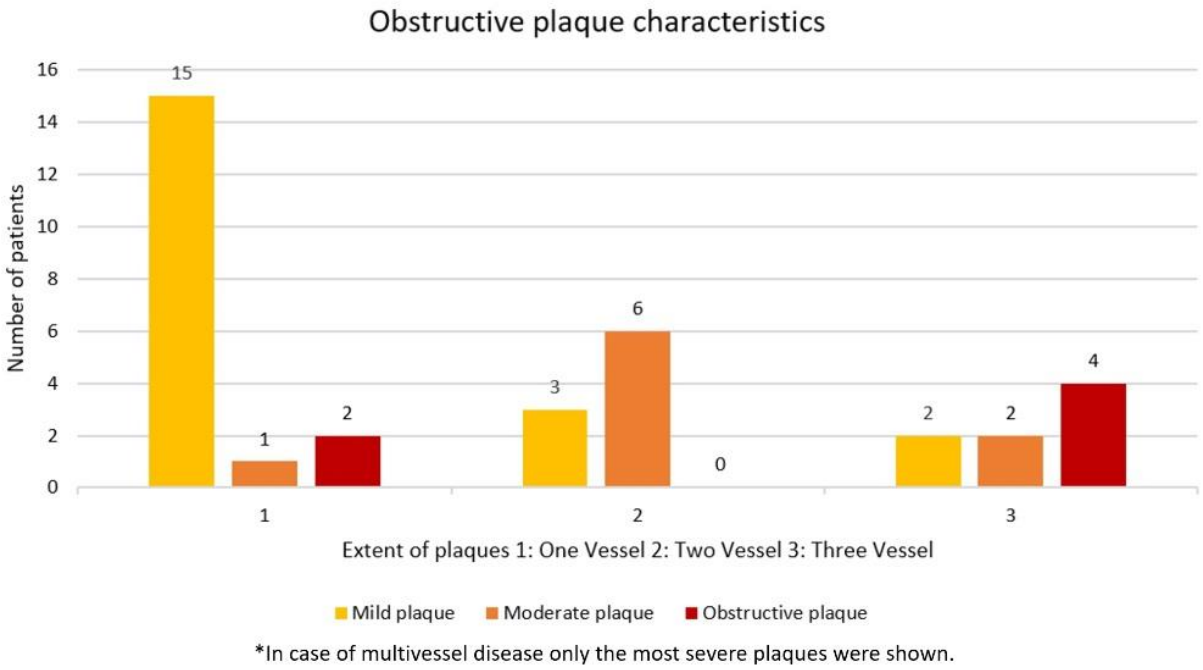
Cardiology, Mugla Sitki Kocman University, Mugla, Turkey

Background and Aims: A zero CAC score has been associated with good prognosis and has a high negative predictive value for the exclusion of obstructive coronary artery disease (CAD); the so called "power of zero". However, it has several limitations such as inability to detect non-calcified plaques. We aimed to investigate obstructive and non-obstructive plaque ratios in patients with a CAC score of zero.

Methods: We retrospectively evaluated symptomatic patients who underwent CAC scoring and coronary computed tomography angiography (CCTA) between January 2021 and June 2021 in our institution.

Results: Of the 196 patients enrolled to the study 107 had a CAC score of zero. Of those patients with a CAC score of zero the mean age was 51.7±10.7 years and 63.6% were male. Of the patients 72 (67.3%) did not have any and 35 (32.7%) had some degree of plaques. Of those 20 (18.7%) had mild plaques, 9 (8.4%) had moderate plaques, and 6 (5.6%) had obstructive plaques on CCTA. The severity and extent of

plaques were shown on Figure.



Conclusions: Our study showed a substantial number of symptomatic patients with CAC score zero had atherosclerotic plaques. As CAC scanning alone misses some cases “power of zero” should be questioned in symptomatic patients.

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340 / #61

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CITRUS BERGAMIA (ENDOBERG®) ATTENUATES SYSTOLIC BLOOD PRESSURE AND PREVENTS CARDIAC OXIDATIVE STRESS, CARDIAC REMODELING AND DYSFUNCTION IN OBESE RATS

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

Matheus Belin[1], Taynara Aparecida Vieira[1], Nubia Alves Grandini[1], Juliana Silva Siqueira[1], Thiago Luiz Novaga Palacio[1], Erika Tiemi Nakandakare Maia[1], Fabiane Valentini Francisqueti-Ferron[1], Artur Junio Togneri Ferron[1], Silméia Garcia Zanati Bazan[1], Dijon Henrique Salome Campos[1], Igor Otávio Minatel[2], Giuseppina Pace Pereira Lima[2], Giuseppe Lombardo[3], Giancarlo Aldini[4], Camila Renata Correa[1]
[1]Pathology, Sao Paulo State University, Botucatu, Brazil, [2]Chemistry And Biochemistry, Sao Paulo State University, Botucatu, Brazil, [3]Products, AKHYNEX, Milan, Italy, [4]Pharmaceutical Sciences, Università degli Studi di Milano, Milan, Italy

Background and Aims: Obesity and oxidative stress are risk factors for cardiovascular diseases, the leading cause of death globally. Therefore, we set out to investigate whether EndoBerg®(E), a bioactive compounds-rich extract, improves markers of cardiac oxidative stress(COS), systolic blood pressure(SBP), and cardiac remodeling and dysfunction in obese rats.

Methods: Forty-eight Wistar rats were distributed into four groups and received by gavage (250mg/Kg/day) of E for 20 weeks as follow: G1- control diet (C); G2 - C+E; G3 - Western Diet (WD); and G4 - WD+ E. The total antioxidant capacity (TAC) of EndoBerg®, by DPPH, FRAP, and ABTS; and the COS, by MDA and protein carbonylation, were evaluated by UV-vis-Spectrophotometry. The adiposity index (AI) was measured. Cardiac structure: diastolic-posterior-wall-thickness(PWT), diastolic-thickness-of-interventricular-septum(IST), left-ventricular-mass-index(LVMI); systolic function: PWSV(posterior-wall-shortening-velocity), EF(ejection fraction); and diastolic function: E/E' ratio, and E/A' ratio, were evaluated by Doppler Echocardiography. Systolic blood pressure(SBP) was evaluated by tail-cuff-plethysmography. The data were compared by two-way ANOVA with Tukey's post hoc ($p<5\%$).

Results: The TAC of EndoBerg® was 1,3-5,4 µg TE/mg (Table 1). The WD groups, compared to the C groups, had higher AI (Figure 1), COS (Figure 2-A,B), SBP (Figure 3), and had cardiac remodeling and dysfunction (Table 2). EndoBerg® supplementation attenuated SBP (Figure 3) and prevented COS (Figure 2-A,B), cardiac remodeling and dysfunction (Table 2).

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Table 1. Total antioxidant capacity of EndoBerg® by three different methods.

Total Antioxidant Capacity	Value
DPPH (µg TE/mg)	5.4 ± 0.1
FRAP (mM FeSO/mg)	2.5 ± 0.3
ABTS (µg TE/mg)	1.3 ± 0.1

Table 2. Echocardiographic study of obese rats after 20 weeks of administering EndoBerg®.

Echocardiographic Variable		Groups				Effects		
		C	C + E	WD	WD + E	Diet	EndoBerg®	Interactions
Structural	PWT (mm)	1.49 ± 0.06	1.52 ± 0.03	1.92 ± 0.12[a]	1.55 ± 0.06[b]	<0.001	<0.001	<0.001
	IST (mm)*	1.52 (1.50-1.53)	1.53 (1.53-1.59)	2.00 (1.88-2.04)[a]	1.53 (1.53-1.55)[b]	<0.001	<0.001	<0.001
	LVMI (g/g)	1.49 ± 0.21	1.59 ± 0.28	1.80 ± 0.32[a]	1.47 ± 0.17[b]	0.173	0.112	0.004
Systolic function	PWSV (mm/s)	83.8 ± 4.6	81.4 ± 4.3	67.2 ± 6.3[a]	85.5 ± 4.9b[d]	<0.001	<0.001	<0.001
	EF (%)	0.94 ± 0.02	0.94 ± 0.01	0.91 ± 0.02[a]	0.94 ± 0.01[b]	<0.001	0.002	0.002
	CD (L/min)	99.5 ± 28.9	100.6 ± 27.1	78.2 ± 2.3[a]	105.5 ± 20.2[b]	0.235	0.043	0.062
Diastolic function	E/E' ratio (m/s)*	11.8 (10.6-12.4)	11.9 (11.1-13.1)	18.6 (15.8-19.9)[a]	11.7 (10.5-12.7)[b]	<0.001	<0.001	<0.001
	E/A ratio (m/s)	1.56 ± 0.07	1.64 ± 0.09c	0.66 ± 0.07[a]	1.57 ± 0.11[bd]	<0.001	<0.001	<0.001

Data presented as mean ± standard deviation or median with interquartile range (*) and submitted to Two-way ANOVA with Tukey's post hoc ($p<0.05$). a = C vs WD; b = WD vs WD + E; c = C vs C + E; d = C + E vs WD + E. C = Control diet; E = EndoBerg®; WD = Western diet. PWT: diastolic posterior wall thickness; IST: diastolic thickness of the interventricular septum; LVMI: Left ventricule mass index; PWSV: left ventricle posterior wall shortening velocity; EF: ejection fraction; CD: cardiac debit.

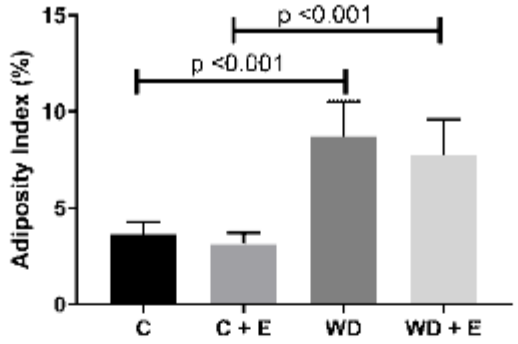

Figure 1. Adiposity Index (%) of obese rats after 20 weeks of administering EndoBerg®.

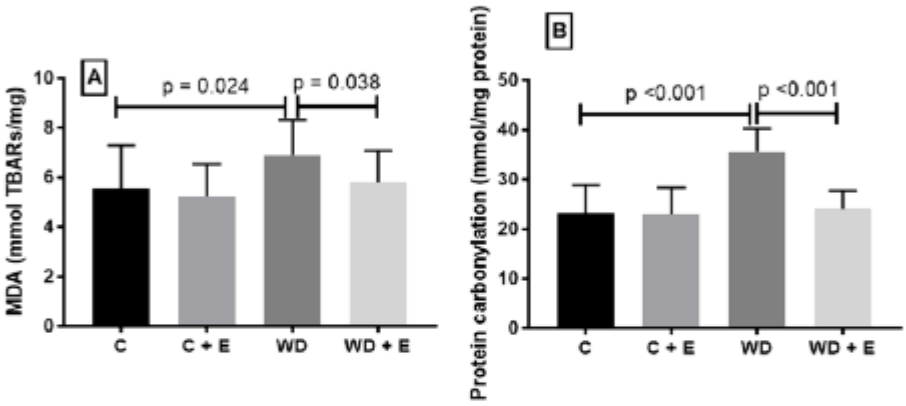

Figure 2. Oxidative Stress in cardiac tissue of obese rats after 20 weeks of administering EndoBerg®. A - Malondyhaldeide (MDA-nmol TBARs/mg); B – protein carbonylation (nmol/mg).

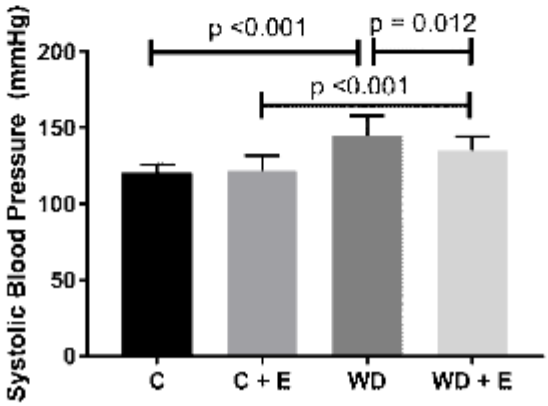

Figure 3. Systolic Blood Pressure (mmHg) of obese rats after 20 weeks of administering EndoBerg®.

Conclusions: The EndoBerg® extract showed interesting *in vitro* antioxidant capacity, attenuated blood pressure, prevented cardiac oxidative stress, and the development of cardiac remodeling and dysfunction in obese rats. Thus, EndoBerg® has great potential as a preventive and/or complementary therapy against cardiovascular disease.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

REMOTE ISCHEMIC PRECONDITIONING DOES NOT PROVOKE METABOLOMIC ALTERATIONS IN PATIENTS UNDERGOING MAJOR VASCULAR SURGERY: A RANDOMIZED CONTROLLED TRIAL

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Remote ischemic preconditioning (RIPC) is a procedure that aims to reduce ischemia-reperfusion injury to ischemia-sensitive organs. Metabolomics is a novel method to explain the effects of RIPC and draw conclusions about its usefulness in clinical practice. This study assesses whether preoperative RIPC affects metabolome after vascular surgery and if these metabolomic changes correlate with heart and kidney injury markers.

Methods: A randomized-controlled, double-blinded trial was carried out in the Tartu University Hospital. Patients undergoing elective vascular surgery were recruited. RIPC consisting of four cycles of 5 minutes of ischemia followed by 5 minutes of reperfusion, was applied before the surgery. Blood samples were collected preoperatively and approximately 24 hours postoperatively. The metabolome was analyzed with the AbsoluteIDQ p180 Kit.

Results: Final analysis included 45 patients from the RIPC and 47 from the sham group. Mean age was 67 (± 9) and 66 (± 10) years in the RIPC and sham groups, respectively (p=0.577). RIPC did not cause significant changes in metabolites 24 hours after surgery. Positive linear correlation of change in the kynurenine/tryptophan ratio with change in hs-troponin T ($r = 0.570$, $p < 0.001$), NT-proBNP ($r = 0.552$, $p < 0.001$), cystatin C ($r = 0.534$, $p < 0.001$) and beta-2-microglobulin ($r = 0.504$, $p < 0.001$) were detected only in the RIPC group.

Conclusions: RIPC did not provoke significant changes in metabolome 24 hours after vascular surgery. The positive linear correlation between the kynurenine/tryptophan ratio and heart and kidney injury markers suggests that the Kynurenine-Tryptophan pathway can play a role in RIPC-associated cardio- and renoprotective effects.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ASSESSMENT OF ATHEROSCLEROSIS IN PATIENTS WITH SUSPECTED CORONARY ARTERY DISEASE BY CAROTID ARTERY DOPPLER ULTRASOUND AND CORONARY CALCIUM SCORE

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Cardiovascular Disease (CVD) is the leading cause of morbidity and mortality in both industrialized and low income to middle-income countries. As atherosclerosis is the underlying cause for most of CAD, so identification of subclinical disease in the asymptomatic phase has emerged as a public health and economic imperative. Aim : The aim of the study was to evaluate the ability of carotid artery Doppler ultrasound and coronary artery calcium score as screening tools for atherosclerosis in patients who underwent CT coronary angiography for suspected coronary artery disease

Methods: This study was conducted on 40 patients (17 males and 23 females) with mean age of 50 years with atypical chest pain underwent Cardiac CT (CCT) and carotid Ultrasound (US) on the same day. Carotid artery atherosclerosis was evaluated by detection of Carotid Intimal Thickness (CIMT) & Carotid Plaque Score (CPS) then coronary arteries were evaluated by CCT. Coronary artery calcium score was obtained from axial non contrast cardiac CT and finally Coronary Artery Disease (CAD) was evaluated. The relation between both carotid artery Doppler findings & CACS and severity of coronary artery disease were detected

Results: There was significant relation between carotid artery disease that was estimated by Carotid intimal thickness, Catotid plaque score and CT coronary score(p=0.045&0.005).

Conclusions: Subclinical atherosclerosis as defined by Carotid intimal thickness, Carotid plaque score and Coronary artery calcium score can be simple, non-invasive yet sensitive risk prediction tools to promptly identify those individuals at risk of CVD

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

COMPARISON OF ULTRASOUND TECHNIQUES IN ASSESSMENT ATHEROSCLEROTIC PLAQUE STABILITY IN THE CAROTID ARTERIES

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: The aim of the study was to compare the usefulness of ultrasound imaging techniques - B-Mode and
VAUS (3D Volumen ultrasound) - in the assessment of atherosclerotic plaque stability

Methods: 62 patients (64 plaques) were included to the study
Patients with confirmed in CT or MRI post CVA (cerebrovascular accident) lesions in the brain, were examined and referred for complementary ultrasound examination, of the carotid arteries. The presence of atherosclerotic plaque in the carotid artery located in the damaged hemisphere of the brain was found.
The protocol included ultrasound examination in B-Mode imaging, Doppler-coded colour examination, VAUS and CEUS (contrast enhanced ultrasound) as a reference examination.

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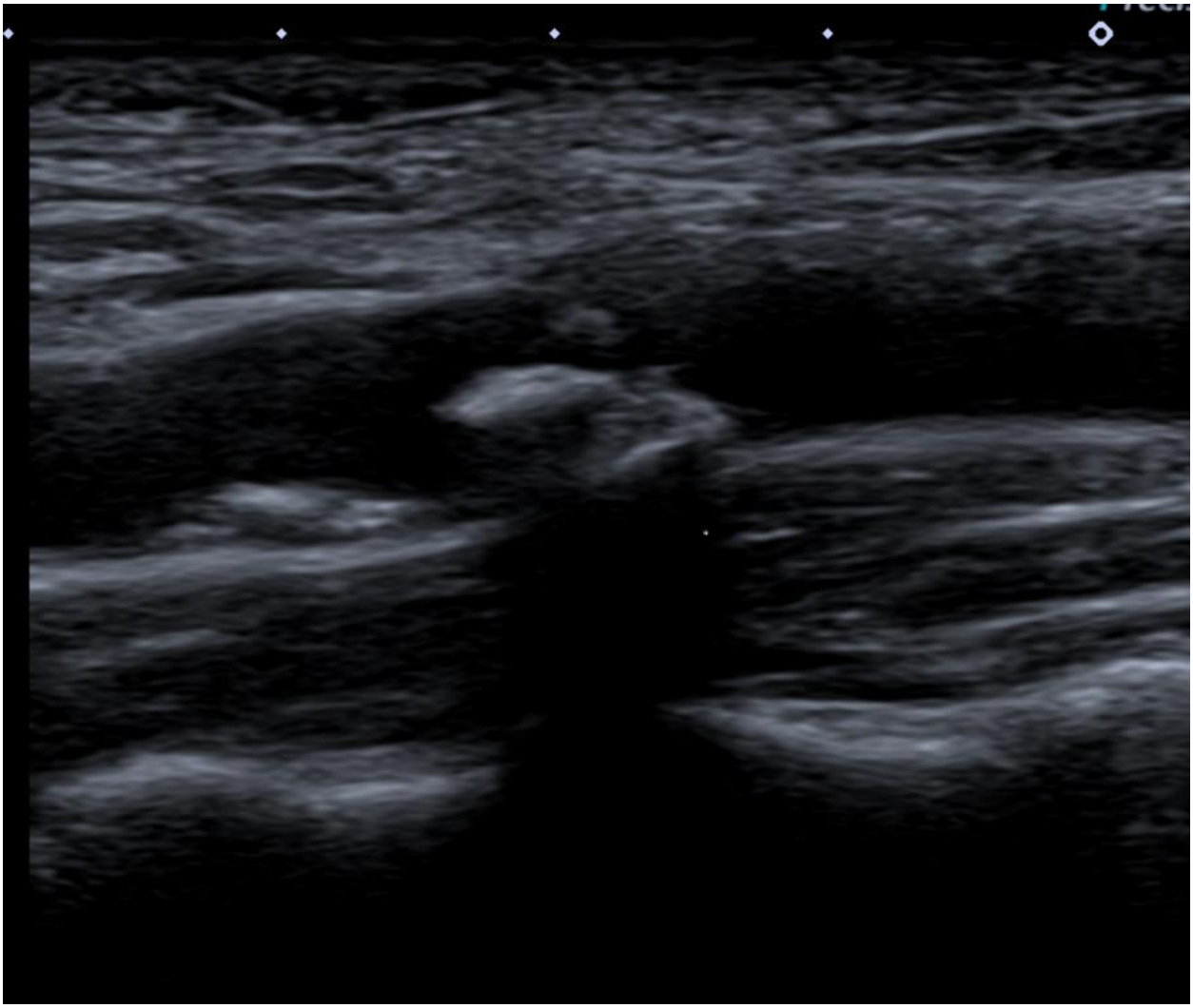

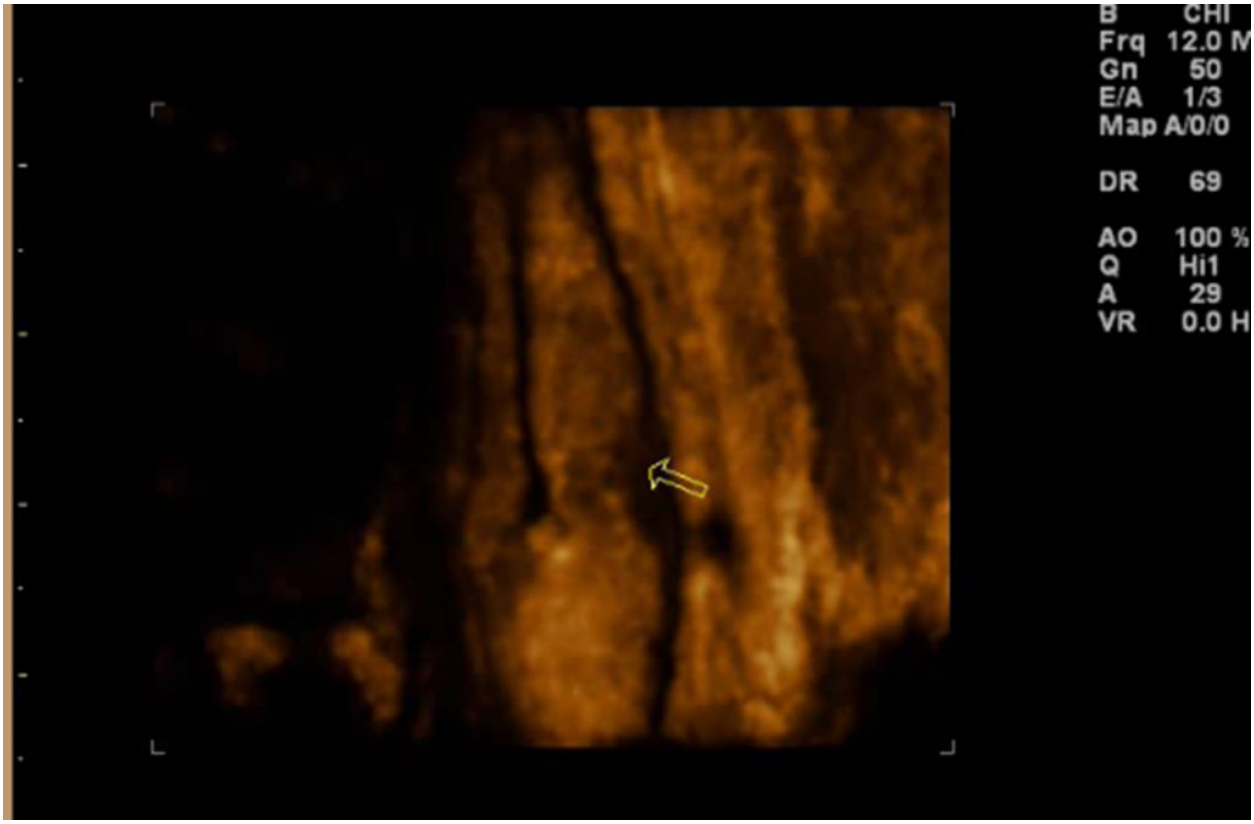
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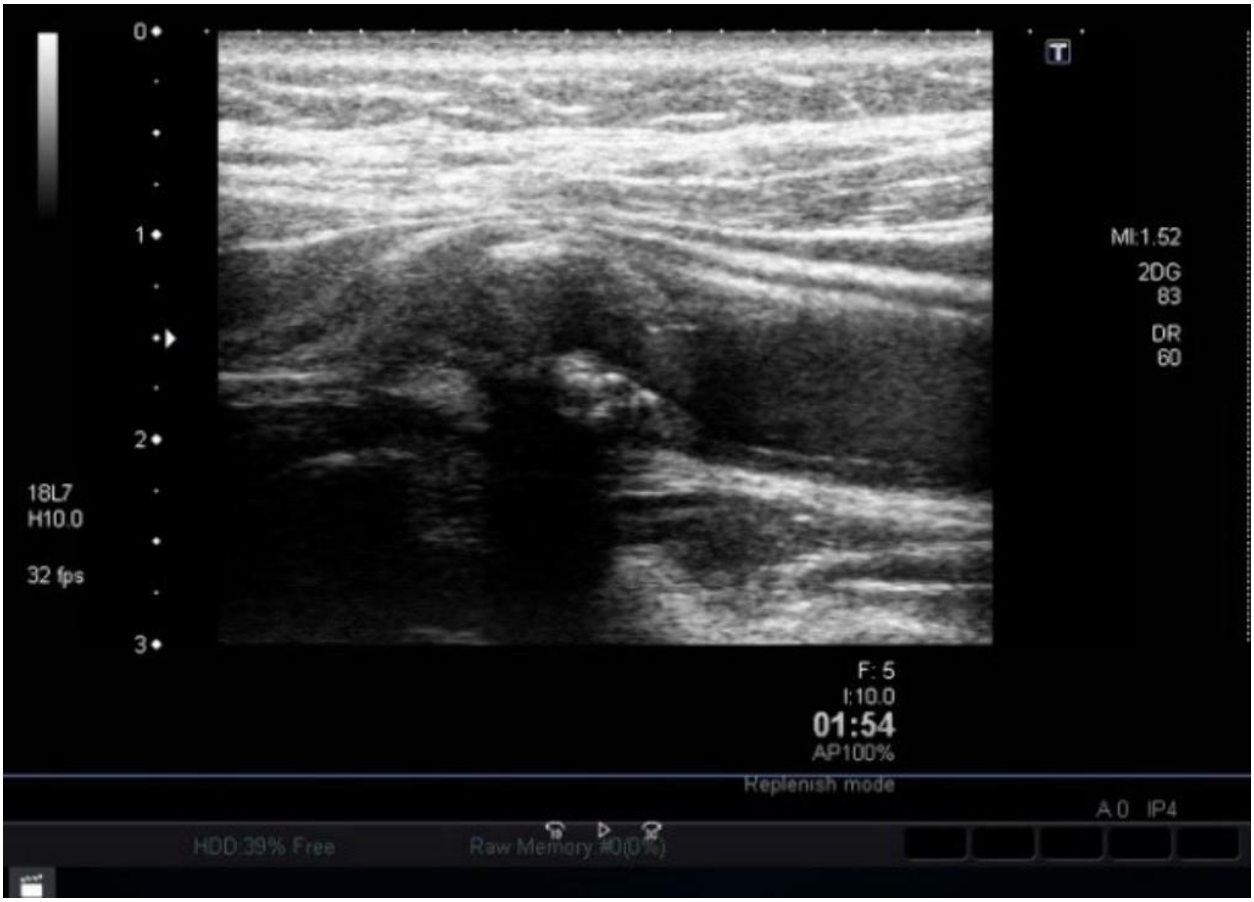

Results: No statistically significant differences were found in the classification of plaques on the Gray-Weill-
Nikolaides (GWN) scale in the B-Mode and VAUS.
The advantage of VAUS over B-Mode was demonstrated in the assessment of atherosclerotic plaque depending on the presence and size of the defect in the surface of the fibrotic cap (statistically significant).
The application of the CEUS technique made it possible to document the neovascularization of all the plaques qualified for analysis, as well as the precise determination of the plaque/vessel border. This made it possible to objectify the B-Mode and VAUS.

Conclusions: The results of the study show that regardless of the ultrasound technique used, the correct morphological evaluation of atherosclerotic plaque as well as its possible vascularization allows the determination of atherosclerotic plaque instability.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MOLECULAR BASIS OF REGENERATIVE ANGIOGENESIS IN MURINE ACUTE MYOCARDIAL INFARCTION: A BIOINFORMATICS ANALYSIS

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

Cristian Nuñez Pedrozo[1], Tomás Peralta[1], Sebastián Ulla[1], Gustavo Giunta[2], Paola Locatelli[1], Daniela Olea[1], Alberto Crottogini[1], Luis Cuniberti[1]
[1]Cardiovascular Regenerative Medicine Laboratory, IMETTyB, Capital Federal, Argentina, [2]Cardiology, Fundación Favaloro, Buenos Aires, Argentina

Background and Aims: The hypoxia-inducible factor-1 (Hif1) is a major regulator of the hypoxic response after acute myocardial infarction (AMI). It is known that mammalian hearts have limited regeneration capacity. Over the last years, molecular therapies have sought to enhance Hif1 expression to induce angiogenesis and cell survival. In the present research we evaluated the Hif1a/Hif3a relation in the transcriptomes of infarcted mice belonging to the regenerative (R) and non-regenerative (NR) evolutionary stages.

Methods: The bulk RNA-Seq files were retrieved from GEO (GSE123868). The heart samples were taken at 1.5, 3 and 7 days post-AMI for both neonatal (R) and infant mice (NR) and non-infarcted mice at equal times. The files were processed on UseGalaxy employing the FastQC/HISAT/featurecount pipeline. Differential gene expression and gene ontology analysis was performed with edgeR/PathFindR.

Results: Bulk analysis showed that at 1.5 days post AMI, R mice had significant lower expression of Hif1a (logFC: -1.24) and higher expression of Hif3a (logFC: 2.15) when compared to NR mice ($p < 0.001$). Gene ontology analysis showed a significant alteration of the biological process named positive regulation of angiogenesis at 1.5 days (FE: 1.54; $p < 0.05$) and 7 days (FE: 1.87; $p < 0.05$) post-AMI in genes with differential expression between R and NR stages.

Conclusions: This study shows that within the first 36 hours post-AMI Hif1a expression is down-regulated in R mice. This temporary silencing is associated with a higher expression of Hif3a in the R infarcted mice. These results support the existence of a Hif1a/HIif3a relation that may fine-tune the positive regulation of angiogenesis post-AMI.

91ST EAS CONGRESS
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345 / #581

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE HIGHEST DOSE OF PITAVASTATIN SIGNIFICANTLY DECREASED INFLAMMATORY CYTOKINES AND CORONARY NEOINTIMAL HYPERPLASIA DURING THE 12-MONTH FOLLOW-UP IN TYPE 2 DIABETIC PATIENTS

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

Soon Jun Hong, Do Sun Lim
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Background and Aims: We compared the effects of highest-dose and lowest-dose pitavastatin therapy on coronary neointimal hyperplasia at 12-month follow-up in diabetic patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) using optical coherence tomography.

Methods: A total of 72 diabetic patients with NSTE-ACS were randomized to the lowest-dose pitavastatin (1mg [n=36]) or the highest-dose pitavastatin (4mg [n=36]) after everolimus-eluting stent implantation.

Results: Neointimal volume was significantly lower in the pitavastatin 4mg group (0.41±0.28 mm^3/1mm vs. 0.74±0.23 mm^3/1mm, $p<0.01$) at 12-month follow-up. Improvement of brachial artery flow-mediated dilation (baFMD) was significantly higher in the pitavastatin 4mg group than in pitavastatin 1mg group (0.15±0.15 mm vs. -0.03±0.19 mm, $p<0.001$). Additionally, the improvement of adiponectin levels was significantly greater in the pitavastatin 4mg group than in the pitavastatin 1mg group (2.97±3.98 μg/mL vs. 0.59±2.80 μg/mL, $p<0.05$).

Conclusions: Pitavastatin 4mg significantly improved inflammatory cytokines and lipid profiles compared to pitavastatin 1mg during the 12-month follow-up, contributing to the reduction of neointimal hyperplasia and to the improvement of baFMD in diabetic patients with NSTE-ACS requiring coronary stenting. Thus, the administration of pitavastatin 4mg can be safely and effectively used in high-risk patients requiring coronary stenting.

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346 / #1565

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

REAL WORLD DATA COMPARING METABOLIC CONTROL IN DIABETIC EGYPTIANS WITH AND WITHOUT ISCHEMIC HEART DISEASE

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Patients with known ASCVD have more stringent metabolic goals requiring polypharmacy. Yet adherence to polypharmacy is disappointing. We decided to retrospectively examine our records on how well are patients with known diabetes and IHD controlled compared to the general population with diabetes.

Methods: We examined the records for a cohort of 500 Egyptians with diabetes. Patients medicated for IHD in this group were identified and then compared to the other patients in this cohort.

Results:

	IHD	Not IHD	Probability
Number	85	415	**P<0.001**
Gender M/F	54/31	221/194	P=0.089
Mean Age	61	48	**P<0.001**
Duration DM	11	7	**P<0.001**
BMI	33.6	32.1	**P=0.04**
Sys BP	134	137	P=0.74
Heart Rate	77	80	P=0.25
HbA1c	9.3	8.5	P=0.056
Chol	163	188	**P<0.001**
TG	151	156.5	P=0.964
HDL	47	51	**P=0.037**
LDL	74	107.5	**P<0.001**
LPa	20.6	25	P=0.79
eGFR	85.5	99	**P<0.001**
Sudoscan	66	69	**P=0.015**
Biothesiometry	33	26	**P<0.001**

The records showed that 85 patients were medicated for IHD, m/F 54/31, are significantly older, had higher BMI, and longer duration of diabetes than the patients with only Diabetes(415), they had significantly lower Chol, HDL, LDL, and eGFR yet are still above target values. There was no difference regarding BP, heart rate, TG, LPa , or HbA1c between both groups. They also had worse markers of peripheral neuropathy.

Conclusions: Egyptian Diabetics with known IHD are more adherent to lipid-lowering agents, yet most are above targets for BP, Chol, LDL, and HbA1c.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

LOW-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS ARE ASSOCIATED WITH SUBSEQUENT STENTED-TERRITORY ISCHEMIC STROKE AFTER CAROTID ARTERY STENTING

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Uncontrolled low-density lipoprotein cholesterol (LDL-C) is an important risk factor for carotid stenosis. However, the role of LDL-C after carotid artery stenting (CAS) is not well known with respect to stented-territory infarction (STI) and in-stent restenosis (ISR). We hypothesized that LDL-C levels after CAS might be independently associated with STI and ISR.

Methods: We conducted a retrospective study for patients with significant carotid stenosis who were subjected to CAS between September 2013 and May 2021. LDL-C levels were measured after six and twelve months following CAS. STI and ISR (newly developed stenosis of the treated artery of >50%) were examined as clinical outcomes after CAS. The association between clinical outcomes and LDL-C was explored using multivariate analysis adjusting for demographics, risk factors for stroke, and other clinical variables.

Results: Of 244 patients enrolled, STI and ISR were observed in 11 (4.5%) and 10 (4.1%) patients, respectively. As shown by multivariate logistical regression analysis, higher white blood cell count (OR, 1.498 per $10^3/mm^3$; 95% CI, 1.101-2.037; p=0.01), higher LDL-C levels after twelve months (OR, 1.026 per 1 mg/dL; 95% CI, 1.003-1.049; p=0.025), and ISR (OR, 32.612; 95% CI, 5.829-182.456; p<0.001) were independent predictors of STI. In addition, higher LDL-C levels after 12 months (OR, 1.036 per 1 mg/dL; 95% CI, 1.013-1.059; p=0.002) were independent predictors of ISR.

Conclusions: We showed that LDL-C levels after twelve months independently predict STI and ISR after CAS. These findings support that strict LDL-C control is essential to prevent future vascular events.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CORRELATIONS BETWEEN CORONARY ARTERY DISEASE, CORONARY ARTERY CALCIUM SCORE, AND LIPOPROTEIN(A) LEVEL IN EAST ASIA

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Lipoprotein(a) (Lp(a)) levels are associated with coronary artery disease (CAD) and aortic valve calcification. This study aimed to determine the correlation between Lp(a) levels and coronary artery calcium (CAC) scores in patients who underwent coronary computed tomography angiography (CCTA).

Methods: This was a single-center observational study. The patients had not been previously diagnosed with CAD and underwent CCTA and Lp(a) measurement in a three-month timeframe. Coronary angiography and further management were performed according to the physician's decision. Of the 252 patients, 81 and 171 patients underwent coronary revascularization and received medical treatment only, respectively. To examine the relationship between Lp(a) and CAC score and between Lp(a) and CAD, we divided the patients by Lp(a) level (50 mg/dL) and CAC score (400).

Results: No relationship was observed between Lp(a) and CAD or other risk factors for CAD. There were no differences in the ratio of patients who underwent coronary revascularization or in the CAC score according to an Lp(a) level of 50 mg/dL. There was no difference in Lp(a) level at a CAC score of 400. The proportion of patients who underwent coronary revascularization was high in the high CAC score group (50.6% vs 23.7%, $p = 0.000$). No association was observed between Lp(a) level and CAC score in the Spearman correlation (0.000, $p < 0.998$).

Conclusions: Correlations between Lp(a) level and CAC score and between Lp(a) and CAD were not observed in this Korean cohort study. However, a high CAC score was correlated with coronary revascularization.

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349 / #94

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ASSOCIATION OF ACE GENE POLYMORPHISM WITH ATHEROSCLEROSIS PROGRESSION AND DURATION OF INDEPENDENT LIVING IN THE ELDERLY

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: To determine were for the effect of genetic polymorphism (GP) on the prevalence of dyslipidemia (DRR), left radial pulse wave propagation velocity as the degree of worsening of arterial stiffness (WAS), and the duration of independent life (IL).

Methods: The method was analysis of variance in a linear model with ACE (GP) as the independent variable and DRR, WAS, and IL as dependent variables in the target population. Independent variables were divided into three groups (II, ID, and DD) according to ACE (GP).The subjects were panel data from a random sample of residents aged 75 years or older in Ogimi Village, Okinawa Prefecture, Japan. The study design was an observational cohort study. The analysis period was 5 years starting in 2016.

Results: Panel data were obtained for 17 individuals in the cohort ; ACE (GP) % was distributed 52.9 for II, 35.2 for ID, and 11.7 for DD; DRR was 11.1% for type II only; mean IL (months) was 26 for type II, 31 for type ID, and The mean IL (months) was 26 for type II, 31 for type ID, and 36 for type DD. Left APWV showed 12.22, 11.17, and 15.0, significant at p=.038 (95%CI,-7.46 to -2.0).

Conclusions: The ACE gene in older adults in long-lived areas with type II, which has superior vasodilatory properties, may progress more rapidly in the degree of deterioration than ID and DD in left radial pulse wave propagation velocity. No association with duration of independent living was observed.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

VALUE OF BLOOD PRESSURE MEASUREMENT EARLIER VERSUS LATER IN LIFE TO PREDICT CARDIOVASCULAR MORTALITY

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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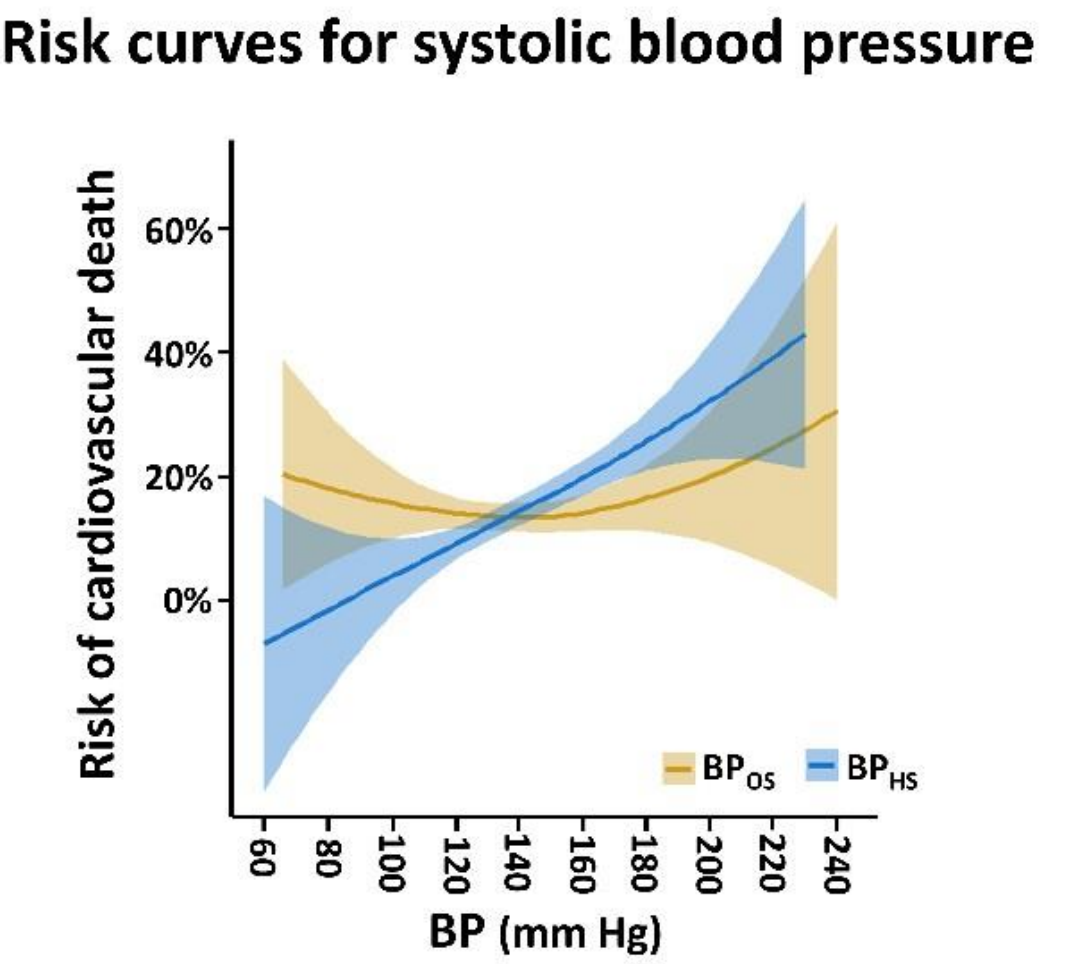
Background and Aims: We here aimed at comparing the value of systolic blood pressure (BP) earlier versus later in life to predict cardiovascular mortality.

Methods: In a cardiovascular observation study (OS) we prospectively recorded fatal cardiovascular events over up to 19 years in 1282 patients of whom 570 had the Metabolic Syndrome (MetS) at baseline. These patients had participated in a health survey (HS) 15 years prior to the OS baseline. BP was measured both at the HS and at the baseline of the OS.

Results:



Risk curves are calculated for blood pressure (BP) assessed at the health survey (HS) and at the baseline of the cardiovascular observation study (OS) according to loess (LOcally WEighted Scatter-plot Smoother) fitting with 95% confidence intervals for cardiovascular death during follow up.

We found that the increase in cardiovascular mortality matched the increase of BP in the HS in a linear way but this is not the case for BP assessed at the OS (figure). A cox regression analysis revealed that each millimeter of mercury (mm Hg) increased the risk for cardiovascular death by 2% (HR = 1.02 [1.01-1.03], p<0.001). Applying a stratification for the presence of MetS, we found that in both groups BP was a

significant predictor of cardiovascular mortality (HR_{MetS} = 1.02 [1.01-1.02], p<0.001 and HR_{noMetS} = 1.02 [1.01-1.03], p<0.001). In contrast, BP as measured at the baseline of the OS was not significantly associated with cardiovascular death during follow-up neither in the total population nor in any subgroup (HR = 1.00 [0.99-1.01], p=0.652; HR_{MetS} = 1.00 [0.99-1.01], p=0.468 and HR_{noMetS} = 1.00 [0.99-1.01], p=4.66).

Conclusions: We thus conclude that BP assessed earlier in life is a better predictor of cardiovascular mortality than BP assessed later in life.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CYSTATIN C PREDICTS MAJOR CARDIOVASCULAR EVENTS IN PATIENTS WITH CORONARY ARTERY DISEASE BOTH AMONG PATIENTS WITH TYPE 2 DIABETES AND IN NON-DIABETIC INDIVIDUALS

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Cystatin C is an established biomarker for renal function, and, given the close association of chronic kidney disease and cardiovascular disease might indicate new-onset or deteriorating cardiovascular disease. However, evidence for cystatin C as a predictor of cardiovascular events is limited and controversial. We therefore aimed at investigating the role of Cystatin C as a predictor of future major adverse cardiovascular events (MACE) in a high risk-cohort of patients with coronary artery disease (CAD).

Methods: Cystatin C was measured in 1098 patients with angiographically proven CAD. Vascular events were recorded over a mean follow-up of 8.0±5.0 years.

Results: At baseline, 239 patients had T2DM and 859 did not have diabetes. During follow-up, 30.0% of our patients suffered MACE. Cystatin C proved to be a strong and independent predictor of vascular events in the total study cohort (standardized adjusted HR 1.20 [1.12-1.28], p<0.001). When diabetes status was taken into account, cystatin C significantly predicted major cardiovascular events in non T2DM patients (HR=1.16 [1.08-1.26], p<0.001) and in patients with T2DM (HR=1.34 [1.13-1.60], p=0.001).

Conclusions: We conclude that cystatin C predicts major cardiovascular events in patients with coronary artery disease both among patients with type 2 diabetes and in non-diabetic individuals.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PRO-B-TYPE NATRIURETIC PEPTIDE STRONGLY PREDICTS MAJOR CARDIOVASCULAR EVENTS AND MORTALITY IN CARDIOVASCULAR DISEASE PATIENTS WITH TYPE 2 DIABETES AS WELL AS IN THOSE WITHOUT DIABETES

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Elevated pro-B-type-natriuretic peptide (pro-BNP) is a strong marker of cardiovascular risk in several high-risk populations. However, the power of pro-B type natriuretic peptide (pro-BNP) to predict major cardiovascular events (MACE) and mortality in patients with established cardiovascular disease and type 2 diabetes (T2DM) is unclear.

Methods: We enrolled 873 patients with established cardiovascular disease, 579 with angiographically proven stable CAD and 294 with sonographically proven peripheral artery disease. Prospectively, cardiovascular events were recorded over a mean follow-up period of 7.9±3.6 years.

Results: At baseline, pro-BNP was significantly higher in patients with T2DM (n=285) than in those who did not have diabetes (1010±2604 vs. 727±2327 mg/dl; p=0.003). During follow-up, 257 patients suffered MACE; the event rate was significantly higher in patients with T2DM than in subjects without T2DM (37.8 vs. 26.0%; p<0.001). Pro-BNP predicted both MACE and mortality in the total study population, with standardized adjusted hazard ratios (HR) of 1.37 [1.26-1.48]; p<0.001 and 1.30 [1.21-1.40]; p<0.001, respectively. Further, pro-BNP predicted MACE and mortality in patients with T2DM (HRs 1.37 [1.21-1.55]; p<0.001 and 1.24 [1.10-1.40]; p<0.001, respectively) and in those who did not have diabetes (HRs 1.45 [1.26-1.67]; p<0.001 and 1.41 [1.25-1.60]; p<0.001, respectively). Interaction terms pro-BNPxT2DM were non-significant for both MACE and mortality (p=0.590 and 0.306 respectively), indicating that the power of pro-BNP to predict MACE and mortality did not differ significantly between cardiovascular disease patients with and without T2DM.

Conclusions: We conclude that pro-BNP strongly predicts MACE and mortality in cardiovascular disease patients with T2DM as well as in those without diabetes.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE A BODY SHAPE INDEX AND TYPE 2 DIABETES ARE MUTUALLY INDEPENDENT PREDICTORS OF MAJOR CARDIOVASCULAR EVENTS IN PATIENTS WITH ESTABLISHED CARDIOVASCULAR DISEASE

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: The A Body Shape index (ABSI) is a validated measure of visceral adiposity that is calculated based on waist circumference, height and BMI. Its power to predict major cardiovascular events in patients with established cardiovascular disease (CVD) is unclear and is addressed in the present study.

Methods: We prospectively recorded cardiovascular events in a large cohort of 1544 patients with established CVD (1297 patients with angiographically proven stable coronary artery disease and 247 patients with sonographically verified PAD) over a mean follow-up time of 10.0±4.6 years.

Results: At baseline, the ABSI was higher in patients with type 2 diabetes (T2DM; n=502) than in those who did not have diabetes (8.4±0.6 vs. 8.3±0.6; p<0.001). Prospectively, the ABSI significantly predicted the incidence of MACE (n=507) after adjustment for age, gender, smoking, hypertension, LDL cholesterol, HDL cholesterol, and T2DM (standardized adjusted HRs 1.14 [1.04-1.24]; p=0.004, respectively). T2DM in turn in this model also significantly predicted MACE with a HR of 1.61 [1.33-1.94]; p<0.001 after adjustment for ABSI.

Conclusions: We conclude that ABSI and T2DM are mutually independent risk factors for MACE in patients with established cardiovascular disease.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ONE YEAR FOLLOW-UP OF CARDIOVASCULAR PROFILE AND THERAPEUTIC MANAGEMENT OF CHILDREN AND ADOLESCENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA: PRELIMINARY DATA FROM THE HELLAS-FH REGISTRY

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: To assess cardiometabolic characteristics and therapeutic management in children and adolescent patients during one-year follow-up.

Methods: Children and adolescents older than 8 years from the HELLAS Familial Hypercholestrolemia (FH) registry were evaluated. Changes in demographics, lipid profile and treatment are reported.

Results: A total of 176 subjects were included (mean age 10.3±3.2 years, 49.2% boys). Of patients, 70.5% were on lipid-lowering therapy at enrollment visit and had the following lipid profile: TCHOL 258±61 mg/dL, LDL-C 187±58 mg/dL, HDL-C 57±12 mg/dL and TG 67 (52-85) mg/dL. Overall, 20 of the children/adolescents (11.3%) were within target for LDL-C (<135 mg/dL) at the time of enrollment. After a median follow-up of 12.1 months (IQR 8.7-15.6), almost all (94.2%) children/adolescents were treated with lipid-lowering therapy. Specifically, 64.0% were on statin therapy, 23.0% on ezetimibe, 28.1% on sterols, and 25.2% on red yeast rice. One year lipid profile was: TCHOL 229±49 mg/dL, LDL-C 162±46 mg/dL, HDL-C 53±11 mg/dL and TG 68 (52-91) mg/dL. A total of 29 children/adolescents (16.5%) achieved LDL-C target levels (p=NS vs baseline).

Conclusions: After a median follow-up of 12 months, intensification of hypolipidemic therapy with improvement of lipid profile was observed in children/adolescents with FH. However, the percentage of subjects achieving LDL-C target remained low.

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Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

CYP2C19 AND CYP3A4 ACTIVITY IS ASSOCIATED WITH SURVIVAL IN TICAGRELOR-TREATED PATIENTS AFTER ST-ELEVATION MYOCARDIAL INFARCTION

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: We assessed the effect of CYP450 activity assessed by lansoprazole metabolism on 7 year-survival of 89 patients with STEMI treated by PCI together with prasugrel (n = 46) and ticagrelor (n = 49).

Methods: Patients were given lansoprazole as a probe drug that is metabolized into 5OH-lansoprazole by CYP2C19 or lansoprazole sulfone by CYP3A4, and concentration of lansoprazole and both metabolites was determined.

Results: There was no difference in survival between groups. In ticagrelor group, both lansoprazole sulfone/lansoprazole (HR per doubling = 2.90; 95%CI = 1.32–6.35; p = 8.10^{-3}) and 5OH-lansoprazole/lansoprazole (HR per doubling = 0.34; 95%CI = 0.19–0.61; p = 3.10^{-4}) ratio correlated with survival. The effect remained significant after adjustment for other significant predictors (age, ejection fraction, previous MI and the number of diseased vessels), and gender, smoking, hypertension, diabetes and dyslipidemia. In post-hoc analysis, the effect was only present in patients treated by atorvastatin (n = 30; HR per doubling of lansoprazole sulfone/lansoprazole = 12.68; HR for 5OH-lansoprazole/lansoprazole = 0.25, respectively). No significant effect on survival was found in prasugrel-treated patients. Similarly, the effect of CYP2C19 polymorphisms on lansoprazole metabolite production was only evident in the ticagrelor group. Only 4 deaths occurred during prasugrel/ticagrelor treatment.

Conclusions: We hypothesize that CYP450 effect on survival was mediated by factors unrelated to P2Y12-blocking treatment, possibly by atorvastatin, degraded by CYP3A4. The effect was evident in ticagrelor group because prasugrel is a moderate CYP3A4 inhibitor and therefore formation of lansoprazole sulfone in high doses of prasugrel may not reflect the long-term activity of CYP3A4.

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356 / #1125

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE ASSOCIATION OF NICOTINE ADMINISTRATION AND MICROSTRUCTURAL CHANGES OF IN-STENT AREAS IN THE PORCINE MODEL – A STUDY PROTOCOL

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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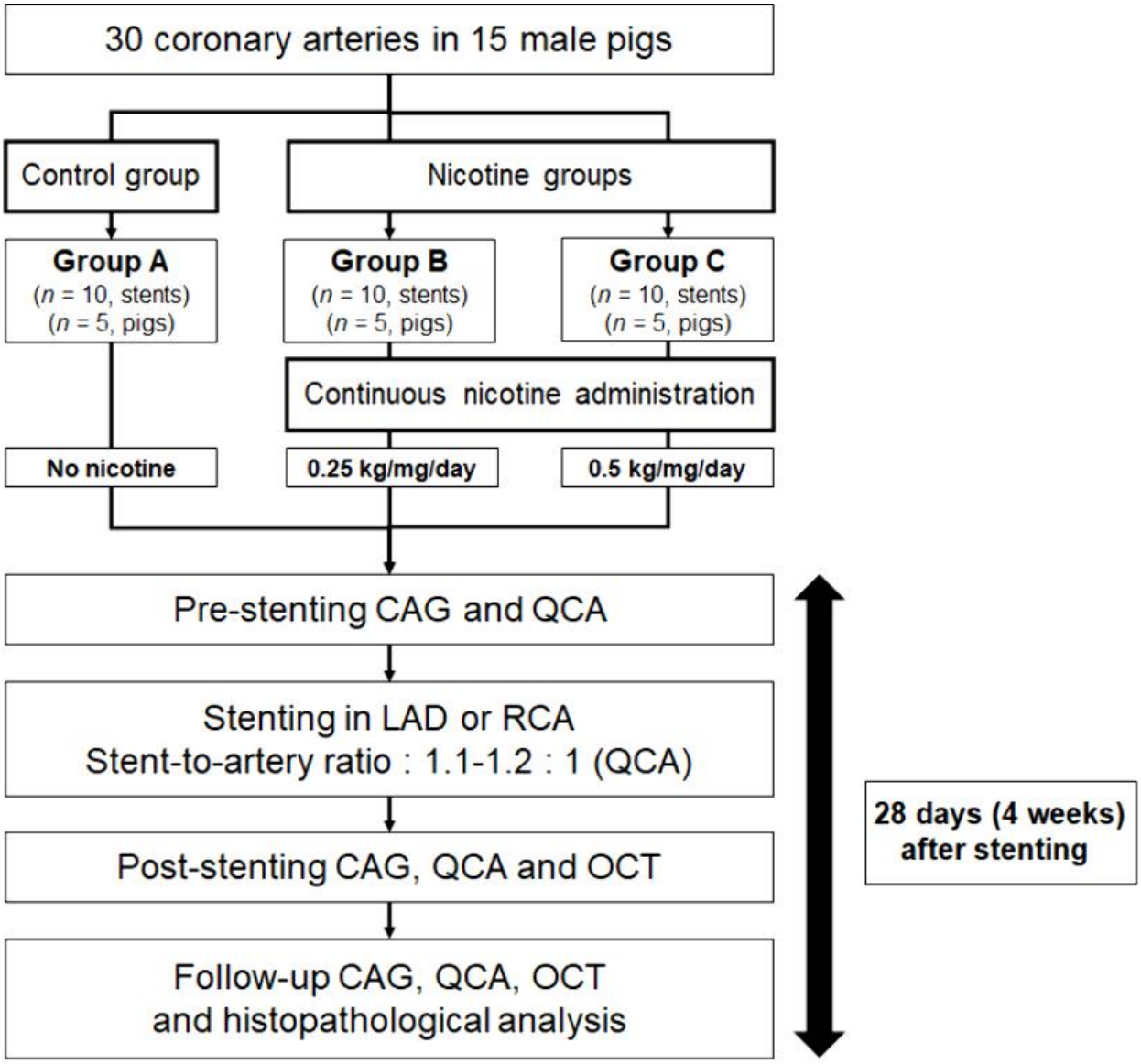
Background and Aims: This animal study aimed to scrutinize the effect of nicotine on microstructural changes including strut coverage, neointimal characteristics, strut malapposition following stenting.

Methods: It is a 4-week, prospective observational trial by a total of 15 male pigs. Among them, a total of 30 commercial sirolimus-eluting stents (SESs) will be implemented at either left anterior descending coronary artery or right coronary artery. All animal subjects may be allocated into different 3 groups: (1) group A (10 stents, and 5 pigs); (2) group B (10 stents, and 5 pigs); (3) group C (10 stents, and 5 pigs). Group A does not receive any nicotine administration, whereas other groups receive continuous nicotine administration after stenting (for 28 days). The daily total dose of nicotine will be set as 0.25 mg/kg/day in group B, and 0.5 mg/kg/day in group C. The study protocol is well-illustrated in **Figure 1**.



After the engagement of a guiding catheter into ostium of each coronary artery, baseline angiogram (CAG) and quantitative coronary analysis (QCA) will be conducted, then stent implantation will be done with one commercial SES with a stent-to-artery ratio of 1.3:1. Post-stenting CAG, QCA and optical coherence tomography (OCT) will be performed. 28 days post-stenting, follow-up CAG, QCA, OCT and histopathological analysis will be conducted.

Results: The results could help to contribute to current evidence that smoking may lead to microstructural changes of in-stent areas such as in-stent restenosis or neoatherosclerosis.

Conclusions: It is not applicable since this abstract is a study protocol.

91ST EAS CONGRESS
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357 / #1246

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PRESCRIPTION PATTERN OF BETA-BLOCKERS IN POST-ACUTE MYOCARDIAL INFARCTION

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: The prescription of beta-blockers after an acute myocardial infarction (AMI) is recommended by relevant guidelines. We sought to evaluate the treatment pathway of beta-blockers in post-AMI patients from 2018 to the first wave of COVID-19 pandemic in Italy and to investigate predictors for treatment non-initiation.

Methods: Healthcare utilization databases of Lombardy Region were investigated. Subjects aged ≥18 years and hospitalised with AMI in the quarter February-March-April of 2018, 2019, and 2020 were included. We searched for a first prescription of beta-blockers in a 30-day period after the discharge date. A multivariate logistic model was performed to evaluate the effect of several covariates on the probability of not receiving a post-AMI beta-blocker therapy.

Results: Overall, 2259, 2383, and 1932 individuals were hospitalised with AMI in the 3-month period of 2018, 2019, and 2020, respectively. In 2020, about 53–59% of individuals with AMI received a prescription of beta-blockers within 30 days after the discharge, compared to about 56-63% in 2018, suggesting a decreasing trend over time. Men were 30% more likely to start the treatment than women, increasing age was associated with significant increasing probability of not receiving a post-infarction beta-blocker therapy, while having received an antihypertensive or lipid-lowering therapy, or having been hospitalized for heart failure prior to the AMI hospitalization increased the likelihood of being treated with beta-blockers.

Conclusions: The initiation of beta-blocker treatment after AMI remains an under-prescribed practice, that does not seem to have been further affected by the first wave of the COVID-19 pandemic in Italy.

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358 / #1331

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE PREDICTIVE VALUE OF THE SMART RISK SCORE IN PATIENTS REFERRED FOR CORONARY ANGIOGRAPHY

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: The SMART Risk Score has been introduced for risk stratification in secondary prevention. The present study was performed to analyze the predictive value of the SMART Risk Score in patients referred for coronary angiography.

Methods: The SMART Risk Score was calculated in 3,135 participants of the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study. 10-year risk categories according to the SMART Risk Score were formed (<10%, 10-20%, 20-30%, 30-40%, and >40%). There was follow-up for cardiovascular mortality with a median (inter-quartile) duration of 9.9 (8.7-10.7) years.

Results: Most LURIC participants had SMART Risk Score of 10-20%. SMART Risk Score categories were strongly predictive of cardiovascular mortality. Compared to SMART Risk Score category <10%as a reference, participants in the categories 10-20%, 20-30%, 30-40%, and >40% had a hazard ratio (95% confidence interval) of 3.2 (1.8-5.6), 9.4 (5.5-16.3), 16.4 (9.4-28.4), and 25.8 (15.0-44.5), respectively (all p<0.001).

Conclusions: The SMART Risk Score is a very useful tool to predict cardiovascular mortality in patients referred for coronary angiography.

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359 / #376

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ENSEMBLE MACHINE LEARNING FOR SCREENING CARDIOVASCULAR DISEASES IN ELECTRONIC HEALTH RECORDS

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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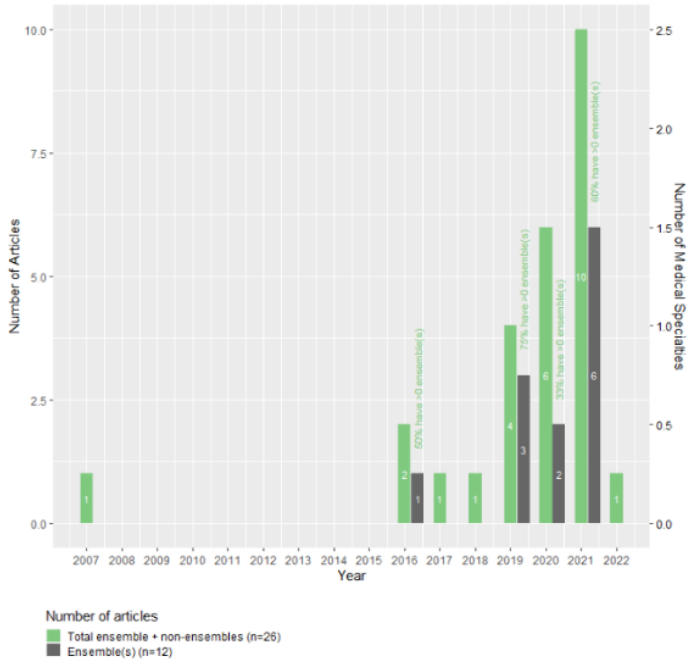
Background and Aims: Machine Learning (ML) methods are increasingly proposed for cardiovascular disease (CVD) screening in Electronic Health Records (EHRs). Among all ML methods, "Ensembles of machine learning models" (EMLs), which work by combining multiple predictions into one, are often acknowledged to provide the best predictive performances. However, the evidence for using EMLs in the context of CVD screening within EHRs has not been systematically reviewed yet.

Methods: We conducted a scoping review within EMBASE and MEDLINE electronic databases using free and MeSH terms related to ML, screening and EHRs. Original articles describing derivation and/or validation of EMLs for EHRs screening were selected. Data sources and processing steps were classified and reported alongside the descriptions of ML algorithms. The cumulative hypergeometric test was used to establish whether specific algorithms performed significantly better.

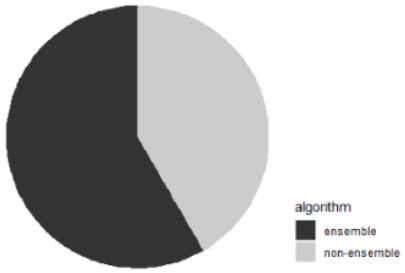
Results: Our search strategy retrieved a total of 3,355 articles. 30 articles reported the use of ML models for screening CVD within EHRs, of which 16 (53.3%) described at least one EML and were included in the analysis. Our results showed that EMLs are increasingly being employed for screening CVD within EHRs (Figure 1A) and outperform non-ensemble approaches (Figure 1B). EMLs with a weighted average fusion strategy were the best performers (Figure 1C). EML methodologies, processing steps and data

sources were often not clearly described, hindering reproducibility.

A) Published articles proposing a machine learning model to screen cardiovascular diseases in Electronic Health Records



B) Proportion of articles where study authors selected an ensemble as the best model.



C) Probability that a model generated by a machine learning algorithm was selected as a best model (by study authors) as many times as observed by chance alone.

Machine Learning Algorithm	Probability of selection as best model by chance alone[1]
Ensemble with weighted vote fusion	0.004
Artifical Neural Network	0.113
Deep Learning Neural Network	0.333
Random Forest	0.870
Multilayer Perceptron	0.929
Extreme Gradient Boosting	1.000
Least Absolute Shrinkage and Selection Operator (LASSO)	1.000

[1] *Two sided hypergeomeric test*

Conclusions: EML methods often provide higher predictive performances than non-ensemble ML methods and should be considered when deriving new predictive models aiming at screening and identifying individuals affected by CVD within EHRs.

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360 / #1609

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

DO COMORBIDITIES AND RESIDUAL RISK FACTORS INFLUENCE CHOICE OF ANTIPLATELET MONOTHERAPY IN PATIENTS WITH PERIPHERAL ARTERY DISEASE? RESULTS FROM THE CROSS-SECTIONAL RESRISK-PAD STUDY

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Background and Aims: Guidelines recommend antiplatelet therapy for the secondary prevention of atherosclerotic cardiovascular disease (ASCVD) in patients with symptomatic peripheral artery disease (PAD). Some guidelines suggest clopidogrel as the preferred option when antiplatelet monotherapy (APMT) is considered the optimal antithrombotic choice. Though aspirin is still largely prescribed. Using real-world data, we examined the characteristics of patients prescribed either clopidogrel or aspirin.

Methods: Cross-sectional study of 80,170 patients with PAD from the UK Clinical Practice Research Datalink (2010-20). Inclusion criteria were age ≥18 years, on APMT with clopidogrel or aspirin, diagnosed with PAD prior to initiating APMT and prior to any other ASCVD diagnosis (if any), and had ≥1 year of baseline data prior to the first APMT prescription. Atrial fibrillation, end-stage renal disease and haemorrhagic stroke led to exclusion.

Results: 13,162 and 67,008 PAD patients were on clopidogrel and aspirin, respectively. Table shows participant characteristics, risk factors, additional manifestations of ASCVD and medications. Mean±SD LDL-cholesterol was 2.3±0.9 and 2.5±1.0 mmol/l in patients on aspirin and clopidogrel, respectively. Attainment of certain thresholds for blood pressure/HbA1c/LDL-cholesterol are shown in Figure. A higher proportion of patients on aspirin attained recommended LDL-C
thresholds.

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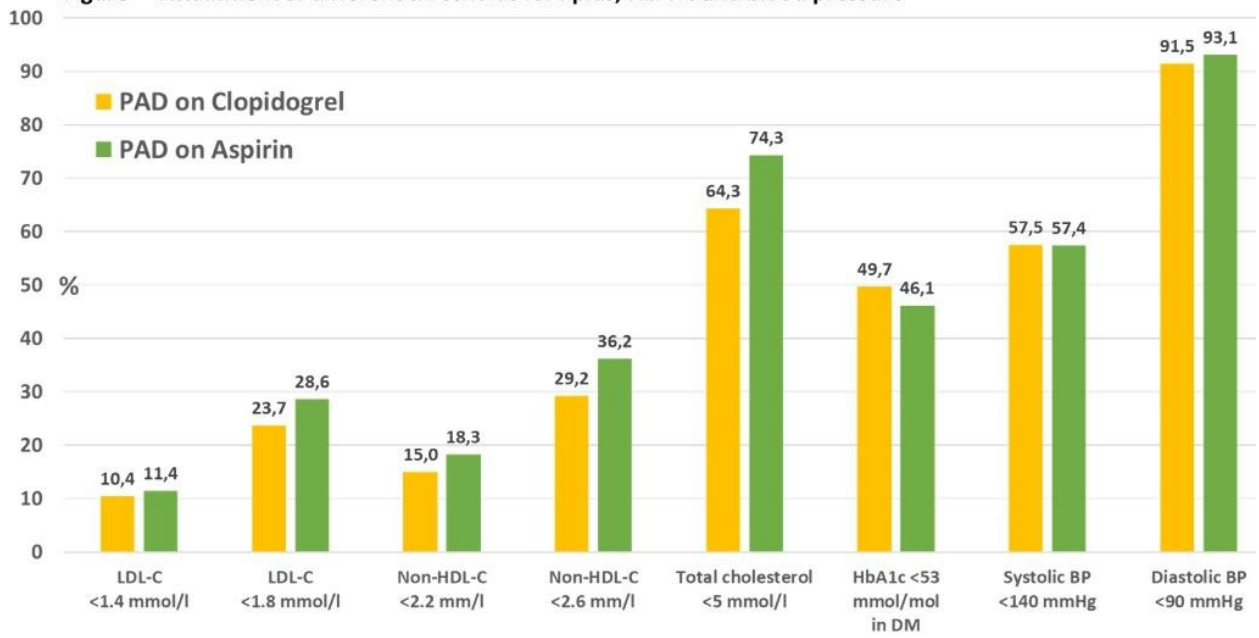
Table. Characteristics of participants.	PAD patients on CLOPIDOGREL	PAD patients on ASPIRIN
	n = 13,162	n = 67,008
Male	56.7%	58.1%
Age (years), mean (SD)	70.6 (11.8)	70.9 (11.5)
Hypertension	56.1%	61.8%
Diabetes	50.3%	58.9%
Dyslipidaemia	43.2%	32.8%
Current smoker	40.4%	34.7%
BMI (kg/m^2), mean (SD)	28.3 (6.21)	29.4 (6.56)
Obesity (≥30 kg/m^2)	33.6%	40.3%
Myocardial infarction	5.9%	3.4%
Heart failure	7.0%	4.5%
Stroke	14.4%	4.4%
Amputation	7.6%	6.5%
Polyvascular disease	26.0%	16.5%
Medication	--	--
• **ACEI/ARB**	52.9%	63.4%
• **Statin**	81.6%	81.7%
• **Ezetimibe**	3.6%	3.9%
• **Metformin**	26.3%	35.1%
• **Sulphonylureas**	13.9%	19.2%
• **DPP4 inhibitor**	4.9%	2.9%
• **GLP1 agonist**	1.5%	1.1%
• **SGLT2 inhibitor**	1.2%	0.4%
• **Insulin**	12.9%	15.7%

Figure **Attainment of different thresholds for lipids, HbA1c and blood pressure**



Conclusions: PAD patients are much more frequently prescribed aspirin than clopidogrel. Patients on clopidogrel were more likely to have polyvascular disease (particularly with stroke), heart failure and history of amputation. Perception of higher risk and/or other ASCVD might be partly driving the selection of clopidogrel instead of aspirin. Risk factor burden remains high in patients on aspirin or clopidogrel, and attainment of guideline-recommended targets remains suboptimal.

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361 / #213

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

IMMEDIATE RESULTS OF PRIMARY PCI IN PATIENTS WITH ACS WITH ST SEGMENT ELEVATION. EXPERIENCE OF THE CENTER OF CARDIOLOGY

POSTER ON BOARD: AS04.12 PREVENTION AND TREATMENT OF CARDIOVASCULARDISEASE; MISCELLANEOUS

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Interventional Cardiology, Republican Specialized Scientific and Practical Medical Center of Cardiology, Tashkent, Uzbekistan

Background and Aims: To assess the immediate results of coronary artery stenting in patients with ST elevated ACS, performed at the Republican Center of Cardiology.

Methods: From January 2021 to February 2022, 114 patients with ACS with ST elevation were urgently admitted to the RSSPMC of Cardiology. Patients subjected to coronary artery stenting were mostly male 59 (77.6%), aged 28 to 81 years. Hypertension was detected in 56 (73.7%) patients, DM in 15 (19.7%) patients. In ICA, 25 (32.9%) patients had single vascular lesion, 26 (34.2%) 2 vascular lesions, and 25 (32.9%) patients had multivessel lesions. Characteristics of patients according to the SYNTAX Score scale had the following: 58 (76.3%) patients had a low score, 13 (17.1%) patients had an average score, and 5 (6.6%) respondents had a high risk.

Results: The immediate angiographic success of the intervention was 94.37% (67). The main part of patients - 95.8% (68) noted a significant clinical improvement after activation. In the ECG, in 94.3% (67) of patients there was a positive trend in the form of a decrease in the ST segment. Complications in the form of no-reflow developed in 8.45% (6) cases (in all cases, the blood flow was restored medically to the level of TIMI III). Acute stent thrombosis developed in 5.6% (4) patients (of which 4.2% (3) patients underwent systemic thrombolysis, 1.4%

Conclusions: Primary PCI in patients with ST elevated ACS is characterized by a good angiographic efficiency of 94.37% and a clinical efficacy of 95.8% with a decrease in the incidence of complications and death

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362 / #981

Topic: *AS04 Clinical Vascular Disease / AS04.13 New lipid lowering therapies*

THE EFFECT OF PCSK9 INHIBITION ON THE STABILIZATION OF ATHEROSCLEROTIC PLAQUE DETERMINED BY BIOCHEMICAL AND DIAGNOSTIC IMAGING METHODS

POSTER ON BOARD: AS04.13 NEW LIPID LOWERING THERAPIES

Marcin Basiak[1], Michal Kosowski[1], Maria Dziubinska-Basiak[2], Marcin Hachula[1], Lukasz Buldak[1], Grzegorz Machnik[1], Robert Krysiak[1], Boguslaw Okopien[1]
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Background and Aims: In addition to high cholesterol levels, several plasma factors play a significant role in the development of atherosclerosis. Interleukin 6 (IL-6), interleukin 18 (IL-18), tumor necrosis factor (TNF-), metalloproteinase 2 (MMP-2) and metalloproteinase 9 (MMP-9) are among the cytokines and molecules that may contribute to the stabilization of atherosclerotic plaque. The purpose of this study was to determine the effect of advanced lipid-lowering therapy using proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors on the levels of these determinants in patients with confirmed high-risk atherosclerotic plaque.

Methods: Ultrasonography confirmed the presence of non-stable atherosclerotic plaque in patients with dyslipidemia who were eligible to begin alirocumab treatment. The levels of IL-6, IL-18, TNF-, and MMPs were measured before and after three months of therapy in this group.

Results: The levels of IL-6, IL-18, TNF-, and MMPs were measured before and after three months of therapy in this group. After treatment, statistically significant decreases in Il-18, Il-6, TNF- ($p<0.001$), and MMP-2 ($p<0.05$) concentrations were observed. In addition, we found that the concentrations of these markers were significantly higher in the patient group prior to therapy initiation compared to the control group.

Conclusions: The results of our study indicate that PCSK-9 inhibitor therapy significantly reduces the concentration of factors that influence the stability of atherosclerotic plaque, which may explain their critical role in reducing cardiovascular risk in patients receiving this treatment.

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363 / #1564

Topic: *AS04 Clinical Vascular Disease / AS04.13 New lipid lowering therapies*

A REAL WORLD SINGLE CENTER EXPERIENCE WITH EARLY USE OF TRIPLE LIPID LOWERING THERAPY

POSTER ON BOARD: AS04.13 NEW LIPID LOWERING THERAPIES

Fabrizio Delnevo, Gianmarco Annibali, Catia De Rosa, Silvia Muccioli, Stefania Civera, Marzia Colopi, Sergio Bongioanni, Nicola Gandolfo, Giuseppe Musumeci
Cardiology, AO Ordine Mauriziano, Torino, Torino, Italy

Background and Aims: We evalueted safety and efficacy of an early triple lipid lowering therapy (LLT) with PCSK9i in patients witn acute coronary syndromes (ACS).

Methods: This is a single-center experience that enrolled patients consecutively arrived for ACS. The prescribed LLT at discharge was evalueted. The triple therapy with high-intensity statins plus ezetimibe and PCSK9i was raccomended at discharged in patients already treated with statin ad LDL-C > 100 mg/dl. Six month visit follow-up was performed to determine achievement of treatment goal, compliance with therapy, side effects, and any cardiovascular disease events after discharge

Results: We enrolled 1024 patients, 95% discharged with high intesitive statin plus ezetimibe and 236 (23%) treated with the addition of PCSK9i (triple therapy) in the in-hospital setting or at discharge via the fast-track pathway, In patients with triple therapy we observed a dramatic lowering of LDL-C values at 6-month follow-up (LDL-C at baseline 125 mg/dl vs 22 mg/dl at 6 months, $p<0.001$), with more than 98% of patients having LDL-C values at target (<55 mg/dl) . We reported only 3% of side effects at the 6-month that were mainly muscle pain and skin reactions at the injection site and lead to discontinuation theapy in only 2% of patients. Regarding the recurrence of cardiovascular events, about 1% of patients experienced new coronary revascularization.

Conclusions: In conclusion, the use of an early hypolipidemic approach with PCSK9i in-hospital or at discharge enables rapid achievement of optimal LDL-C values and reduced morbidity rates while maintaining absolute safety profiles with very low LDL-C values.

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364 / #1126

Topic: *AS04 Clinical Vascular Disease / AS04.14 SGTL2 inhibitor and cardiovascular diseases*

RESULTS FROM THE NATIONWIDE FRENCH GLUCOSE (GLP1RA AND SGLT2I USE BY CARDIOLOGISTS SURVEY).

POSTER ON BOARD: AS04.14 SGTL2 INHIBITOR AND CARDIOVASCULAR DISEASES

Pierre Sabouret[1], Raul Santos[2], Ali Sharareh[3], Serge Cohen[3], Leon Ouazana[3], Dominique Guedj-Meynier[3], Thierry Garban[3], Julien Rosencher[3], Julien Adjedj[3], Jean Claude Dib[3], Patrick Khanoyan[3], Mattia Galli[4], Lale Tokgozoglu[5], Giuseppe Biondi-Zoccai[6], Maciej Banach[7], Nicolas Lellouche[8], François Dievart[3]
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Background and Aims: Guidelines on Diabetes type 2 have recently been updated due to new data from randomized clinical trials. However, real world data are lacking regarding the implementation among the community of French cardiologists.

Methods: The survey was performed during October and November 2022 in France with an online questionnaire on the site of the National College of French Cardiologists. Four mailings were sent to cardiologists to invite them to answer to the questionnaire.

Results: 60% of cardiologists declared they prescribed or advised to prescribed antidiabetic agents. Among these responders, SGLT2i, Metformine, GLP1RA, DPP4i, Insulin, Sulfamids represented 73%, 65%,44%, 15%,7% and 5% respectively of the initiation. For GLP1RA, the main barriers reported were the lack of experience with injectable, lack of time to prescribe, and because cardiologists consider that's the field of diabetologists in 34%,30%,31% respectively.
The 3 main indications of preferred strategy by GLP1RA versus SGLT2i were expected weight loss, presence of documented atherosclerosis and a glycated hemoglobin above 8%, whereas the 3 main indications to prescribe a SGLT2i versus a GLP1RA were presence of HF and/or CKD patients and the oral formulation.

Conclusions: In this contemporary French survey about the management of type 2 diabetic patients, cardiologists seem well informed of the guidelines, preferred indications of both new classes, with identified main barriers to prescription of GLP1RA which highlight the need of a better network with other healthcare providers to better implement this anti-diabetic drug, whereas SGLI2i are easily initiated, mainly for non-diabetic indications (HF, CKD).

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

365 / #1271

Topic: *AS04 Clinical Vascular Disease / AS04.14 SGTL2 inhibitor and cardiovascular diseases*

INFLUENCE OF DAPAGLIFLOZIN ON LIPID PARAMETERS IN PATIENTS WITH CORONARY ARTERY DISEASE AND TYPE 2 DIABETES MELLITUS

POSTER ON BOARD: AS04.14 SGTL2 INHIBITOR AND CARDIOVASCULAR DISEASES

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Background and Aims: Sodium glucose co-transporter 2 inhibitors (SGCT-2) have shown several favorable effects in patients with type 2 diabetes mellitus (T2DM). Aim of the study was to evaluate influence of sodium glucose co-transporter 2 inhibitor – dapagliflozin on lipid spectrum in patients with coronary artery disease (CAD) and T2DM.

Methods: 86 patients with CAD and T2DM were enrolled in the prospective study (aged 45-73 years, mean age 61.2±12.54 years, male=54%). Patients were divided into 2 groups and Group I were assigned dapagliflozin along with standard therapy and Group II only standard therapy. Anthropometry, laboratory and instrumental data were assessed at baseline and after the 12 weeks of the treatment. All statistical analysis were performed using STATA software.

Results: During the treatment total cholesterol has been decreased in each group from baseline, however there were not statistically significant changes between groups (P>0.05). High-density lipoprotein – cholesterol (HDL-C) has been improved in Group I than Group II (21% vs 11%, P<0.05). Low-density lipoprotein-cholesterol (LDL-C) and remnant cholesterol have been reduced significantly in Group I than group II (P<0.05). Besides, non HDL-cholesterol has been decreased significantly in Group I than Group II (P<0.05). Regarding the triglycerides there were not statistically significant changes between groups (P>0.05). When we analyzed by gender there were not observed any statistically significant changes between sexes (P>0.05).

Conclusions: SGCT-2 – dapogliflozin improve HDL-C and reduce non-HDL and remnant cholesterol in patients with CAD and T2DM. Further studies are needed with large amount of patients to understand exact mechanisms.

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366 / #905

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

CLINICAL AND ECHOCARDIOGRAPHIC CHARACTERISTICS IN PATIENTS WITH POST-COVID SYNDROME

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: The persistence of symptoms beyond acute COVID-19 is known as Post-COVID syndrome (PCS). There is controversy regarding its physiopathology and characterisation. The purpose of this work is to describe the clinical and echocardiographic characteristics, along with inflammatory conditions in patients (pat) with PCS.

Methods: In this prospective cohort study we included pat between 20 and 60 years old, who had been diagnosed with acute COVID-19, 3 to 12 weeks before enrollment. The trial was made between june 2021 and february 2022. Patients were divided into two groups: those with PCS (CSP, n=13) and those who were asymptomatic (CAP, n=14). A third control group was incorporated, with patients without diagnosis of COVID 19 in the last year (CTR, n=12).

Results: Pat in group CSP were older than CAP and CTR (CSP (46 ± 13) vs. CAP (32 ± 9,5) vs. CTR (36 ± 14); p=0,05), with no difference in sex, systolic blood pressure or BMI. Pat in CAP presented dyspnea 69%, palpitations 54% and asthenia 46%. In this group, a higher Borg scale value was seen (CTR(1,6 ± 1) vs. CAP (1,2 ± 1)vs. CSP (3,5 ± 1,9); p=0,017). A no significant increase in ferritin values was seen in CSP. Moreover, a lower EA ratio was detected in this group (CTR (1,6 ± 0,5) vs.CAP (2,1 ± 0,8) vs.CSP (1,16 ± 0,4); p= 0,0052).

Conclusions: Patients in CSP had higher Borg scale score and a lower EA ratio. The age and inflammatory markers could explain the persistence of symptoms of PCS.

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367 / #1161

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

NITRIC OXIDE RELEASING NANOFIBER STIMULATES REVASCULARIZATION IN RESPONSE TO ISCHEMIA VIA CGMP-DEPENDENT PROTEIN KINASE

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: Nitric oxide (NO) promotes angiogenesis via various mechanisms; however, the effective transmission of NO in ischemic diseases is unclear. we tested whether NO-releasing nanofibers modulate therapeutic angiogenesis in an animal hindlimb ischemia model.

Methods: Male C57BL/6 mice with surgically-induced hindlimb ischemia were treated with NO-releasing 3-ethylaminopropyltrimethoxysilane (MAP3)–derived nanofiber or control fiber, by applying them to the wound for 20 min, three times every two days. The amount of NO from the nanofiber into tissues was assessed by NO fluorometric assay. The activity of cGMP-dependent protein kinase (PKG) was determined by western blot analysis. Perfusion ratios were measured 2, 4, and 14 days using laser doppler imaging(LDPI). On day 4, Immunohistochemistry (IHC) with F4/80 and gelatin zymography were performed. IHC with CD31 was performed on day 14. To determine the angiogenic potential of NO-releasing nanofibers, aorta ring explants were treated with MAP3 or control fiber for 20 min, and the sprout lengths were examined after 6 days.

Results: As per either LDPI ratio or CD31 capillary density measurement, angiogenesis in the ischemic hindlimb was improved in the MAP3 nanofiber group; further, the total nitrate/nitrite concentration in the adduct muscle increased. The number of macrophage infiltrations and MMP-9 activity decreased. Vasodilator-stimulated phosphoprotein (VASP), one of the major substrates for PKG, increased phosphorylation in the MAP3 group. MAP3 nanofiber or NO donor SNAP (s-nitroso-n-acetyl penicillamine)-treated aortic explants showed enhanced sprouting in an ex vivo aortic ring assay, which was partially abrogated by KT5823, a potent inhibitor of PKG.

Conclusions: These findings suggest that the novel NO-releasing nanofiber, MAP3 activates PKG and promotes therapeutic angiogenesis in hindlimb ischemia.

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368 / #1188

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

THE ASSOCIATION OF SARC-F SCORE WITH ATHEROSCLEROSIS IN ELDERLY RESIDENTS OF CARE HOMES.

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: Ischemic Heart Disease, Cerebrovascular Disease and Peripheral Arterial Disease are the leading atherosclerosis-related diseases and the main admission-associated conditions in Residential Care and Nursing Homes. The SARC-F questionnaire is a simple and reproducible screening tool for low physical performance. In this cross-sectional study, the physical performance of elder Care Homes' residents in association with atherosclerosis-related diseases was assessed.

Methods: 389 elderly (older than 60 y.o.) residents of Care Homes were recruited. Health records of all participants were analysed for the presence of established atherosclerosis-related conditions, including Ischemic Heart Disease, Cerebrovascular Disease and Peripheral Arterial Disease. For physical performance evaluation, the SARC-F questionnaire was used.

Results: 54% (211) residents were diagnosed with atherosclerosis-related diseases. The mean SARC-F score of atherosclerotic residents was reliably higher compared to participants without atherosclerosis-related diseases (5.27±0.18 vs. 4.61±0.25, p-value=0.005). The prevalence of atherosclerosis was significantly higher among residents with SARC-F ≥ 4 (low physical performance threshold) (60.2% vs. 37.0%, p-value=0.000). In addition, the prevalence of low physical performance was also significantly higher among residents with atherosclerosis-related diseases (85.5% vs. 64.6%, p-value=0.000). The Tay-b Kendall correlation revealed the low positive relationship between atherosclerosis-related diseases and SARC-F score (r=0.086, p-value=0.049).

Conclusions: The atherosclerosis-related diseases are associated with higher rates of low physical performance among elderly residents of Care Homes.

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369 / #192

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

CLINICAL DETERMINANTS OF GROWTH DIFFERENTIATION FACTOR 15 PLASMA LEVELS IN OUTPATIENTS WITH PERIPHERAL ARTERIAL DISEASE

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: Growth differentiation factor 15 (GDF-15) is a robust prognostic biomarker in patients with cardiovascular disease. A better understanding of its pathophysiology in patients with atherosclerosis is desirable. We aimed to study the associations of circulating levels of GDF-15 with clinical variables in outpatients with peripheral arterial disease (PAD).

Methods: A cross-sectional study (Study of Atherosclerosis in Vastmanland, Västerås, Sweden) included consecutive outpatients with carotid or lower extremity PAD (n=439). The mean age was 70 (SD 7) years, and 41% were female. Plasma levels of GDF-15 were obtained together with clinical data, including medical history, biochemical data, echocardiographic measures of left ventricular geometry and function, ankle-brachial index (ABI), and carotid ultrasonographic data on intima-media thickness (IMT) and occurrence of carotid stenosis. The relations between GDF-15 plasma concentrations and the clinical variables were evaluated using uni- and multivariable linear regression models. In the multivariable model, all prespecified variables were included.

Results: In the univariable models, GDF-15 levels were significantly related to several clinical variables (table 1). The multivariable analysis identified independent relations of GDF-15 with age, body mass index, diabetes, physical activity, renal function, low-density-lipoprotein cholesterol, and high-sensitive C-reaction protein (R^2=0.51). In contrast, much weaker associations with GDF-15 was observed for cardiac geometry and function, ABI, IMT, or carotid

stenosis.

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Table 1. *Uni- and multivariable associations of log GDF-15 with clinical variables in patients with peripheral arterial disease.*

	Univariable analysis			Multivariable analysis (R^2 = 0.51)		
	Coefficient	**95% CI**	**p-value**	**Coefficient**	**95% CI**	**p-value**
Clinical variables						
Male sex	0.17	0.07 to 0.28	0.001	0.06	-0.03 to 0.14	0.173
Age (years)	0.21	0.14 to 0.28	<0.001	0.08	0.03 to 0.12	<0.001
Ever smoked	0.08	-0.04 to 0.20	0.169	0.09	-0.01 to 0.19	0.055
BMI (kg/m2)	0.03	-0.03 to 0.10	0.343	-0.04	-0.09 to -0.00	0.038
Hypertension	0.18	0.06 to 0.30	0.003	-0.05	-0.144 to 0.05	0.322
Diabetes	0.46	0.35 to 0.57	<0.001	0.37	0.24 to 0.50	<0.001
Previous MI	0.22	0.09 to 0.35	0.001	0.08	-0.03 to 0.19	0.162
Previous stroke	0.18	0.01 to 0.35	0.040	0.09	-0.04 to 0.21	0.180
Physical activity			<0.001			0.002
Low	0 (reference)			0 (reference)		
Moderate	-0.23	-0.35 to -0.11		-0.16	-0.26 to -0.07	
High	-0.35	-0.50 to -0.21		-0.17	-0.28 to -0.05	
Systolic BP (mmHg)	0.00	-0.07 to 0.07	0.98	-0.01	-0.05 to 0.03	0.679
Biochemical variables						
eGFR*			<0.001			<0.001
From 60 to 70 (mL/min/1.73m^2)	-0.19	-0.23 to -0.14		-0.14	-0.18 to -0.10	
From 70 to 80 (mL/min/1.73m^2)	-0.09	-0.16 to -0.02		-0.06	-0.12 to 0.00	
LDL*			<0.001			0.009
From 1.5 to 2.5 (mmol/L)	-0.33	-0.50 to -0.16		-0.22	-0.34 to -0.09	
From 2.5 to 3.5 (mmol/L)	-0.04	-0.15 to 0.08		0.03	-0.06 to 0.11	
hsCRP (mg/L)	0.21	0.14 to 0.28	<0.001	0.08	0.04 to 0.12	<0.001
HbA1c (mmol/mol)	0.15	0.11 to 0.20	<0.001	0.00	-0.06 to 0.05	0.954
Peripheral atherosclerotic burden						
ABI	0.21	0.11 to 0.31	<0.001	0.07	-0.01 to 0.16	0.105
IMT (mm)	0.11	0.04 to 0.17	<0.001	0.00	-0.04 to 0.04	0.919
ICA-stenosis	0.11	-0.01 to 0.23	0.060	0.07	-0.03 to 0.17	0.193
Cardiac geometry & function						
LV mass index (g/m^2)	0.16	0.10 to 0.23	<0.001	0.04	-0.01 to 0.09	0.096
LVEF (%)	-0.03	-0.08 to 0.23	0.278	0.03	-0.01 to 0.08	0.164
LA volume index (mL/m^2)	0.12	0.06 to 0.17	<0.001	0.04	-0.01 to 0.08	0.109

Presented are linear regression models with GDF-15 (transformed to its natural logarithm) as the dependent variable. For continuous variables, coefficients represent the change in log-GDF-15 for every one standard deviation increase in the independent variable unless otherwise stated.

*Visual inspection of plots with clinical variables against log GDF-15 indicated a non-linear relationship for some of the variables. These variables were analyzed using restricted cubic splines with 3 knots in the regression models.

Abbreviations: ABI, ankle-brachial index; BMI, body mass index; BP, blood pressure; CI, confidence interval; CV, cardiovascular; EF, ejection fraction; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitive C-reaction protein; ICA, internal carotid artery; IMT, intima-media thickness; LDL, low-density-lipoprotein cholesterol; LV, left ventricle; MI, myocardial infarction.

Conclusions: Circulating GDF-15 levels were independently associated with several clinical variables among outpatients with PAD, where diabetes had the strongest association. However, weaker associations were seen in variables reflecting atherosclerotic burden or cardiac dysfunction. Further studies are needed to confirm the generalizability of these findings.

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370 / #619

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

ENDOGENOUS SUPPRESSION OF DOUBLE-STRANDED RNA-INDUCED MDA5 AUTOINFLAMMATORY SIGNALING IS ESSENTIAL FOR THE MAINTENANCE OF VASCULAR INTEGRITY IN ADULT MICE

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: Long double-stranded RNA (dsRNAs) are recognized as danger-associated molecules by the cytosolic innate immune sensors inducing thus innate immune responses. RNA editing is a post-transcriptional modification induced by the binding of Adenosine Deaminases Acting on RNA (ADARs) to dsRNAs. We have recently reported that ADAR1 is the main RNA editor in endothelial cells (ECs) but the role of ADAR1 in vascular physiology remains yet elusive.

Methods: Mice carrying a conditional *Adar1* or *Ifh1* allele were crossed with either a *Tie2*-Cre or tamoxifen-inducible VE-Cadherin-CreERT2 mouse line. Culture of primary human and murine ECs, dsRNA metabolism studies, gene-silencing/overexpression approaches and fluorescence-based confocal microscopy were used to assess the role EC-ADAR1 and corroborate the phenotypes observed in vivo

Results: Depletion of the endothelial ADAR1 is embryonically lethal, evidencing its pivotal role in vascular homeostasis. In adult mice, inducible EC-ADAR1 ablation elicited premature death due to pulmonary vascular leakage and pleural effusion, reflecting a compromised ECs barrier function. Mechanistically, the silencing of the EC-ADAR1 disrupted long-to-short dsRNA metabolism, leading to an accumulation of cytoplasmic long dsRNAs, to aberrant levels of interferon-β and activation of innate immune system. Finally, activation of the cytosolic dsRNA sensors caused the dissociation of β-catenin from VE-cadherin in EC junctions. Interestingly, the silencing of the dsRNA sensor MDA5 restored the integrity of the ADAR1-deficient endothelium and was sufficient to prevent the lethal phenotype.

Conclusions: Endogenous suppression of double-stranded RNA-induced MDA5 autoinflammatory signaling by the RNA editor ADAR1 is essential for the maintenance of vascular integrity in adult mice.

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371 / #1566

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

ADHERENCE TO TREATMENT AND RISK FACTOR CONTROL IN PATIENTS AFTER CORONARY STENTING DEPENDING ON REGULAR OR REMOTE FOLLOW-UP

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: The remote monitoring after coronary stenting (CS) may facilitate adherence to treatment and risk factor control. Aim: to evaluate the adherence to drug therapy and risk factor control in patients after CS receiving remote monitoring or care with outpatient visits.

Methods: 279 consecutive stable CAD patients after CS were randomized into groups of regular outpatient visits (group 1, n=96, cardio exam and blood testing), remote monitoring (group 2, n=95, videoconference, telephone care and blood tests interpretation) and control group (group 3, n=88, cared by a physician at the residence place). Adherence to medical therapy using four-item Morisky Green Levine Medication Adherence Scale was assessed at baseline, 1, 3, 6 and 12 mo after CS in groups 1 and 2 and at baseline and 12 mo in group 3.

Results: An increase in the number of highly adherent individuals vs. baseline (33 vs. 17 and 42 vs. 13, respectively, $p < 0.05$), was observed in groups 1 and 2. The non-adherence to DAAT was 1-2%, while 32,3%, 29,5%, 57.9% of patients in groups 1, 2, 3 reduced/ceased statins 12 mo after CS ($p<0.05$ group 3 vs. 1 and 2). BP level decrease was observed in groups 1 and 2, the number of smokers decreased in group 2 (46.3 to 31.6%, $p < 0.05$).

Conclusions: The remote monitoring is a safe and effective strategy for improving adherence to treatment and risk factor control in patients after CS.

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372 / #1567

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

CORONARY ATHEROSCLEROSIS PROGRESSION AFTER CORONARY STENTING, DEPENDING ON REGULAR OUTPATIENT OR REMOTE MONITORING FOR 12 MONTHS

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: The remote monitoring is a safe strategy for maintaining the adherence to treatment in CAD patients.The purpose was to determine the incidence of coronary atherosclerosis progression in patients after coronary stenting (CS) receiving remote monitoring or care with outpatient visits.

Methods: 279 consecutive stable CAD patients (61.5±9.5 years) underwent scheduled CS were randomized into groups of regular outpatient visits (group 1, n=96), remote monitoring (group 2, n=95) and control group (group 3, n=88). The visits (cardio exam and blood testing) and remote monitoring (videoconference, blood tests interpretation) were performed at 1, 3, 6 and 12 months after CS (groups 1 and 2). Patients in group 3 were cared by a physician at the residence place. 12 months after CS the test for stress-induced myocardial ischemia was performed in each patient.

Results: 96 patients (34.4%) required repeat coronary angiography (CA) – 30(31.2%)/20(21.1%)/46(52.3%) in groups 1/2/3*, respectively ($p<0.05$ gr. 3 vs. gr. 1 and 2). Restenosis of the previously stented segment was detected in 8 (2.9%) patients, progression of coronary atherosclerosis - in 38 (13.6%) ($p<0.01$ vs. rate of restenosis). Progression of coronary atherosclerosis was observed in 10(10.4%)/9(9.5%)/19(21.6%)* of cases in groups 1,2,3, respectively (*$p<0.05$ gr. 3 vs. gr. 1 and 2), the rate of restenosis was comparable in the groups.

Conclusions: The progression of coronary atherosclerosis was the main cause for repeat CA 12 months after CS. The groups of patients receiving active regular outpatient or remote monitoring demonstrated a lower rate of coronary atherosclerosis progression and repeat CA.

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373 / #1497

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

ASSOCIATION OF CORONARY COMPUTED TOMOGRAPHIC ANGIOGRAPHY PARAMETERS DEFINED IN PATIENTS WITH ACUTE CORONARY SYNDROME WITH RISK OF LONG-TERM SIGNIFICANT CARDIAC EVENTS

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: To explore the association of characteristics defined by coronary computed tomographic angiography (CTCA) in acute coronary syndrome (ACS) with risk of long–term significant cardiac events.

Methods: We examined cohort of 201 patients (161 male – 80,1%, 58,2±10,7 years) with ACS (71,1% patients with myocardial infarction – MI and 28,9% with unstable angina – UA). CTCA (320–row CT scanner) performed in 3–6 days after percutaneous coronary intervention (PCI), using semi-automatic quantitative and qualitative analysis of coronary arteries (CA). In non–calcified plaques (NCPs) we assessed characteristics including CTCA instability signs (CTCAIS) – low-attenuation plaques (LAP) quantified by HU<30 and <46, napkin-ring sign, positive remodeling, spotty calcifications, rough contour.

Results: For 33,8 [18,8;46] months after ACS composite primary endpoint (CPE) of cardiac events defined as nonfatal MI, UA, cardiac death, late coronary revascularization and ischemic stroke occured in 42 (20,9%) patients. We identified significant association CPE risks with such CTCA characteristics as CA number with NCPs (adjusted Hazard Ratio – HR=2.997, 95% Confidence Interval – CI:1.850–4.856,p<0,0001, Harrell's C index – C=0,87); NCP number (HR=1.494;CI:1.190–1.875,p<0,0005,C=0,86); stenosis>50% (HR=3.933,CI:1.191–12.988,p<0,025,C=0,83); number of NCP with stenosis>50% (HR=1.991,CI:1.451–2.733,p<0,0001,C=0,87); maximal plaque length (HR=1.176,CI:1.083–1.278, p<0,0001,C=0,87); maximal plaque burden (HR=1.070,CI:1.027–1.115,p<0,0014,C=0,86); NCP with spotty calcification (HR=2.458,CI:1.041-5.804, p<0,04,C=0,83) and their number (HR=1.494,CI:1.184–1.886,p<0,0007,C=0,85); NCP with LAP<46HU (HR=5.843,CI:2.326–14.676,p<0,0002,C=0,87) and their number (HR=5.845,CI: 2.773–12.320,p<0,0001,C=0,88).

Conclusions: The results of this study in patients with ACS demonstrated definite association long–term significant cardiac events with several baseline CTCA characteristics related not only to CA obstruction, but also to plaque's number and morphological features.

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376 / #460

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM, NEUROHUMORAL AXIS AND CARDIOVASCULARMORTALITY IN LURIC

POSTER ON BOARD: AS04.15 OTHER

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Background and Aims: Although neurohormones and Renin-Angiotensin-Aldosterone-System (RAAS) components
are important predictors of cardiovascular mortality (CVM), their importance
for predicting outcomes in patients with/without RAAS-blockers and different degrees
of arterial stiffness is less understood.

Methods: We therefore analyzed long-term data from the Ludwigshafen Risk and Cardiovascular Health (LURIC) study in 3316 patients
subdivided according to pulse pressure (PP) and RAAS-blocker use.

Results: Patients on RAAS-inhibition had higher renin and noradrenaline, lower aldosterone and aldosterone/
renin quotient (ARQ). Renin and noradrenaline significantly predicted CVM in
patients without RAAS-blocker (HR=1.17, 1.15) and in patients receiving angiotensinconverting-enzyme (ACE) inhibitors (HR = 1.17, 1.29), whereas aldosterone predicted
CVM only in patients receiving ACE-inhibitors (HR = 1.13). CVM was predicted independently
from PP by renin, noradrenaline and angiotensin II. Independently from
RAAS inhibition renin decreased and ARQs increased with rising PP.Furthermore,
noradrenaline increased with PP, but only without ACE-inhibition.HR for CVM in
the ACE-inhibitor group were 1.29, 1.28, 1.29 for renin in the first, second and third
PP quartiles and 1.22, and 1.19 for aldosterone in the second and fourth quartile.
Furthermore, we showed that noradrenaline predicts CVM in all PP quartiles in
patients with ACE-inhibition. In the RAAS-blocker-free group, HR for renin for
CVM were 1.36 and 1.18 in the third and fourth PP quartiles, but neither aldosterone
nor noradrenaline were predictive for CVM within the PP quartiles

Conclusions: Renin and noradrenaline are strong predictors of CVM regardless of RAAS blockade, whereas
aldosterone is predictive only in the ACE-inhibitor group. Catecholamines but not
renin are associated with rising PP.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

Board Onsite / #449

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

COMPARISON OF EFFECTS OF BLOOD PRESSURE, BLOOD GLUCOSE AND LIPID VARIABILITY ON CARDIOVASCULAR PROGNOSIS IN DIABETIC PATIENTS

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Metabolic abnormalities such as dyslipidemia, glucose and high blood pressure are common in diabetic patients. Variabilities in these measures have been reported as a potential residual cardiovascular risk factors. This study aimed to analyze the relationship between variabilities of blood pressure, blood glucose, total cholesterol and triglyceride levels (metabolic variability parameters) and their effects on cardiovascular prognosis in diabetic patients.

Methods: A total of 24,857 diabetic patients aged 40 years or older who had their blood pressure, blood glucose, total cholesterol, and triglyceride levels measured three or more times for three years after January 1, 2017 at three tertiary general hospitals were selected. They were divided into high/low groups based on their systolic blood pressure (SBP), blood glucose, total cholesterol (TC) and triglyceride coefficient of variation (CV) over a 3-year period. The incidence of major adverse cardiovascular events (MACE), a composite of cardiovascular death, myocardial infarction, and stroke, was compared between groups.

Results: The correlation between the CV of SBP and the CV of glucose was highest, and the correlation between the CV of SBP and the CV of triglycerides was the lowest. All groups with high CV had a higher incidence of MACE than those with low CV (table1). Cox regression analysis suggested sex, alcohol, creatinine, SCORE2, SBP CV, TC CV, triglyceride CV, mean TC, and mean glucose as independent risk predictors for MACE in diabetic

patients.

Table 1. Incidence of MI, stroke, cardiovascular death and MACE

	SBP CV			TC CV			triglyceride CV			Glucose CV		
	Low	High	*p*	Low	High	*p*	Low	High	*p*	Low	High	*p*
MI	278 (2.2)	877 (7.1)	<.01	312 (2.5)	843 (6.8)	<.01	468 (3.8)	687 (5.5)	<.01	262 (2.1)	893 (7.2)	<.01
Stroke	38 (0.3)	226 (1.8)	<.01	61 (0.5)	203 (1.6)	<.01	116 (0.9)	148 (1.2)	0.05	48 (0.4)	216 (1.7)	<.01
CVD	2 (0.02)	40 (0.3)	<.01	9 (0.1)	33 (0.3)	<.01	24 (0.2)	18 (0.1)	0.40	4 (0.03)	38 (0.3)	<.01
MACE	316 (2.5)	1,087 (8.8)	<.01	370 (3.0)	1,033 (8.3)	<.01	581 (4.7)	822 (6.6)	<.01	311 (2.5)	1,092 (8.8)	<.01

CV, coefficient of variation; CVD, cardiovascular death; MACE, major adverse cardiovascular event; MI, myocardial infarction; SBP, systolic blood pressure; TC, total cholesterol.

Conclusions: Metabolic variability parameters, especially SBP CV, TC CV and TG CV, are important residual risk factors for cardiovascular events in diabetic patients.

91ST EAS CONGRESS
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Board Onsite / #1328

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

WHAT DO FRENCH CARDIOLOGISTS THINK ABOUT INHIBITOR OF SGLT2 FOR PATIENTS WITH TYPE 2 DIABETES? A SURVEY FROM THE NATIONAL COLLEGE OF FRENCH CARDIOLOGISTS (CNCF)

POSTER ON BOARD: AS03.01 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES AND RISK FACTORS

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Background and Aims: Background : to assess criteria that lead French cardiologists to prescribe a SGLT2 inhibitor (SGLT2i) for patients with type 2 diabetes (T2D).

Methods: Method : A survey of 20 questions was sent 3 times in October 2022 to 1 200 cardiologists in private practice in France.

Results: 102 answers were collected (23 % from women cardiologists, 40 % of cardiologists with more than 30 years of pratice). Among patients with T2D seen by cardiologists, 25 % received an iSGLT2. Cardiologists prescribed or recommended a SGLT2i for 82 % of their patients with T2D in secondary prevention or at high CV risk who don't yet receive one. The main reasons of non prescription were " I prefer that a diabetologist do it". They "always or often" prescribed an iSGLT2 for 82 % of their patients without diabetologists and 54 % of those followed by diabetologists. The two main criteria for choosing an iSGLT2 are the oral formualtion and the proven clinical efficacy on MACE, in chronic kidney disease (63%), secondary prevention (57%). and surprisingly when HbA1c level wasn't at goal (47%).

Conclusions: French cardiologists are aware of clinical benefits provided by SGLT2i in T2D patients and indeed 82 % of cardiologists prescribed or
recommended this therapeutic class especially when patiens don't benefit from a management by diabetologists. Knowledge remains suboptimal about efficacy on glycated hemoglobin compared with GLP1RA, about optimal combinations and management with insulin, advocating further efforts in medical education.

91ST EAS CONGRESS
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#1272

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

MONOCYTE ACTIVATION IN PATIENTS WITH CORONARY HEART DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: Coronary heart disease (CHD) and atherosclerosis are the most significant cardiovascular diseases, which account for the majority of deaths from this pathology. Today, it's well known that chronic systemic inflammation plays a leading role in the pathogenesis of CHD. The aim of this study was to evaluate the pro-inflammatory activation of monocytes in patients with CHD.

Methods: Totally, 33 patients with CHD and 23 healthy subjects were included in the study. The groups were comparable by traditional cardiovascular risk factors such as age, gender, body mass index, blood pressure and history of arterial hypertension, family history of CHD, blood lipids profile. CD14+ monocytes were isolated from whole blood by the standard ficoll gradient method followed by magnetic cell separation. Non-stimulated and stimulated after 24-hour incubation with LPS, monocyte secretion of the pro-inflammatory cytokine TNF-α was assessed by ELISA.

Results: It was shown that in patients with coronary heart disease pro-inflammatory activation of circulating monocytes by TNF-α was higher than in healthy subjects, and amounted 33.1 vs. 28.2, but this difference didn't reach the statistical significance, p=0.141. At the same time, patients in CHD group with severe carotid atherosclerosis had significantly increased monocyte activation, namely 35.9 vs. 23.4 in carotid atherosclerosis free group, p=0.047.

Conclusions: Increased pro-inflammatory activation of monocytes was determined in CHD patients with severe carotid atherosclerosis that confirms the role of chronic inflammation in atherosclerosis development. Further research is needed to identify the mechanisms of monocyte activation in patients with CHD. This grant was supported by Russian Science Foundation (Grant #22-15-00134).

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1289

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

FEATURES OF BLOOD PARAMETERS IN ELDERLY AND SENILE PATIENTS WITH CARDIOVASCULAR COMORBIDITY AND CHRONIC KIDNEY DISEASE

VIRTUAL E-POSTER SESSION

Elena Efremova, Alexander Shutov
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Background and Aims: Chronic kidney disease (CKD) is a defining pathology in the structure of comorbidity of patients of the older age group with cardiovascular diseases. The aim of this study was to investigate the features of blood parameters, including the lipid profile, in patients with cardiovascular comorbidity, depending on the presence of 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).The content of hemoglobin, the number of erythrocytes, the number of leukocytes with a leukocyte formula, the number of platelets, lipid profile, blood ions were assessed. Follow-up period was 1 year, primary endpoint - all-cause mortality.

Results: Compared to patients without CKD, elderly patients had lower levels of hemoglobin (p=0.02), blood erythrocytes (p=0.04). Hemoglobin indices depended on the severity of CKD (comparison of CKD stages 3a and 4, p=0.001; CKD stages 3b and 4, p=0.009).There were differences in lipid metabolism in patients with CKD: higher triglycerides (p=0.02) compared with patients without CKD. More than half of the elderly and senile patients with CKD had hypercholesterolemia (171; 61.7%), hypertriglyceridemia was observed in 62 (22.4%) patients. Half of the elderly and senile patients with CKD (139; 47.3%) had serum potassium level more than 4.5 mmol/l, every fifth (54, 19.5%) - the serum potassium level exceeded 5 mmol/l. An increase in serum potassium concentration was noted with the progression of CKD ($p<0.05$).

Conclusions: Features of blood parameters in elderly patients are associated with comorbidity, including CKD

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#1288

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

APOB-DEPLETED SERUM-MEDIATED MACROPHAGE CHOLESTEROL EFFLUX IS PRESERVED IN ERYTHEMATOTELANGIECTATIC ROSACEA

VIRTUAL E-POSTER SESSION

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Background and Aims: Rosacea is an inflammatory condition with a high prevalence of cardiovascular (CV) disease. Excess cholesterol removal from macrophages prevents atherosclerosis although inflammation may compromise HDL function aggravating CV risk.

Methods: The present investigation aimed to evaluate, in subjects with erythematous-telangiectatic rosacea, the profile of plasma lipids, and the apoB-depleted serum-mediated ^{14}C-cholesterol efflux from macrophages. Subjects with rosacea (n = 41; 30F, 11M) were recruited at the Dermatology Clinic of the Universidade Nove de Julho and matched, by sex and age, with control subjects (n = 41; 30F, 11M). Anthropometric and clinical data were obtained from all individuals. Plasma lipids and apolipoproteins were determined, respectively, by enzymatic and immunoturbidimetric methods. ApoB-depleted serum was used as a cholesterol acceptor from macrophages, previously overloaded with acetylated LDL and ^{14}C-cholesterol. Comparisons were done by the Mann-Whitney test.

Results: The mean disease duration was 1 to 10 years in 73% of individuals with rosacea, predominantly on the face (95%). Most individuals (76%) were not undergoing any type of treatment. The control and rosacea groups were similar regarding BMI, waist circumference, smoking prevalence, alcohol consumption, menopausal status, plasma lipids, and atherogenic indices (apoB/apoAI; CT/apoB; TG/HDLc). The efflux of ^{14}C-cholesterol from macrophages [% (25-75% interquartile intervals)], mediated by apoB-depleted serum, was similar between the control [8.3% (5.9-9.6)] and rosacea [8.2% (5.7-11.2)] groups.

Conclusions: In individuals with erythematous-telangiectatic rosacea, matched with controls regarding the main CV risk factors, cholesterol removal from macrophages is preserved, not constituting an aggravation of CV risk in this disease.Funding: FAPESP, CNPq, Brazil

91ST EAS CONGRESS
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#468

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

THE EFFECTIVENESS OF SINUS RHYTHM RESTORATION IN PATIENTS WITH LONG-TERM EPISODES OF PERSISTENT ATRIAL FIBRILLATION: THE ASSOCIATION WITH CARDIOVASCULAR RISK FACTORS AND STRUCTURAL HEART DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the association of cardiovascular risk factors and structural heart disease with the effectiveness of sinus rhythm (SR) restoration in patients with persistent atrial fibrillation lasting ≥90 days (AFper90+).

Methods: The cohort study analyzed clinical and instrumental data from 115 AFper90+ patients, who underwent an elective direct current cardioversion (DCCV). Patients were subdivided into the compared groups with effective (G1: n=59 [51,3 %]) and ineffective DCCV (G2: n=56 [48,7 %]) (restored and non-restored SR, respectively).

Results: G2 was characterized by more severe heart failure and more frequent percutaneous coronary intervention cases, as opposed to G1. Diabetes mellitus (DM) tended to be more frequent in G2, as compared to G1. According to the transthoracic echocardiography data, G2 patients (vs. G1) presented with more left ventricular dilatation and pulmonary hypertension cases. Transesophageal echocardiography revealed a decrease of left atrial appendage flow velocity (LAAFV) ≤40 cm/s in 65 % of patients. Left atrial spontaneous echo contrast (LASEC) was visualized in 15 (25 %) G1 patients, in contrast to G2 (n=54 [96 %]). The frequency of dense LASEC (grades «3+» and «4+») was numerically, but insignificantly higher in G2 (vs. G1: 25 % vs. 15 %, respectively; p=0,169). The multivariable logistic regression analysis revealed LASEC as an independent predictor of SR restoration. Additionally, DM and lower LAAFV were strongly associated with dense LASEC.

Conclusions: Freedom from LASEC appeared to be the independent predictor of effective DCCV in AFper90+ patients, with DM and lower LAAFV being strongly associated with dense LASEC.

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#551

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

CLINICAL CHARACTERISTICS AND MAJOR ADVERSE EVENTS IN RURAL DWELLERS WITH ARTERIAL HYPERTENSION AND HIGH VISIT-TO-VISIT BLOOD PRESSURE VARIABILITY

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the clinical characteristics and the history of major adverse cardio- and cerebrovascular events (MACCE) in rural dwellers with arterial hypertension (HTN) and high visit-to-visit blood pressure variability (BPVVV).

Methods: The retrospective cohort study analyzed available data from the random sample of 132 rural males with HTN (mean age 51 ± 6 years). BPVVV (of systolic and diastolic BP) was assessed by means of standard deviation and coefficient of variation (derived from the four consecutive visits). The enrolled sample was subdivided into the groups with high (n=78; 59,1 %) and low (n=54; 40,3 %) BPVVV (HBPV and LBPV, respectively).

Results: The HBPV group was characterized by longer HTN duration, the higher frequency of positive family history of cardiovascular diseases, obesity (the tendency) and smoking, higher levels of plasma lipids and more frequent reduced renal filtration function (Table). The history of myocardial infarction (MI) was more frequent in HPBV group (vs. LBPV: 26 (33,3 % [95 % CI 23,2-44,3 %]) vs. 8 (14,8 % [95 % CI 6,5-25,7 %]) cases, respectively; p=0,017). Additionally, all the acute cerebrovascular events (ACVE) (transient ischemic attack or stroke) occurred previously in HBPV group (vs. LBPV: 14 (17,8 % [95 % CI 10,2-27,3 %]) vs. 0 (95 % CI 0-3,5 %) cases, respectively;

p=0,001).

Table. The certain clinical characteristics of rural males with arterial hypertension and different blood pressure visit-to-visit variability

Parameters	LBPV N=54	HBPV N=78	p
Age, years, Me (IQR)	50 (46-56)	53 (47-56)	0,234
HTN duration, years, Me (IQR)	6 (3-10) n=50*	11 (8-16) n=75*	<0,001
Smoking, n/N* (%)	22/47 (46,8)	54/68 (79,4)	<0,001
Obesity, n/N* (%)	13/51 (25,5)	29/70 (41,4)	0,069
Family history of CVD, n/N* (%)**	11/51 (21,6)	30/75 (40,0)	0,034
TPC, mmol/l, Me (IQR)	5,4 (4,7-6,2)	6,0 (5,2-6,8)	0,024
TG, mmol/l, Me (IQR)	1,2 (1,0-1,9)	2,0 (1,6-2,8)	<0,001
eGFR <60 ml/min/1,73 m^2, n/N* (%)	7/47 (14,9)	29/68 (42,6)	0,002

Notes: MACCE – major adverse cardio- and cerebrovascular events; LBPV – low blood pressure visit-to-visit variability; HBPV – high blood pressure visit-to-visit variability; Me – median; IQR – interquartile range; HTN – hypertension; CVD – cardiovascular diseases; TPC – total plasma cholesterol; TG – triglycerides; eGFR – estimated glomerular filtration rate (by CKD-EPI equation); * – available data; ** – both paternal and maternal

Conclusions: The concomitant HBPV in rural hypertensive males was associated with a worse cardiovascular risk profile and more frequent history of MACCE, namely MI and ACVE. Further research on the prognostic value of HBPV is needed for HTN patients, aimed at MACCE risk reduction.

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#1294

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

PROGONOSTIC VALUE OF KIDNEY RESISTANCE INDEX IN ELDERLY AND SENILE PATIENTS WITH CHRONIC KIDNEY DISEASE AND CARDIOVASCULAR COMORBIDITY

VIRTUAL E-POSTER SESSION

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Background and Aims: The kidney resistance index (intrarenal vascular resistance) is considered as one of the early markers of kidney damage. The aim of this study was to investigate progonostic value of the kidney resistance index in elderly and senile patients with chronic kidney disease (CKD) and cardiovascular comorbidity.

Methods: 62 patients with stable cardiovascular diseases (25 males, mean age 69.4±7.4 years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). The kidney resistance index (the ratio of the difference for the renal artery between the maximum systolic velocity and the final diastolic velocity to the maximum systolic velocity) was determined according to the standard method during ultrasound examination of the kidneys.Follow-up period was 1 year, primary endpoint - all-cause mortality.

Results: 32 (51.6%) patients had CKD with eGFR less than 60 ml/min/1.73 m^2. The kidney resistance index was higher in men than in women (0.8 (0.64; 0.90) and 0.6 (0.53; 0.73), respectively, p=0.02). In the analysis of comorbidity, an increase in the kidney resistance index was observed in patients with atrial fibrillation compared with patients without atrial fibrillation: 0.95 (0.86; 0.97) and 0.68 (0.6; 0.78) , respectively, p=0.02. The kidney resistance index of more than 0.73 determined an unfavorable annual prognosis (mortality and hospitalizations during the year) in patients with stable cardiovascular disease (sensitivity - 88%, specificity - 71.43% (AUC = 0.86) ; p=0.0001).

Conclusions: The renal resistance index more than 0.73 determines an unfavorable prognosis during the year in elderly and senile patients with CKD and cardiovascular comorbidity.

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#1285

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

BASELINE ECG CHANGES COULD PREDICT MAJOR MACE AMONG HOSPITALIZED CKD PATIENTS

VIRTUAL E-POSTER SESSION

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Background and Aims: As data on cardiovascular complication among chronic kidney disease patients has been limited, the present study aimed to understanding the association between electrocardiogram changes with clinical outcomes among hospitalized patients with chronic kidney disease.

Methods: We performed a single-centre, observational prospective cohort study among stage V CKD patients who haven't experienced haemodialysis. CKD was diagnosed based on the KDIGO 2012 criteria. The cumulative all-cause mortality and cardiovascular death, MACE and non-fatal MI were analysed using Kaplan-Meier.

Results: Total of 350 patients were enrolled, 96 patients were excluded due to previous history of haemodialysis and 56 patients were excluded due to incomplete data. The rest of 198 patients were analysed. Their mean age was 39.87 years and 41.52% were women. They were followed up for 12 months on average, with 129 incident cases (65.15%) being identified during 1-years at risk. Pathologic Q wave at baseline (HR 3.15, 95% CI [1.81-5.37]; P<0.01), peak T wave (HR 1.93, 95% CI [1.07-2.84]; P=0.04), left axis deviation (HR 2.14, 95% CI [1.03-4.47]; P=0.04), and non-specific ST/T changes (HR 2.70, 95% CI [1.65-3.78]; P=0.01) were all independently associated with all-cause mortality, cardiovascular death, and MACE. On the contrary, left ventricular hypertrophy and fragmented QRS weren't associated with clinical outcomes.

Conclusions: Several changes of electrocardiogram were significantly associated with the incidence of all-cause mortality, cardiovascular mortality, MACE, and rehospitalization independently of level and change in cardiovascular disease risk factors, and may have clinical utility for prognostication among hospitalized CKD patients.

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#108

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

LIPID PROFILE FEATURES IN WOMEN OF REPRODUCTIVE AGE WITH METABOLIC SYNDROME

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the features of the lipid profile in MS in women of reproductive age.

Methods: The main adolescent group included 92 patients 15-20 years old; the main reproductive group - 214 patients aged 21-45 years. In both groups MS was diagnosed according to the IDF criteria (2005), adjusted for sex and age. The control groups consisted of 40 teenage girls and 60 women of reproductive age. In all patients BMI, waist-to-hip ratio (WHO); fblood pressure; glucose, insulin and C-peptide fasting and postprandial levels, total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C), uric acid and leptin levels were measured. Also low density lipoprotein cholesterol (LDL-C) and very low density (VLDL-C), atherogenic coefficient (CA), leptin / BMI index, glucose-insulin ratio (GIS), HOMAIR and HOMAβ-cell) were calculated.

Results: In the main adolescent group hypertriglyceridemia in the upper quartile of the control group was observed in 59.5%. Hypercholesterolemia in the upper quartile of the control group was observed 72.5%. VLDL-C increase in the upper quartile of the control group was observed in 59.5%, LDL-C in 64.6%, CA in 67,1%. TG,TC and lipoprotein levels correlated with SBP, BMI, waist circumference, basal and postload insulin levels, HOMAIR and HOMAβcell, leptin and leptin/BMI index. Inverse relationship was mentioned with HDL and GIS. Hypoalphacholesterolemia in the lower quartile of the control group was observed in 57.0% and correlated with the postload insulin, C-peptide, leptin and leptin/BMI index. Lipid profile disorders were more common in reproductive women.

Conclusions: The most common disorders in adolescent women with MS were hypercholesterolemia and an increase in LDL-C, in reproductive patients - hypertriglyceridemia (83.3%) and hypoalphacholesterolemia.

91ST EAS CONGRESS
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#1270

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.11 Gut microbiome*

FEATURES OF THE INTESTINAL MICROBIOTA METABOLOME IN PATIENTS WITH ARTERIAL HYPERTENSION AND ABDOMINAL OBESITY

VIRTUAL E-POSTER SESSION

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Background and Aims: Cardiovascular disease (CVD) remains leading cause of death and disability in developed world. Significant recent interest has focused on the role of intestinal microbiota (IM) as a risk factor for development of CVD. The aim was to compare intestinal metabolome parameters and their relationship to target organ damage in patients with arterial hypertension (AH) and abdominal obesity (AO).

Methods: 141 patients were divided into 3 groups: Gr1-control group without AH (n=34), Gr2-with AH (n= 49), Gr3-with AH and AO (n=58). Gr2 and Gr3 were comparable in BP stage. In Gr3 BMI and obesity degrees were significantly increased ($p<0.001$). Examination included questionnaire on actual nutrition, ABPM, measurement of pulse wave velocity (PWV) and endothelial dysfunction (ED), EchoCG. Complete blood count, lipid profile parameters, inflammatory markers, metabolic parameters: trimethylamine oxide (TMAO), short-chain fatty acids (SCFA) in coprofiltrate were measured.

Results: Daily fiber intake was lower reference limits in Gr2, Gr3. Excessive simple carbohydrates intake was mostly found in Gr3. In Gr3, significant elevation of 24-hour SBP, DBP, DBP and heart rate variability at night, increased ED were registered; rise of leukocytes, hemoglobin, liver enzymes, uric acid, LDL-CH, triglycerides, C-peptide, resistin, hs-CRP, IL-1b, 6, TMAO, decreased SCFA vs Gr1 and partially Gr2. Correlations of VDBP with TMAO, PWVr with SCFA, hs-CRP, insulin, leptin and resistin were registered. Correlations of EchoCG parameters with GDF15 were revealed.

Conclusions: Early detection of intestinal microbiota metabolome disorders, timely implementation of therapeutic preventive measures will provide additional means to control risks for CVD development and progression in AH patients with AO.

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#109

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

NON-OBSTRUCTIVE CORONARY ARTERY DISEASE AND HEART FAILURE WITH PRESERVED EJECTION FRACTION: PROGNOSTIC MARKERS

VIRTUAL E-POSTER SESSION

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Background and Aims: To evaluate prognostic markers of adverse outcomes in patients with heart failure with preserved ejection fraction (HFpEF) and non-obstructive coronary artery disease (CAD) during 12 months of follow-up period.

Methods: A total of 63 patients (62.0 (58.0; 69.0) years) were enrolled. Dynamic CZT SPECT, echocardiography and coronary computed tomography angiography studies were performed baseline. Serum levels NT-proBNP, matrixmetalloproteinase-9 (MMP-9), tissue inhibitor of metalloproteinase-1 (TIMP-1), soluble ST2 (sST2), tetranectin, high sensitive C-reactive protein (hsCRP), interleukin-1β, 6 and 10 were measured by enzyme immunoassay.

Results: Group 1 comprised patients with adverse outcomes (n=12), group 2 comprised those without it (n=51). In group 1 the levels of NT-proBNP were 3.5 times higher (p<0.001), sST2 by 17.1% (p<0.001), TIMP-1 by 31.1% (p=0.012), MMP-9 by 23.4% (p=0.049), and hsCRP was 1.9 times (p=0.004) and interleukin-1β was 2 times higher (p=0.048) compared to group 2. Myocardial flow reserve (MFR) were lower by 48.2% (p<0.001) and stress-MBF by 32.3% (p<0.001), rest-myocrdial blood flow (MBF) was higher by 22.2% (p=0.043), and GLS was lower by 27.1% (p=0.003) in group 1 than in group 2. Univariate analysis revealed that MFR ≤ 1.62 (p=0.014), stress-MBF ≤ 1.35 ml/min/g (p=0.012), GLS ≤-18% (p=0.018), NT-proBNP ≥ 760.5 pg/mL (p=0.018) were risk factors of HFpEF progression. Multivariate analysis demonstrated that NT-proBNP ≥ 760.5 pg/mL (OR 1.87, p=0.027) and MFR levels ≤ 1.62 (OR 2.801, 95%, p=0.018) were predictors of adverse outcomes.

Conclusions: The impaired MFR ≤1.62 obtained with dynamic CZT imaging and NT-proBNP ≥ 760.5 pg/mL can individuate patients with non-obstructive CAD at risk of HFpEF progression during 12 month follow-up period. Funding: MK-4257.2022.3

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#107

Topic: *AS02 Lipids and Lipoproteins / AS02.11 Liver metabolism and steatosis*

DEVELOPMENT OF A NOVEL PET TRACER 68GA-NOTA-KS FOR EVALUATION OF HEPATIC FUNCTION IN ANIMAL MODELS OF LIVER FIBROSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: The preoperative assessment of hepatic function is a crucial factor for successful liver surgery to reduce postoperative mortality and morbidity. However, conventional methods including the Child-Pugh classification, the model for end-stage liver disease (MELD), and the indocyanine green clearance are the indirect methods of measuring hepatic function, which often lead to inaccurate assessment. Asialoglycoprotein receptors are expressed on normal hepatocytes of mammals and a novel synthetic compound KS was designed to bind specifically to asialoglycoprotein receptors. Thus, ^{68}Ga-labeled KS could be suitable for visualization of asialoglycoprotein receptors in the liver by using positron emission tomography (PET) and could directly reflect the hepatic function. Here, we investigate whether a novel PET tracer ^{68}Ga-labeld KS could reflect the hepatic function in rats with liver fibrosis.

Methods: Synthesized KS was conjugated with 2-(p-isothiocyanatobenzyl)-1,4,7-triazacyclononane-1,4,7-triacetic acid (SCN-NOTA) and labeled with ^{68}Ga. Liver fibrosis animal models were induced by an intraperitoneal injection of thioacetamide (300 mg/kg) three times a week for 4 weeks using the male Sprague-Dawley rat. Images were acquired after injection of ^{68}Ga-NOTA-KS in the rat tail vein before sacrifice. The liver uptake value (LUV) of ^{68}Ga-NOTA-KS was calculated as the whole liver uptake divided by the heart uptake.

Results: Functional hepatocyte imaging was successfully visualized by using ^{68}Ga-NOTA-KS PET/CT in live animals. Furthermore, LUV of ^{68}Ga-NOTA-KS was significantly decreased in rats with liver fibrosis, compared to normal rats.

Conclusions: ^{68}Ga-NOTA-KS PET/CT could reflect the hepatic function in liver fibrosis rat model. Thus, LUV assessed by ^{68}Ga-NOTA-KS PET/CT could serve as a direct surrogate marker of hepatic function.

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#1274

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

ASSOCIATION OF ATHEROSCLEROSIS-RELATED MITOCHONDRIAL MUTATIONS WITH THE MITOCHONDRIAL DYSFUNCTION

VIRTUAL E-POSTER SESSION

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Background and Aims: Many mtDNA mutations were found to be associated with chronic human diseases, including cardiovascular disorders. Recent studies have identified the involvement of mitochondrial dysfunction in the pathogenesis of atherosclerosis and describe the mtDNA mutations identified so far that are associated with atherosclerosis and its risk factors. Aim of this research to identify a statistically significant relationship among several mitochondrial mutations and processes, which underlying mitochondrial dysfunction.

Methods: The initial data were the results of biological experiments with 14 hybrid monocyte-derived macrophages obtained from patients with varying stages of atherosclerosis. For each macrophages line, the level of heteroplasmy was detected for each of the 10 mutations of the mitochondrial genome. Models based on network analysis, linear and nonlinear models, models based on frequency analysis of proton leak, ATP production, maximal respiratory capacity and reserve respiratory capacity 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 (m.12315G>A, m.3256C>T), rRNA (m.1555A>G,), Coenzyme Q - cytochrome c reductase (m.15059G>A), NADH dehydrogenase (m.14459G>A, m.5178C>A, m.3336T>C, m.13513G>A) and Coenzyme Q - cytochrome c reductase (m.14846G>A) don`t statistically significantly affect proton leak, ATP production, maximal respiratory capacity and reserve respiratory capacity (adjusted p-values are from 0.13 to 1). However, the mutation in the gene rRNA (m.del652G) is statistically significantly related to proton leak ($r = 0.87$, adjusted p-value = 0.04).

Conclusions: It was found strong direct correlation between mutation in gene MT-RNR1 (12S rRNA) and proton leak. This study can be applied to study the contribution of mitochondrial mutations to processes of atherogenesis.

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#122

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

A STUDY ON PREVALENCE OF FAMILIAL HYPERCHOLESTEROLAEMIA (FH) IN SRI LANKA: A MULTICENTER STUDY

VIRTUAL E-POSTER SESSION

Anne Thushara Matthias[1], Sitheeg Mahbooba[1], Jayamini Kaushalya[1], T M R Jinasena[2], Peduru Hewa Saman[2], T S P Samaranayake[3], Anthony Fernandopulle[4]
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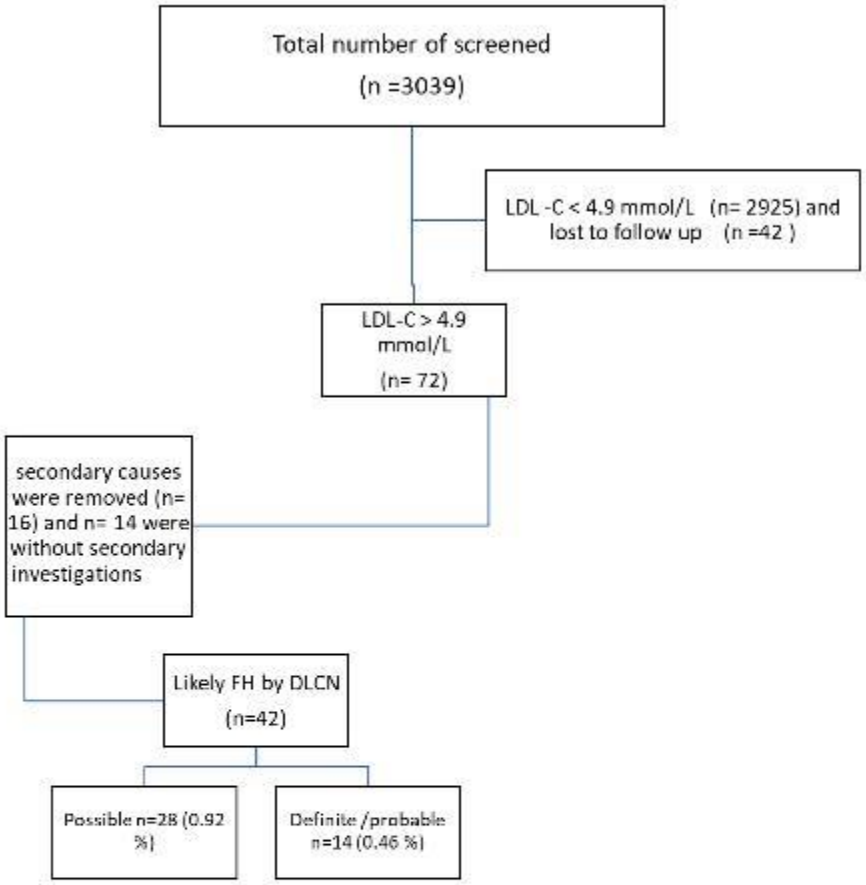
Background and Aims: Familial hypercholesterolemia (FH) is one of the commonest inherited metabolic diseases which predisposes to cardiovascular diseases. There is no literature on the prevalence of FH in Sri Lanka. This study was aimed at finding the prevalence of FH in Sri Lanka as it is helpful in planning further studies in FH in the country and optimize the care of patients with FH.

Methods: The diagnosis of FH was based on Dutch Lipid Clinic Network Criteria (DLCNC) score and the data was evaluated over six-months at a tertiary-care hospital and a primary-care center.

Results:


Total number of screened
(n =3039)
LDL -C < 4.9 mmol/L (n= 2925) and lost to follow up (n =42)
LDL-C > 4.9 mmol/L
(n= 72)
secondary causes were removed (n= 16) and n= 14 were without secondary investigations
Likely FH by DLCN
(n=42)
Possible n=28 (0.92 %)
Definite /probable n=14 (0.46 %)

Res

ults: Out of 3039 serum lipid profiles reviewed, 42 (1.38 %) had LDL-cholesterol of 4.9 mmol/L after exclusion of 16 (0.52%) with identified secondary causes [untreated hypothyroidism (n = 13), nephrotic syndrome (n=3)], no secondary investigations (n=14) and lost to follow up (n=42) .(Figure 1) 0.92 % of all patients who had LDL-cholesterol measured over the six months had a DLCNC score of 3–5, 0.26 % scored 6–8 and 0.197 % scored > 8 indicating a possible, probable and definite diagnosis of FH respectively. The point prevalence of likely phenotypical FH based on DLCNC (probable or confirmed) was calculated as approximately 14/3039 (1: 217)

Conclusions: The prevalence of FH in patients investigated on lipid profile in a tertiary-care hospital and a primary-care was 1:217. This is comparable with prevalence of FH in global population (1 in 200–250). This is the first study to assess the prevalence of FH in Sri Lanka.

91ST EAS CONGRESS
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#384

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

RESIALYLATION OF LOW-DENSITY LIPOPROTEINS: A PROMISING WAY TO REDUCE LOW-DENSITY LIPOPROTEINS ATHEROGENICITY

VIRTUAL E-POSTER SESSION

Raisa Surkova[1], Dmitry Kashirskikh[1], Igor Sobenin[1,2], Ulyana Zotova[3], Alexander Markin[3], Victor Glanz[4], Alexander Orekhov[1,4,5]
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Background and Aims: Low-density lipoproteins (LDL) undergoes many modifications, which leads to an increase in their atherogenicity, but the primary and most important atherogenic modification of LDL is desialylation. The aim of the study was to establish the possibility of reducing the atherogenicity of LDL using an enzymatic resialylation reaction.

Methods: LDL from human serum samples were isolated using ultracentrifugation. LDL were incubated for 1 hour at 37°C with ST6GAL1-Fc enzyme and substrate (5 mM sialic acid, 100 mM MnCl2, 100 mM MgCl2, 100 mM Tris-HCl, 50 mM DTT, PBS). The resulting samples were incubated with cell line THP-1. To determine the atherogenicity of resialylated LDL, the concentration of intracellular cholesterol was measured using commercial kits.

Results: As a result of the study, we compared the data obtained during the incubation of cell line THP-1 with samples of resialylated LDL and naturally occurring desialylated LDL (substrate and enzyme were not added). The concentration of intracellular cholesterol was measured on the second day of incubation. A significant decrease in the concentration of intracellular cholesterol was found during the incubation of cell line THP-1 with samples of resialylated LDL compared with naturally occurring desialylated LDL.

Conclusions: The data obtained indicate the promising possibility of using the resialylation reaction to reduce the atherogenicity of LDL. This requires additional research to determine the mechanisms that underlie resialylation.
This work was supported by the Russian Science Foundation (Grant # 20-15-00264)

91ST EAS CONGRESS
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#1267

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

ASSESSMENT OF MYOCARDIAL PERFUSION WITH SPECT IN OBESE PATIENTS WITH HIGH AND VERY HIGH CARDIOVASCULAR RISK DURING GLP-1 RECEPTOR AGONISTS THERAPY, PRELIMINARY RESULTS

VIRTUAL E-POSTER SESSION

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Background and Aims: to evaluate myocardial perfusion with 99mTc-MIBI SPECT in obese patients with high and very high cardiovascular risk (CVR) at baseline and after 6 months of therapy with glucagon-like peptide-1 (GLP-1) receptor agonists.

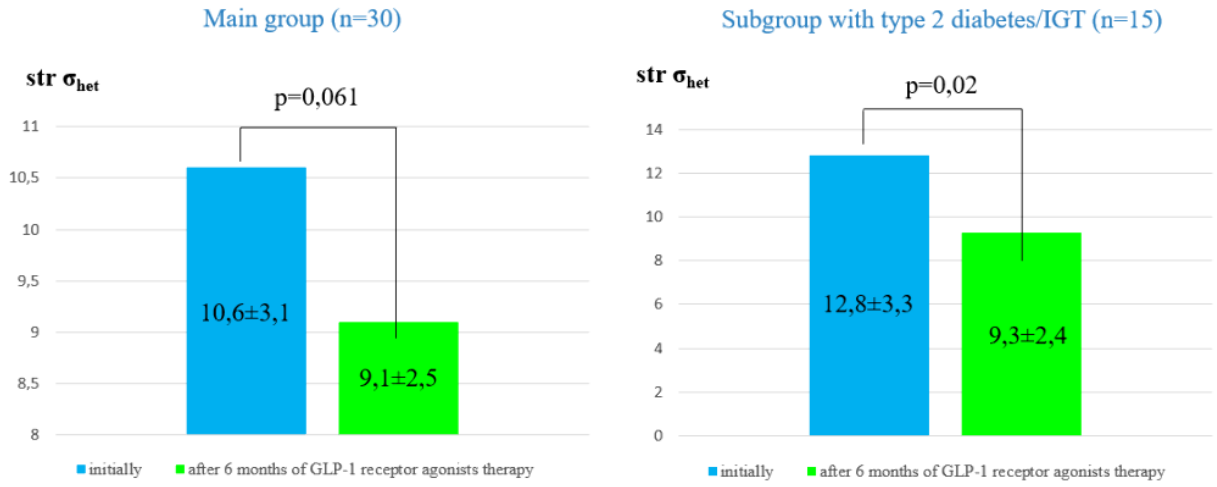
Methods: The study includes obese (BMI ≥30 kg/m2) patients with high and very high CVR, planned for treatment with GLP-1 receptor agonists. The main group (Group I), for today, consists of 15 patients with type 2 diabetes mellitus (DM) or impaired glucose tolerance (IGT). Group II includes 15 patients without carbohydrate metabolism disorders (type 2 DM and/or IGT). Physical examination, assessment of lipid profile parameters, perfusion myocardial SPECT (rest/stress) with perfusion inhomogeneity assessment (σsev* - impairment severity index, and σhet* - heterogeneity index; *lower is better) were performed at baseline and after 6 months of GLP-1 receptor agonists therapy.

Results: After 6 months of GLP-1 receptor agonists treatment, a significant reduction of weight, waist circumference, BMI ($p < 0.0001$ for each indicator), total cholesterol levels ($p=0.0001$) and LDL cholesterol levels ($p=0.0004$) was
detected.

Averages	Initially	After 6 months of GLP-1 RA therapy
Weight, kg	97,7±3,2	91,66±3,2
BMI, kg/m²	34±1,08	31,83±1,05
Waist circumference, cm	106,2±2,38	100,0±3,23
total cholesterol, mmol/l	5,65±0,28	4,60±0,24
LDL cholesterol, mmol/l	3,62±0,25	2,68±0,22

Myocardial SPECT perfusion inhomogeneity parameters decreased significantly (stress σsev= 26,8±5,7 to 22,6±4,7, $p=0.03$, stress σhet= 10,6±3,1 to 9,1±2,5, $p=0.061$) predominantly due to DM/IGT patients

(Group I) (stress σsev= 27,7±5,8 to 22,4±4,5, p=0.01, stress σhet= 12,8±3,3 to 9,3±2,4, p=0.02).



Conclusions: GLP-1 receptor agonists affect not only constitutional parameters and lipid profile indicators, but also improve myocardial perfusion at the microcirculation level. Further research is required to expand the indications for GLP-1 receptor agonists prescription in obese patients with high and very high CVR and also expand efficacy control parameters.

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#1222

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

DYSLIPOPROTEINEMIA AS A RISK FACTOR FOR ENDOTHELIOCYTE DAMAGE

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the possible relationship between the concentrations of cholesterol, LDL and the degree (%) of induced hemolysis of erythrocytes as a marker of the functional competence of the cell membrane.

Methods: Whole blood of apparently healthy donors (n=24) and persons with clinical manifestations of atherosclerosis (n=27) was used. Determination of cholesterol and LDL concentrations was carried out by methods generally accepted in the clinic. The assessment of the degree of hemolysis was determined by the change in the light transmission of a suspension of erythrocytes suspended in 0.9% NaCl in the presence of HCl (hemolytic) at 500 nm. It is not hemolysis that is recorded, but damage to the erythrocyte membrane, since light scattering changes due to the collapse of the membrane and the erythrocyte cytoskeleton.

Results: In the group of apparently healthy donors, the cholesterol level was 4.1±0.5 mmol/l, the concentration of LDL was 2.1±0.3 mmol/l, the degree of HCl-induced erythrocyte hemolysis was 31.5±4.6%. In the group of patients with atherosclerosis, the cholesterol level was 6.9±1.3 mmol/l, the LDL concentration was 4.7±0.8 mmol/l, the degree of erythrocyte hemolysis induced by HCl was 48.4±8.2%.

Conclusions: The high levels of cholesterol and LDL are associated with the degree of HCl-induced erythrocyte hemolysis ($p<0.01$).
HCl-induced hemolysis of erythrocytes reflects the degree of metabolic damage to cells. An increase in the degree of induced hemolysis of erythrocytes can be a marker for assessing damage to endothelial cells.

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#1177

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

CORRELATION BETWEEN AORTIC VALVE CALCIFICATION AND C-REACTIVE PROTEIN LEVELS IN PATIENTS WITH AORTIC VALVE SCLEROSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: Aortic valve calcification (AVC) is presently the most common cause of aortic valve stenosis (AVS) resulting in significant morbidity and mortality. This study aimed to evaluate and associate the effect of C-reactive protein (CRP) levels on AVC progress for individuals with aortic valve sclerosis (AVSc).

Methods: We present the preliminary results of a prospective study of 65 patients with AVSc, who underwent non-contrast ECG-guided multi-slice computed tomography (MSCT) for quantification of calcium score by Agatston units (AU) and blood sampling for biochemical analysis. Primary endpoints were the quantification of (1) AVC score; and (2) blood CRP levels. The study took place between 4 tertiary hospitals in Greece.

Results: The median age of all participants was 75.3 years old (IR=7.4) with median blood CRP levels being 0.7mg/dl (IR 1.1). The median AVC score was 673.5 AU (IR=878.2). According to the results of a bivariate analysis, a statistically significant correlation between AVC score with CRP was noted. Increased CRP levels were related to increased AVC scores (p=0.028).

Conclusions: A significant relationship between elevated blood CRP levels and increased calcium score in the aortic valve in individuals with AVSc was confirmed. The above results serve as a standpoint for further research to clarify the exact underlying pathophysiology mechanisms, as inflammation could possibly contribute to the accelerated progression of cardiac valve calcification.

91ST EAS CONGRESS
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#448

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

LABORATORY MONITORING OF THE EFFICACY AND SAFETY OF COMBINATION THERAPY WITH ATORVASTATIN AND EZETIMIB IN PATIENTS WITH MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

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Background and Aims: to study the severity of the lipid-lowering effect and the safety of combined therapy with atorvastatin and ezetimibe in patients with acute myocardial infarction (MI) during 24 weeks.

Methods: 60 patients with MI (57.8±8.2 years) were included. In the first 24-96 hours from the onset of the disease, patients were prescribed atorvastatin 80mg. Low-density lipoproteins (LDL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine phosphokinase (CPK) were determined initially and repeatedly after 4-6 and 24 weeks. If the target LDL was not reached (<1.4mmol/l and a decrease of ≥50%), ezetimibe 10mg was additionally prescribed after 4-6 weeks. According to the results of the study, the patients were divided into groups: group 1 (25 patients) received atorvastatin monotherapy; group 2 (41 patients) took atorvastatin+ezetimibe. The compared groups were comparable in age, gender, anthropometric indicators.

Results: In group 1 LDL decreased by 48.5% ($p<0.001$). AST was initially 37.8(26.4;62.6) IU/l, after 24 weeks – 25.1±7.2 IU/l ($p=0.007$). ALT, CPK did not change. CPK>10 upper limits of the norm (ULN) and ALT>3 ULN were not detected. In group 2 LDL decreased by 60% ($p<0.001$). AST initially 35.3(29.8;86.4) IU/l, repeatedly – 30.2(24.5;38) IU/l ($p=0.014$); CPK initially 290 (149.3;630.3) IU/l, repeatedly – 137(102;175) IU/l ($p=0.005$). ALT hasn't changed. An increase in CPK>10 VGN has not been registered. An increase in ALT>3 VGN was detected in 2.4% (n=1; $p_{1gr-2gr}=0.343$).

Conclusions: In patients with MI, therapy with atorvastatin and ezetimibe contributed to a pronounced lipid-lowering effect in the absence of unfavorable dynamics of hepatic transaminases, CPK.

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#1191

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

LP(A) LEVELS AND ACHIEVEMENT OF LDL-C TARGETS

VIRTUAL E-POSTER SESSION

María Riestra Fernández[1,2], Vanesa García Moreira[3], Marta Diéguez Felechosa[1,2], Juan Rondan[4], Jose Miguel Vegas Valle[4], Nuria Valdés Gallego[1,2]
[1]Endo Group, Instituto de Investigación Sanitaria del Principado de Asturias, Oviedo, Spain, [2]Endocrinology And Nutrition, Hospital Universitario de Cabueñes, Gijón, Spain, [3]Clinical Analysis, Hospital Universitario de Cabueñes, Gijon, Spain, [4]Cardiology, Hospital Universitario de Cabueñes, Hospital Universitario de Cabueñes, Spain

Background and Aims: Lp(a) contributes to the reported LDL-C concentration. The achievement of LDL-C targets in patients with high cardiovascular risk may be a challenge, and high levels of Lp(a) could make it more difficult. Our aim is to evaluate whether Lp(a) influences the achievement of LDL-c targets

Methods: We conducted a retrospective observational study. Patients with high or very high cardiovascular risk were selected according to the ESC 2019 guidelines. Sociodemographic variables, LDL-C and Lp(a) values, and lipid-lowering treatment were obtained. We consider Lp(a) ≥ 75 nmol/L as high Lp(a). SPSS v25 was used for the statistical analysis.

Results: We obtained data from 103 patients with high or very high cardiovascular risk. 71.8% were male, median age 64.1 years (41.8-83.9, SD 10.1). Median LDL-C levels were 67 mg/dl (8-255, DS 35.5). Median Lp(a) 74.2 nmol/L (0.6-1101.4, DS 187.8). 49.5% had levels above 75 nmol/L. 61.2% of patients received high-intensity statin + ezetimibe lipid-lowering treatment, followed by 24.3% high-intensity statin. 3.9% received I-PCSK9. 70.9% of all did not achieve LDL-C targets, without differences based on levels of LP(a). Compared to patients with normal Lp(a) values, patients with high Lp(a) required more combined treatment (high intensity statin + ezetimibe and/or I-PCSK9) to achieve the same LDL-C values (68.6% patients receiving combined treatment Vs 53.8%, p 0.042)

Conclusions: Patients with high levels of Lp(a) require more intense lipid-lowering treatment to reach LDL-c targets than patients with normal Lp(a). This should be considered when selecting the initial lipid-lowering treatment in patients with high or very high cardiovascular risk.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#140

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

DEEP LEARNING-BASED PREDICTION FOR SIGNIFICANT CORONARY ARTERY STENOSIS FROM CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY AMONG ASYMPTOMATIC POPULATION

VIRTUAL E-POSTER SESSION

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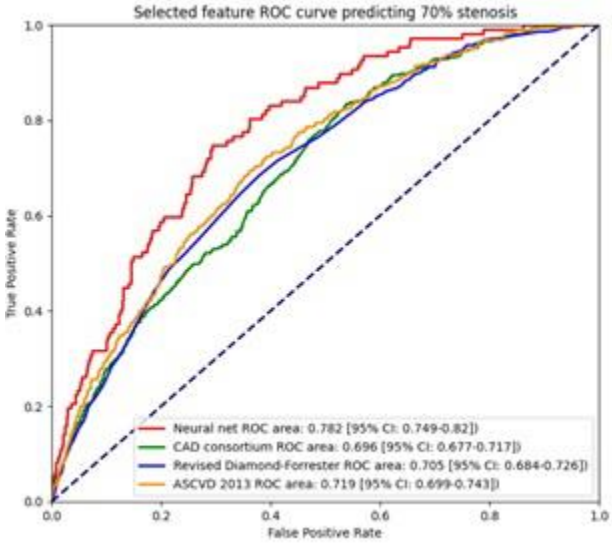
Department Of Internal Medicine, Seoul National University Hospital Healthcare System Gangnam Center, Seoul, Korea, Republic of

Background and Aims: Although coronary computed tomography angiography (CCTA) is currently utilized as the frontline test to accurately diagnose coronary heart disease (CHD) in clinical practice, there are still debates as the screening tool for asymptomatic population. Using deep learning (DL), we sought to develop the prediction model for significant coronary artery stenosis on CCTA among apparently healthy asymptomatic adults.

Methods: We retrospectively reviewed 11,180 cases that included CCTA for a routine health check-up between 2012 and 2019. Main outcome was the presence of obstructive CHD, defined as coronary artery stenosis of ≥70% on CCTA. Prediction model was developed using various DL methods, and the performance was compared with pretest probabilities, including pooled cohort equation (PCE), CAD consortium, and updated Diamond-Forrester (UDF) scores.

Results: In the cohort comprising 11,180 apparently healthy asymptomatic adults (mean age 56.1 years; men 69.8%), 516 (4.6%) had obstructive CHD. Among DL methods, we chose the neural network with multi-task (19 selected features) since it produced the best performance (AUC, 0.782) with high diagnostic accuracy of 71.6%. Our DL-based model demonstrated a better prediction than PCE (AUC, 0.719), CAD consortium score (AUC, 0.696), and UDF score (AUC, 0.705). Age, sex, HbA1c, and HDL

cholesterol were the highly ranked features. Personal education and monthly income levels were included as important features in the model.



Conclusions: A neural network with multi-task model was successfully developed for detecting CCTA-derived obstructive CHD among asymptomatic population. In clinical practice, we could provide more precise indications for CCTA as a screening tool and identify individuals at higher risk.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1193

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

CLINICAL, LABORATORY AND INSTRUMENTAL PARAMETERS, ASSOCIATED WITH IN-HOSPITAL FUNCTIONAL RECOVERY OF PATIENTS, SUFFERED FROM ACUTE CORONARY SYNDROME

VIRTUAL E-POSTER SESSION

Liana Babii[1], Valentyn Shumakov[1], Tetiana Talaieva[2], Nataliia Tereshchenko[1], Yuliia Kovalchuk[1], Iryna Tretiak[2], Oksana Voloshyna[1], Olena Pogurelska[1], Kyrylo Mikhaliev[3]
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Background and Aims: To study clinical, laboratory and instrumental parameters, associated with in-hospital functional recovery of patients, suffered from acute coronary syndrome (ACS).

Methods: The cohort study enrolled and analyzed clinical, laboratory and instrumental data from 44 male patients (mean age 58±10 years), admitted to hospital for ACS. STEMI was diagnosed in 39 of 44 patients, unstable angina – in 5 cases. Coronary angiography was performed in all the patients (with urgent PCI in case of STEMI). Exercise tolerance (ET) test was performed at the second week of in-hospital stay. According to ET-test results, patients were subdivided into the groups with low (G1; n=24 [55 %]) and high ET (G2; n=20 [45 %]). Circulating endothelial progenitor cells (EPCs) (CD34/CD45+) were detected by means of flow cytometry in peripheral blood before and after ET-test (EPCs1 and EPCs2, respectively).

Results: G1 (vs. G2) was characterized by older age, higher glycated hemoglobin level, worse kidney filtration function, and more frequent left anterior descending artery disease. G1 and G2 did not differ significantly in the frequency of multivessel disease and complete coronary revascularization (Table). Both EPCs1 and EPCs2 correlated negatively with age (ρ= – 0,332 (p=0,028) and ρ= – 0,304 (p=0,045), respectively) and serum aspartate to alanine aminotransferase levels ratio (ρ= – 0,402 (p=0,007) and ρ= – 0,331 (p=0,028),

respectively).

Table. The certain clinical, laboratory and instrumental characteristics of patients with different ET, assessed at the second week of in-hospital stay for ACS

Parameters	Low ET N=24	High ET N=20	p
Age, years, Me (IQR)	63 (57-70)	55 (49-57)	0,001
Glycated hemoglobin, %, Me (IQR)	6,3 (5,4-7,0) n=16*	5,3 (5,1-5,7) n=13*	0,025
eGFR, ml/min/1,73 m^2, Me (IQR)	58 (51-69)	74 (63-87)	0,003
eGFR <60 ml/min/1,73 m^2, n/N (%)	12 (50)	3 (15)	0,015
AST, U/L, Me (IQR)	54 (31-126)	33 (24-41)	0,129
ALT, U/L, Me (IQR)	48 (32-57)	32 (27-55)	0,185
AST/ALT ratio, c.u., Me (IQR)	0,99 (0,62-2,01)	0,90 (0,66-1,29)	0,583
EPCs1/ml, Me (IQR)	3491 (2084-4541)	2514 (1665-5622)	0,616
EPCs2/ml, Me (IQR)	3278 (1990-5297)**	2740 (2030-5477)***	0,880
LAD stenosis ≥75 %, n (%)	20 (83)	10 (50)	0,018
Multivessel disease, n (%)	6 (25)	7 (35)	0,522
Complete revascularization, n (%)	11 (46)	7 (35)	0,547

Notes: ACS – acute coronary syndrome; ET – exercise tolerance; Me – median; IQR – interquartile range; eGFR – estimated glomerular filtration rate (by CKD-EPI equation); AST – aspartate aminotransferase; ALT – alanine aminotransferase; EPCs1 – circulating endothelial progenitor cells (CD34/CD45+), assessed before ET-test; EPCs2 – circulating endothelial progenitor cells (CD34/CD45+), assessed after ET-test; * – available data; ** – p=0,304 (vs. EPCs1 in the corresponding group); *** – p=0,911 (vs. EPCs1 in the corresponding group)

Conclusions: Low in-hospital ET in patients, suffered from ACS, was associated with older age, higher glycated hemoglobin level, and worse kidney filtration function. These factors, in addition to the completeness of revascularization, should be considered while assessment of in-hospital functional recovery after ACS.

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#577

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

MONOSODIUM GLUTAMATE (UMAMI) INDUCES METABOLIC SYNDROME AND ATHEROSCLEROSIS IN FEMALE APOE-/- MICE

VIRTUAL E-POSTER SESSION

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Background and Aims: Consumption of umami foods containing monosodium glutamate (MSG) have been suggested to increase the risk for obesity and metabolic syndrome. It remains elusive whether MSG accelerate atherosclerotic cardiovascular disease. The present study was designed to evaluate the effect of dietary intake of MSG in $ApoE^{-/-}$ mice fed with a western-type diet (WD).

Methods: In this study, 6-week-old female $ApoE^{-/-}$ mice were employed. MSG (300 mM) was administered to mice via dietary intake in drinking water. All mice were sacrificed on week 18. Students t-test or one-way analysis of variance (ANOVA) were used to test and analyze the data when appropriate. P value less than 0.05 is considered to be statistically significant.

Results: In comparison to mice taking regular water, MSG-treated mice showed much higher body weight on week 2 and markedly reduced blood glucose after 12 weeks of WD feeding. Total oxygen consumption (VO2) was significantly higher in MSG mice compared to the control littermates, implying that MSG mice exhibited higher energy expenditure. Furthermore, the respiratory exchange ratio (RER) did not change between the two groups. Mice on MSG developed insulin resistance. MSG produced significant reduction in serum high-density lipoprotein (HDL) levels and no difference is observed in other lipid profiles. More importantly, en-face Oil Red O staining of mouse aorta reveals a trend increase in the lesion size in MSG treated mice compared with vehicle.

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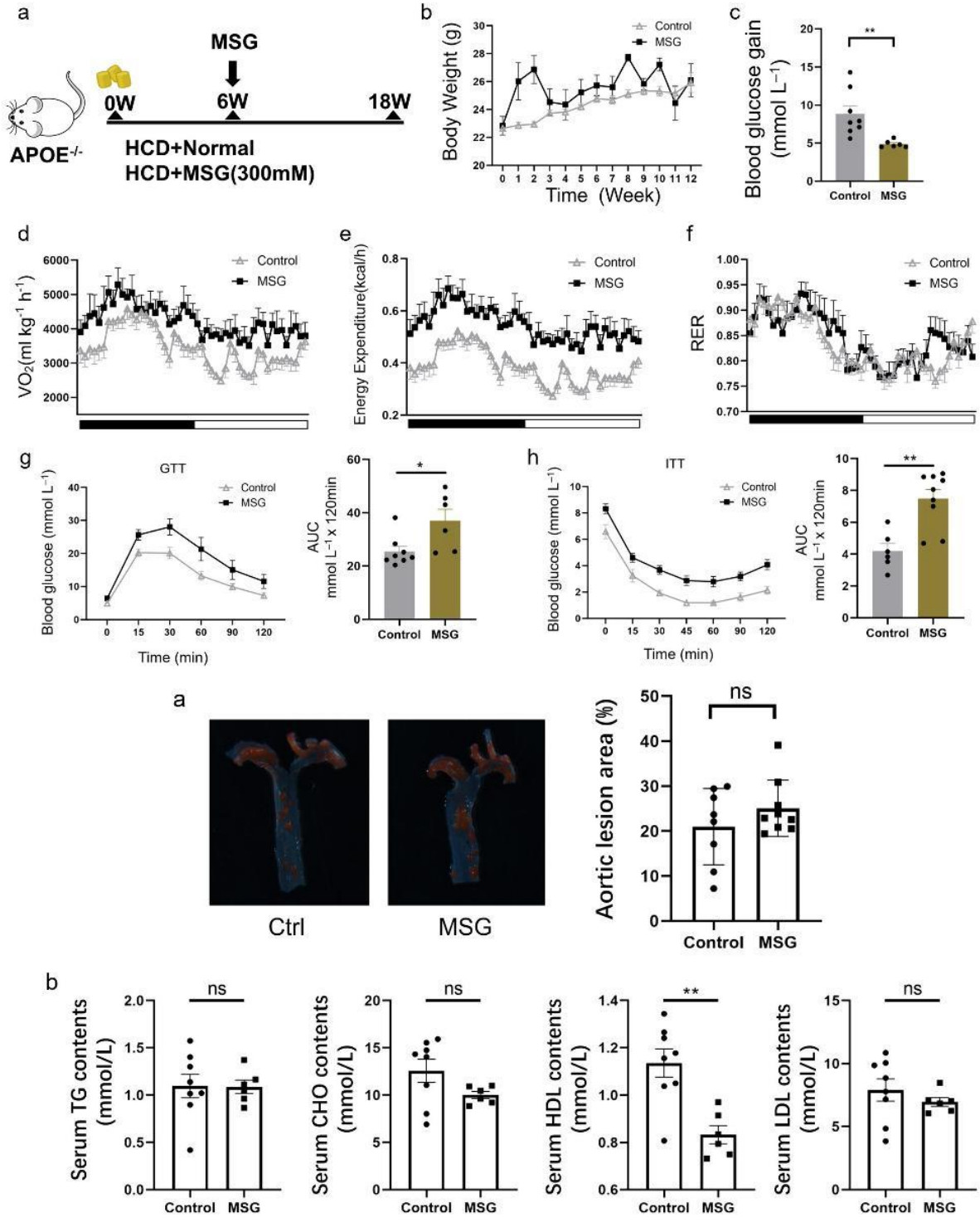

Conclusions: The present study reveals that dietary intake of MSG induces obesity and metabolic disorders, while reducing circulating HDL level, which may possibly aggravates atherosclerosis.

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#1202

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

FEATURES OF STRUCTURAL AND FUNCTIONAL CHANGES OF THE HEART IN PATIENTS WITH CORONARY HEART DISEASE AND DIABETES MELLITUS.

VIRTUAL E-POSTER SESSION

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Background and Aims: Evaluation of the influence of diabetes mellitus in patients with coronary artery disease on the structural, morphological and functional indicators of the state of the myocardium.

Methods: The study included 40 patients (45-65 years). 20 IHD patients with clinical manifestations of type 2 DM (Group 1) and 20 IHD patients without DM (Group 2). Echocardiography assess the state of myocardial function of the left ventricle (the mass calculated using the R.B.Devereux formula).

Results: LVPWd, cm 1.17±0.03 and 1.03±0.02 ($p<0.001$); LVPWs, cm 1.53±0.03 and 1.41±0.02 ($p=0.0021$); IVSd, cm 1.18±0.04 and 1.07±0.03 ($p=0.0026$); IVSs, cm 1.55±0.04 and 1.46±0.02 ($p=0.0040$). In patients with IHD and DM and without DM, significant differences were found in the thickness of the posterior wall in systole and diastole of the LV and in the thickness of the interventricular septum in systole and diastole. In patients with IHD and DM, these indicators were higher than in patients of the 2nd group. The mean myocardial mass in patients with DM manifestations was 308.14±11.98 and was also higher in patients without DM-275.42±9.36 ($p=0.001$). The functional parameters: EDD, cm 5.67±0.07 and 5.35±0.09 ($p=0.294$); ESD, cm 3.50±0.08 and 3.80±0.09 ($p=0.994$); EF,% 55.82±0.76 and 60.32±1.25 ($p=0.722$).

Conclusions: Diabetes mellitus type 2 had an impact on changes in the structural, morphological and functional parameters of the LV, manifested by an increase in the linear dimensions of the left ventricle and myocardial mass and a decrease in functional parameters. Detection and timely treatment of DM can prevent exacerbation of LV remodeling processes and the development of CHF.

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#451

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

POLYVASCULAR DISEASE, PULSE PRESSURE AND MORTALITY

VIRTUAL E-POSTER SESSION

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Background and Aims: Peripheral arterial disease (PAD), coronary artery disease (CAD) and carotid stenosis (CS) are robust mortalitypredictors. The value of individual vascular beds in polyvascular disease (PVD) to predict mortality in patients with atherosclerotic burden is not clear. Therefore, we have examined the predictive value of PAD, CAD and CS in patients at risk of cardiovascular (CV) disease.

Methods: We analyzed baseline data from the Ludwigshafen Risk and Cardiovascular Health (LURIC) study, a monocentric cohort study of 3316 patients referred to coronary angiography.

Results: As the number of atherosclerotic vascular beds increased, the hazard ratios (HRs) for both all-cause and CV mortality significantly increased in a multivariate analysis after adjusting for age, sex, BMI, diabetes mellitus and eGFR, with HRs of 1.36 (95%CI:1.11–1.68), 2.56 (95%CI: 2.01–3.26), 2.84 (95%CI: 1.93–4.17) and 1.56 (95%CI: 1.19–2.06), 2.70 (95%CI: 1.97–3.72), 3.50 (95% CI: 2.19–5.62), respectively. The combination of PAD with either CAD or CS was associated with higher HRs for all-cause (HR
2.81 and 7.53, respectively) and CV (HRs 2.80 and 6.03, respectively) mortality compared with the combination of CAD and CS
(HRs 1.94 and 2.43, respectively). The presence of PVD was associated with higher age, systolic blood pressure, pulse
pressure (PP), former smoking and inversely with lower eGFR.

Conclusions: We show that as the number of atherosclerotic vascular beds increases, all-cause and CV mortality rates increase in parallel. Simultaneous
prevalence of PAD is associated with significantly higher all-cause and CV mortality compared with CS coexistence.
Furthermore, increasing atherosclerotic load may contribute to vascular stiffness and impaired renal function.

91ST EAS CONGRESS
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#135

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE FREQUENCY OF BREAST ARTERY CALCIFICATION DURING SCREENING MAMMOGRAPHY OF UZBEK WOMEN OLDER THAN 40 YEARS OLD

VIRTUAL E-POSTER SESSION

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Background and Aims: The presence of breast artery calcification (BAC) is associated with cardiovascular (CV) risk factors. Early detection of coronary heart disease (CHD) is important because nearly 40% of initial CV events in women are fatal, highlighting the need for methods to identify women at increased CV risk. The aim of work was to study the frequency of BAC during screening mammography as a marker of CV risk in Uzbek women over 40 years.

Methods: Bilateral digital mammography was performed on 386 women aged 40 to 71 years (mean age 47+/-7 years). The studies were carried out in mediolateral oblique and craniocaudal projections using a digital mammography system «SINO MDT» (China). On mammograms were assessed the presence of BAC, the number of affected vessels, and the distribution of calcification in the vessel wall.

Results: Subjects were questioned in terms of CV risk factors, including diabetes mellitus, hypertension, dyslipidemia, as well as a history of CHD, stroke, transient ischemic attack, and heart failure. From 386 examined women 79 had BAC (20.5%). Amoung them, 13 (20.2%) were over 60 years, 63 (79.8%) were from 40 to 60 years old. The frequency of BAC among women older than 60 years was 1.5 times higher. Approximately 65% of women with BAC had a family history of CHD compared to 35% of women without BAC.

Conclusions: Evaluation of BAC during routine mammography is extremely important in identifying asymptomatic women with increased cardiovascular risk. BAC varies significantly by age and ethnicity, which should be taken into account when comparing different studies.

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#453

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

INDICATORS OF MYOCARDIAL ELECTRICAL INSTABILITY DURING HIGH-DOSE ATORVASTATIN THERAPY IN PATIENTS AFTER ACUTE MYOCARDIAL INFARCTION IN COMBINATION WITH COVID-19

VIRTUAL E-POSTER SESSION

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Background and Aims: Assess the electrophysiological parameters of the heart in patients with myocardial infarction (MI) and COVID-19 during high-dose atorvastatin therapy with multi-day monitoring of the electrocardiogram (MM ECG).

Methods: 64 patients were included on the fourth day after MI, mean age 54.3±6.8years. MM ECG performed within 48-120 hours. We determined the heart rate turbulence (HRT), late ventricular potentials (VLPs), QT dispersion (dispQTe). The treatment was carried out in according to clinical guidelines (ESC, 2017) including atorvastatin (80 mg/day). 2 groups were distinguished: 25 people with MI and COVID-19 ("MICov"), 39 MI patients without COVID-19 ("MInoCov"). Total cholesterol, triglycerides, low and high density lipoproteins were assessed.

Results: VLPs in the "MInoCov" group were registered in 15% patients within 24 hours vs. 18% in the "MICov" group (p=0.03), for 120 hours – in 28% of patients in the group "MInoCov" vs. 33% in the group "MICov" (p=0.04). For 72 hours in the "MInoCov" group higher QRSf values were recorded - 103 (97-105) ms (p=0.009). In a group "MInoCov" less frequently recorded pathological HRT in 48 hours: 5.1% vs. 16% patients (p=0.027). For the entire monitoring period, the dispQTe was higher in the group "MICov" - 40.9(13.1-33) vs. 26.3(17.9-29.2) ms (p_{120}= 0.014). In the group "MInoCov" was lower triglyceride level (p=0.031).

Conclusions: In patients with myocardial infarction and COVID-19 during high-dose atorvastatin therapy, myocardial electrical instability in early postinfarction period was recorded more often.

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#1220

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

THE CONDITION OF THE MAIN ARTERIES IN PATIENTS WITH CHRONIC HEART FAILURE AND DIABETES MELLITUS

VIRTUAL E-POSTER SESSION

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Background and Aims: To assess the condition of the main arteries in patients with CHF with concomitant type 2 diabetes mellitus.

Methods: 165 patients with CHF of functional class I–III (FC) of ischemic genesis aged 40 to 65 years were examined. All patients were divided into 2 groups depending on the presence of DM. Group 1 (n-86) is represented by patients with CHF without DM, group 2 (n-79) — patients with CHF and concomitant DM. To study the condition of the main arteries, the pulse wave propagation velocity (PWV) was determined along the elastic (PWVe) and muscular (PWVm) arteries. All patients underwent a test with post-occlusive reactive hyperemia.

Results: In patients with CHF and DM, there was a significant increase in PWVe compared with patients with CHF without DM: 11.6 [9.3; 12.1] m/s vs 8.9 [8.1; 9.2] m/s in the 2nd and 1st groups, respectively. The frequency of occurrence of persons with SRPVe exceeding normal indicators was significantly higher in patients with CHF and DM than among patients with CHF without DM (78.7% vs 24.6%, respectively). PWVm/PWVe was more significantly reduced in the group of patients with CHF and DM. During the occlusion test in the group of patients with CHF and DM, normal reactivity of the main arteries is significantly less common (14.6% vs 31.8%).

Conclusions: In patients with CHF with the same FC, significantly worse indicators reflecting the stiffness of the arterial wall were revealed among patients with concomitant diabetes.

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#1224

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

DISCORDANCE BETWEEN LDL CHOLESTEROL AND APOLYPOPROTEIN B. WHICH TO PREFER TO GUIDE TREATMENT?

VIRTUAL E-POSTER SESSION

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Background and Aims: Current cardiovascular risk guidelines recommend target values of low-density lipoprotein cholesterol (LDLc) < 55 mg/dL and apolipoprotein B (apoB) < 65 mg/dL. Our objective was to establish the prevalence of LDLc and ApoB discordance in a secondary prevention population in our cardiac rehabilitation unit and describe the size of LDLc particles in this cohort.

Methods: We conducted a retrospective observational study including patients with previous ischemic heart disease with lipid-lowering treatment in secondary prevention followed up in our cardiac rehabilitation unit.

Results: We present a series of 100 patients with a mean age of 60.5 years (S.D. 9.7), 79% male, with high prevalence of cardiovascular risk factors (59% hypertension, 26% diabetes mellitus, 52% smokers). All patients received lipid-lowering therapies, with statins alone or in combination with Ezetimibe. **30 patients (30%) had LDLc > 55 mg/dL and ApoB < 65 mg/dL,** 37 (37%) reached target LDL and ApoB levels (LDLc < 55 mg/dL and ApoB < 65 mg/dL), and 33 (33%) did not reach any of the target levels (LDLc > 55mg/dL and ApoB > 65 mg/dL). **No patient had LDLc < 55mg/dL and ApoB > 65mg/dL**. Among patients with ApoB target level achieved and LDLc > 55mg/dL, the mean LDLc/ApoB ratio was 1.1 (S.D. 0.1). The mean ratios stratified by LDLc level are represented in Figure 1.

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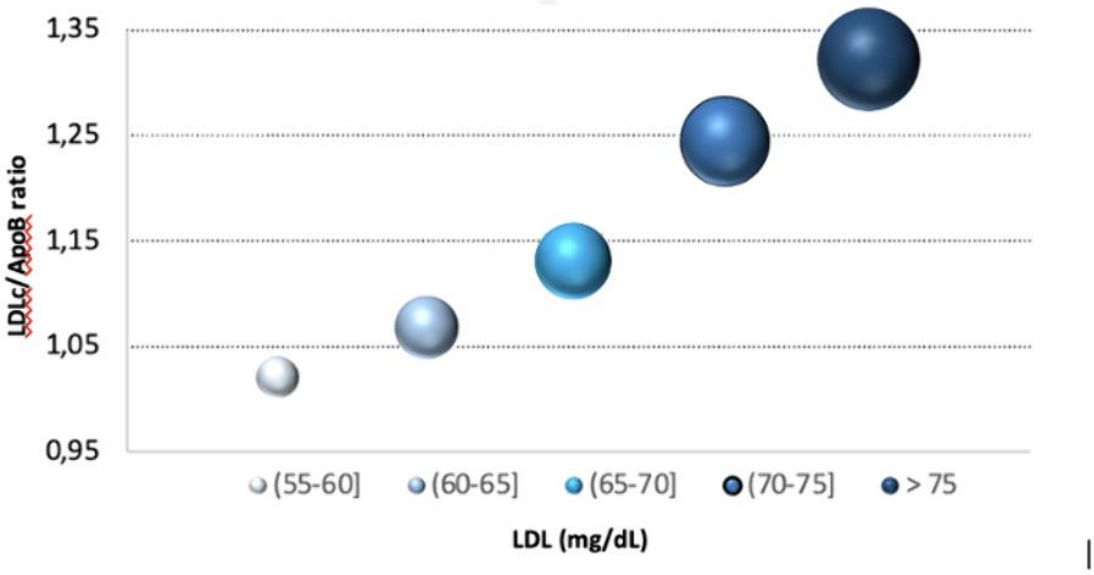

LDLc (mg/dL)	n	Mean LDLc/ApoB	S.D.
(55-60]	10	1.02	0.08
(60-65]	6	1.07	0.12
(65-70]	9	1.12	0.03
(70-75]	3	1.24	0.14
> 75	2	1.30	0.05

Conclusions: The conclusion of our study is that in clinical practice we find a group of patients with discrepancy between LDLc and ApoB levels that is not represented in the main studies of cardiovascular outcomes.

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#1262

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

MONOCYTE ACTIVATION IN TYPE 2 DIABETES AND ASSOCIATED ATHEROSCLEROSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: Atherosclerosis is one of the main vascular complications of diabetes mellitus (DM) that leads to a significant increase in cardiovascular mortality in diabetic patients. Chronic systemic inflammation plays an important role in the pathogenesis of DM and atherosclerosis. The aim of this study was to evaluate the pro-inflammatory activation of monocytes in patients with DM with/without atherosclerosis.

Methods: Totally, 27 patients with newly diagnosed DM were included, with average glucose level of 7.8 (0.9) mmol/l. Assessment of atherosclerotic status was carried out using ultrasound scanning of the carotid arteries. CD14+ leukocytes were isolated from whole blood by immunomagnetic cell separation. Proinflammatory monocyte activation was evaluated as the ratio of non-stimulated and LPS-stimulated secretion of pro-inflammatory cytokine IL-1β measured by ELISA after 24-hour incubation.

Results: In the group of DM and atherosclerosis, non-stimulated secretion of IL-1β was significantly higher than in the group of diabetic patients without atherosclerosis, and amounted to 91.4 (9.5) pg/ml versus 65.4 (7.2) pg/ml, respectively, $p<0.05$. Stimulated secretion of IL-1β was also higher in the group of patients with DM and atherosclerosis compared to the group without atherosclerosis and amounted to 1040.5 (122.8) pg/ml versus 530.6 (72.7) pg/ml, respectively, $p< 0.01$.

Conclusions: Increased pro-inflammatory monocytes activation in diabetic patients with atherosclerosis may be associated with increased chronic systemic inflammation, 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 in patients with DM. This work was supported by the Russian Science Foundation (grant no. 22-25-00149).

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#133

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

GENDER-RELATED ASSOCIATION OF PERCEIVED STRESS WITH METABOLIC SYNDROME COMPONENTS

VIRTUAL E-POSTER SESSION

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Background and Aims: Exposure to a job-specific stress among police officers is associated with a higher prevalence of hypertension and metabolic syndrome (MetS). The study's principal focus rested on investigating the association of perceived stress with arterial hypertension, an essential causative factor for CVD morbidity and mortality.

Methods: Cross-sectional data from a cohort of non-diabetic subjects (n=233; 19F), aged 30-58 years, were analysed. MetS conformed to IDF criteria, whereas perceived stress with Cohen's 10-item Perceived Stress Scale (PSS). Presence of coronary plaque and carotid artery intima-media thickness were also determined. Separately for men and women, regression analyses were applied. Results are expressed as crude and adjusted (for age and current smoking) odds ratios (OR) and 95% confidence intervals (CI).

Results: Positive associations were established between PSS score and waist circumference, and blood pressure (p=0.01), although in men only. The effect of perceived stress (OR=1.135, 95% CI [1.058-1.218], p=0.001), waist circumference (OR=1.900, 95% CI [1.054-1.127], p<0.0001), triglycerides (OR=1.298, 95% CI [1.031-1.611], p=0.02), and glucose (OR=2.093, 95% CI [1.204-3.639], p=0.02) on the prevalence of hypertension, were also encountered in men only. After adjustment for perceived stress (OR 1.101, 95% CI [1.001-1.202], p=0.03), waist circumference (OR=1.138, 95% CI [1.064-1.218], p=0.0001) and glucose (OR=2.696, 95% CI [1.081-6.725], p=0.03) hypertension was still found prevalent. None of the referenced variables had any effect on the prevalence of hypertension in women, neither in univariate, nor in multivariate analyses.

Conclusions: All outcomes were conclusively gender-related across the study population.

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#106

Topic: *AS02 Lipids and Lipoproteins / AS02.12 Adipose tissue biology and pathology*

ASSESSMENT OF MACROPHAGE INFLAMMATORY ACTIVITY ON VISCERAL ADIPOSE TISSUE IN HIGH-FAT DIET-INDUCED OBESE MICE BY 18F- FDG PET/CT

VIRTUAL E-POSTER SESSION

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Background and Aims: Obesity induced inflamed visceral adipose tissue (VAT) secretes pro-inflammatory cytokines thereby promoting systemic inflammation and insulin resistance which further exacerbate obesity-related cardiovascular disease (CVD). Macrophages are the key players in the development of obesity-associated VAT inflammation. Extensive clinical studies have reported that ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) can be used to evaluate the macrophage inflammatory activity on VAT in human beings. However, due to difficulty in human VAT biopsy, pathologic correlations were lacking and there was a few study on preclinical animal models. Here, we investigated whether ^{18}F-FDG PET/CT could reflect the macrophage inflammatory activity on VAT in high-fat diet-induced obese mice.

Methods: Obese animal models were induced by a high-fat diet (60% fat) for 20 weeks using the male C57BL/6 mice. All animals underwent ^{18}F-FDG PET/CT before sacrifice. Macrophage inflammatory activity was evaluated using the maximum standardized uptake value (SUVmax). Flow cytometry-, histological-, and molecular analyses were performed on harvested VAT.

Results: All obese animals showed insulin resistance which resembled the human metabolic syndrome, a key pathophysiological process that contributes to increase CVD risk. VAT SUVmax was increased in obese mice and significantly correlated with the levels of C-reactive protein (CRP). Furthermore, VAT from obese mice showed increased macrophage infiltration, compared to normal mice.

Conclusions: ^{18}F-FDG PET/CT could visualize and evaluate the macrophage inflammatory activity on obesity-driven inflamed VAT in obese mice model. Our preclinical study strongly supports the clinical application of ^{18}F-FDG PET/CT in the assessment of VAT inflammation to patients who are vulnerable to CVD.

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#457

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

PARAMETERS OF REGIONAL ARTERIAL STIFFNESS IN YOUNG AGE PATIENTS WITH CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: to study the state of the arterial bed in patients with coronary artery disease (CAD) with different types of coronary artery lesions.

Methods: 155 people were included (48 (42; 52)years). Depending on the coronary angiography results, patients were divided into groups: 1 - patients without hemodynamically significant stenoses (HSS) of the coronary arteries (CA), 2 - HSS of one CA, 3 - HSS of two or more CAs. The compared persons were comparable in age, sex, office blood pressure. The subjects underwent volume sphygmography (Fukuda Denshi, Japan). Cardio-ankle vascular index (CAVI), PWV in predominantly elastic arteries (R/L-PWV), and biological age were recorded.

Results: R/L-PWV was 11.5±1.6m/s in group 1, 12.1±1.7m/s in group 2, and 12.9±3.5m/s in group 3 (p_{1-2}=0.102; $p_{1,2-3}$<0.001). The biological age in the 1st group was 42.6±11.1years, in the 2nd group - 47 (37;52)years, in the 3rd group - 52.6±10.4years (p_{1-2}= 0.598, $p_{1,2-3}$<0.001). Differences in the CAVI index were registered between patients without HSS and with the presence of HSS of two or more arteries: in the 1st group - 7.3 (6.8;7.9), in the 2nd group - 7.5 (7.1;8.1), in the 3rd group - 8.2 (7.4;9.5) (p_{1-2}=0.104, $p_{1,2-3}$<0.001).

Conclusions: according to volume sphygmography, significant differences in arterial stiffness parameters were registered in patients with coronary artery disease with various types of coronary lesions. The most pronounced changes were found in patients with lesions of two or more coronary arteries according to the results of coronary angiography.

91ST EAS CONGRESS
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#130

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

BLOOD LIPID PROFILE AND SIGNAL AVERAGED ECG PARAMETERS IN PATIENTS WITH HYSTORY OF MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

Ergashali Tursunov, Amayak Kevorkov, Nodir Zakirov, Alisher Rasulov
Cardiac Arrhythmias, Republican Specialized Scientific Practical Medical Center of Cardiology, Tashkent, Uzbekistan

Background and Aims: Purpose: Assessment of relationship between signal averaged ECG (SAECG) parameters and blood lipid profile in patients with history of myocardial infarction and preserved left ventricle ejection fraction (LVEF).

Methods: Methods: study enrolled 525 patients with a history of MI (median age 63 [57; 69] years) and preserved LVEF. All patients underwent lipid profile determination and 12-lead ECG. In blood lipid profile total cholesterol (TC), triglycerides (TG), high density (HDL-C), very low density (VLDL-C), low density lipoprotein cholesterol (LDL-C) were determined. Also, non-high density lipoprotein cholesterol (non-HDL-C), TC/HDL-C ratio and plasma cholesterol coefficient (PCC) were calculated. Three criteria are used to detect late ventricular potentials as follows: filtered QRS duration (fQRSd), the duration of the terminal part of the QRS complex with an amplitude below 40 μV (LAS40) and the root mean square (RSM) signal amplitude of the last 40 ms of the signal <20 μV (RMS40).

Results: Results: The results obtained are presented in the table 1. Our data indicate the presence of a positive correlation between fQRSd parameter of SAECG with TC, LDL-C, nonHDL-C and TC/HDL-C ratio. LAS40 parameter demonstrated positive correlation with TC, TG, VLDL-C, LDL-C and nonHDL-C. RMS40 parameter did not demonstrate a significant relationship with any of the studied blood lipid profile

indicators.

Blood lipid profile	fQRSd	LAS40	RMS40
TC	0,189*	0,219*	-0,094
TG	0,101	0,179*	-0,033
HDL-C	-0,005	0,112	-0,063
VLDL-C	0,098	0,200*	-0,039
LDL-C	0,205*	0,162*	-0,109
nonHDL-C	0,199*	0,191*	-0,079
TC/HDL-C	0,208*	0,124	-0,056
PCC	0,047	0,071	0,031
All data presented as Spearmen correlation coefficient (R); * - p<0.05			

Conclusions: Conclusion: our study demonstrates the existence of a certain relationship between the level of blood lipids and such markers of electrical myocardial instability as ventricular late potentials, detected using signal averaged ECG, in patients with history of myocardial infarction and preserved left ventricle ejection fraction

91ST EAS CONGRESS
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#459

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

LIPID-LOWERING THERAPY STRIKES AGAIN

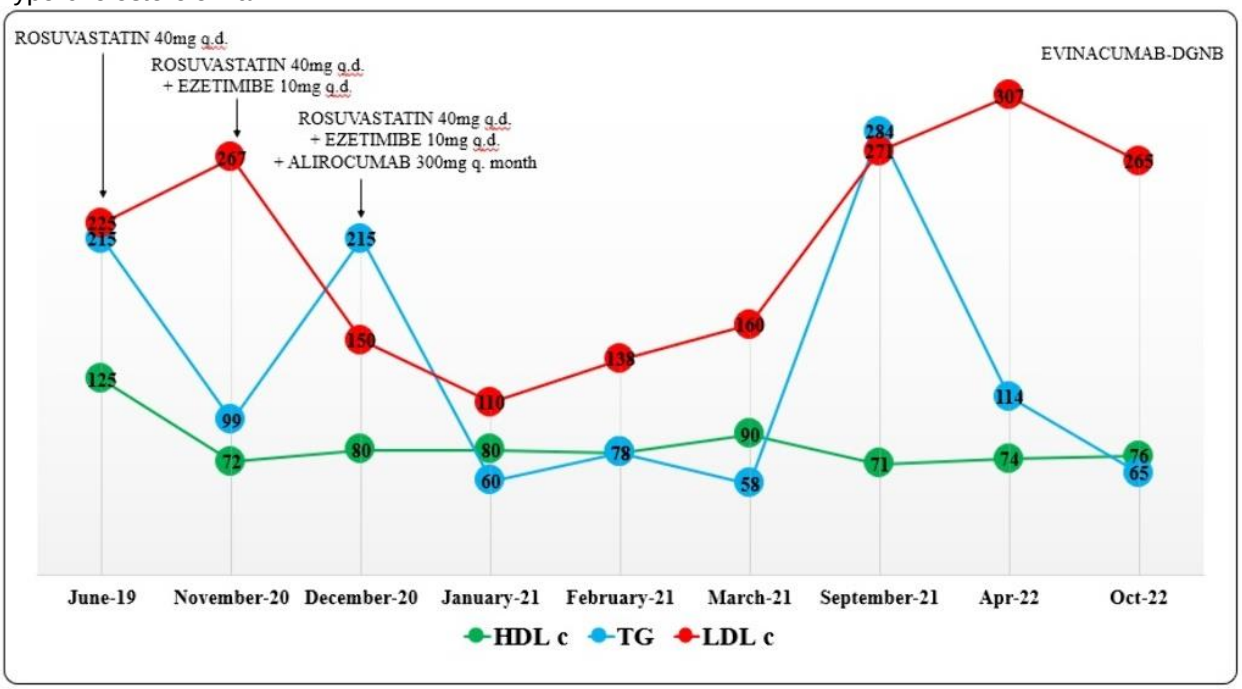
VIRTUAL E-POSTER SESSION

Rebecca Pântea[1], Cornelia Zara[1], Adela Chirita-Emandi[2], Mădălina Ivașcu[1], Ana-Maria Balahura[3]
[1]Cardiology, Theracardia, Brasov, Romania, [2]Genetics, University of Medicine and Pharmacy Victor Babes, Timisoara, Romania, [3]Cardiology, Emergency Clinical Hospital, Bucharest, Romania

Background and Aims: Long-term exposure to high LDL cholesterol is a key predictor of atherosclerotic cardiovascular disease risk. Familial hypercholesterolemia is a rare genetic disorder, which increases the risk of coronary heart disease at a young age. LDL mutation: APOB, LDLR, LDLRAP1 or PCSK9 gene are the most frequent cause of this condition.

Methods: We present the case of a 52 year old female patient with 3 known cardiovascular risk factors- hypertensive, dyslipidemia and overweight and a history of coronary revascularization at a young age (43 years old). She associates mild to moderate progressive aortic valve degenerative disease after coronary surgery. She has also history of Non-Hodgkin lymphoma in remission. Under intensive LLT -lipid lowering therapy **(**rosuvastatin 40 mg plus ezetimibe) and lifestyle intervention, she did not reach the guideline-recommended target of LDL cholesterol level. She was therefore put on PCSK9i with poor response. Genetic test for familial hypercholesterolemia showed a homozygous pathogenic variant NM_015627.2:c.89-1G>C in LDLRAP1, confirming the diagnosis of autosomal recessive familial hypercholesterolemia. Additionally, The Dutch score of 13 points pointed to a diagnosis of familial

hypercholesterolemia.



Results: She is eligible for treatment with evinacumab, a recombinant human IgG4 monoclonal antibody or other specific treatments.

Conclusions: Familial hypercholesterolemia must be definitely hunted for, whenever red flags such as a patient with premature multisite atherosclerotic disease or unexplained early aortic stenosis or the inability to reach target LDL cholesterol levels despite intensive LLT.

91ST EAS CONGRESS
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#126

Topic: *AS02 Lipids and Lipoproteins / AS02.12 Adipose tissue biology and pathology*

IDENTIFICATION OF MAJOR HUB GENES INVOLVED IN HIGH-FAT DIET-INDUCED OBESE VISCERAL ADIPOSE TISSUE BASED ON BIOINFORMATICS APPROACH

VIRTUAL E-POSTER SESSION

Yu Jiang
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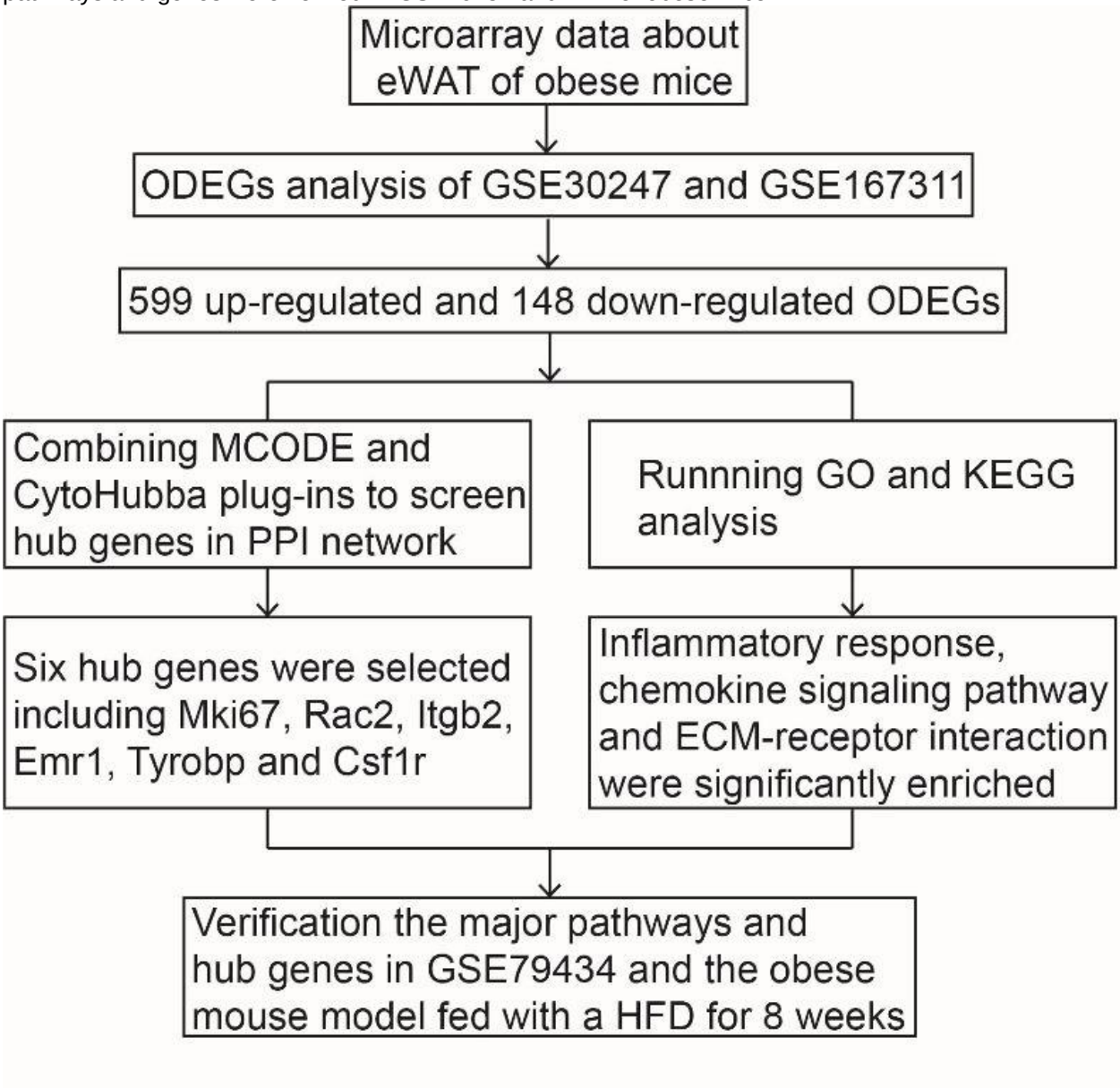
Background and Aims: High-fat diet (HFD) can cause obesity, inducing dysregulation of the visceral adipose tissue (VAT). This study aimed to explore potential biological pathways and hub genes involved in obese VAT, and for that, bioinformatic analysis of multiple datasets was performed.

Methods: The expression profiles (GSE30247, GSE167311 and GSE79434) were downloaded from Gene Expression Omnibus. Overlapping differentially expressed genes (ODEGs) between normal diet and HFD groups in GSE30247 and GSE167311 were selected to run protein-protein interaction network, GO and KEGG analysis. The hub genes in ODEGs were screened by Cytoscape software and further verified in GSE79434 and obese mouse model.

Results: 747 ODEGs (599 up-regulated and 148 down-regulated) were screened, and the GO and KEGG analysis showed that the up-regulated ODEGs were significantly enriched in inflammatory response and extracellular matrix receptor interaction pathways. On the other hand, the down-regulated ODEGs were involved in metabolic pathways; However, there were none significant KEGG pathways. Furthermore, six hub genes, Mki67, Rac2, Itgb2, Emr1, Tyrobp, and Csf1r were acquired. These

pathways and genes were verified in GSE79434 and VAT of obese mice.



Conclusions: This study revealed that HFD induced VAT expansion, inflammation, and fibrosis, and the hub genes could be used as therapeutic biomarkers in obesity.

91ST EAS CONGRESS
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#1240

Topic: *AS04 Clinical Vascular Disease / AS04.11 Anti-inflammatory therapies*

INHIBITION OF RESTENOSIS AFTER ORBITAL ATHERECTOMY OF SEVERELY CALCIFIED ATHEROSCLEROTIC ARTERY USING POLYHYDROXY FULLERENE – LOADED MICROBUBBLES-MEDIATED PULSED LOW LEVEL FOCUSED ULTRASOUND SONODYNAMIC THERAPY

VIRTUAL E-POSTER SESSION

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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”. The orbital atherectomy method that are currently in use, cause to inflammation and subsequent restenosis. The aim of this study was to evaluate the effect of pulsed low- level focused ultrasound sonodynamic therapy on inflammation and restenosis reduction after mechanical atherectomy of the animal model of severely calcified common carotid artery, wherein diagnostic ultrasound is adjuncted with atherectomy and combination therapy system, with a goal of increased safety.

Methods: Briefly, New Zealand white rabbits were submitted to common carotid artery severely calcified atherosclerotic stenosis. Then treatment group underwent B- mode ultrasound- guided orbital atherectomy followed by pulsed low- level focused ultrasound (F= 1.1 MHz, 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.

Results: from histopathology and ultrasonography showed a significant reduction in the mean value for macrophages and smooth muscle hyperplasia cells density after orbital atherectomy in the treated group compared with the other groups ($p<0.05$).

Conclusions: Anti- inflammatory effect of ultrasound, accompanied by enhanced anti- inflammatory effect of Polyhydroxy Fullerene, induced by enhanced sonodynamic therapy, dinduced by collapsed microbubbles, can cause to reduce the inflammation and smooth muscle hyperplasia cells in the intimal layer. These findings provide the basis for developing of sonodynamic therapy for a successful clinical application in the treatment of restenosis after orbital atherectomy.

91ST EAS CONGRESS
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#1245

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

STUDY OF THE EFFECT OF IL6 AND CCL2 ON THE CHOLESTEROL CONTENT IN THE THP-1 CELL LINE

VIRTUAL E-POSTER SESSION

Anastasia Bogatyreva[1], Taisiya Tolstik[1], Diana Kiseleva[2], Ulyana Zotova[1], Vadim Cherednichenko[1], Yuliya Markina[1,3], Alexander Markin[1,4]
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Background and Aims: The aim of the study was to analyze data of cholesterol accumulation in THP-1 cells, which were incubated with various cytokines and LDL isolated from the plasma of patients with inflammatory diseases.

Methods: Cells were cultured in RPMI 1640 medium with the addition of either cytokines and atherogenic LDL, or cytokines without LDL, or only LDL as the positive control. The negative control contained a pure medium. Cytokines IL 6, CL2 were used. The cells were labeled the BDP 630/650. Cholesterol content was measured by flow cytometry.

Results: The average value of fluorescence intensity in the negative control was 39.9 (SD=2.6); in the positive control 45.5 (SD=2.7). Addition IL6 and CCL2 have led to an increase in cholesterol level in the cells. The average fluorescence intensity in the IL6 group 37.4 (SD=4.1); in the group IL6+LDL 48.1 (SD=4.8); CCL2 51.6 (SD=1.3); CCL2+LDL 62.3 (SD=1.8). For all groups p value < 0.05.

Conclusions: IL6 have demonstrated tendention to increase cholesterol level compared to a positive control. In the other side the addition of CCL2 was showed a significant increase in the cholesterol content in cells with and without LDL, which may indicates its high pro-atherogenic activity. This work was supported by the Russian Science Foundation («Research Institute of Human Morphology» Grant # 22-25-00190).

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#556

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.02 Smooth muscle cell biology*

VASCULAR SMOOTH MUSCLE CELL CONTRACTILE PROTEINS ARE BETTER MARKERS OF VASA VASORUM AS COMPARED TO ENDOTHELIAL CELL PROTEINS

VIRTUAL E-POSTER SESSION

Victoria Markova, Leo Bogdanov, Elena Velikanova, Anastasia Kanonykina, Daria Shishkova, Anton Kutikhin
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Background and Aims: Currently, vasa vasorum (VV) are quantified using specific immunohistochemical or immunofluorescence staining against endothelial cell (EC) markers, e.g. CD31/PECAM1 or VE-cadherin. Although EC staining is quite sensitive and specific for VV, it does not allow to perform an objective evaluation of vascular geometry and the signal-to-noise ratio is often quite low. Here, we demonstrated that contractile proteins specific for vascular smooth muscle cells (VSMCs) outperform EC proteins as VV markers.

Methods: Cryosectioned rat aortas and human saphenous veins were analysed by serial staining for ECs (CD31, VE-cadherin, ERG), VSMCs (SM-MHC and α-smooth muscle actin (α-SMA)), markers of arterial specification (HES1, HEY1), venous lineage (NR2F2, NRP2), lymphatic differentiation (PROX1, LYVE1, VEGFR3), and mechanosensitive transcription factors (KLF2 and KLF4). Samples were visualised using confocal microscopy.

Results: Immunostaining for the VSMC markers (contractile proteins SM-MHC and α-SMA) permitted measurement of VV area regardless of vasospasm and provided significantly higher signal-to-noise ratio as compared with the EC markers (CD31 or VE-cadherin). Notably, ERG was defined as a sensitive and specific marker of endothelial lineage in both rat and human blood vessels. Although KLF2 and PROX1 were specific for venous endothelial cells in rats and HEY1 was abundant in rat capillaries, none of the endothelial markers was specific for any of vascular lineages in human VV.

Conclusions: Staining for VSMC contractile proteins (regardless of the marker) is an optimal staining for VV quantification. This study was supported by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities), grant number 0419-2021-001 (https://www.rosrid.ru/ikrbs/detail/V7B4FOKSN5NU0QCFLCPK75S1).

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#465

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

RENAL FUNCTION AND EARLY COMPLICATIONS AFTER SURGICAL REVASCULARIZATION IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: To evaluate the influence of renal filtration function upon early postoperative complications (EPOCs) in patients with stable coronary artery disease (SCAD) undergoing isolated coronary artery bypass grafting (CABG).

Methods: We enrolled 595 consecutive SCAD patients (mean age 61±8 years, 508 (85,4 %) males), undergoing isolated CABG. Renal filtration function was assessed by estimated glomerular filtration rate (eGFR) (by CKD-EPI). According to the baseline eGFR value, patients were subdivided into three groups: ≥90 ml/min/1,73 m^2 (G1; n=100 [16,8 %]); 60-89 ml/min/1,73 m^2 (G2; n=346 [58,2 %]); and <60 ml/min/1,73 m^2 (G3; n=149 [25,0 %]). We analyzed perioperative clinical and instrumental data, and EPOCs cases. Totally, EPOCs were registered in 111 (18,7 %) patients.

Results: G3 was characterized by older age, higher frequency of females, atrial fibrillation (Table), history of repeated myocardial infarction (vs. [G1+G2]: 22,8 % vs. 13,7 %, respectively; p=0,014), left ventricular systolic dysfunction (vs. [G1+G2]: 35,6 % vs. 24,7 %, respectively; p=0,011), and 3-vessel disease (vs. [G1+G2]: 85,9 % vs. 76,2 %, respectively; p=0,015). EPOCs were more prevalent in G3, namely due to the higher frequency of acute kidney injury (Table). Acute postoperative heart failure tended to be more frequent in G3 (vs. [G1+G2]: 12,1 % vs. 7,3 %, respectively; p=0,091). Consequently, the perioperative profile of G3 patients included longer inotropic support and intensive care unit

stay.

Table. The perioperative characteristics of SCAD patients with different baseline renal filtration function, undergoing CABG

Parameters	G1 N=100	G2 N=346	G3 N=149	p
Age, years, Me (IQR)	54 (49-60)	62 (56-67)	65 (60-71)	p_{1-2}<0,001 p_{1-3}<0,001 p_{2-3}<0,001
Females, n (%)	5 (5,0)	38 (11,0)	44 (29,5)	p_{1-3}<0,001 p_{2-3}<0,001
Atrial fibrillation, n (%)	4 (4,0)	28 (8,1)	26 (17,4)	p_{1-3}=0,004 p_{2-3}=0,022
EPOCs, n (%)	8 (8,0)	62 (17,9)	41 (36,9)	p_{1-2}=0,049 p_{1-3}<0,001 p_{2-3}=0,082
AKI, n (%)	3 (3,0)	26 (7,5)	25 (16,8)	p_{1-3}=0,002 p_{2-3}=0,020

Notes: SCAD – stable coronary artery disease; CABG – coronary artery bypass grafting; Me – median; IQR – interquartile range; EPOCs – early postoperative complications; AKI – acute kidney injury; p_{1-2} – statistical significance of difference between G1 and G2; p_{1-3} – statistical significance of difference between G1 and G3; p_{2-3} – statistical significance of difference between G2 and G3

Conclusions: The concomitant baseline impairment of renal filtration function worsens perioperative profile in patients undergoing isolated CABG, namely by the higher frequency of EPOCs, prolonging intensive care.

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#466

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

THE ASSOCIATION OF SYNTAX SCORE WITH FUNCTIONAL SIGNIFICANCE OF CORONARY STENOTIC LESIONS IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Mykola Stan[1], Kyrylo Mikhaliev[2], Oleg Zharinov[3], Andriy Khokhlov[1], Oksana Stan[1], Oleg Zelenchuk[4], Boris Todurov[5]
[1]Interventional, Endovascular And Angiography Department, Heart Institute of the Ministry of Health of Ukraine, Kyiv, Ukraine, [2]Scientific Department Of Internal Medicine, SIS «RPC PCM» SAD, Kyiv, Ukraine, [3]Department Of Functional Diagnostics, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine, [4]Department Of Cardiac Surgery, X-ray Endovascular 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 study the association of SYNTAX score with functional significance of stenotic coronary lesions in patients with stable coronary artery disease (CAD).

Methods: The study consecutively enrolled 68 patients with stable CAD (mean age (63±8,0) years; 45 (66 %) males) and angiographically intermediate coronary lesions (diameter stenosis 50-90 %). The stenotic range 70-90 % was considered a «severe» coronary stenosis (SCS) (n=46 [68 %]). The overall CAD complexity was evaluated by SYNTAX score. Functional significance of coronary lesions was assessed by fractional flow reserve (FFR). Forty (59 %) patients presented with at least one functionally significant coronary lesion (FFR ≤0,80). We stratified the enrolled sample in a binary manner according to several FFR cut-offs (from ≤0,80 to ≤0,60, with 0,05 decrement).

Results: The SCS was strongly associated with all but one (≤0,60) of the selected FFR cut-offs (≤0,80: OR 10,82 (95 % CI 3,67-31,87) (p<0,001); ≤0,75: OR 9,29 (95 CI 3,20-27,01) (p<0,001); ≤0,70: OR 5,47 (95 CI 1,84-16,31) (p=0,002); and ≤0,65: all the FFR ≤0,65 patients presented with SCS; all the AUCs for logistic regression models were ≥0,8). The SYNTAX score was strongly associated with FFR ≤0,70 (OR 1,26 (95 % CI 1,06-1,49); p=0,009) and ≤0,65 (OR 1,21 (95 CI 1,03-1,43); p=0,023). Additionally, SYNTAX score was the only factor, (moderately) associated with FFR ≤0,60 (OR 1,23 (95 % CI 1,04-1,47); p=0,017) (0,8>AUC≥0,7).

Conclusions: The SYNTAX score was associated with more functionally affected (FFR ≤0,70) stenotic coronary lesions in patients with stable CAD, thus should be considered as an additional factor favoring revascularization.

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#123

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ULTRASOUND ASSESSMENT OF TOTAL CEREBRAL BLOOD FLOW IN UZBEK PATIENTS WITH CAROTID ATHEROSCLEROSIS

VIRTUAL E-POSTER SESSION

Gulnora Rozikhodjaeva[1], Zulfiya Ikramova[2], Feruza Rozikhodjaeva[3]
[1]Functional Diagnostic, Central Clinical Hospital №1 of the Head Medical Department under the Administration of the President of the Republic of Uzbekistan, Tashkent, Tashkent, Uzbekistan, [2]Ultrasound Diagnostic, Center for the Development of Professional Qualifications of Medical Workers, Tashkent, Republic of Uzbekistan, Tashkent, Uzbekistan, [3]Medizinische Klinik I, Klinikum Ingolstadt, Ingolstadt, Germany

Background and Aims: Total cerebral blood flow (CBF) is an important but little studied indicator in patients with cerebrovascular disorders. Ultrasound dopplerography occupies a leading position among the diagnostic techniques used in the assessment of CBF. The aim of the study was an ultrasound assessment of the total CBF in patients with carotid atherosclerosis (CA).

Methods: We included in the study 304 subjects aged 18 to 85 years, of which 84 were healthy persons without cardiovascular diseases.
220 patients with CA. The total CBF calculated as the sum of the volumetric blood flow in the internal carotid artery ICA, external carotid artery ECA and vertebral artery VA of both sides. The diameter was measured in B-mode using four different methods: B-mode, color, power doppler,advanted flow imaging AFI modes. CBF was calculated using a semi-automatic program based on spectral doppler and diameter on the ultrasound scanner Aplio500(Toshiba) with linear probe 5,5-10 MHz.

Results: With age, a decrease in CBF values was observed. Until the age of 60, there was no significant dynamics of CBF (19.27 ml/min or 0.74 ml/year) (CBF 983,70 ml/min). A more significant decrease of CBF was in older age groups: by 12.26 ml/year in the group of 60–74 years old (CBF 812 ml/min), 10.51 ml/year at the age of 75 years and older (CBF 664,9 ml/min)($p<0.05$). The gradual decrease in CBF was mainly associated with a significant decrease in the volume of blood flow in the ICA.

Conclusions: The ultrasonic assessment of total CBF provide a diagnostic tool for identifying patients more prone to cerebral ischemia.

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#1297

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

ATHEROSCLEROSIS PROGRESSION IN SUBJECTS WITH VERY HIGH CARDIOVASCULAR RISK IN TREATMENT WITH A HIGH-INTENSITY LIPID-LOWERING REGIMEN. AN OBSERVATIONAL STUDY.

VIRTUAL E-POSTER SESSION

Estibaliz Jarauta[1], Carmen Vicente-Langarita[1], Ana Maria Bea-Sanz[2], Victoria Marco-Benedi[3], Fernando Civeira[1]
[1]Internal Medicine, Hospital Universitario Miguel Servet, Zaragoza, Spain, [2]Cibercv, Instituto de Salud Carlos III, Zaragoza, Spain, [3]Grupo De Dislipemias Primarias, Instituto de Investigación Sanitaria de Aragón, Zaragoza, Spain

Background and Aims: Intima media thickness (IMTc) regression on carotid arteries has been associated with the reduction of cardiovascular disease. There are few data about the progression of atherosclerosis measured by 2D ultrasound after intensive lipid-lowering treatment. Our study aimed to describe the progression of IMTc and plaque prevalence in subjects with very-high cardiovascular risk in treatment with high-intensity statins with or without ezetimibe plus PCSK9i in real clinical practice.

Methods: IMTc were measured at baseline and follow-up by 2D ultrasound. Lipid profile and prevalence of cardiovascular risk factors were collected in both visits.

Results: Thirty-four subjects with familial hypercholesterolemia and 12 with a previous history of CVD were included. After a median follow-up of 15 years and a median time treatment with PCSK9i of 5 years, a median progression of IMTc of 0.00065 mm/year was observed in the common and internal carotid artery and 0.0098 mm/year in the carotid bulb. There was no difference in the number of plaques. In the same period, values of low-density lipoprotein cholesterol (LDLc) decreased by 77% ($p<0.001$), whereas high-density cholesterol (HDLc) increased by 5.9% ($p=0.021$). The prevalence of hypertension and diabetes increased from 16 to 57% and 7 to 33%, respectively. The variables associated with atherosclerosis progression were baseline IMTc, high LDLc, low HDLc and development of hypertension and diabetes mellitus, with the highest predictive value for the common carotid artery, $R^2= 0.55$.

Conclusions: Atherosclerosis progression in subjects receiving very intensive lipid-lowering treatment was lower than in the general population and was associated with LDLc reduction and HDLc increase.

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#1324

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ULTRASOUND- GUIDED BALLOON ANGIOPLASTY OF OCCLUDED ARTERY ACCOMPANIED BY COMBINED DISULPHONATED ALUMINUM PHTHALOCYANINE - MEDIATED PHOTODYNAMIC THERAPY AND IODINE-125- MEDIATED GAMMA RAY- INTRAVASCULAR BRACHYTHERAPY

VIRTUAL E-POSTER SESSION

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[1]Department Of Physics, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [2]Laboratory Of Novel Technologies In Non- Invasive Treatments, Islamic Azad University, Tabriz Branch, Tabriz, Iran, [3]Division Of Translational Medicine Development Of Noninvasive Treatments, Mehrad Research Lab, Tabriz, Iran

Background and Aims: The balloon angioplasty methods that are currently in use, cause to inflammation and subsequent restenosis. The aim of this study was to evaluate the effect of combined photodynamic therapy and brachytherapy on inflammation and restenosis reduction after balloon angioplasty of the animal occluded common carotid artery model, wherein diagnostic ultrasound is adjuncted with angioplasty and combination therapy system, with a goal of increased safety.

Methods: Briefly, Golden Syrian Hamsters were submitted to common carotid artery advanced atherosclerotic occlusion by primary perivascular Co_2 thermal laser 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 combined photodynamic therapy with red diode laser (WL= 635 nm, E/A= 125 J/cm2), accompanied by photosensitizer Disulphonated Aluminum Phthalocyanine (AlS2Pc) administration.

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for macrophages and smooth muscle hyperplasia cells density after balloon angioplasty in the treated group compared with the other groups ($p<0.05$).

Conclusions: Anti- inflammatory and cytotoxic effect of photodynamic therapy, accompanied by apoptotic effect of gamma ray brachytherapy, can cause to reduce the inflammation and smooth muscle hyperplasia cells in the intimal layer. These findings provide the basis for developing of combined Disulphonated Aluminum Phthalocyanine (AlS2Pc)- mediated photodynamic therapy and ^{125}I- mediated gamma ray- intravascular brachytherapy for a successful clinical application in the treatment of restenosis after balloon angioplasty.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#549

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

METABOLIC PROFILE IN PATIENTS WITH HYPERTENSION AND FREQUENCY VENTRICULAR EXTRASYSTOLE

VIRTUAL E-POSTER SESSION

Anastasia Ivankova[1], Nataliia Kuzminova[1], Evgenia Ivanova[2], Olena Kulchytska[1]
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Background and Aims: Essential hypertension rarely occurs in isolation and often forms clusters with cardiometabolic risk factors, such as decreased glucose tolerance, hyperuricemia, and dyslipidemia. The aim: is to evaluate the metabolic profile in patients with essential hypertension and ventricular extrasystole.

Methods: 82 patients with stage II essential hypertension entered the study. The main group consisted of 50 persons with essential hypertension and frequent ventricular extrasystole. In addition, we examined 32 patients without any cardiac arrhythmias, who entered the comparison group. We also examined 30 people without any cardiovascular pathology, who were included in the control group. The statistical analysis indicated the age and gender homogeneity of patients. All patients underwent full comprehensive clinical, laboratory, and instrumental examination: 1) measurement of blood pressure; 2) electrocardiography in 12 standard leads; 3) daily blood pressure monitoring; 4) echocardiography; 5) the level of serum lipid spectrum, uric acid level.

Results: The level of uric acid in patients with frequent ventricular extrasystole was significantly higher than in patients without arrhythmias (381 μmol / l vs. 318 μmol / l, p = 0.001) and persons without cardiovascular pathology (303 μmol / l, p <0.001). In turn, the number of patients with hyperuricemia was also highest in patients with ventricular extrasystolic arrhythmia (48.0 %), which was significantly different compared with patients without arrhythmias, where the number of patients with hyperuricemia was only 9.4 % (p <0.0003).

Conclusions: Patients with frequent ventricular exrtasystole had more pronounced proatherogenic shifts in the blood lipid spectrum and a significantly higher level of uric acid (p <0.05).

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#53

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.16 Cardiometabolic factors implicated in the development of heat failure with preserved ejection fraction*

DYSLIPIDEMIA AND MYOCARDIAL STRAIN IN YOUNG ADULTS WITH METABOLIC SYNDROME

VIRTUAL E-POSTER SESSION

Svetlana Bartosh-Zelenaya[1], Viktoria Stepanova[2], Olga Mamaeva[2], Tatyana Naiden[1]
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Background and Aims: To assess lipid metabolic disorders and right and left ventricular strain in young people with metabolic syndrome to identify early markers of myocardial dysfunction.

Methods: 50 young people (18–44 years old) were examined; 26 of them had a newly established clinical and laboratory diagnosis of MS. The control group consisted of 24 young healthy people. Anthropometric data included height, body weight, waist circumference (WC), waist-to-height ratio , body mass index (BMI). Lipid profile was assessed including total cholesterol (TC), triglycerides (TG), high and low density lipoprotein cholesterol (HDL and LDL cholesterol), as well as glucose levels. Longitudinal (GLS), circular (GCS), and radial (GRS) strain were measured using 4D echocardiography.

Results: In individuals with MS, the mean values of circular (GCS), radial (GRS) strain and area strain (GAS) of the LV were also significantly lower compared to the control group (p1=0.002, p2=0.002, p3=0.001). Mean RV GLS values of 20.4% in the main group were lower compared to the control group (24.3%, p=0.02), although they were at the lower limit of the norm. The TC level had a strong direct correlation with tLV GLS in 2D and 4D, GAS, GCS, GRS; direct moderate correlation with LV EF in 4D. LDL-C was correlated with 2D and 4D LV GLS (r1=0.63, r2=0.69), GAS (r=0.81), GRS (r=0.77).

Conclusions: In young people with MS, 2D and 4D RV and LV strain is an earliest marker of myocardial dysfunction associated with changes in the lipid profile, namely, an increase in the level of total cholesterol and low-density lipoprotein cholesterol . 3

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#1474

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

HYPOPHOSPHATEMIA AND CARDIOVASCULAR DISEASE: DATA FROM A GREEK POPULATION STUDY

VIRTUAL E-POSTER SESSION

Efstathia Megapanou[1], Matilda Florentin[1], Georgia Anastasiou[2], George Liamis[1]
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Background and Aims: While hyperphosphatemia is associated with cardiovascular toxicity and atherosclerosis, low phosphate levels are not fully described in patients with cardiovascular disease (CVD). Aim of our study was to investigate the incidence of hypophosphatemia in hospitalized patients with cardiovascular disease as well as their connection with in- and out-of-hospital mortality.

Methods: We conducted a prospective study of 176 patients with hypophosphatemia who were consecutively hospitalized at the 2nd Department of Internal Medicine of University Hospital of Ioannina. Out-of-hospital mortality was reported within one month from patients' discharge.

Results: From our study population's history, 18,2% reported coronary heart disease (CHD), 26,7% peripheral arterial disease (PAD), 6,8% carotid stenosis and 26,1% stroke. Out of 176 hypophosphatemic patients, 126 presented the disorder on admission and 50 during their hospitalization. Persons with history of CHD (OR 2,43 CI 1,03 - 5,73) had increased risk of exhibiting hypophosphatemia on admission, with CHD proven to be an independent risk factor (OR 3,90 CI 1,49 - 10,21) for the appearance of this disorder. Patients with CHD (OR 3,42 CI 1,28 - 9,15), PAD (OR 9,33 CI 3,60 - 24,20), carotid artery stenosis (OR 5,72 CI 1,07 - 30,61) and stroke (OR 8,09 CI 3,44 - 19,06) were more likely to present hypophosphatemia during their hospitalization. History of stroke (P=0,026) was a risk factor for in-hospital mortality and CHD (P=0,026) for out-of-hospital mortality of hypophosphatemic patients.

Conclusions: Hypophosphatemia in patients with CVD is not uncommon and their association may be linked to increased mortality.

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#91

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

PREMATURE VENTRICULAR CONTRACTIONS AS A RISK FACTOR FOR ATHEROSCLEROSIS

VIRTUAL E-POSTER SESSION

Olga Germanova
International Centre For Education And Research In Cardiovascular Pathology And Cardiovisualization, Samara State medical university, Samara, Russian Federation

Background and Aims: In the list of reasons of atherosclerosis, there are no premature ventricular contractions (PVCs). Aim. To study the main arteries hemodynamics in patients with PVCs and to determine their influence on the atherosclerotic process.

Methods: 286 patients with PVCs: 1 (142) – patients with PVCs less 3000 per 24 hours, 2 (144) – more 3000 per 24 hours. Groups were similar in age, gender, comorbidities. By Doppler-ultrasound and shygmography we determined the parameters of heart biomechanics and arteries kinetics (common carotid, posterior tibial artery): speed, acceleration, power, work. The volume of cardiac output and transmitral blood flow were measured by echocardiography. We identified the moment of extrasysyoles' appearance by apex-cardiography and ECG. We classified the PVCs up to the moment of their appearance in cardio cycle: before the transmitral blood flow peak; after the transmitral blood flow peak.

Results: The prevalence of atherosclerotic process was observed in group 2 ($p<0,05$). The maximums of hemodynamic parameters were in first post-extrasystolic contraction in PVCs before the transmitral peak flow. PVCs caused the mechanic damage of endothelium and as a result lipid deposition. The "weak places" – are the places of the main effect of the first post-extrasystolic wave: aorta arch in large radius, carotid bifurcation, aorta bifurcation.

Conclusions: PVCs change intra-arterial hemodynamics and cause the mechanical injury of intima, existing atherosclerotic plaques that can lead to progressing of atherosclerosis. PVCs are the risk factor for atherosclerosis.

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#1479

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

PEDIATRIC REFERENCE VALUES FOR NON-FASTING LIPIDS IN FRENCH-CANADIAN CHILDREN

VIRTUAL E-POSTER SESSION

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Background and Aims: Dyslipidemias, including familial hypercholesterolemia (FH), are a risk factor for cardiovascular diseases (CVD). FH is a genetic disorder that impairs cholesterol metabolism, resulting in elevated levels of LDL-C and the onset of early cardiovascular disorders. The heterozygous form of FH (HeFH) is the most common form of this condition, with a higher prevalence in the French-Canadian population due to a founder effect. Atherosclerosis can begin in childhood, highlighting the importance of screening for dyslipidemia during this period, using reference values adapted to the target population. This study aimed to establish age- and gender-specific reference values for non-fasting lipid profiles in healthy French-Canadian children, considering the stage of puberty.

Methods: Non-fasting blood samples were obtained from 386 children enrolled in the GESTE cohort in Sherbrooke, Quebec. Lipid profiles, including total cholesterol (TC), HDL-C, LDL-C, triglycerides (TG), non-HDL cholesterol (non-HDL-C), and apolipoprotein B (ApoB), were measured. Using the *GAMLSS* method in RStudio, age- and gender-specific reference values and percentile curves were estimated.

Results: Reference curves and percentile values (5^{th}, 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th} and 95^{th}) were established based on the lipid profiles of 356 healthy, non-obese children (204 aged 6-7 years and 152 aged 9-13 years), with 82 children present at both follow-ups. Boys in the prepubertal stage had higher levels of TC ($p<0.0001$), HDL-C ($p<0.0001$), and TG ($p<0.05$) than those in puberty.

Conclusions: Here, we reported for the first-time reference values for the French-Canadian children that could lead to a better diagnosis of dyslipidemia and better prevention against CVD.

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#487

Topic: *AS04 Clinical Vascular Disease / AS04.11 Anti-inflammatory therapies*

APPLICATION FOR DISSOLUTION OF CORONARY ATHEROSCLEROTIC PLAQUE: A NEW TREATMENT?

VIRTUAL E-POSTER SESSION

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Background and Aims: In atherosclerosis, the accumulation of fat in and between cells and the LDL coating of the vessel is called the atheroma stage. The plaque is now called fibroatheroma with the proliferation of smooth muscle cells, which transforms it from the beginning into a more robust structure (Hanson et al., 2013). With the dissolution of this lipid formation, which increases inflammation, the formed atherosclerotic plaque will disappear.

Methods: 10 autopsy samples with coronary artery disease prepared for phosphatidylcholine/deoxycholate application. This mixture was applied to a part of 10 autopsy specimens with coronary artery disease, whose autopsy specimens were divided into two equal parts before administration. Other parts were placed in a protective liquid of 0.9% benzyl alcohol only. The applied and untreated tissue pieces were kept in solutions for 10 minutes, then washed with distilled water and cleaned.

Results: When the microscopic examination of the samples with and without phosphatidylcholine/deoxycholate application was compared, it was observed that the lipid-weighted tissues in the atherosclerotic plaque were fragmented.
It was shown with the microscope image that the application of phosphatidylcholine/deoxycholate, which dissolves the unwanted subintimal lipid accumulation, did not damage the tissue structure.

Conclusions: It has been determined that the staining and preparation tissue pieces and the application, which allows the structural features of the tissues with and without phosphatidylcholine/deoxycholate application to be examined under the microscope, break up the unwanted subintimal fat accumulation. Microscopic images have also shown that phosphatidylcholine/deoxycholate application does not disrupt the structure of the tissues while dissolving the fat deposit.

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#488

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

THE ASSOCIATION BETWEEN CORONARY ARTERY CALCIUM SCORE AND MYOCARDIAL BLOOD FLOW IN NON-OBSTRUCTIVE CORONARY ARTERY DISEASE PATIENTS

VIRTUAL E-POSTER SESSION

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Background and Aims: The interplay between anatomical lesions of coronary arteries, specifically coronary artery calcium score (CAC), and myocardial blood flow (MBF) in non-obstructive coronary artery disease (NOCAD) patients remains unclear. The aim of the study was to assess the relationships between CAC and MBF and myocardial flow reserve (MFR) in NOCAD patients (stenosis<50%).

Methods: All patients underwent coronary computed tomography angiography with assessment of CAC by using Agatston method and dynamic SPECT on solid-state detectors gamma camera. Standard indexes of myocardial perfusion imaging (MPI) and quantitative global parameters (stress/rest MBF, MFR) were assessed. Based on the CAC results was divided patients' sample into three groups: 1. CAC=0 Agatston Units (n=19); 2. CAC=1-100 Agatston Units (n=21); 3. CAC=101-400 Agatston Units (n=12).

Results: The study included 52 patients (36 men, age 55.0±9.8 years). Standard indexes of MPI and rest MBF did not differ significantly in groups. Stress-MBF and MFR were significantly decreased from the first group compared to the third one: stress-MBF 1.52 (1.31;1.66), 1.33 (1.02;1.63) and 0.91 (0.64;1.4) ml/min/g, MFR 2.84 (2.18;3.9), 2.54 (2.18;3.08) and 1.6 (1.48;2.07), in groups, respectively ($p<0.05$). The Spearman analysis showed negative significant correlations ($p<0.05$) between CAC and stress-MBF ($\rho=-0.46$, $p=0.003$) as well as MFR ($\rho=-0.48$, $p=0.001$).

Conclusions: Decreased stress-MBF and MFR and increased CAC can use like early marker of risk in NOCAD patients. The combined assessment of CAC and scintigraphic parameters of MBF might be used to improve diagnostic accuracy of clinical status in NOCAD patients.

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#1486

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

PROTECTIVE ROLE FOR BODY FAT MASS IN ATHEROGENESIS AMONG LOW CARDIOVASCULAR RISK PATIENTS

VIRTUAL E-POSTER SESSION

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Background and Aims: Dietary, pro-inflammatory and lipid factors contribute to the atherogenesis in humans. The study aim was to evaluate a potential association between central obesity, multiply modified LDL (mmLDL) and subclinical atherosclerosis in individuals with low SCORE risk.

Methods: A pilot study, including patients without carotid atherosclerosis at low risk according to SCORE, was designed. Anthropometry and bioimpedance analysis were performed in every subject alongside with laboratory tests for cholesterol profile and multiply modified LDL (mmLDL). The epicardial fat thickness (EFT) and intima-media thickness (IMT) were assessed by ultrasound methods. Multivariate linear regression analysis was used to assess the impact of different metabolic parameters on subclinical atherosclerosis prevalence.

Results: 86 adult subjects were screened (mean age: 42.9(2.3) years; BMI 22.9(5.4) kg/m^2; and 35% male). 44 (51%) participants with CO. The level of mmLDL was significantly higher in the CO group, regardless of gender: 26 [18; 32] U vs 14 [10; 16] U, respectively ($p<0.01$). IMT average were correlated with WC, body fat mass, TG, TC, LDL, and mmLDL ($r = 0.4; 0.3; 0.3; 0.4; 0.4; 0.5$, respectively, $p = 0.001$). According to multivariate analysis IMT was directly associated with age ($\beta=0,4$; $p = 0.001$), EFT ($\beta=0,3$; $p = 0.02$) and inversely associated with body fat mass ($\beta= - 0,4$; $p = 0.02$).

Conclusions: Body fat mass plays an beneficial role in the atherogenesis in low risk patients. Excessive accumulation of fat mass is a compensatory mechanism for the elimination of triglycerides from the bloodstream and deposition in adipocytes, thereby providing a protective effect against hyperlipidemia and atherosclerosis.

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#490

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

CALCIPROTEIN PARTICLES ARE INTERNALISED BY CIRCULATING MONOCYTES AND INDUCE MONOCYTE-DERIVED CHEMOKINE RELEASE

VIRTUAL E-POSTER SESSION

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Laboratory Of Molecular, Translational, And Digital Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Background and Aims: Calciprotein particles (CPPs) represent a mineral buffering system which scavenges excessive Ca^{2+} and PO_4^{3-} ions to prevent extraskeletal calcification, yet causing endothelial dysfunction upon the internalisation by arterial endothelial cells. Here we revealed that circulating CPPs are also internalised by monocytes, causing release of pro-inflammatory chemokines (MIP-1α, MIP-3α, CINC-1, CINC-3, CXCL10) into systemic circulation.

Methods: Peripheral blood of healthy volunteers was co-incubated with CPPs (0.4×10^5 particles per mL, ≈15% increase in CPP concentration previously reported in patients with end-stage renal disease) in the flow culture system (15 dyn/cm^2) to investigate the effects of CPPs on the human blood *ex vivo*. For *in vivo* modeling, we intravenously administered CPPs to Wistar rats (0.8×10^5 particles per mL, ≈8% increase in CPP amount if recalculated into animal equivalent dose).

Results: Among the blood cells, monocytes were exclusively responsible for CPP internalisation, whereas neutrophils, eosinophils, lymphocytes, red blood cells, and platelets were devoid of CPPs upon the co-incubation. Co-incubation of CPPs did not affect the complete blood count yet caused a donor-dependent pro-inflammatory response in human serum ex vivo (upregulation of MIP-1α/1β and SDF-1α/CXCL12). Moreover, intravenous administration of CPPs to Wistar rats enhanced the release of monocyte-derived chemokines (MIP-1α, MIP-3α, CINC-1, CINC-3, CXCL10), whilst elevated serum sICAM-1 and IL-8 indicated an involvement of endothelial cells to the systemic inflammatory response provoked by CPPs.

Conclusions: Pathological effects of circulating CPPs are not limited to endothelial dysfunction, as they also induce release of monocyte-derived chemokines into systemic circulation. This research was funded by the Russian Science Foundation, grant number 22-15-00107 (https://rscf.ru/en/project/22-15-00107/).

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#82

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MYOKINE PROFILE AND GLYCEMIC CONTROL IN TYPE 2 DIABETES MELLITUS PATIENTS WITH HEART FAILURE

VIRTUAL E-POSTER SESSION

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[1]Internal Medicine, Zaporozhye State Medical University, Zaporozhye, Ukraine, [2]Internal Medicine, Zaporozhye Medical Academy of Postgraduating Education, Zaporozhye, Ukraine, [3]Internal Medicine, Medical Academy of Postgraduating Education, Zaporozhye, Ukraine

Background and Aims: Type 2 diabetes mellitus (T2DM) remains a powerful predictor of progressive heart failure (HF), but it is not clear whether altered glycemic control interferes with HF progression via an impaired profile of circulating myokines. The aim was to investigate plausible effects of glucose control on signature of myokines in T2DM patients affected by chronic HF

Methods: A total of 372 patients with T2DM from our local database were prescreened in the study. We used any medical records, discharge reports, laboratory reports, and communications with general practitioners to qualify the patients as candidates for participating in the study. Finally we included 314 individuals suffering from chronic HF and subdivided them into two groups according to glycosylated hemoglobin (HbAc1) < 6.9% and ≥ 7.0%, respectively. Echocardiography and Doppler examinations along with biomarker measurements were performed at baseline of the study.

Results: The results showed that irisin levels were significantly lower in patients with an HbAc1 ≥ 7.0% than in those with an HbAc1 < 6.9%, whereas concentrations of apelin, myostatin and adropin did not significantly distinguish between these two groups. We also identified numerous predictors of poor glycemic control, but only N-terminal brain natriuretic pro-peptide (odds ratio [OR] = 1.07; 95% confidence interval [CI] = 1.02-1.10, p = 0.04) and irisin (OR = 1.09; 95% CI = 1.04-1.17, p = 0.001) remained independent predictors of the dependent variable

Conclusions: We found that decreased levels of irisin were associated with poor glycemic control in T2DM patients with HF regardless of clinical conditions and other biomarkers

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#77

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

CASE REPORT: ADHERENCE TO THERAPY, MTTP GENE VARIANTS, COURSE OF ATHEROMA IN TWO HOFH PATIENTS ON LOW DOSE LONG TERM LOMITAPIDE THERAPY

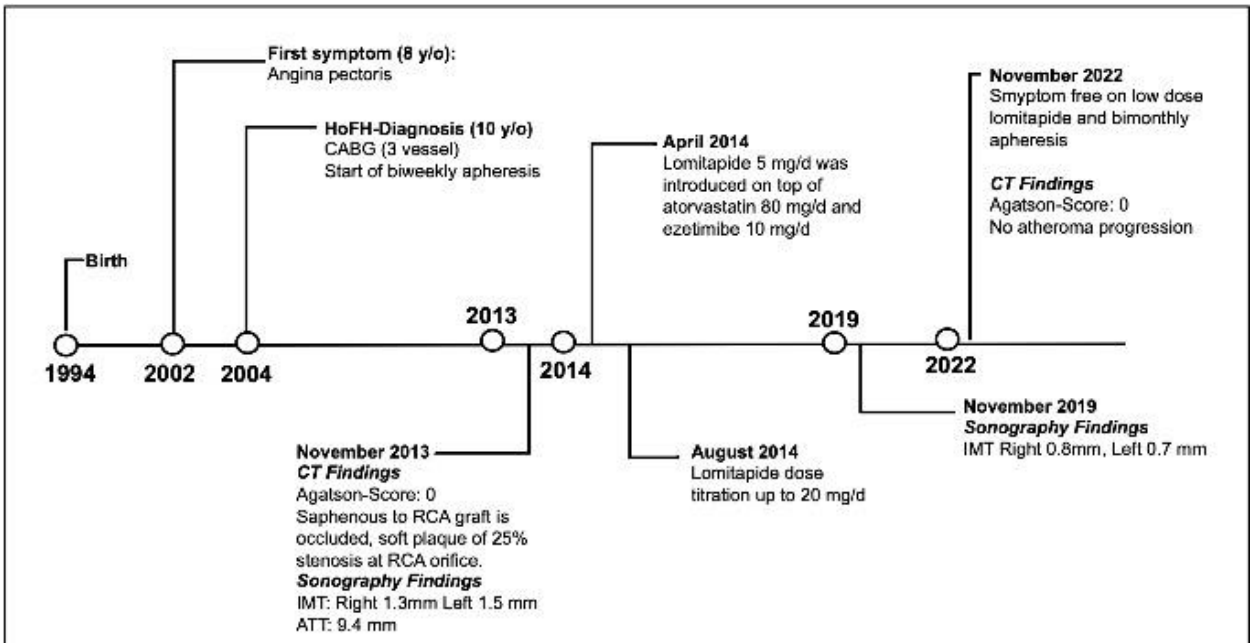
VIRTUAL E-POSTER SESSION

Burcu Yagmur
Cardiology, EGE UNIVERSITY, IZMIR, Turkey

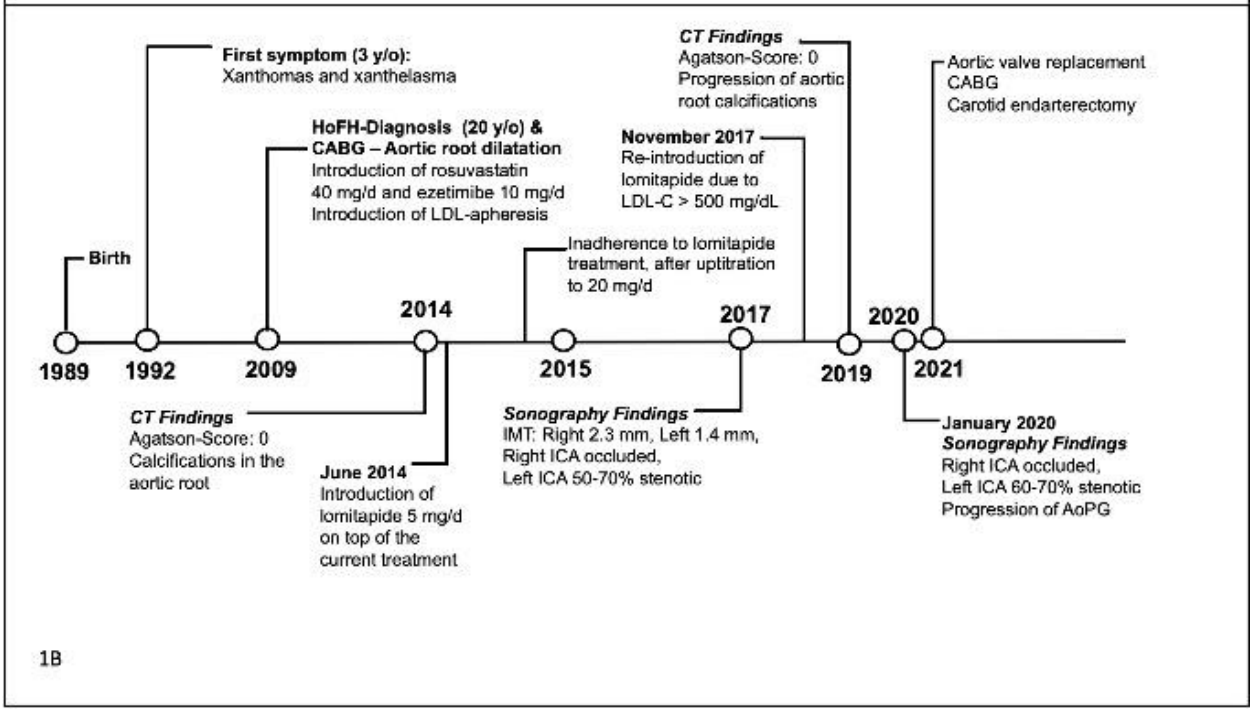
Background and Aims: Homozygous familial hypercholesterolemia (HoFH) is a rare genetic condition characterized by extremely high levels of low-density lipoprotein cholesterol (LDL-C) leading to an increased risk of early atherosclerosis.HoFH patients mostly present with mutations in the LDLR, but here we present two cases with concomitant MTTP mutations Our aim was to present the possibility of preventing the progression of atherosclerotic burden with effective and safe LDL-C reduction in HoFH patients with low dose Lomitapide therapy and to emphasize the role of treatment adherence in therapy success.

Methods: We present two patients with phenotypically HoFH, a compound heterozygous female and a simple homozygous male, both with LDLR and additional MTTP mutations, who were treated with the MTTP-inhibiting agent lomitapide, with different treatment compliances. The role of impulsivity was investigated through Barratt Impulsivity Scale 11, and the extent of the atherosclerotic burden was followed up using coronary artery calcium scoring, echocardiographic and sonographic findings, and eventually through a strict follow-up of laboratory parameters.

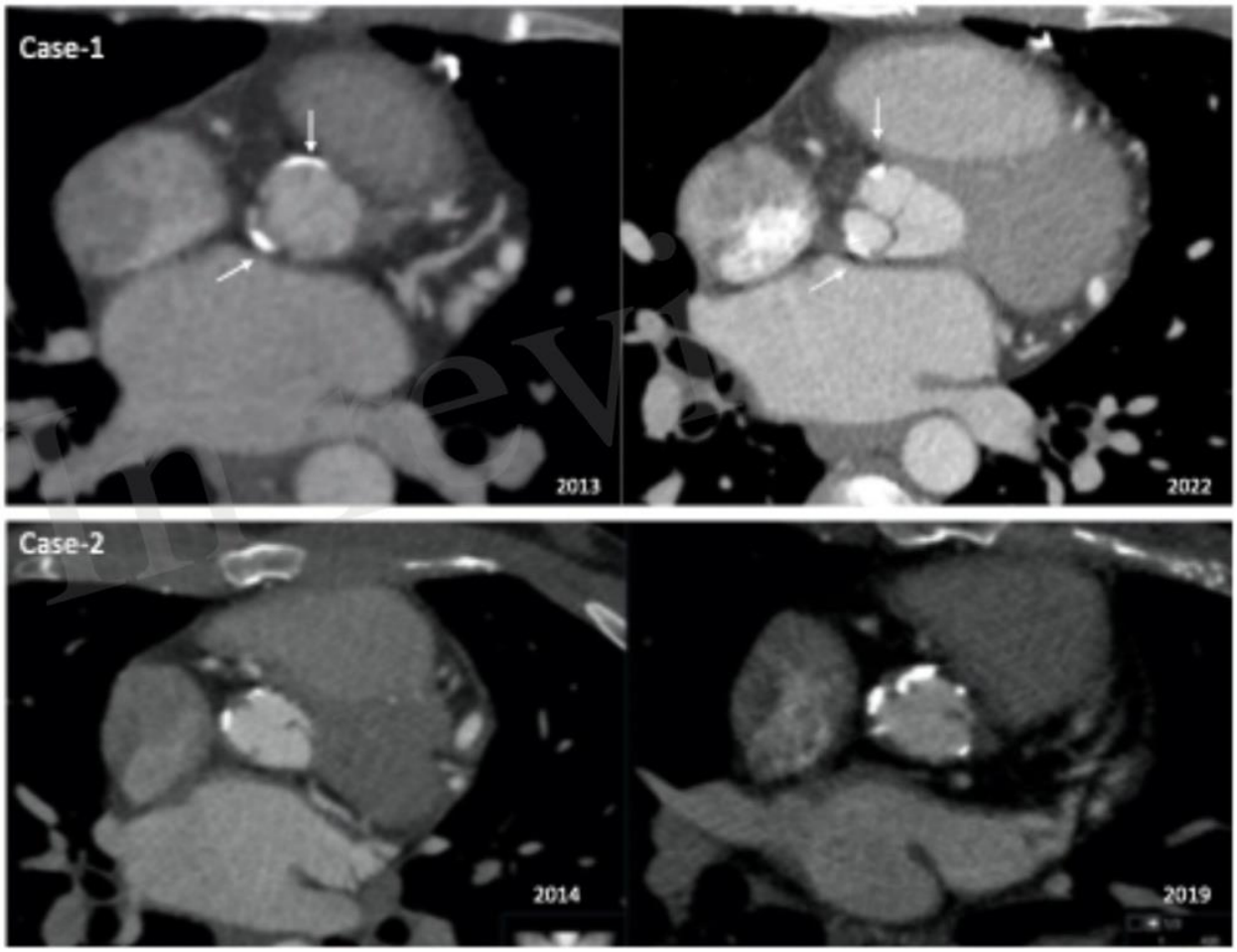
Results: Two real-life cases demonstrate that effective lipid-lowering therapy (LLT) with low-dose lomitapide combined with long-term apheresis safely inhibits the progression of atheroma in both the coronary and vascular regions and delays the progression of aortic
stenosis.


First symptom (8 y/o):
Angina pectoris
HoFH-Diagnosis (10 y/o)
CABG (3 vessel)
Start of biweekly apheresis
April 2014
Lomitapide 5 mg/d was introduced on top of atorvastatin 80 mg/d and ezetimibe 10 mg/d
November 2022
Smyptom free on low dose lomitapide and bimonthly apheresis
CT Findings
Agatson-Score: 0
No atheroma progression
Birth
1994
2002
2004
2013
2014
2019
2022
November 2013
CT Findings
Agatson-Score: 0
Saphenous to RCA graft is occluded, soft plaque of 25% stenosis at RCA orifice.
Sonography Findings
IMT: Right 1.3mm Left 1.5 mm
ATT: 9.4 mm
August 2014
Lomitapide dose titration up to 20 mg/d
November 2019
Sonography Findings
IMT Right 0.8mm, Left 0.7 mm

1A


First symptom (3 y/o):
Xanthomas and xanthelasma
CT Findings
Agatson-Score: 0
Progression of aortic root calcifications
Aortic valve replacement
CABG
Carotid endarterectomy
HoFH-Diagnosis (20 y/o) &
CABG – Aortic root dilatation
Introduction of rosuvastatin 40 mg/d and ezetimibe 10 mg/d
Introduction of LDL-apheresis
November 2017
Re-introduction of lomitapide due to LDL-C > 500 mg/dL
Inadherence to lomitapide treatment, after uptitration to 20 mg/d
Birth
1989
1992
2009
2014
2015
2017
2019
2020
2021
CT Findings
Agatson-Score: 0
Calcifications in the aortic root
June 2014
Introduction of lomitapide 5 mg/d on top of the current treatment
Sonography Findings
IMT: Right 2.3 mm, Left 1.4 mm,
Right ICA occluded,
Left ICA 50-70% stenotic
January 2020
Sonography Findings
Right ICA occluded,
Left ICA 60-70% stenotic
Progression of AoPG

1B



Conclusions: Low dose Lomitapide on top of standard LLT with decreased frequency of lipid apheresis, enabled the prevention of the progression of atherosclerotic burden if associated with good adherence to therapy. The cause of incompliance might be explained by the impulsive behavior of the patients and non-adherence to low-fat diet.

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#1518

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

ASSOCIATION OF PRECONCEPTION FACTORS WITH TYPE 2 DIABETES, IN THE URBAN POPULATION OF NORTH INDIA.

VIRTUAL E-POSTER SESSION

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Background and Aims: Type 2 diabetes mellitus (T2DM) has become a public health problems due to its association with risk factors; obesity, physical inactivity, western diet, alcoholism. The role of preconception factors such as, western diet, tobacco and alcohol intake during conception among parents and their effects on risk of T2DM among offspring are not well known. This study aims to find out the association of biological risk factors with cognitive impairment and dementia.

Methods: After written informed consent and approval from hospital ethic committee, all subjects (n=2002) above 25 years of age (1016 males and 986 females) were randomly selected and recruited from urban population of Moradabad, North India. Assessment of preconception factors; western diet, tobacco and alcohol intake was made by validated questionnaires used for elucidation of family history of the subjects. Biological risk factors were assessed by physical examination, sphygmomanometer and electrocardiography. The association of risk factors with T2DM was calculated by multivariate logistic regression analysis.

Results: Obesity, physical inactivity, alcoholism, were highly prevalent independent risk factors of T2DM. Among preconception factors, tobacco and alcohol intake by men and western diet intake by both sexes, were common preconception risk factors of T2DM.

Conclusions: It is possible that increased frequency of obesity, physical inactivity, alcoholism and preconception risk factors; western diet, tobacco and alcohol intake were significant risk factors of T2DM. Cessation tobacco and alcohol intake and increased intake of Mediterranean type of foods by the parents may be useful in the prevention of T2DM among offspring during adult life.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#508

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

CARDIOMETABOLIC RISK FACTORS AND COGNITIVE DECLINE IN AN AGEING POPULATION

VIRTUAL E-POSTER SESSION

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Background and Aims: Risk factors (RF) associated with cardiovascular disease (CVD) may also affect cognitive function (CF) during an ageing. In a 9-year prospective study, we investigated associations between decline of CF and baseline cardiometabolic RF and their changes during 9 years in Novosibirsk population sample from the age of 47-74 to 55-84 years.

Methods: A random population sample (n=3153, baseline age 47-74 years) from the HAPIEE project cohort was examined in 2006-2008 and 2015-2018. The average follow-up period was of 9.2 (SD = 0.7) years. Medical history of CVD, RF and CF (memory, semantic verbal fluency, attention and processing speed) were assessed in repeated serial examinations by standard methods.

Results: In a linear regression analysis, cognitive decline in men was independently associated with high baseline levels of systolic blood pressure (p=0.005) and fasting blood glucose (FG) (p=0.003), relatively low baseline body mass index (BMI) (p=0.011) and a 9-year decrease of total cholesterol (p=0.027); in women, with a 9-year decrease of BMI (p=0.024 and 0.012). Relationship between a 9-year increase of FG and the dynamics of CF in women was bidirectional (reverse - with semantic verbal fluency (p=0.049), direct - with immediate recall (p=0.030)).

Conclusions: In a 9-year prospective follow-up of Novosibirsk population sample (from 47-74 to 55-84 years old), we revealed the associations between age-related cognitive decline and cardiometabolic RF. These findings emphasize the importance to control the modifiable RF of CVD to prevent cognitive decline. Supported by WT (106554/Z/14/Z); NIA (1RO1AG23522); RAS (122031700094-5).

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1529

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

INTRACARDIAC HEMODYNAMICS AND HEART RATE VARIABILITY IN STABLE CORONARY ARTERY DISEASE PATIENTS WITH CONCOMITANT COVID-19

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the intracardiac hemodynamics (IH) and heart rate variability (HRV) in stable coronary artery disease (SCAD) patients with concomitant COVID-19.

Methods: The cross-sectional study analyzed clinical and instrumental data from the sample of 80 patients, being subdivided into three groups: group 1 (G1) – SCAD without COVID-19 (n=30; average age 62±14 ys; males – 18 [60 %]); group 2 (G2) – SCAD with concomitant COVID-19 (n=25; 62±11 ys; males – 21 [84 %]); group 3 (G3) – COVID-19 without SCAD (n=25; 52±19 ys; males – 21 [80 %]). The control group included 30 relatively healthy volunteers (47±15 ys; males – 23 [77 %]).

Results: The changes of IH and HRV in G2 were characterized by the impaired left ventricular (LV) systolic and diastolic function, dilation of both ventricles and elevated systolic pulmonary artery pressure. LV end-diastolic volume was higher in G2 (205±21 ml), in comparison to G1 (176±33 ml; p<0,001) and G3 (130±21 ml; p<0,001). G1-3 patients, as compared to controls, presented with the decrease of the overall HRV (by SDNN, SDANN and SDNNi) and parasympathetic activity (by rMSSD, pNN50 and HF), along with the increase of QT interval duration and its variability. G2 demonstrated the most advanced changes of HRV (by SDNN and pNN50) and both QT interval characteristics.

Conclusions: SCAD patients with concomitant COVID-19, along with both ventricles dilation and IH impairment, presented with the sings of autonomic dysfunction and the increase of QT interval duration and its variability. HRV and QT interval characteristics should be additionally considered while the management of such patients.

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#1547

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

FOXP3+ T LYMPHOCYTES ARE ASSOCIATED WITH THE SEVERITY OF ATHEROSCLEROSIS AND DIABETIC STATUS IN PATIENTS WITH CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Irina Kologrivova[1], Elena Kravchenko[1], Alexey Dmitriukov[1], Olga Kharitonova[2], Oksana Trubacheva[1], Olga Koshelskaya[2], Tatiana Suslova[1]
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Background and Aims: Regulatory FoxP3+ T lymphocytes (Treg) control the development of inflammation and their frequency is impaired both during coronary artery disease (CAD) and diabetes mellitus type 2 (DM2). CD4+CD25^{lo}FoxP3+ Treg subset represents previously activated cells and increases during chronic inflammatory disorders, but were never evaluated during CAD and DM2. The objective of the present study was to estimate relationships between the subsets of FoxP3+ Treg cells and the severity of atherosclerosis in patients with CAD depending on the presence of DM2.

Methods: We recruited 62 CAD patients (36 men; 64 (59; 67) y.o.). DM2 was diagnosed in 24 patients. The severity of atherosclerosis was evaluated by calculation of Gensini Score (GS). We measured numbers of CD4+CD25^{hi}FoxP3+ and CD4+CD25^{lo}FoxP3+ T-lymphocytes and evaluated FoxP3 nuclear translocation, which reflects cellular functional activity.

Results: Patients were divided into 3 groups based on the GS tertiles: group 1 - GS<17 points; group 2 - GS 17-45 points; group 3 – GS>45 points. Only patients in group 2 with DM2 had elevated absolute numbers of CD4+CD25^{lo}FoxP3+ T-lymphocytes (1,7 (1,4; 2,1) vs. 0,8(0,6; 0,9)´10$^{7/}$L, p=0.041) and increased absolute numbers of cells with FoxP3 nuclear translocation among FoxP3+CD25^{hi} (7,6 (7,0; 13,5) vs. 6,2 (2,2; 6,8)´10$^{7/}$L, p=0.048) and FoxP3+CD25^{lo} T-lymphocytes (1,3 (1,2; 1,3) vs. 0,8(0,3; 0,9)´10$^{7/}$L, p=0.048) compared to patients without DM2.

Conclusions: We have demonstrated for the first time that presence of DM2 in CAD with intermediate severity of atherosclerosis is accompanied by elevation of CD4+CD25^{lo}FoxP3+ T lymphocytes, which further may be considered for elaboration of the personalized diagnostic and therapeutic approach.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1556

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

AGE AND GENDER PECULIARITIES OF THE LIPID SPECTRUM IN THE URBAN POPULATION BEFORE AND DURING THE COVID 19 EPIDEMIC

VIRTUAL E-POSTER SESSION

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Background and Aims: The aim of this cross-sectional study was to evaluate the influence of Covid 19 infection on lipid parameters in the urban population of European Russia.

Methods: Lipid profiles of 57536 patients aged 13-94 in 347 cities of European Russia estimated before Covid 19 epidemic in 2016 year and those from 65500 patients during 2020-2021 years were compared with usage of descriptive statistics, sample comparison, and two-factor analysis of variance.

Results: The average level of total cholesterol (TC), as well as LDL-C, was the highest in the age group of 43-62 years for both sexes in both compared samples: before and during the Covid-19 epidemic. The peaks of the average values of TC and LDL-C in men appeared 10 years earlier than in women in both the pre-epidemic and epidemic populations. The average values of TC and LDL-C decreased with age and reached their minimum in the elderly. Nevertheless mean HDL-C levels in men increased monotonously with age, while levels in women rose sharply from a minimum at age 13 to a maximum at age 25, followed by a slight decrease with age and a downward trend across all age groups during the epidemic. Mean HDL-C levels in Covid-19 positive patients were significantly reduced: 1.39 [1.35, 1.43] compared with 1.47 [1.45, 1.48] in patients with negative test results ($p<0.001$).

Conclusions: The results of a cross-sectional study showed a statistically significant dependence of lipid parameters on sex, age and Covid 19 infection. This study was supported by Research grant № 075-15-2022-1110.

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#52

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

INSULIN-LIKE GROWTH FACTOR-IAS AN ADDITIONAL COMPONENT OF METABOLIC SYNDROME IN FEMALES OF REPRODUCTIVE AGE

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the role of insulin-like growth factor-I (IGF-I) in the pathogenesis of insulin resistance (IR) and its correlation with the components of the metabolic syndrome (MS).

Methods: The main group consisted of 306 women (92 adolescent 15-20 years old and 214 of reproductive age 21-45 years old) with MS according to the following "summary" criteria: WHO glucose intolerance), modified WHO criteria (fasting plasma insulin level above the upper quartile in the study population) and criteria of IDF, adjusted for sex, age, percentile values for lipid levels, blood pressure and obesity rates. Tthe fasting glucose level and in oral glucose tolerance test, fasting immunoreactive insulin level and 2 hours after an oral reception of 75 g of glucose, the total cholesterol (CH), triglycerides and high-density lipoprotein (HDL) cholesterol levels were determined. Polycystic ovary syndrome (PCOS) was evaluated according to the Rotterdam criteria. The level of sex hormone-binding globulin (SHBG); total testosterone; DEA; 17-OH-progesterone; DEA-S; androstenedione; prolactin; IGF-I level were determined.

Results: In the main adolescent group, the mean IGF-I level was 250.4 ng/ml and correlated with BMI, waist circumference, total CH, tal testosterone, basal and postprandial C-peptide, SHBG level, LVMI. In the main reproductive group, the mean IGF-I level was 256.1 ng/ml and correlated with postprandial insulin level, oligomenorrhea, prolactin, 17-OH-progesterone, with DEAS level, mean ovarian volume, TW and LVMI.

Conclusions: In female patients elevated IGF-I levels may be an additional component and an early predictor of MS, similar to hyperinsulinemia. Low IGF-I levels may be an independent risk factor for the development of CAD in patients MS.

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#1466

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

EXOSOMES AS POTENTIAL TRANSPORTERS OF PROTEINS WITH SIALIDASE ACTIVITY

VIRTUAL E-POSTER SESSION

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Background and Aims: Sialidase activity circulating in the blood is responsible for atherogenic modification of low-density lipoprotein (LDL). The aim of this study was to isolate and identify proteins possessing sialidase activity.Sialidase activity circulating in the blood is responsible for atherogenic modification of low-density lipoprotein (LDL). The aim of this study was to isolate and identify proteins possessing sialidase activity.

Methods: The blood serum of atherosclerotic patients was screened for the presence of significant sialidase activity using commercial kits. Isolation of proteins with sialidase activity was performed using affinity chromatography followed by polyacrylamide gel electrophoresis (PAGE). In order to identify the isolated proteins, the MALDI-TOF mass spectrometry method was used.

Results: About 700 blood serum samples were tested and 84 samples with sialidase activity were selected. Proteins of 65 kDa and 116 kDa were isolated from the eluate after affinity chromatography using PAGE. Mass spectrometry revealed a wide range of proteins, but no known human neuraminidase was found among them. During chromatography, exosomes are isolated together with an affinity-binding protein, which explains the wide range of proteins identified by mass spectroscopy and masking the real result of affinity isolation.

Conclusions: The data obtained suggest that an unidentified protein with sialidase activity circulates in the blood, both in free form and non-covalently bound to the extracellular vesicles membrane (exosomes). This work was supported by the Russian Science Foundation (Grant # 20-15-00264).

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#1592

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

ENDOTHELIAL DYSFUNCTION AND P2X7 ANTAGONISM IN TTOP SYSTEM

VIRTUAL E-POSTER SESSION

Maria Lombardi[1], Sabrina Nicolò[1], Lorenzo Coppadoro[2], Monica Soncini[2], Gianfranco Fiore[2], Chiara Foglieni[1]
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Background and Aims: Mechanisms promoting endothelial dysfunction include the activation of P2X7 and TNF-α pathways. Technologically advanced systems for modeling endothelial barrier represent useful tools for the study of mechanism regulating atherosclerosis development. Our aim was to investigate the relationship between P2X7 antagonism and TNF-α in endothelial dysfunction

Methods: We have developed a microphysiological system called True Tissue On Platform (TToP), i.e. a bicompartmental platform with an open-well design based on laser micromachined cartridge, allowing sample retrieval without cell damage. EaHy926 endothelial cells (EC) were settled ($3.5x10^4$ cell/system) over a polycarbonate membrane allocated into the cartridge. Live imaging on Acridine Orange (AO) labeled EC assessed viability and distribution. P2X7 antagonist (A740003, 100mM for 2h) was applied in the upper chamber of TToPs to modulate the effect of TNF-a (100ng/ml, overnight). EC monolayers were destinated to immunofluorescence for confocal microscopy, or dedicated to RT-qPCR

Results: AO labeling before EC treatment demonstrated the formation of tight monolayers of homogenously distributed. TNF-α significantly up-regulated IL-1β (p=0.0029) and NF-kB (p=0.0059) genes, and variably affected P2X7. Confocal microscopy in TToP cartridge with CD31/PECAM or von Willebrand Factor antibodies confirmed the phenotype preservation, that with phalloidin-TRITC showed cytoskeletal stress following TNF-α. Addition of A740003 either prior/after EC treatment with TNF-α globally reverted the activation status, significantly restoring NF-kB gene expression (p=0.003).

Conclusions: Preliminary data suggest TToP suitability to study EC dysfunction and perform pharmacological approaches aimed at modulating atherosclerosis relevant pathways. In perspective, we envisage the development of more complex vessel models, including a dynamic system to study cells under perfusion/chemical gradients.

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#7

Topic: *AS02 Lipids and Lipoproteins / AS02.11 Liver metabolism and steatosis*

THE THERAPEUTIC EFFECT OF JIGUCAO CAPSULE IN NONALCOHOLIC HEPATITIS(NASH) MOUSE

VIRTUAL E-POSTER SESSION

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Background and Aims: Jigucao capsule is a classic traditional Chinese medicine used to treat acute and chronic hepatitis and cholecystitis with liver and gallbladder damp heat syndrome in clinic, but whether it has the therapeutic effect on Nonalcoholic steatohepatitis (NASH) and the underlying mechnism is not clear.

Methods: The C57BL/6 mice were fed with MCD to obtain NASH mouse model. HE staining, PAS staining and oil red O staining were used to evaluate the histopathological changes before and after jigucao capsule treatment; biochemical analysis were used to determined the biochemical changes; Western blotting and gene sequencing analysis were used to detect the potential mechanisms.

Results: The results of HE staining, PAS staining and oil red O staining demonstrated that jigucao capsule could alleviate the symptoms of MCD-induced NASH mouse, biochemical analysis indicated that jigucao capsule could decrease the expression of Alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol(TC), and Triglyceride (TG). gene sequencing analysis demonstrated that ECM-receptor interaction, PI3K-AKT signaling pathway, Rap1 signaling pathway, chemokine signaling pathway, AGE-RACE signaling pathway, B cell receptor signaling pathway, NF-kappa B signaling pathway were related to the jigucao capsule treatment on MCD-induced NASH, and western blotting confirmed it.

Conclusions: Here, our data demonstrated that jigucao capsule could alleviate the symptoms of MCD-induced NASH model by multiple signaling pathway, which may help us understanding the therapeutic mechanism of traditional medicine and for clinical medication guidance.

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#1607

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

ASSOCIATIONS BETWEEN HYPOTHYROIDISM AND SUBCLINICAL ATHEROSCLEROSIS AMONG MALE AND FEMALE PATIENTS WITHOUT CLINICAL DISEASE REFERRED TO COMPUTED TOMOGRAPHY

VIRTUAL E-POSTER SESSION

Sumaya Al Helali
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Background and Aims: BACKGROUND: Patients without clinical coronary artery disease (CAD) may have higher risk of subclinical atherosclerosis. However, there are conflicting findings when the results are stratified by gender and the underlying risk of CAD. **OBJECTIVES:** To examine gender-specific associations of hypothyroidism with coronary calcification and plaques

Methods: Retrospective cross-sectional study was conducted among adult patients referred to (64 multidetector spiral) computed tomography (CT) at a specialized Cardiac Centre between July 2007 and December 2017. Those with pre-existing CAD were excluded. Hypothyroidism was defined as TSH ≥ 4.5 mU/L. Plaques were determined based on quantification of coronary calcium and coronary CT angiography

Results: A total 2499 patients (1544 males and 955 females) were included. The prevalence of hypothyroidism was significantly higher in females than males (18.0% versus 12.9%, p<0.001), in all patients and those <65 years. Hypothyroidism in males was significantly associated with higher coronary calcium score (CCS)>0, higher CCS groups, and both soft and calcified plaques (p=0.027, p=0.032, p=0.005, and p=0.017, respectively). After adjusting for traditional coronary risk factors, the higher risk in males remained significant for coronary plaque but not for CCS>0. On the other hand, hypothyroidism in females was not significantly associated with coronary calcification nor plaques in both univaraite and multivariate analysis

Conclusions: There is gender-specific differences in the association of hypothyroidism with subclinical atherosclerosis. The higher risk of coronary plaques but not calcification in males was independent of traditional coronary risk factors. The lack of risk in females may be related to lower underlying risk of CAD.

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#26

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

DEEP SEA WATER INCREASES MESENCHYMAL STEM CELL CAPABILITY THROUGH EXPRESSION OF IGF1R IN THE TREATMENT CARDIAC AGING INDUCED BY MIRNA-THERAPEUTIC POTENTIALS IN HUMANS

VIRTUAL E-POSTER SESSION

Weisyun Hu
Cardiology, China Medical University Hospital, Taichung, Taiwan

Background and Aims: Aging is capable of inducing decrease of heart function, and stem cells show potential in the treatment of aging heart. Deep sea water is obtained from the ocean layer under 200 meters. Research findings confirm that deep sea water shows cellular protective effect due to its antioxidant and anti-inflammatory properties.

Methods: This study aimed to investigate whether co-cultureing deep sea water with stem cells can increase stem cell functions or not. If yes, which cellular signaling is involved between deep sea water and increase of stem cell functions. In addition, cell and animal models for aging heart would be designed in order to explore the protective effect of stem cells after incubation with deep sea water. From experimental data, we found that deep sea water increases stem cell viability through expression of membrane protein IGF1R. In addition, research findings confirmed that activation of miR 880-3p/SOD2/p53 axis in aging cardiomyocytes.

Results: Co-culturing with aging cardiomyocytes with deep sea water pretreated stem cells showed better cardiac protective effect than stem cells without pre-treatment of deep sea water through regulation of miR 880-3p/SOD2/p53 axis. Furthermore, animal experiment also confirmed that cardiac protective effect on stem cells pretreated with deep sea water was better than stem cells without pretreated with deep sea water in the treatment of aging heart.

Conclusions: These findings suggest that stem cells pretreated with deep sea water may show clinical potential in the treatment of aging heart.

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#27

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

A COMPARISON OF ATRIAL FIBRILLATION INCIDENCE AMONG PHYSICIAN AND THE GENERAL POPULATION: UNRAVEL THE HEALTH MYTHS FOR PHYSICIANS

VIRTUAL E-POSTER SESSION

Weisyun Hu
Cardiology, China Medical University Hospital, Taichung, Taiwan

Background and Aims: Purpose: To explore the association of atrial fibrillation (AF) among physician specialist.

Methods: Method: We used Cox proportional hazards models to estimate the incidence rate and the adjusted hazard ratios (aHR) with 95% confidence intervals (CIs) to determine the risk of atrial fibrillation in the physician study cohort relative to the comparison cohort, and further analyzed stratified by age and comorbidities.

Results: Result: The Cox proportional hazard regression model revealed that male physician was significantly associated with an increased risk of AF than non-physician after adjusting for potential confounders (adjusted HR, 1.05; 95% CI: 1.00– 1.11). In age-specific analysis, male physician age less than 35 years old showed the strongest association with AF (adjusted HR, 3.70; 95% CI: 3.01– 4.55). When stratified by comorbidity, the male physician cohort exhibited a significantly higher risk of AF than controls (adjusted HR, 1.45; 95% CI: 1.34– 1.57).

Conclusions: Conclusion: Association of AF among physicians was shown.

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#28

Topic: *AS04 Clinical Vascular Disease / AS04.14 SGTL2 inhibitor and cardiovascular diseases*

DIABETIC PATIENTS WITH AND WITHOUT SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS USE WITH INCIDENT CANCER RISK- THE GOOD, THE BAD AND THE UGLY

VIRTUAL E-POSTER SESSION

Weisyun Hu
Cardiology, China Medical University Hospital, Taichung, Taiwan

Background and Aims: The burden of diabetes mellitus is growing dramatically, mainly through its atherosclerotic cardiovascular impact . On the contrast, diabetes is also associated with cancer development and the mechanism underlying this phenomenon is complicated . Recently, novel antidiabetic agent with sodium-glucose cotransporter-2 (SGLT2) Inhibitors was introduced and several pluripotent effect was proposed . In this regard, to identify the role of pharmacologic intervention in incident cancer among diabetic individuals is truly novel and interesting and clearly of importance for health care delivery and quality control efforts. Thererfore, this study was conducted for evaluation of the relation between SGLT2 Inhibitors and risk of incident cancer among diabetic patients with large size of the database examined, and the clinical importance of the question examined

Methods: Methods: This study identified a non- SGLT2 inhibitor cohort of 325,989 patients and a SGLT2 inhibitor cohort of 325,990 patients. The primary interest of this study was the occurrence of cancer. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using univariate Cox proportional hazard models.

Results: Results: Patients receiving SGLT2 inhibitor (adjusted HR=0.79, 95%CI=0.76-0.83) had significantly lower risk of contracting cancer than patients without receiving SGLT2 inhibitor.

Conclusions: Conclusion: The results demonstrated that diabetic patients receiving SGLT2 had significantly lower risks of cancer.

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#29

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

ASSOCIATION OF HEART FAILURE PATIENTS WITH AND WITHOUT SACUBITRIL-VALSARTAN USE WITH INCIDENT CANCER RISK -REFINE THE ROLE OF SACUBITRIL-VALSARTAN

VIRTUAL E-POSTER SESSION

Weisyun Hu
Cardiology, China Medical University Hospital, Taichung, Taiwan

Background and Aims: Purpose :This study was to evaluate the association between heart failure (HF) patients with and without sacubitril-valsartan use with incident cancer risk.

Methods: Methods: This study consisted of 18072 patients receiving sacubitril-valsartan and 18072 controls. In the Fine and Gray model, which extends the standard Cox proportional hazards regression model, we estimated the relative risk of developing cancer between the sacubitril-valsartan cohort and the non- sacubitril-valsartan cohort by using subhazard ratios (SHRs) and 95% confidence intervals (CIs).

Results: Results: The incidence rates of cancer were 12.02 per 1000 person-years for the sacubitril-valsartan cohort and 23.31 per 1000 person-years for the non- sacubitril-valsartan cohort. Patients receiving sacubitril-valsartan had a significantly lower risk of developing cancer with an adjusted SHR of 0.57(0.49, 0.67).

Conclusions: Conclusion: Sacubitril-valsartan users were less to be associated with the development of cancer.

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#504

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

TRANSCRIPTOME ANALYSIS OF MIRNA AND MRNA IN THE MYOCARDIAL TISSUE OF MICE WITH LMNA-DILATED CARDIOMYOPATHY

VIRTUAL E-POSTER SESSION

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Background and Aims: Lamin A/C (*LMNA*) gene mutations are a known cause of familial dilated cardiomyopathy (DCM). DCM linked to *LMNA* gene mutation (*LMNA*-DCM) is a highly penetrant and arrhythmogenic cardiomyopathy that leads to transplantation and premature sudden cardiac death. The precise mechanisms triggering disease progression remain unknown. In the current study, we investigated the mRNA and miRNA transcriptome in the myocardial tissue of 50-week-old wild-type and *LMNA*^{R249W} mice to gain insights into the molecular pathogenesis of *LMNA*-DCM.

Methods: We analyzed the mRNA and miRNA trascriptome by next-generation sequencing in cardiac tissue from six 50-week-old wild type mice with normal cardiac function and six *LMNA*^{R249W} mice with DCM. Functional enrichment analysis of differentially expressed genes (DEGs) were performed using over representation analysis (ORA) for Gene Ontology, KEGG and Reactome. We analyzed miRNA-mRNA interactions to find miRNA-target regulation pairs (mTPs). The functions of miRNA target genes, previously validated in other studies, were also analyzed using ORA. All expression data analysis was performed using the ExpHunter suite.

Results: 2148 genes (1485 upregulated and 663 downregulated) and 53 miRNAs (21 upregulated and 32 downregulated) were diferentially expressed in *LMNA*^{R249W} hearts. Funtional enrichment analysis identified extracellular matrix regulation, fatty acid metabolism and calcium signaling among the most enrichment pathways. We found 1800 validated mTPs and the most significant functions of the targets are related to extracellular matrix, actinin and cytoeskeleton organization, and regulation of inflamatory response.

Conclusions: These results revealed novel miRNA-mRNA interaction networks and signaling pathways for *LMNA*-DCM, providing novel insights into the development of this disease.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#506

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

SUBCLINICAL CAROTID ATHEROSCLEROSIS: ROLE OF INFLAMMATION, CHOLESTEROL, HEMODYNAMIC LOAD AND SEX IN ROTATIONAL SHIFT WORKERS IN THE ARCTIC

VIRTUAL E-POSTER SESSION

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Background and Aims: The mechanisms of atherosclerosis development, including immune ones, differ in men and women. To study feasibility of atherosclerotic plaque (AP) detection in individuals working in the Arctic via rotating shifts (ARS) regarding sex, arterial hypertension (AH), immune inflammation.

Methods: In Yamburg village (68° 21' 40" N), 99 males (M) and 81 females (F) with AH 1,2 stages and normotensive individuals, comparable in age, work experience in ARS, office blood pressure were examined. Ultrasound examination of carotid arteries (CA), biochemical blood test was performed. Statistica 8,0 (Stat Soft, USA), IBM SPSSS Statistics 23. (IBM. USA).

Results: Analysis was conducted in M and F groups with AP (n=98)/without AP (n=82): among them 57 M (58%), 41F (51%) were with AP, Pχ2=0.6116; with/without AH. In AH M, more often than in normotensive M, AP was visualized in CA lumen: 72% (44 out of 61) vs 34% (13 out of 38), Pχ2=0.0209. Probability of AP in M was associated with hs-CRP (p=0.052), level of VLDL CH (p=0.038), C-peptide (p=0.004), IL6 (p=0.048); with level of VLDL CH (p=0.052) in F only. In M with AP, strong association with mean daily blood pressure parameters was found.

Conclusions: CA AP associated with AH in ARS was frequently detected in M. Regardless of blood pressure, AP in M was associated with systemic inflammation, raise of pro-inflammatory cytokines and increase in VLDL CH level. ROC-analysis revealed relationship of AP only with VLDL CH in F. In AH M and F, AP was associated with systemic inflammation, pro-inflammatory cytokines due to AH presence.

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#1578

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

ATHEROGENIC WSS EFFECTS ON AORTIC ENDOTHELIAL CELLS: APPLICATION OF A NOVEL BIOREACTOR

VIRTUAL E-POSTER SESSION

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Background and Aims: Altered blood flow acts on mechanotransduction, playing a role in aortic atherosclerosis. Endothelial cells (EC) respond to fluidodynamic changes, i.e. tangential wall shear stress (WSS), through modifying adhesion and growth. Our aim was to evaluate EC response to atherogenic WSS using a new generation bioreactor reproducing the WSS multidirectional nature *in vivo* sensed by EC.

Methods: Primary human aortic EC cultured over PMMA supports (untreated or human collagen typeI pre-coated) till ≈70% confluence were hosted in specifically developed novel devices allowing application of multidirectional, complex WSS patterns under controlled sterile conditions. Unidirectional (WSS=0.1Pa, Oscillatory Shear Index OSI=0) and multidirectional (WSS=0.1Pa,OSI=0.2, rotating motor) were compared. Experiments were carried out for 24 and 48 hours. Cell viability and distribution were assessed by Acridine Orange, or multilabelling with Phalloidin–TRITC, anti-CD31/PECAM1-AlexaFluor488 and DAPI at fluorescence or confocal microscope, respectively.

Results: No changes in EC density after 24h into bioreactor in static vs. unidirectional WSS with both untreated and coated supports, but massive EC detachment from untreated supports after 48h were found. Conversely, 48h of unidirectional WSS lead to a scarce detachment of EC settled over collagen typeI (mean detachment vs. pre-flow number=24±37%). The multidirectional WSS increased the EC detachment to 35±22%. This effect was partially compensated by increase of cell dimensions: the surface covered by EC was significantly lower in samples submitted to unidirectional vs. multidirectional WSS (Δ area covered by=-17,5%, p=0.0485).

Conclusions: Preliminary results show an effect of atherogenic multidirectional WSS on EC detachment and dimensions in comparison with unidirectional WSS.

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#30

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

TRANSPLANTATION OF MESENCHYMAL STEM CELLS INCREASES EXPRESSION OF ANTIOXIDANT PROTEINS AND AMELIORATES GP91/ROS/INFLAMMASOME SIGNALING IN DIABETIC CARDIOMYOPATHY.-FIRST IN HUMAN STUDY

VIRTUAL E-POSTER SESSION

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Background and Aims: Cardiomyopathy is one of complications associated with diabetes. Due to its high prevalence, diabetic cardiomyopathy becomes an urgent issue in patients with diabetes. Various pathological signalings are related to progress of diabetic cardiomyopathy, including inflammasome. Transplantation of mesenchymal stem cells is full of potentials in the treatment of diabetic cardiomyopathy because of cardiac regenerative capability of stem cells.

Methods: This study aimed to investigate whether transplantation of mesenchymal stem cells shows therapeutic effect on diabetic cardiomyopathy through regulation of inflammasome signaling. Wistar male rats were divided into three groups including Sham, T1DM (rats with type 1 diabetes) and T1DM+WJSC (T1DM rats receiving 1 x 10^6 stem cells per rat). Compared to Sham, experimental results indicated that several pathological conditions can be observed in heart tissues with T1DM, including structural change, fibrosis, elevation of oxidative stress and expression of inflammasome related proteins.

Results: All the pathological conditions were significantly improved in T1DM rats receiving transplantation of mesenchymal stem cells (T1DM+WJSC). Furthermore, experimental findings suggested that transplantation of mesenchymal stem cells exerted expression of antioxidant proteins in diabetic heart tissues, resulting in decrease of oxidative stress and blockage of inflammasome signaling.

Conclusions: Therefore, these findings imply that transplantation of mesenchymal stem cells shows therapeutic effect on diabetic cardiomyopathy through regulation of inflammasome induced by oxidative stress.

91ST EAS CONGRESS
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#1575

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

P2X7 AND ITS TARGET MIRS IN PATIENTS WITH ABDOMINAL AORTIC ANEURYSM AND CAROTID ATHEROSCLEROSIS: A PROOF OF CONCEPT STUDY

VIRTUAL E-POSTER SESSION

Maria Lombardi[1], Lucia Spartano[1], Sabrina Nicolò[1], Vincenzo Ardita[2], Renata Castellano[2], Germano Melissano[2], Roberto Chiesa[2], Domenico Baccellieri[2], Chiara Foglieni[1]
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Background and Aims: Carotid atherosclerotic plaques (CPL) and abdominal aortic aneurysm (AAA) are co-morbidities. If/how CPL may affect AAA is poorly investigated. P2X-purinoceptor-7 (P2X7) is expressed both in human AAA and CPL lesions and is instability-associated in CPL. P2X7 is functionally related to two microRNAs, i.e. miR-150, miR-186 (modulators of vascular cell proliferation) and may be shed into the bloodstream in correlation with C-reactive protein increase. Our aim is exploring the possible relationship between circulating P2X7, its target miRs and clinical status or lesion dimensions in patients with AAA +/- CPL.

Methods: Male patients with AAA undergoing aneurysmectomy were characterized and CPL stenosis assessed by Ecocolordoppler-TSA. Ten patients were allocated to group A (0<stenosis ≤40%), 10 to group B (stenosis >40%). Seven healthy volunteers (group C) served as controls. P2X7 was evaluated into serum by ELISA. P2X7 gene, miR-150 and miR-186 were determined by RT-qPCR.

Results: In group A, CPL appeared mainly localized at carotid bulb, in group B extended along branches. Circulating P2X7 positively correlated to C-reactive protein and negatively to P2X7 tissue levels in AAA patients. P2X7 was lower in group B, than in others (p=0,0065, p=0,0009 vs. group A, C, respectively). Although P2X7 gene was undetermined into serum, both miRs were detected, and miR-186 was lower in group B vs. A (p=0,0221, n=6 samples/group), not different vs. C. AAA diameter was linearly related to miR-186 in group B (p=0.0351).

Conclusions: Preliminary data suggest a role for P2X7 axis in patients with AAA and hemodinamically significant CPL, deserving further investigations.

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#1574

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

CLINICAL CHARACTERISTICS OF ADULT AND PAEDIATRIC PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA: A REAL-LIFE CROSS-SECTIONAL STUDY FROM THE TURKISH NATIONAL DATABASE

VIRTUAL E-POSTER SESSION

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Background and Aims: Familial hypercholesterolemia (FH) is the most common cause of premature ASCVD. Türkiye is among the countries with the highest rate of ASCVD. However, no population-based study has been published so far on the prevalence of FH, demographic and clinical characteristics, burden of ASCVD, treatment compliance, and attainment of LDL-C) targets.

Methods: We performed a study using the Turkish Ministry of Health's national electronic health records involving 83,063,515 citizens as of December 2021 dating back 2016. Adults fulfilling the diagnostic criteria of definite or probable FH according to the Dutch Lipid Network Criteria (DLNC), and children and adolescents fulfilling the criteria of probable FH according to the European Atherosclerosis Society (EAS) Consensus Panel report formed the study population (n=157,790). The primary endpoint was the prevalence of FH.

Results: Probable or definite FH was detected in 0.63% (1/158) in the adults and 0.61% (1/164). Proportion of adults with LDL-C levels > 190 mg/dL was 4.56% (1/22). The prevalence of FH among children and adolescents was 1 in 270. The proportion of adults and children and adolescents on lipid-lowering treatment (LLT) was 32.1% and 1.5%, respectively. Overall discontinuation rate of LLT was 65.8% among adults and 77.9% among children. Almost no subjects on LLT were found to attain LDL-C targets.

Conclusions: This nationwide study showed a very high prevalence of FH in Türkiye. Patients with FH are diagnosed late and treated sub-optimally. These results denote the urgent need for country-wide initiatives for early diagnosis and effective management of FH patients.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1573

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

PHENO-GENOTYPIC FEATURES OF FAMILY HYPERCHOLESTEROLEMIA IN CHILDREN

VIRTUAL E-POSTER SESSION

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Background and Aims: Familial hypercholesterolemia (FH) is the most common genetic disease in the world. Mutations in LDLR, APOB and PCSK9 genes play a leading role in the pathogenesis of FH. Without treatment, people with FH have a 20 times higher risk of disease and death from CVD. Difficulties in the timely diagnosis of FH in children are due to the clinical asymptomatic course and the phenotypic heterogeneity of the disease. In order to reduce the burden of CVD and mortality in people with FH, it seems relevant to study the pheno-genotypic manifestations of the disease in childhood.

Methods: The study was selected 85 patients with a clinical diagnosis of FH aged 0 to 17 years inclusive. All children underwent a detailed medical history, lipid profile analysis and clinical examination. Genetic testing was carried out by high throughput sequencing using a panel of 5 genes: LDLR, APOB, APOE, LDLRAP1, PCSK9.

Results: In our study, none of the children with heFH had such characteristic clinical manifestations. As a result of DNA sequencing of 85 children with heFH, isolated LDLR mutations were detected in 30 (35.29%), APOB mutations in 10 (11.76%), and PCSK9 mutations in 1 (1.17%) children. In addition, two mutations were identified: LDLR+APOB in 6 children (7.05%), LDLR+PSCK9 in 5 patients (5.88%). The most common variants of LDLR: c.906C>G, c.986G>A; in APOB: c.10580G>A, c.9811G>A.

Conclusions: Thus, in 61% of patients, the diagnosis was confirmed genetically. The results obtained justify the need for early pheno-genotypic diagnosis of FH in childhood for timely start treatment and prevention of CVD at a young age.

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#45

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

GLOBAL CIRCUMFERENCE STRAIN OF THE THORACIC AORTA AS A NEW SURROGATE MARKER OF AORTIC AND CORONARY ATHEROSCLEROSIS: 2D SPECKLE-TRACKING TRANSOESOPHAGEAL ECHOCARDIOGRAPHIC ASSESSMENT

VIRTUAL E-POSTER SESSION

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Background and Aims: Global circumference strain (GCS) is a new diagnostic marker assessing the disturbances of mechanical properties of the thoracic aorta (TA). We aimed to study the role of GCS as a predictor of aortic and coronary atherosclerosis using 2D speckle-tracking transoesophageal echocardiography (2D ST TEE).

Methods: 2D ST TEE was performed in 182 consecutive CAD patients and 11 healthy volunteers using Epiq 7G (Philips) and X8-2t multiplane probe. The ascending aorta, accessible parts of the arch, and descending aorta were visualized. The height (cm) of each atheroma was measured. 5 grades of TA atherosclerosis were distinguished. The GCS, % and GCS normalized to pulse pressure (GCS/PP) in the descending aorta were calculated. All patients underwent coronary angiography. The stenosis >50% was assessed as significant. SYNTAX Score was calculated.

Results: Based on multivariate logistic regression analysis GCS and GCS/PP are independent factors for predicting significant TA atherosclerosis, grades 3-5 (OR 0.81 and OR 0.63, both $p<0.05$) and coronary atherosclerosis (OR 0.76 and OR 0.81, both $p<0.05$). GCS ≥5.9% (AUC 0.94±0.03, $p<0.001$) and GCS/PP ≥11.4 (AUC 0.97±0.02, $p<0.001$) are predictors of intact TA. GCS ≤4.85% (AUC 0.82±0.04, $p<0.001$) and GCS/PP ≤8.06 (AUC 0.87±0.03, $p<0.001$) are predictors of significant TA atherosclerosis. GCS ≤4.05% (AUC 0.62±0.04, $p=0.007$) and GCS/PP ≤5.95 (AUC 0.61±0.04, $p=0.018$) are predictors of significant coronary stenosis, while GCS ≤3.75% (AUC 0.67±0.07, $p=0.039$) and GCS/PP ≤5.15 (AUC 0.64±0.07, $p=0.045$) are predictors of coronary atherosclerosis with SYNTAX Score ≥22.

Conclusions: GCS and GCS/PP are new informative predictors of the severity and prevalence of aortic and coronary atherosclerosis.

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#1467

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ASSOCIATION BETWEEN SERUM MATRIX METALLOPROTEINASE-12 AND LDL/HDL RATIO IN PATIENTS WITH HEART FAILURE

VIRTUAL E-POSTER SESSION

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Background and Aims: Matrix metalloproteinase-12 **(**MMP-12) is an enzyme capable of degrading major extracellular matrix (ECM) proteins. Studies have suggested that MMP-12 deficiency is related with increased vascular ECM degradation and development of atherosclerotic plaques. Relatively little is known whether MMP-12 interacts with atherogenic lipoproteins in heart failure (HF). The aim of our study was to investigate a possible association between MMP-12 and atherogenic indices in chronic heart failure.

Methods: 56 patients with chronic HF with midrange ejection fraction (HFmrEF) were examined, mean age 65.62±9.69 years, and 22 age and sex-matched healthy subjects, mean age 56.4±5.53 years. ELISA was used for measuring MMP-12 levels. The lipid profile and atherogenic indices (log TG/HDL, LDL/HDL, TC/HDL and TG/HDL) were also studied.

Results: Serum MMP-12 levels were statistically significantly lower in patients than in controls: 0.0033 (0.0022-0.0071) vs. 0.0075 (0.0068-0.016) (KW=7.37; p=0.006). There was not statistically significant difference between the lipid indices in patients compared to healthy controls (p>0.05). MMP-12 showed correlation with LDL/HDL (r=0.39; p=0.03).

Conclusions: Our data show an association between LDL/HDL ratio and MMP-12 in HF. A possible relationship is suggested between abnormal ECM degradation and serum lipoproteins in HF. Further studies are needed to clarify the role of MMP-12 in development of atherosclerotic plaques in HF.

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#1464

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.14 Epigenetics and microRNA*

ANALYSIS OF CIRCULATING MIRNAS SPECIFICALLY INCREASED IN INSULIN RESISTANCE AND/OR HIGH-LDL CHOLESTEROLEMIA - ANALYSIS OF METABOLOME, CORRELATION WITH RELATED DISEASES, AND ATHEROSCLEROTIC RISK ASSESSMENT -

VIRTUAL E-POSTER SESSION

Ayano Sayama[1], Saki Ikeda[1], Erina Shigematsu[1], Saeko Sugawara[2], Terumi Hasegawa[1], Mizusa Suzuki[1], Miki Igawa[1], Mizuha Ominato[1], Yuuka Kuroda[1], Chiho Masuko[1], Nodoka Matsuda[1], Nanae Kondo[1], Masashi Omura[1], Kimie Kawachi[1], Kouji Hirota[3], Seiichi Oyadomari[4], Kazuki Tajima[5], Makoto Ujihara[5], Taiji Ito[1]
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Background and Aims: Micro (mi) RNAs are small RNAs that collectively suppress the expression of various genes. Among the miRNAs are blood-secreted miRNAs (circulating miRNAs) that are secreted from secreting cells and act on target cells through the blood. In this study, we performed comprehensive identification of insulin resistance- and/or high-LDL cholesterolemia (Cho)- specific circulating miRNAs, target gene prediction and Gene Ontology (GO) analysis, and aimed to predict the effect on metabolome and causality with related diseases.

Methods: Serum miRNA expression in healthy subjects and subjects with insulin resistance or high-LDL Cho who had IC in men in their 40s and 50s was comprehensively analyzed by microarray. Then, target gene prediction was performed using Targetscan and miRDB, and GO analysis was conducted in conjunction with Human Metabolome Database and Disease Jensen Database by Shiny GO application.

Results: We identified 12 circulating miRNAs with increased expression specific to insulin resistance, and 4 those to high-LDL Cho. Based on predicted target genes of these miRNAs, we searched the database for metabolites commonly affected in both diseases. As a result, alterations of metabolites such as phosphatidic acid and Phosphoric acid were identified. Surprisingly, these miRNAs were also predicted to be commonly involved in the development of diseases associated with high-LDL Cho, including carcinoma and Alzheimer's disease.

Conclusions: Although insulin resistance and high-LDL Cho are closely related to each other, it was predicted that miRNA groups with increased blood expression in each disease would be involved in the variation of common metabolite and related disease development.

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#1301

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

NON-ALCOHOLIC FATTY LIVER DISEASE AND METABOLIC SYNDROME AMONG YOUNG ADULTS

VIRTUAL E-POSTER SESSION

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Background and Aims: Aim. To assess the association between non-alcoholic fatty liver disease **(**NAFLD) and metabolic syndrome (MS) among young adults.

Methods: . This study included 60 patients. All the study patients were divided into two groups: group 1 – with MS, n=20; group 2 – without MS, n=40, comparable in age and gender.

Results: . Individuals in group 1 had higher values of systolic BP (143.5 [142–151] vs 127 [117.5–130.5] mmHg; p<0.001) and diastolic BP (85 [76–96] vs 75 [70–83] mmHg, p=0.027), body mass index (29.5 [27.7–32.7] vs 26.6 [24.4–27.0] kg/m2, p=0.002), WC/HC ratio (1.00 [0.96 -1.04] vs 0.88 [0.85 - 0.97], p=0.002), visceral fat mass (11 [9–18] vs 7.0 [5,2-11,7] kg, p=0,02) compared with group 2. There were some differences in serum levels of LDL-C (1,9 [1,4-2,1]; 4,0 [3,5-4,7] vs 3.0 [2.6–3.5] mmol/l, p=0.001), ALT (28.9 [21-49] vs 21.0 [15.5–25.3] U/l, p=0.005), uric acid (304.6 [257.5–394.4]; vs 284.5 [235.9–328.4]; mmol/l, p=0.047) and resistin (5.0 [2.4-5.1]; vs 1.2 [0.8–1.8], ng/ml, p=0.017). Correlations between Fatty Liver Index (FLI) and systolic BP (r=0.52; p=0.01), visceral fat mass (r=0.57; p=0.02) were found among young people with NAFLD. The optimal cut-off value of FLI and HSI was 30 (sensitivity 93.3% and specificity 76.7%). The AUROC of FLI for predicting NAFLD was 0.931.

Conclusions: . Our study revealed a high frequency of MS in young patients with NAFLD. The revealed changes in the part of the liver were accompanied by more pronounced changes in lipid and purine metabolism along with an imbalance of adipokines.

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#1314

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

MONITORING OF INDICATORS OF OXIDATIVE STRESS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

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Background and Aims: The most formidable pathology of the cardiovascular system is acute myocardial infarction (AMI). The prognosis of such patients is due to endothelial dysfunction, oxidative stress. A change in the balance between the pro- and antioxidant systems leads to the formation of the earliest markers of cell damage - oxidized modified proteins (OMP), which can lead to a violation of the integrity of the endothelium.
The purpose of the study. Study of changes in clinical and biochemical parameters in patients with acute myocardial infarction

Methods: The study involved 93 patients diagnosed with AMI.

Results: When comparing the indicators of oxidative stress, a statistically significant increase in the products of oxidized modification of proteins and a decrease in the activity of the key antioxidant enzyme SOD were found. During the correlation analysis, reliable positive relationships were established between the presence of AMI and gender (r=0.250, p=0.001), the level of OHS (r=0.470, p=1.3E-10), the level of LDL cholesterol (r=0.658, p=3.4E-22), ADFGn (r=0.543, p=2.7E-14), KDFGn (r=0.387, p=2.2E-07), ADFGo (r=0.344, p=5.1E-06), KDFGo (r=0.552, p=3.4E-22), between the level of CFK-MV and ADF- Gn (r=0.378, p=0.002), KDFGn (r=0.298, p=0.05), ADFGo (r=0.453, p=0.0001), KDFGo (r=0.385, p=0.004), and negative links between AMI and SOD activity (r=-0.358, p=0.00004), CPK-MF and SOD activity (r=-0.329, p=0.0001).

Conclusions: A correlation has been established between AMI and indicators of oxidative stress, which reflects an increase in the products of oxidized modification of proteins and a decrease in the activity of SOD.

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#1323

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

EVENT-FREE FAMILIAL HYPERCHOLESTEROLEMIA IN THE ELDERLY: A RETROSPECTIVE ANALYSIS OF THE CHARACTERISTICS AND CLINICAL CONTRIBUTORS

VIRTUAL E-POSTER SESSION

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Background and Aims: Familial Hypercholesterolemia (FH) is characterized by lifelong high cumulative LDL burden and increased risk of atherosclerotic events. Nonetheless, there is a subgroup of FH patients, who do not develop atherosclerotic events despite not using any lipid lowering agent. The aim of this study was to evaluate the clinical characteristics of event-free elderly FH patients.

Methods: Medical records of patients aged ≥65 years with a statin-free LDL level ≥160 mg/dL were reviewed retrospectively. Patients were divided into two groups according to the presence and absence of known and/or documented atherosclerotic cardiovascular disease. Lipid profile and clinical characteristics were compared and multivariate analysis was performed to assess independent variables associated with resilient FH.

Results: A total of 143 (66.4% female, mean age 72.49 +/- 6.35 years) patients fulfilled the study criteria. Among them, 57.3% had no known or documented atherosclerotic disease. Female gender, higher HDL, younger age and lower Lp(a) levels were univariate correlates of event-free FH, whereas frequency of hypertension, diabetes, hsCRP, LDL, HbA1c and eGFR did not have a statistically significant association. In multivariate analysis, low Lp(a) was the strongest determinant of event-free FH (seen in Table).

	B	S.E.	Wald	df	Sig.	Exp(B)
Age	.086	.031	7.714	1	.005	1.090
Gender	-.971	.416	5.456	1	.019	.379
Lp(a)	.025	.007	11.249	1	<.001	1.025
HDL	-.024	.013	3.358	1	.067	.976

Conclusions: Beside of age, lower Lp(a) levels and female gender were found to be associated with event-free (resilient) FH elderly individuals.

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MANNHEIM GERMANY | MAY 21-24, 2023

#1320

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

THE ASSOCIATION OF BLOOD LIPIDS LEVELS WITH VITAMIN STATUS OF YOUNG AND HEALTHY ADULTS

VIRTUAL E-POSTER SESSION

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Background and Aims: Vitamins are essential micronutrients that are demanded for physiological functioning and metabolism. According to the last scientific data, the problem of deficient vitamin status is a major concern all over the world. For the past decades, the issue of marginal vitamin status and insufficient vitamins levels causes the growing research interest. The aim of this study was to compare the blood lipids levels in young and healthy adults with normal or deficient vitamin status.

Methods: 138 young and healthy adults (33% males) with normal body weight and absence of chronic medical conditions were recruited. Serum levels of vitamins (B1, B2, B6, Folic acid, D12, C, D3, A, E, and K2) and blood lipids (TCH, LDL-CH, HDL-CH, and TG) were measured after 8 weeks of wash-out period (inc. any vitamin supplements or vitamin fortified food products).

Results: 27 participants (19.6%) had normal vitamin status; 63 (45.7%) - insufficient/deficient levels of 1 vitamin from the list; and 48 (34.8%) participants had insufficient and/or deficient levels of 2 and more vitamins that were considered as deficient vitamin status. TCH and LDL-CH levels were reliably higher in the deficient vitamin status group compared to the normal vitamin status group (4.90±0.99 mmol/l vs 4.42±0.73 mmol/l for TH with p=0.035 and 3.05±0.75 mmol/l vs 2.61±0.69 mmol/k for LDL-CH with p=0.017). The levels of HDL-CH and TG were comparable between groups.

Conclusions: The deficient vitamin status was associated with reliably higher TCH and LDL-CH levels in young and healthy adults.

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#480

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

LONG NON-CODING RNA EXPRESSION IN CALCIFIED CAROTID PLAQUES

VIRTUAL E-POSTER SESSION

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Background and Aims: We have reported the molecular activities in calcified carotid plaques including epigenetic profiles. In this study, we investigated the expression of long non-coding RNAs (lncRNAs) in carotid plaques based on the calcium score.

Methods: Eight specimens removed by carotid endarterectomy (mean age 71.8 years, mean stenosis rate 75.6%)were classified into high- and low-calcified plaques (HCP and LCP) according to the Agatston calcium score (average 856.1 vs. 54.5). A highly sensitive RNA-Seq, SMART (Switching Mechanism At 5' End of RNA Template)-Seq v4, was performed, and differences in lncRNA expression were examined between the groups by bioinformatics data mining.

Results: Total expressed transcripts were 229647 (60715 genes). Filtering out low-quality transcripts, lncRNAs with a difference (between HCP and LCP) showing $|\log_2 FC| \geq 1$ and $p<0.05$ in mean $\log_2 TPM$ expression were chosen. Fifteen genes were extracted from the HCP group, and 33 genes from the LCP group. The lncRNA selected for both selections (A:significant lncRNAs with a $p<0.01$ difference between the two groups, B:lncRNAs showing a difference for $\log_2 TPM$ expression of $|\log_2 FC| \geq 1/p \leq 0.05$ in more than 13/16 of the individual comparisons of each sample) were NR2F2-16, GRM1-12, and SBNO1-AS1 in the HCP group, and ZNF184-2, DLEU2L, Z97192.2 etc. in the LCP group. The lncRNA NR2F2-AS1 in HCP promotes cell proliferation, migration, and invasion and suppresses apoptosis by uptake of miR4429 regulating MBD1. In LCP, the lncRNAs were involved in transcriptional regulation (ZNF184) etc., while others were novel.

Conclusions: Profiles of lncRNA expression were shown with possible regulation of cell proliferation in calcified carotid plaques.

91ST EAS CONGRESS
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#476

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

ANTIATHEROGENIC EFFECT OF BLUEBERRY FRUIT POLYPHENOLS EXTRACTS (VACCINIUM ANGUSTIFOLIUM AIT.) REDUCES OXIDATIVE STRESS AND ENHANCES THE CHOLESTEROL EFFLUX PROCESS

VIRTUAL E-POSTER SESSION

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Background and Aims: The purpose of this study is to investigate the antiatherogenic effects of blueberry (*Vaccinium angustifolium Ait*) fruit polyphenols and their ability to mediate atherosclerosis-related oxidative stress**.**

Methods: We used *pH* differential, colorimetric aluminum chloride, Folin-Ciocalteu, and vanillin-HCl methods to quantify respectively total anthocyanins, total flavonoids, total polyphenols, and total condensed tannins content. *In vitro* determination of the antioxidant activity was carried out using the $DPPH^{\bullet}$ scavenging, FRAP, and TAA assays, as well as by monitoring conjugated diene formation (CD) in copper oxidized LDL. Cholesterol efflux to apoA1 was measured in J774 ^{3}H-cholesterol loaded.

Results: Our data show that blueberry fruit extracts were rich in polyphenols and anthocyanins (111,20 ± 2,96 mg GAE/g dw; 16,29 ± 1,02 mg C-3-GE/g dw, respectively). The obtained IC 50 values from DPPH experiment were (322,02 ± 11,59 vs 232,33 ± 15,59 µg/ml, $p<0,01$), respectively for blueberry fruit phenolic compounds extract and for its purified anthocyanins extract. The respective extracts show a significant dose-response increase ($p<0,05$) of ferric-reducing antioxidant power which is arranged from [(25,84 ±1,24 to 68,06±2,26) vs (11,6 ± 3,90 to 34,2 ± 0,7) mg AAE/gE]. Results from total antioxidant capacity ranged from [(70,36 ± 15,59 to 396,98 ± 20,72) vs (89,75 ± 16,82 to 634,33 ± 74,53) mg AAE/gE], respectively for the same extracts. Moreover, blueberry polyphenols and anthocyanins (160 and 320 µg/ml) significantly inhibit CD formation in oxidized human LDL and enhance cholesterol efflux.

Conclusions: We showed that the blueberry extracts possess interesting *in vitro* antioxidant and antiatherogenic capacities.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1316

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE STRUCTURE OF PRESCRIBING AND TAKING MEDICATIONS IN ELDERLY AND SENILE PATIENTS WITH CARDIOVASCULAR COMORBIDITY AND CHRONIC KIDNEY DISEASE

VIRTUAL E-POSTER SESSION

Elena Efremova, Alexander Shutov
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Background and Aims: Comorbidity and polypharmacy are typical for older patients. The aim of this study was to investigate the structure of prescribing and taking medications in elderly and senile patients with cardiovascular comorbidity and chronic kidney disease

Methods: 447 older patients with stable cardiovascular disease and chronic kidney disease (CKD) (219 males, mean age was 69,6±7,3 years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). The structure of drug prescriptions a month before seeking medical help and the reasons for refusing therapy was studied.

Results: Diuretics, anticoagulants, mineralocorticoid receptor antagonists and angiotensin II receptor blockers were more often prescribed to elderly and senile patients with CKD compared to patients without CKD. Nephroprotective therapy with blockers of the renin-angiotensin-aldosterone system was received by 99.3% of patients with CKD. In the month prior to seeking medical attention, only 77.3% of patients were using RAAS blockers, and only 40.1% of patients with CKD were taking statins. Every fifth patient with cardiovascular comorbidity and CKD took non-steroidal anti-inflammatory drugs. There was an under-prescription of mineralocorticoid receptor antagonists given that the majority of patients with CKD (81.9%) had chronic heart failure. Elderly and senile patients with CKD most often named forgetfulness (64.5%), unwillingness to constantly take drugs (35.9%) and good health (32.6%) among the reasons for intermittent use or refusal of drugs.

Conclusions: The structure of prescribing and taking medications in elderly and senile patients due to comorbidity, including CKD. There is a lack of adherence to drug therapy in real clinical practice.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1315

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

GALECTIN LEVEL 3 IN MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

Yulia Kotova
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Background and Aims: Recently, an actively studied biomarker is galectin-3, used in laboratory diagnostics as a marker of tumor transformation and a biomarker of CHF. Goal. Evaluation of the clinical and prognostic significance of galectin-3 in patients with myocardial infarction (MI) with ST segment elevation.

Methods: Material and methods. 87 patients were examined who were diagnosed with MI with ST segment elevation. On the 1st-2nd day of the disease, the level of galectin-3 was determined by the enzyme immunoassay in all patients.

Results: The concentration of galectin-3 on day 1-2 was 10.5 [7.4; 13.9] ng/ml, by day 10-14 the concentration of this biomarker increased and reached 15.6 [9.2; 24.2] ng/ml. There were ($p = 0.04$) higher concentrations of galectin-3, estimated on the 10th-14th day of the disease in patients with a previous acute cerebral circulatory disorder (ACCD) compared with patients without a history of ACCD. In patients with a history of hypercholesterolemia, the level of galectin-3 on the 10th-14th day of MI was 47% higher ($p =0.0002$) compared with patients without it. Similar results were noted in the group of patients with hereditary CHD ($p = 0.023$). Patients with type 2 diabetes mellitus were also characterized by higher values of the analyzed marker, assessed on the 10th-14th day of MI.

Conclusions: The results of this work showed the possibility of using the galectin 3 level for risk stratification of patients with MI. Despite a large number of experimental and clinical studies of galectin 3, some questions remain unanswered and require more detailed and in-depth analysis.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1311

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

LEFT MAIN CORONARY ARTERY CALCIFICATION AND CAROTID ARTERY STENOSIS IN PATIENTS WITH AORTIC VALVE SCLEROSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: Studies have suggested that the incidence of carotid artery stenosis in patients with left main (LM) coronary artery disease (CAD) is higher than in the general population, with the prevalence of CAD being higher in this group. CAD and aortic valve calcification (AVC) share common pathophysiological mechanisms and risk factors. The aim of this study was to evaluate possible correlations between LM coronary artery calcification (CAC) and carotid artery stenosis in individuals with aortic valve sclerosis (AVSc).

Methods: We present the preliminary results of a prospective study of 64 patients with AVSc, who underwent non-contrast ECG-guided multi-slice computed tomography (MSCT) for quantification of calcium score by Agatston units (AU) and carotid duplex ultrasound scan (CDUS). Primary endpoints were the quantification of (1) AVC score;(2) LM CAC score; and (3) grading of carotid artery stenosis.The study took place between 3 tertiary hospitals in Greece.

Results: The median age of all participants was 75.3 years old (IR=7.4) with median AVC and LM CAC scores being 673.5 AU (IR=878.2) and 83.7 AU (IR=95) respectively. According to the results of bivariate regression analysis, males show statistically significantly increased LM CAC scores compared to females ($p<0.001$). For both sexes, it was noted that individuals with LM CAC had a greater degree of left carotid artery stenosis compared to individuals without LM CAC ($p=0.031$).

Conclusions: The significant correlation between LM CAC and the degree of left carotid artery stenosis for individuals with AVSc has major potential for further research on the local hemodynamic flow and on tissue pathophysiological adaptation.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#96

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

ANTIDYSLIPIDEMIA PHARMACOTHERAPY IN CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND BAYESIAN NETWORK META-ANALYSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: Background and Aims: The benefits and safety of antidyslipidemia pharmacotherapy in patients with chronic kidney disease were not well defined so the latest evidence was summarized by this work.

Methods: Methods: This systematic review and Bayesian network meta-analysis (NMA) included searches of PubMed, Embase, and Cochrane Library from inception to Feb. 28, 2022, for randomized controlled trials of any antilipidaemic medications administered to adults with chronic kidney disease [CKD: estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73 m^2 not undergoing transplantation], using the Grading of Recommendations Assessment, Development, and Evaluation system (GRADE) tool to assess the certainty of the evidence.

Results: Results: 55 trials and 30 works of them were included in our systematic review and NMA respectively. In comparisons with no antidyslipidemia therapy or placebo, proprotein convertase subtilisin/Kexin type 9 inhibitors plus statin (PS) was the most effective drug regimen for reducing all-cause mortality (OR 0.62, 95% CI [0.40, 0.93]; GRADE: moderate), followed by moderate-high intensity statin (HS, OR 0.76, 95% CI [0.60,0.93]; I2=66.9%; GRADE: moderate). PS, HS, low-moderate statin (LS), ezetimibe plus statin (ES), fibrates (F) significantly decreased the composite cardiovascular events. The subgroup analysis revealed the null effect of statins on death (OR 0.92, 95% CI [0.81, 1.04]) and composite cardiovascular events (OR 0.94, 95% CI [0.82, 1.07]) in dialysis patients.

Conclusions: Conclusion: In nondialysis CKD patients, statin-based therapies could significantly and safely reduce all-cause death and composite cardiovascular events despite the presence of arteriosclerotic cardiovascular disease and LDL-c levels. Aggressive medication regimens, PS and HS, appeared to be more effective.

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#1309

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

DETERMINATION OF THE CONTENT OF CYTOMEGALOVIRUS AND HERPES SIMPLEX VIRUS 1 IN PATIENTS WITH CORONARY HEART DISEASE

VIRTUAL E-POSTER SESSION

Yulia Kotova
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Background and Aims: Coronary heart disease (CHD) occupies a leading position among all chronic non-communicable diseases. The main substrate for the development of coronary artery disease is coronary atherosclerosis, but today special attention is paid to new aspects of the formation of coronary atherosclerosis.
The purpose of the study is evaluating the relationship of the previous infection caused by cytomegalovirus (CMV) and herpes simplex virus 1 (HVS 1) with the occurrence of coronary heart disease during prospective follow-up.

Methods: The levels of antibodies to CMV and HVS 1 were determined in serum samples tduring the initial examination in participants without CHD. The analyses were performed in those who developed a case of CHD (n=72) during 5 years of follow-up from the initial examination and in a stratified random sample of all participants (n=84).

Results: In the population with the highest level of antibodies to CMV, there was an increased relative risk (RR) of CHD 1.76 (95% confidence interval (CI) 1.00—3.11) when adjusted for age and gender. he RR of CHD at the highest levels of antibodies to CMV in people with diabetes is especially high, the relationship between high levels of antibodies to CMV and diabetes is statistically significant (p=0.05). There was no association of CHD with the highest levels of antibodies to HVS 1 (adjusted HR 0.77; 95% CI 0.36—1.62).

Conclusions: The high level of antibodies to CMV is largely associated with the occurrence of coronary heart disease. CMV infection may be an important risk factor for CHD, which requires further study.

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MANNHEIM GERMANY | MAY 21-24, 2023

#1308

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

POLYPHARMACY IN ELDERLY AND SENILE PATIENTS WITH CARDIOVASCULAR COMORBIDITY

VIRTUAL E-POSTER SESSION

Elena Efremova, Alexander Shutov
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Background and Aims: The aim of this study was to investigate polypharmacy in elderly and senile patients with cardiovascular comorbidity.

Methods: 447 older patients with stable cardiovascular disease (219 males, mean age was 69,6±7,3 years) were studied. Chronic kidney disease (CKD) was diagnosed and classified according to the KDIGO guidelines (2012). Modified Charlson comorbidity index (CCI) was estimated (added scores for chronic kidney disease). Comorbidity was regarded as high at index ≥ 6 scores. GerontoNet ADR Risk Score was used for predicting adverse drug reactions (ADRs).

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 total number of drugs taken by elderly and senile patients with cardiovascular comorbidity was higher than in patients without CKD: 6 (5;8) and 6 (4;7) drugs, respectively, p=0.01. The number of drugs depending on the stage of CKD did not differ (p=0.74). Patients with CKD had higher rates GerontoNet ADR Risk Score than in patients without CKD: 4 (3; 4) and 3 (2; 3) points, respectively, p<0.0001. In 55 (19.9%) elderly and senile patients with CKD (n=277), the GerontoNet score exceeded 5 points, which is an unfavorable prognostic factor. There was no effect of a high risk of drug therapy complications on the mortality of patients with cardiovascular comorbidity and CKD (RR 1.03; 95% CI 0.44–2.39; p=0.94) .

Conclusions: The total number of drugs taken by patients with CKD is greater than in patients without CKD. Every fifth patient had a high risk of drug therapy complications.

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#1306

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

EFFECT OF HDL-C LEVELS ON CORONARY ARTERY CALCIFICATION IN PATIENTS WITH AORTIC VALVE SCLEROSIS

VIRTUAL E-POSTER SESSION

Symeon Evangelos Mavroudeas[1], S Tsiamis[2], C Mantis[3], A Gkogkos[3], K Loukopoulos[1], K Grammatikopoulos[1], I Feskou[4], K Sotirakou[5], S Tsalamandris[1], N Anousakis[1], A Synetos[1], N Kafkas[3], Costas Tsioufis[1], K Toutouzas[1]
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Background and Aims: Coronary artery calcification (CAC) is an important pathophysiological event and predictive indicator for patients with coronary heart disease. Two distinct types of CAC have been recognized, the intimal and medial calcification, each of them with different risk factors. The aim of this study was to evaluate and associate the effect of high-density lipoprotein cholesterol (HDL-C) levels on CAC progression in individuals with aortic valve sclerosis (AVSc).

Methods: We present the preliminary results of a prospective study of 64 patients with AVSc, who underwent non-contrast ECG-guided multi-slice computed tomography (MSCT) for quantification of calcium score by Agatston units (AU) and blood sampling for biochemical analysis. Primary end points were the quantification of (1) aortic valve calcification (AVC) score; (2) CAC score; and (3) blood HDL-C levels.

Results: The median age of all participants was 75.3 years (IR=7.4) with the median blood HDL-C level being 46.9 mg/dl (IR 12.4). The median CAC and AVC scores levels were 242.7 AU (IR=298.1) and 673.5 AU (IR=878.2) respectively. According to the results of the bivariate analysis, a statistically significant relation between HDL-C levels and left anterior coronary artery (LAD) calcification score was noted. Increased HDL-C levels were related to decreased levels of LAD calcification score (p=0.001).

Conclusions: The significant inverse relationship between HDL-C levels and LAD calcification has major potential for further research on the use of HDL-C in CAC and cardiovascular risk evaluation and management.

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#1304

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

EFFECT OF STATINS ON IL-1 SECRETION BY MONOCYTES IN EX VIVO MODEL

VIRTUAL E-POSTER SESSION

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Background and Aims: The anti-atherosclerotic efficacy of statins is explained not only by hypolipidemic, but also by anti-inflammatory action. The aim of this study was to evaluate the effect of statins administration on pro-inflammatory cytokine IL-1 secretion in ex vivo model in primary culture of human monocytes.

Methods: Totally 35 participants with severe atherosclerosis in carotid or coronary arteries aged 54-78 years were included in the study, 17 patients on statins therapy and 18 without statins. Primary culture of circulating monocytes was obtained from whole blood of study participants by gradient centrifugation followed by magnetic separation of CD14+ cells. Basal and lipopolysaccharide(LPS)-stimulated secretion of IL-1 was evaluated by ELISA after 24-hour incubation of cultured cells with and without LPS. Proinflammatory monocyte activation was calculated as the ratio of basal to stimulated IL-1 secretion.

Results: Basal secretion of IL-1 was 117.7 pg/ml in patients receiving statins and 143.3 pg/ml in patients without statins, p=0.394. LPS-stimulated IL-1 secretion was significantly lower in the statins group and amounted to 1116.3 pg/ml vs. 1939.3 pg/ml in the group without statins, p=0.002. Proinflammatory monocyte activation was 10.9 in the statins group vs. 30.9 in the statins-free group, p=0.015.

Conclusions: The results of the study allow considering the suppression of pro-inflammatory activation of monocytes as one of the possible mechanisms of the anti-inflammatory action of statins, but further studies are needed. This work was supported by the Russian Science Foundation (Grant #22-25-00498).

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1303

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

THE MODIFIED RESISTANCE INDEX IN ELDERLY AND SENILE PATIENTS WITH CHRONIC KIDNEY DISEASE AND CARDIOVASCULAR COMORBIDITY

VIRTUAL E-POSTER SESSION

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Background and Aims: There is an association between a decrease of kidney function and indicators of arterial stiffness, which determines the possibility of modified the kidney resistance index to indicators of vascular stiffness.The aim of this study was to investigate the modified kidney resistance index in elderly and senile patients with chronic kidney disease (CKD) and cardiovascular comorbidity.

Methods: 62 patients with stable cardiovascular diseases (25 males, mean age 69.4±7.4 years) were studied. CKD was diagnosed and classified according to the KDIGO guidelines (2012). Vascular stiffness was assessed as the ratio of LV stroke volume (ml) to pulse pressure (mm Hg). The kidney resistance index (the ratio of the difference for the renal artery between the maximum systolic velocity and the final diastolic velocity to the maximum systolic velocity) was determined according to the standard method during ultrasound examination of the kidneys. The kidney resistance index was indexed to an indicator of vascular stiffness - the modified resistance index (MIR).

Results: 32 (51.6%) patients had CKD with eGFR less than 60 ml/min/1.73 m^2. MIR was higher in the presence of CKD: 0.68 (0.65; 0.72) with CKD and 0.61 (0.59; 0. 64) without CKD, resp., p=0.02. There was a direct relationship between the MIR and body mass index (r=0.35, p=0.007), body fat mass index (r=0.36, p=0.005). There was a direct relationship between MIR and the Charlson comorbidity index (r=0.42, p=0.02) and the total number of diseases (r=0.48, p=0.005).

Conclusions: The increase in the modified kidney resistance index is due to the high comorbidity of elderly and senile patients.

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#105

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

SAFFRON ETHANOLIC EXTRACT SUPPRESSED BIOMARKERS OF ENDOTHELIAL DYSFUNCTION IN EARLY AND ADVANCED ATHEROSCLEROTIC RABBITS

VIRTUAL E-POSTER SESSION

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Background and Aims: Cell adhesion molecules mediate leukocyte activation and recruitment into the vessel wall causing endothelial dysfunction, which contributes to the development of atherosclerosis. Previous studies showed that saffron exhibits anti-atherogenic effects. However, the mechanisms underlying the effects of saffron on endothelial dysfunction are still not well understood. Thus, this study aims to investigate the effects of saffron ethanolic extract (SEE) on endothelial dysfunction via protein expressions of vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1) and e-selectin in early and advanced atherosclerotic rabbits.

Methods: Thirty male New Zealand White rabbits were fed with a high-cholesterol diet for 4 and 8 weeks to induce early and advanced atherosclerosis respectively. They were then divided into 2 groups: (1) intervention groups, given 50mg/kg/day SEE (n=10) and 100mg/kg/day SEE (n=10) for 8 weeks, and (2) control group, given distilled water for 8 weeks (n=10). After euthanasia, aortas were excised for immunohistochemical staining. Tissue blocks of the aortas were sectioned and stained with monoclonal antibodies against VCAM-1, ICAM-1 and e-selectin. The immunohistochemical expressions were assessed using the Pearson chi-square test.

Results: VCAM-1 expression significantly decreased post-treatment with 100mg/kg/day SEE compared to control in early atherosclerosis group ($p<0.01$). Rabbits given 50mg/kg/day SEE showed lower expression of ICAM-1 and e-selectin in early atherosclerosis group compared to control group ($p>0.05$). The expression of ICAM-1 and e-selectin reduced post-treatment with 100mg/kg/day SEE in advanced atherosclerosis group compared to control group ($p>0.05$).

Conclusions: SEE could improve endothelial dysfunction and attenuate atherosclerosis by suppressing the protein expression of VCAM-1, ICAM-1 and e-selectin.

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#1174

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

ASSOCIATION OF SUBCLINICAL ATHEROSCLEROSIS AND IL-1 SECRETION BY MONOCYTES IN PATIENTS WITH RHEUMATOID ARTHRITIS

VIRTUAL E-POSTER SESSION

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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: 41 patients with RA aged 49(14.4) were included. 23 participants were atherosclerosis-free and 18 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 216.0(74.9)pg/ml; LPS-stimulated - 1204.9(408.4)pg/ml ($p<0.01$). After rest period, IL-1 concentration decreased to 125.6(87.9)pg/ml, ($p=0.02$). After re-stimulation with LPS, IL-1 secretion was 122.4(55.9)pg/ml. In carotid atherosclerosis group unstimulated secretion of IL-1 was 195.5(88.6)pg/ml; LPS-stimulated – 841.3(112.6)pg/ml, ($p=0.03$). After rest period, IL-1 concentration decreased to 120.8(181.3) pg/ml, ($p=0.07$). After re-stimulation with LPS, the secretion of IL-1 was 114.0(66.5)pg/ml and did not differ significantly from the secretion of cells incubated without LPS ($p=0.725$). The difference between groups wasn't significant in all points.

Conclusions: IL-1 secretion by cultivated monocytes of RA patients did not differ between patients with and without carotid atherosclerosis. A study on a larger cohort is necessary. This work was supported by the Russian Science Foundation (Grant № 22-15-00199).

91ST EAS CONGRESS
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#1327

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

A SURVEY ON AWARENESS CARDIOVASCULAR MORTALITY IN WOMEN

VIRTUAL E-POSTER SESSION

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Background and Aims: Cardiovascular disease constitutes the major reason of mortality worldwide for both genders. However, women are overlooked as victims of cardiovascular disease. World Health Organization data underscores ischemic heart disease as the leading cause of death for both men and women, as is the case according to Turkish Statistical Institute data. A 2019 AHA survey found that only 44% of respondents knew that heart disease is the leading cause of female mortality.

Methods: Our study was designed as a survey aiming to seek for awareness of cardiovascular disease as the leading cause of female mortality. Individuals between 18-80 years of age were enrolled and asked to participate in a short survey

Results: The study included 7920 individuals aged between 18-80 years. Fifty eight percent (n=4643) of the population were female. Cardiovascular disease was pointed out as the leading cause of women's mortality by %35 (n=2813) of the participants. Malignant diseases were declared to be the leading cause by %44 (n=3522). Breast cancer was chosen as the major reason by %25 of the study population (n=2015) while 14% reported they had no idea. Education was not found to be a determinant in the awareness of causes of female mortality.

Conclusions: Cardiovascular disease is the leading cause of mortality in women worldwide. Awareness of this fact is deficient due to sex specific differences in risk factors and clinical presentation, the belief that poor lifestyle habbits are the only reasons for cardiovascular disease. This may culminate in inadequate risk factor modification and late diagnosis of cardiovascular disease in women. .

91ST EAS CONGRESS
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#1460

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE RELATIONSHIP BETWEEN ATHEROGENIC INDICES AND TISSUE INHIBITOR OF METALLOPROTEINASE-3 IN CHRONIC HEART FAILURE

VIRTUAL E-POSTER SESSION

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Background and Aims: Atherogenic indices are used to predict coronary artery disease (CAD) risk. Tissue inhibitor of matrix metalloproteinase-3 (TIMP-3) is a natural inhibitor of matrix metalloproteinases and also a protein with inhibitory effects on angiogenesis. The aim of our study was to investigate a possible association between atherogenic indices and TIMP-3 in chronic heart failure (CHF).

Methods: 56 patients with chronic HF with midrange ejection fraction (HFmrEF) were examined, mean age 65.62±9.69 years, and 22 age and sex-matched healthy subjects, mean age 56.4±5.53 years. ELISA was used for measuring TIMP-3 levels. The lipid profile and atherogenic indices (log TG/HDL, LDL/HDL, TC/HDL and TG/HDL) were also studied.

Results: Serum levels of TIMP-3 were significantly lower in patients compared to controls: 6.460 (1.007-12.520) vs. 5.051 (2.062-10.463); ($p<0.05$). There was not statistically significant difference between the lipid indices in patients compared to healthy controls ($p>0.05$). TIMP-3 showed correlation with LDL/HDL ($r=0.33$; $p=0.02$) and TC/HDL ($r=0.30$; $p=0.04$).

Conclusions: Our data show an association between atherogenic indexes LDL/HDL**,** TC/HDL and TIMP-3 in CHF. A possible lipid interaction with tissue inhibitor of matrix metalloproteinase-3, favoring up-regulation of different pathogenic pathways of HF is suggested. Further studies are needed to clarify the underlying mechanisms of cross-talk between TIMP-3 and lipoproteins in heart failure.

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#1346

Topic: *AS04 Clinical Vascular Disease / AS04.07 Nutrition, nutraceuticals*

CARDIOVASCULAR RISK CLARIFICATION WITH THE FOOD SCALE

VIRTUAL E-POSTER SESSION

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Background and Aims: The aim was to determine the quality characteristics of nutrition in individuals with low risk (SCORE 2 < 2,5%) and to assess the relationship of nutritional characteristics with adiposopathy.

Methods: The study included 86 patients: 42.9 ± 2.3 years, 30 men (35%). 46 (51%) participants with central obesity (CO), low cardiovascular risk (SCORE 2 < 2,5%). All patients were provided with a nutritional questionnaire consisting of 11 questions. The epicardial fat thickness (EFT) was assessed by ultrasonic methods.

Results: Inappropriate nutrition was registered in all patients with CO. A number of diet factors has a correlation with TG, mLDL, 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), fish less than once a week (r = 0.6; r = 0.5; r = 0.5; r = 0.7; r = 0.7; r = 0.5; r = 0.5, 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). According to the nutritional scale, due to an unbalanced diet, the risk of cardiovascular diseases became higher in 57% of patients.

Conclusions: The low cardiovascular risk group is very heterogeneous due to the high prevalence of CO and unbalanced nutrition. The food scale helps to identify diet and stratify the true risks within 2 minutes.

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#1459

Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

HEARING LOSS AND ASSOSIATION WITH DYSLIPIDEMIA: A STUDY

VIRTUAL E-POSTER SESSION

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Background and Aims: Dyslipidemia have been widely studied in patients with sudden sensorineural hearing loss, but it has been unclear whether dyslipidemia associates with it. Whether there is a simple and feasible blood lipid index to predict the onset of hearing loss remains to be further investigated

Methods: This study reviewed 43 patients with hearing loss and 46 healthy ones who received relevant clinical examination and audiometry in our hospital outpatient department, from July 2019 to June 2021. The demographic, clinical characteristics and lipid levels a of the two groups were compared

Results: No signicant differences between the hearing loss group and the control group in age, sex, BMI and smoking habits were observed. Meanwhile, it can be seen the mean (SD) concentrations of total cholesterol (TC) (194.59 [38.22] vs 176.83 [23.55] mg/dL; MD, 17.76 mg/dL; 95% CI, 26.64-46.72 mg/dL), the mean (SD) concentrations of low density lipoprotein cholesterol (LDL-C) (116.99 [33.59] vs 96.91 [22.01] mg/dL; MD, 20.08 mg/dL; 95% CI, 32.43-48.26 mg/dL) and apolipoprotein (apo) B (89.82 [21.38] vs 81.16 [16.17] mg/dL; MD, 8.66 mg/dL; 95% CI, 12.03-23.21 mg/dL) were signicantly higher than the control group. In addition, it was also observed that the median concentrations of high density lipoprotein cholesterol (HDL-C) (1.51 [1.33-1.76] vs 1.56 [1.40-1.84] mg/dL) and the median concentrations of apolipoprotein (apo) AI (118.50 [103.00-141.25] vs 133.00 [115.25-1.52.75] mg/dL) were lower than those in the control group

Conclusions: There were signicant differences in blood lipid levels and lipid metabolism between the hearing loss group and the control group. LDL-C, apo AI and apo B were important independent predictors

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#484

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

PERICORONARY ADIPOSE TISSUE ATTENUATION DETERMINED BY CT PREDICTS CARDIOVASCULAR EVENTS IN PATIENTS WITH SUSPECTED CORONARY ARTERY DISEASE: A RETROSPECTIVE COHORT STUDY

VIRTUAL E-POSTER SESSION

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Background and Aims: Recent studies showed that pericoronary adipose attenuation (PCATA) on coronary computed tomography angiography (CCTA) is a non-invasive biomarker for pericoronary inflammation. This study aimed to investigate whether PCATA is a useful predictor for cardiovascular events in patients with suspected coronary artery disease (CAD).

Methods: A total of 533 patients who underwent clinically indicated CCTA in our institute from August 2011 and December 2015 were enrolled. We assessed PCATA in Hounsfield units (HU) of proximal 40-mm segments of all 3 major coronary arteries. For analyses, the average PCATA of all 3 coroanry arteries was applied. The outcome was the composite of cardiovascular death, acute coronary syndrome, late coronary revascularization.

Results: During a median follow-up of 4.7 years, we observed 58 cardiovascular events. PCATA was significantly higher in patients with cardiovascular events than that in patients without cardiovascular events (- 65.3 ± 6.6 HU vs – 67.9 ± 5.7 HU, p=0.02). High PCATA was significantly associated with the incidence of cardiovascular events in a model that included traditional risk factors and adverse CCTA findings, such as significant stenosis and high-risk plaque (hazard ratio; 1.41, 95% confidence interval; 1.08–1.84, p=0.01). Finally, the incremental prognositc value of PCATA was evaluated. After adding PCATA to the prediction model with adverse CCTA findings, global chi-square values increased significantly from 75.4 to 79.3 (p=0.04).

Conclusions: In patients with suspected CAD undergoing clinically indicated CCTA, high PCATA could predict cardiovascular events.

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#1356

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

SIALIDASE-INDUCED DESIALYLATION OF BLOOD PLASMA LOW-DENSITY LIPOPROTEINS IN MICE.

VIRTUAL E-POSTER SESSION

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Background and Aims: Sialidases can contribute significantly to atherosclerosis development due to their ability to modify low-density lipoproteins (LDL). An association of desialylated LDL with atherosclerosis progression was found several decades ago. Nevertheless, the detailed information about all factors causing LDL desialylation is still to be clarified. A proper model can help with the understanding of the factors causing LDL desialylation. The task of the study was to create a model of desialylation of LDL in mice upon an injection of immobilized sialidase.

Methods: The experimental group of wild type C57BL6 mice received bacterial (*Vibrio cholerae)* sialidase conjugated with mouse IgG (the control group of C57BL6 mice was subjected to a single injection of saline). Termination of mice was carried out at fixed periods of time before and after single injection (1-7 days). Ultracentrifugation was applied for LDL isolation from serum, and then the content of sialic acid was detected using Warren's method as well as lipids of serum were identified using commercially available kits.

Results: Up to 30%-decrease of LDL sialylation was found up to 5 days after sialidase injection with no change of serum levels of triglycerides, total cholesterol and HDL-cholesterol.

Conclusions: A new model of LDL desialylation *in vivo* was established using mice and exogenous sialidase. This model can help with research of factors affecting sialylation of lipoproteins in blood.
Research was supported by the Russian Science Foundation (grant#20-15-00264).

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#1354

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

THE INFLUENCE OF ANTIOXIDANTS ON RESPIRATION OF CELLS CARRYING MITOCHONDRIAL DNA MUTATIONS ASSOCIATED WITH ATHEROSCLEROSIS.

VIRTUAL E-POSTER SESSION

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Background and Aims: Atherosclerosis is associated with a thickening of the inner surface of large arteries, leading to a decrease in blood flow and impaired circulation. It is the leading disease in mortality in the world. An association of mutations of mitochondrial DNA with atherosclerosis was found earlier. 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. The addition of certain antioxidants and vitamins to cybrids carrying mitochondrial mutations associated with different diseases promoted the survival of cells, normalized the level of ROS generation, restored mitochondrial functions including aerobic respiration and ATP synthesis, and increased the content of mtDNA. A convenient model for studying the role of mitochondrial mutations is cytoplasmic hybrids (cybrids) - cells with the same nuclear DNA and specific mtDNA transferred from the donor cells. The study of the effect of antioxidants on cell cybrids with specified mitochondrial mutations is promising in terms of practical application.

Methods: A set of cybrids carrying atherosclerosis-associated mitochondrial mutations was created. The detection of the viability of cells and consumption of oxygen in the presence of antioxidants was carried out.

Results: The effects of different antioxidants 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.

91ST EAS CONGRESS
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#1349

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

COMPARISON OF CORONARY ARTERY AND CARDIAC VALVE CALCIUM SCORE BETWEEN MEN AND WOMEN WITH AORTIC VALVE SCLEROSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: Aortic valve calcification (AVC) remains the most common cause of aortic valve stenosis leading to significant deterioration of patients' life quality and life expectancy reduction. Pathogenetic mechanisms and risk factors associated with the progression of aortic valve calcification oftentimes result in coronary artery calcification (CAC). The aim of this study was to evaluate and compare the cardiac valve calcification and CAC score between men and women with aortic valve sclerosis (AVSc).

Methods: We present the preliminary results of a prospective study of 64 patients with AVSc, who underwent non-contrast ECG-guided multi-slice computed tomography (MSCT) to quantify calcium score by Agatston units (AU). Primary endpoints were the quantification of (1) cardiac valve calcification score; and (2) coronary artery calcification score, for both sexes. The study took place between 3 tertiary hospitals in Greece.

Results: The median age of all participants was 75.3 years old (IR=7.4) with the median cardiac valve calcification score being 230.5 AU (IR=702.0) for males and 343.5 AU (IR=1197.0) for females. According to the results of a bivariate analysis, females show higher cardiac valve calcification scores without statistically significant differences compared to males (p=0.469). In contrast, males show a higher CAC score 204.5 AU (IR=433.3), compared to females 15.0 AU (IR=81.4) with a statistically significant difference (p<0.001).

Conclusions: The study showed increased CAC in men compared to women, while the same was not found for cardiac valve calcification. More studies are needed in order to investigate and clarify the exact underlying pathophysiological mechanism.

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#1347

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

THE EFFECTS OF HETEROPLASMY LEVEL OF ATHEROSCLEROSIS-ASSOCIATED MITOCHONDRIAL DNA MUTATIONS ON GROWTH RATE OF CELLS.

VIRTUAL E-POSTER SESSION

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Background and Aims: Aim: Atherosclerosis is one of the leading diseases causing death in developed countries. The pathogenesis of this disease is related to a thickening of the inner surface of large arteries, leading to a decrease in blood flow and impaired circulation. There is no complete understanding of the mechanism of atherogenesis at the molecular and cellular levels. Mitochondrial mutations can be the first link in a series of pathological changes, including the activation of the immune response, which lead to the development of atherosclerosis. An association of mitochondrial DNA (mtDNA) mutations with atherosclerosis was described lately. Cytoplasmic hybrids (cybrids) carrying these mutations were created as a convenient tool to study these mutations.

Methods: RT-PCR based detection of heteroplasmy of mtDNA mutations, detection of cellular growth rate and viability, cybrids carrying atherosclerosis-associated mtDNA mutations (THP-1 is a parental line).

Results: The data on cell viability and growth rate were obtained for 10 cybrids and parental cell line. Cybrids were ranked on the basis of data on their growth rates and viability. Heteroplasmy levels were identified for 10 mtDNA mutations in each cell line.

Conclusions: Conclusion: Heteroplasmy levels of 10 mtDNA mutations (652delG, A1555G, C3256T, C3336T, C5178A, G12315A, G13513A, G14459A, G14846A, G15059A) associated with asymptomatic atherosclerosis apparently does not affect the rate of cell growth in cybrids studied. The research was supported by Russian Science Foundation, grant # 22-25-00457.

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#538

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

THE ASSOCIATION OF VISIT-TO-VISIT BLOOD PRESSURE VARIABILITY WITH CARDIOVASCULAR RISK FACTORS IN RURAL DWELLERS WITH ARTERIAL HYPERTENSION

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the association of blood pressure (BP) visit-to-visit variability (VVV) with cardiovascular risk factors in rural dwellers with arterial hypertension (HTN).

Methods: The cross-sectional study enrolled 160 rural males with uncomplicated primary HTN (mean age 50 ± 6 years). BP VVV (of systolic and diastolic BP) was assessed by means of standard deviation and coefficient of variation (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 %) BP VVV (HBPV and LBPV, respectively).

Results: The HBPV group was characterized by a worse cardiovascular risk profile, as compared to LBPV patients, particularly regarding the higher frequency of severe HTN, positive family history of cardiovascular diseases (both parental and maternal), obesity, smoking, more frequent alcohol consumption, higher levels of plasma lipids, and higher SCORE and SCORE2 risk (Table). We determined the cardiovascular risk factors, strongly associated with HBPV, namely as follows: active smoking (OR 6,101 [95 % CI 2,111-17,632]; p=0,001), severe HTN (OR 5,557 [95 % CI 1,830-16,871]; p=0,002) and low-density lipoprotein (LDL) cholesterol level (OR 1,434 [95 % CI 1,228-1,676]; p<0,001) (AUC for logistic regression model: 0,991 [95 % CI 0,961-

0,999]).

Table. The cardiovascular risk profile in rural males with uncomplicated hypertension and different blood pressure visit-to-visit variability

Parameters	LBPV N=78	HBPV N=82	p
Age, years, Me (IQR)	50 (46-56)	51 (45-56)	0,529
Severe HTN*, n (%)	6 (7,7)	59 (72,0)	<0,001
BMI, kg/m², Me (IQR)	25,3 (24,1-27,5)	29,0 (26,8-32,8)	<0,001
Obesity, n (%)	7 (9,0)	34 (41,5)	<0,001
WC, cm, Me (IQR)	86 (79-94)	99 (89-105)	<0,001
WC ≥94 cm, n (%)	22 (28,2)	48 (58,4)	<0,001
Family history of CVD, n (%)**	9 (11,5)	60 (73,2)	<0,001
Active smoking, n (%)	16 (20,5)	69 (84,1)	<0,001
Alcohol consumption*, n (%)**	14 (20,0)	63 (76,8)	<0,001
Fasting glucose, mmol/l, Me (IQR)	4,2 (3,8-4,6)	4,9 (4,7-5,1)	<0,001
TPC, mmol/l, Me (IQR)	5,5 (5,2-5,8)	7,3 (7,0-8,1)	<0,001
LDL cholesterol, mmol/l, Me (IQR)	3,3 (3,2-3,7)	5,2 (4,9-6,0)	<0,001
HDL cholesterol, mmol/l, Me (IQR)	1,3 (1,2-1,4)	0,9 (0,8-1,0)	<0,001
VLDL cholesterol, mmol/l, Me (IQR)	0,8 (0,7-0,9)	1,2 (1,1-1,3)	<0,001
Non-HDL cholesterol, mmol/l, Me (IQR)	4,1 (3,9-4,5)	6,4 (6,0-7,3)	<0,001
TG, mmol/l, Me (IQR)	1,9 (1,8-2,3)	3,2 (2,9-3,9)	<0,001
AIP#, c.u., ,Me (IQR)	0,2 (0,1-0,3)	0,5 (0,5-0,7)	<0,001
SCORE, %, Me (IQR)	4 (2-6)	12 (6-20)	<0,001
SCORE2, %, Me (IQR)	12 (8-16)	33 (26-41)	<0,001
«Vascular» age, years, Me (IQR)	61 (47-70)	80 (70-89)	<0,001

Notes: LBPV – low blood pressure visit-to-visit variability; HBPV – high blood pressure visit-to-visit variability; Me – median; IQR – interquartile range; HTN – hypertension; BMI – body mass index; WC – waist circumference; CVD – cardiovascular diseases; TPC – total plasma cholesterol; LDL – low-density lipoproteins; HDL – high-density lipoproteins; VLDL – very low-density lipoproteins; TG – triglycerides; AIP – atherogenic index of plasma; * – anamnestic and/or index visit data; ** – both paternal and maternal; *** – once a week and more frequent; # – by the equation: AIP = log(TG/HDL)

Conclusions: The concomitant HBPV is associated with a worse cardiovascular risk profile in rural hypertensive males. Active smoking, severe HTN, and higher LDL level appeared to be strongly associated with HBPV.

91ST EAS CONGRESS
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#1332

Topic: *AS04 Clinical Vascular Disease / AS04.11 Anti-inflammatory therapies*

IMPROVING OF THE BIOMECHANICAL PARAMETERS IN AN EXPERIMENTAL ANIMAL ABDOMINAL AORTA MODEL OF EARLY STAGE ATHEROSCLEROSIS USING ULTRASOUND-GUIDED EXTRACORPOREAL LOW- LEVEL FOCUSED SONOTHERAPY

VIRTUAL E-POSTER SESSION

Hossein Mehrad[1,2,3]
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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 experimental sonotherapy system and investigated its effectiveness on macrophage foam cells density reduction, wherein diagnostic B- mode ultrasound is combined with 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 results showed the early stage atherosclerosis formation in all of the rabbits' arteries. Then, treatment group underwent extracorporeal pulsed low- level focused sonotherapy (F= 1.1 MHz, I= 24 w/cm^2, PD= 120 ms). Arterial biomechanical parameters were evaluated in the different groups using B- mode ultrasound images.

Results: 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, longitudinal strain, compliance and distensibility index in the treatment group compared with the other groups ($P<0.05$).

Conclusions: Anti- inflammatory effect of sonotherapy reduces the immune cells density and increase the Nitric Oxide (NO) synthase, resulting in lipid efflux, macrophage egress, arterial biomechanical parameters improvement and early stage atherosclerosis regression.

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#92

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.11 Plaque remodelling*

PHYSICAL MODELING OF COMPLICATED ATHEROMA IN PREMATURE VENTRICULAR CONTRACTIONS

VIRTUAL E-POSTER SESSION

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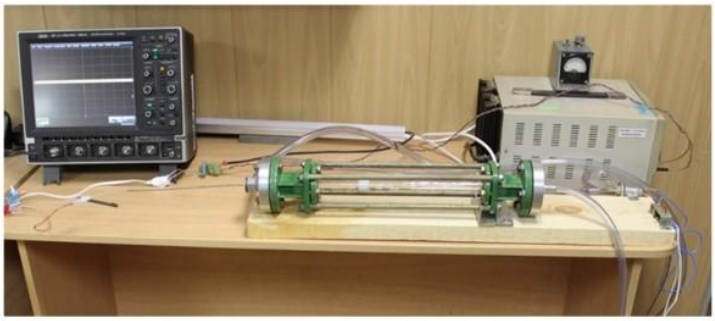
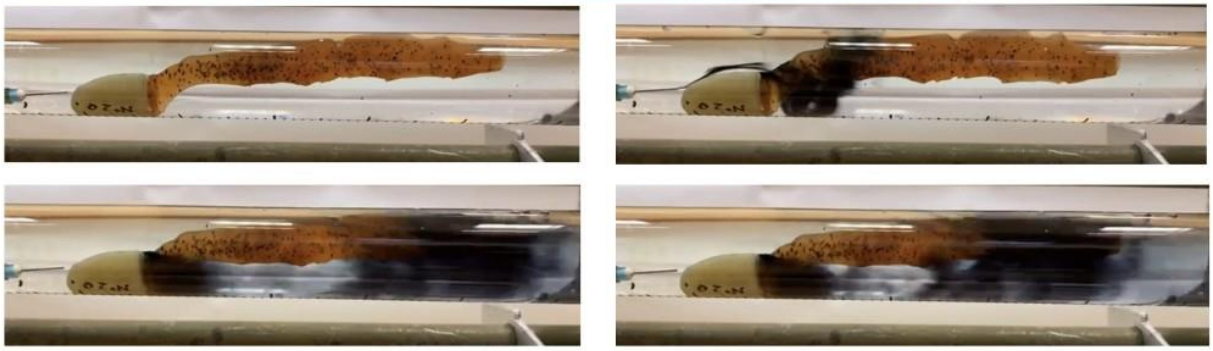
Background and Aims: To study intravascular hemodynamics in premature ventricular contractions (PVCs) with complicated atheroma of the artery in the experiment.

Methods: We used an original "Device for modeling intra-arterial circulation" (document 202780 03/05/2021). Main part of the device is 365 mm long rotameter tube. On both sides, flexible silicone hoses are attached to the rotameter, with their free ends connected to an electric water pump with different modes of work that can simulate regular heart rhythm, as well as PVCs. A fitting is installed at the input end, through which it is possible to introduce into the rotameter a dye, a piezoelectric pressure sensor or an indicator - a silk thread. The closed circuit of the device is filled with an aqueous solution of glycerin with viscosity similar to the human blood.

Results: Inside the rotameter tube, to one of the walls, we fixed a plastic hardening material imitating a marginal atheroma with 50% stenosis with thrombus imitation of silicone 5 cm length. We put a silk thread or a dye to the area of the plaque. In PVCs during the first post-extrasystolic wave behind the plaque, we observed the reflected, standing waves, and turbulent blood flow. The sensor recorded an increase in pressure by 160% compared to the regular heart rhythm. This can lead to the thrombus defragmentation with further embolism in real artery.

Conclusions:





First post-extrasystolic wave causes an increase in intravascular pressure, the appearance of standing, reflected waves, turbulent flow. It can cause the complicated atheroma with further embolism in real arterial vessel.

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#1340

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.04 Adipose tissue homeostasis*

CENTRAL OBESITY DURATION AND LIPID PROFILE AMONG LOW RISK PATIENTS

VIRTUAL E-POSTER SESSION

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Background and Aims: The phenomenon of residual risk of cardiovascular events in the low-risk group is described. Among the causes of heart attacks and strokes in this group, inflammatory and metabolic factors are distinguished.Our aim was to determine the duration of obesity in individuals with central obesity of low cardiovascular risk and to evaluate the relationship of central obesity experience with lipid metabolism.

Methods: The study included 86 patients: 42,9 ± 2.3 years, 56 women (65%) with low risk (SCORE <1%). 44 (51%) participants with central obesity (CO). To determine the duration of central obesity, the indicator "obese years" was used, which was calculated as the difference between the initial age of the patient and the age at which discomfort appeared from a persistent increase in waist circumference.

Results: The “obese years” in the CO group were 2,8 [2,3 - 3,2], and in the control group were 0,6 [0 - 1,0] ($p<0.0001$). “Obesity years” were associated with BFM ($r=0.8$), SBP ($r=0.7$), DBP ($r=0.6$), ectopic distribution of adipose tissue (hepatic and pancreatic steatosis, EFT: $r=0.6$), uric acid ($r=0.5$), chronic inflammation (CRPhs, $r=0.4$; C3-convertase, $r=0.7$; classical pathway of CS, $r=0.4$), lipid metabolism disorders (mLDL, $r=0.6$; TG, $r=0.3$; non-HDL, $r= 0.5$) and IMT ($r=0.4$) ($p<0.0001$).

Conclusions: The experience of central obesity in the group of low risk according to SCORE is a factor in the aggravation of all metabolic markers and signs of chronic inflammation. In clinical practice, it is important not only to state the presence of central obesity, but also to assess it over time.

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#539

Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

PRINTZMETAL ANGINA COMPLICATED BY ARRHYTHMIC STORM

VIRTUAL E-POSTER SESSION

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Background and Aims: We present the case of a 55 year old man, active smoker, admitted to Perugia Hospital on July 2022. He suffered a witnessed out-of-hospital cardiac arrest; cardiopulmonary resuscitation manoeuvres were performed waiting for emergency service (ES);when ES arrived,ECG showed ventricular fibrillation (VF) and many DC-Shock was delivered, until spontaneous circulation was restored.

Methods: The patient was transferred to our hospital under invasive mechanical ventilation. During the transfer,13 VF was treated successfully.The electrocardiogram performed didn't show significant repolarization abnormalities;the echocardiogram showed hypokinesia of the interventricular septum,with normal global ejection fraction.

Results: To rule out an acute coronary syndrome,a coronary invasive angiography (ICA) was immediately performed,which showed mild stenosis of ostial left anterior descending (LAD);during ICA the patient experienced many FV treated with DC-Shock, preceded by transient right bundle branch block and anterior ST elevation; hence, selective angiography of LAD was repeated, which showed a tight spasm at the level of the mild ostial stenosis previously seen; an Impella device was placed due to cardiogenic shock for arrhythmic storm.The patient was transferred to Intensive Care Unit;he was treated with nitrate and verapamil i.v.:no more arrhythmias were observed after that.After 3 days Impella was removed and a new coronary angiography with optical coherence tomography (OCT) was performed; it confirmed mild stenosis of LAD with no evidence of plaque rupture, so no coronary angioplasty was performed. The patient was transferred to the Cardiology ward and an ICD was implanted before discharge.

Conclusions: This is a notable case of Printzmetal angina with a catastrophic onset at first diagnosis.

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#1336

Topic: *AS04 Clinical Vascular Disease / AS04.11 Anti-inflammatory therapies*

ULTRASOUND- GUIDED LASER- MEDIATED THERMAL ANGIOPLASTY OF OCCLUDED ARTERY ACCOMPANIED BY COMBINED DELTA- AMINOLEVULINIC ACID- MEDIATED PHOTODYNAMIC THERAPY AND CATHETER- BASED IRIDIUM-192- MEDIATED BRACHYTHERAPY

VIRTUAL E-POSTER SESSION

Hossein Mehrad[1,2]
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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 combined photodynamic therapy and brachytherapy on inflammation and intimal hyperplasia reduction after angioplasty, wherein diagnostic ultrasound is adjuncted with 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 ^{192}Ir- mediated β^- brachytherapy (^{192}Ir, 15 Gy) in combination with photodynamic therapy with violet diode laser (WL= 405 nm, E/A= 125 J/cm^2) accompanied by intravascular photosensitizer Delta-Aminolevulinic Acid administration.

Results: from ultrasonography and histopathology showed a significant reduction in the mean value for immune cells and smooth muscle hyperplasia cells density after angioplasty in the treatment group compared with the other groups ($p<0.05$).

Conclusions: Apoptotic effect of brachytherapy in combination with anti- inflammatory and cytotoxic effect of photodynamic therapy, can cause to reduce the density of macrophage cells and smooth muscle hyperplasia cells in the intimal layer. These findings provide the basis for developing of combined brachytherapy and photodynamic therapy for a successful clinical application in the treatment of neointimal hyperplasia after laser angioplasty.

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#93

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.11 Plaque remodelling*

MODELING OF INTRA-ARTERIAL HEMODYNAMICS IN THE ATHEROMA PROGRESSION

VIRTUAL E-POSTER SESSION

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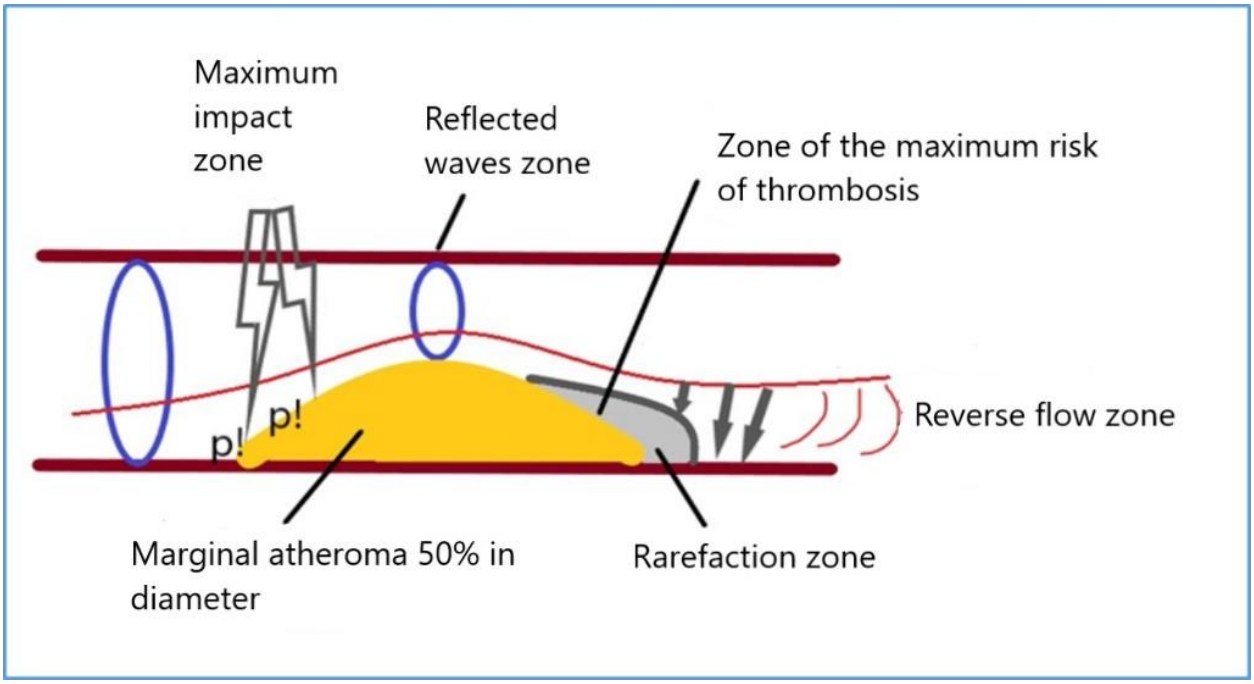
Background and Aims: Prototype models of intra-arterial circulation is one of the priority aims of experimental cardiology, also for the study of atherosclerosis. Aim. To study the intra-arterial hemodynamics in the area of atheroma of the artery in physical modeling.

Methods: We used an original "Device for modeling intra-arterial circulation". The main parts of the model: glass rotameter tube in the form of a truncated cylinder, inlet and outlet ends of which are fixed with elastic tubes connected to an electric pump immersed in container with glycerol solution. Inside the rotameter, using a fitting from the inlet, it is possible to install a pressure sensor that transfers data to the oscilloscope; indicators - a silk thread or dye - ink. The variable pump mode allowed us to simulate a regular heart rhythm, extrasystole (ES) and atrial fibrillation (AF).

Results: In the first post-extrasystolic wave, a turbulent fluid flow, standing waves and waves reflected were observed; the sensor registered an increase in pressure 1,6 times more compared with a regular heart rate. The marginal plaque zones along and against the fluid flow, especially the areas bordering the intact arterial vessel, underwent the main mechanical impact. The same patterns were observed in AF with a maximum duration of a pause between pulse waves of ≥1,5 s.

Conclusions:



Heart arrhythmias play an important role in the intra-arterial hemodynamics pathophysiology of atherosclerosis. The main danger is not the ES itself, but by the first post-extrasystolic contraction or the first pulse wave after a long pause between ventricular contractions in AF.

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#481

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.04 Adipose tissue homeostasis*

ADIPOKINES IN MEN WITH CORONARY ATHEROSCLEROSIS AND ABDOMINAL OBESITY

VIRTUAL E-POSTER SESSION

Evgeniia Garbuzova (Striukova)[1], Victoriya Shramko[1], Elena Kashtanova[1], Yana Polonskaya[1], Ekaterina Stakhneva[1], Alexey Kurguzov[2], Alexander Chernyavsky[2], Yuliya Ragino[1]
[1]Laboratory Of Clinical, Biochemical, Hormonal Investigations Of Therapeutical Diseases, Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics, Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russian Federation, [2]Coronal And Peripheral Arteries Surgery Center, Federal State Budgetary Institution "National Medical Research Center named after Academician E.N. Meshalkin" of the Ministry of Health of the Russian Federation (NMRC named after ak. E.N. Meshalkin), Novosibirsk, Russian Federation

Background and Aims: Obesity is closely related to dyslipidemia, and excess adipose tissue in the body is associated with unfavorable levels of adipokines and inflammatory markers **The goal of research.** To study the levels of adipokines and markers of inflammation (C-peptide, glucose-dependent insulinotropic polypeptide, glucagon-like peptide-1, glucagon, interleukin-6, insulin, leptin, monocyte chemoattractant protein-1, tumor necrosis factor alpha), their associations with unstable atherosclerotic plaques in men with coronary atherosclerosis against the background of abdominal obesity.

Methods: Materials and methods. The study involved 82 men aged 40–77 years with coronary atherosclerosis after endarterectomy from the coronary arteries. We divided all men into two groups: 37 men (45.1%) with unstable atherosclerotic plaques, and 45 men (54.9%) who had stable plaques. Obesity was established at a BMI of ≥30 kg/m2. The levels of adipokines and markers of inflammation in the blood were determined by multiplex analysis.

Results: Results. Groups of men with obesity and without it were comparable in age, SBP, DBP, smoking status, the presence of type 2 diabetes regardless of the type of plaque. In patients with obesity and unstable plaques, the levels of C-peptide, TNFa and IL-6 were 1.8, 1.6, and 2.8 times higher, respectively, than in patients with obesity and stable plaques. The chance of having an unstable plaque increases with an increase in TNFa by 49% in obese patients and decreases with an increase in insulin by 3% in non-obese patients.

Conclusions: Conclusion. In men with coronary atherosclerosis and obesity, unstable atherosclerotic plaques in the coronary arteries are directly associated with the level of TNF-α.

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#145

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

ARTERIAL STIFFNESS AND GLYCOMETABOLIC CONTROL IN OLDER PATIENTS WITH TYPE 2 DIABETES

VIRTUAL E-POSTER SESSION

David Karásek[1], Jaromira Spurna[1], Dominika Macakova[1], Ondrej Krystynik[1], Veronika Kucerova[2]
[1]3rd Department Of Internal Medicine, University Hospital Olomouc, Olomouc, Czech Republic, [2]Department Of Clinical Biochemistry, University Hospital Olomouc, Olomouc, Czech Republic

Background and Aims: Diabetes is one of the main determinants of arterial stiffness and endothelial dysfunction. The aim of this study was to compare indicators of glycometabolic control and parameters of vascular damage in patients with type 2 diabetes (T2D) in different age categories.

Methods: A total of 160 patients with T2D who were divided into four age quartiles were included in this cross-sectional study. All subjects were evaluated for arterial stiffness parameters along with markers of endothelial damage (von Willebrand factor (vWF) and plasminogen activator inhibitor-1 (PAI-1)) and parameters of glycometabolic control.

Results: The oldest participants showed significantly increased parameters of arterial stiffness (aortic augmentation, augmentation index, aortic pulse pressure and pulse wave velocity) despite having similar glycometabolic control compared to other subjects. Arterial stiffness was mainly associated with age and systolic blood pressure. The oldest patients also had the highest levels of vWF, but the lowest levels of PAI-1. Markers of endothelial dysfunction correlated with metabolic parameters.

Conclusions: Age together with systolic blood pressure seems to be the main determinant of arterial stiffness in patients with T2D regardless of glycometabolic control. While endothelial dysfunction is mainly related to an adverse metabolic profile. Supported by MH CZ DRO (FNOl, 00098892).

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#435

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

DEFORMATIONAL BIOMECHANICS AND VAGOSYMPATIC BALANCE IN ADVERSE POSTINFARCTION LEFT VENTRICULAR REMODELING DURING HIGH-DOSE ATORVASTATIN THERAPY

VIRTUAL E-POSTER SESSION

Valentin Oleynikov, Alena Golubeva, Anastasia Babina, Yulia Barmenkova, Irina Avdeeva
Therapy, Penza State University, Penza, Russian Federation

Background and Aims: to evaluate the dynamics of left ventricular (LV) deformation parameters and vagosympathetic balance parameters in patients with adverse remodeling (AR) after STEMI during high-dose atorvastatin therapy.

Methods: The study included 96 patients (52.3±8.4) with primary STEMI. Patients from day 1 and within 6 months after the index event took atorvastatin (40-80mg/day). On days 7-9 and after 6 months, echocardiography was performed with the assessement of global longitudinal strain (GLS,%), apical rotation (Rotapex,°), as well as daily ECG monitoring with analysis of heart rate variability. The criterion for AR LV was considered to be an increase in the EDV index≥20%. The assessment of lipid-lowering therapy was based on a decrease in the level of low-density lipoproteins (LDL) by 6 months to 1.4 mmol/l and by 50% of the initial value.

Results: Among patients (n=39) with DR LV, the following groups were retrospectively identified: A (17 people) who reached the target values of LDL; B (22 patients) with LDL above the target level. In group A, there were no significant changes in GLS (p=0.9) and Rotapex (p=0.07), but there was a regression of the L/H vagosympathetic balance by 40% (p=0.002). In patients with AR, regardless of the achievement of the target level of LDL, only a few indicators underwent significant changes: SDNN and SDANN, TotP and ULFP (p<0.01), while positive dynamics of GLS (p=0.001) and Rotapex (p=0 .01).

Conclusions: The achievement of the optimal level of LDL favorably affects the formation of biomechanics and vagosympathetic regulation of cardiac activity.

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#1173

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE BASAL AND STIMULATED SECRETION OF TNF BY CULTURED MONOCYTES FROM THE BLOOD OF SYSTEMIC SCLERODERMA PATIENTS

VIRTUAL E-POSTER SESSION

Elena Gerasimova[1], Tatiyana Popkova[1], Tatyana Kirichenko[2], Alexander Markin[2], Yuliya Markina[2], Anastasia Bogatyreva[2]
[1]Systemic Arthritis, The V.A. Nasonova Institute of Rheumatology, Moscow, Russian Federation, [2]Laboratory Of Cellular And Molecular Pathology Of The Cardiovascular System, Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Moscow, Russian Federation

Background and Aims: The aim of this study is to determine the basal and stimulated secretion of TNF-α cultured monocytes from the blood of patients with untreated systemic scleroderma (SS).

Methods: Twenty nine patients with untreated SS (mean aged 49[43;59]years) and 22 controls (48[45;57]years) without autoimmune and cardiovascular diseases were included in the study. 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 Lipopolysaccharide (LPS). Secretion of TNF-α was determined by ELISA.

Results: The basal secretion of TNF-α by cultured monocytes from the blood of SS patients was significantly (2.3 times) higher (119.19 [94.56; 149.65] pg/ml of culture medium) compared with healthy individuals (51, 18 [27.28; 61.57] pg/ml, $p<0.001$). LPS-stimulated TNF-α secretion by monocytes in SS patients was 5473.05 [4430.85; 7821.49] pg/ml of the culture medium, which significantly (1.9 times) differed from the control group (2911.24 [1752.11; 4569.66] pg/ml of the culture medium, $p<0.01$).

Conclusions: We obtained a significant increase in the activity of M1-monocytes in patients with untreated SS in comparison with the control, which was manifested by a significant increase in their secretion of pro-inflammatory cytokine TNF-α both in the basal and stimulated states. This work was supported by the Russian Science Foundation (Grant № 22-25-00358).

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#815

Topic: *AS02 Lipids and Lipoproteins / AS02.08 Cellular lipid metabolism and lipid droplets*

RELATIONSHIP BETWEEN MITOPHAGY, MUTATIONS OF MITOCHONDRIAL DNA AND LDL

VIRTUAL E-POSTER SESSION

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Background and Aims: The accumulation of cholesterol induced by atherogenic low-density lipoproteins (LDL) in monocytic cells (and macrophages) can induce the development of atherosclerosis. Previously, our laboratory showed the association of certain mutations in mitochondrial DNA (mtDNA) with atherosclerosis, and obtained the cultures of cytoplasmic hybrids based on the THP1 cell line containing these mutations in varying proportions. It seems necessary to show the existence of a relationship between the accumulation of cholesterol, heteroplasmy of these mutations and its possible changes, as well as the level of mitophagy in cells. **Aim:** determine the existence of relationships between the accumulation of cholesterol induced by atherogenic LDL and mtDNA mutations.

Methods: Confocal microscopy, measurement of heteroplasmy level by RT-PCR, measurement of cholesterol by an enzymatic colorimetric test, descriptive parametric and nonparametric statistics, testing of statistical hypotheses, computer modeling using linear and non-linear regression methods. We measured the accumulation of cholesterol, the level of mitophagy in the cell models, in control and upon the addition of atherogenic LDL.

Results: Differences in the accumulation of cholesterol in different cultures have not been identified. Nevertheless, differences in mitophagy in cultures, as well as changes in heteroplasmy upon incubation of cytoplasmic hybrids with LDL were discovered. Non-ahterogenic LDL stimulated mitophagy in cells studied to a higher degree than atherogenic ones. Different cells with differences in the mitochondrial genome react differently to atherogenic LDL

Conclusions: The relationship between mitophagy, LDL and heteroplasmy of atherosclerosis-associated mutations is complex and should be studied further. Funding source: RSF grant 23-25-00237

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#827

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE EFFECT OF ABDOMINAL OBESITY ON THE LEVEL OF INFLAMMATORY MARKERS IN YOUNG PEOPLE WITH HYPERTENSION

VIRTUAL E-POSTER SESSION

Yana Polonskaya, Elena Kashtanova, Ekaterina Stakhneva, Victoriya Shramko, Evgeny Sadovski, Yuliya Ragino
Laboratory Of Clinical, Biochemical, Hormonal Investigations Of Therapeutical Diseases, Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics, Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russian Federation

Background and Aims: To investigate pro- and anti-inflammatory blood markers in young people with arterial hypertension against the background of abdominal obesity (AO).

Methods: 267 people with hypertension (169 with AO). In the control group there were 263 people comparable in gender and age, with AO - 106 people. The content of TNF-α, IL-6, IL-8, MCP-1, PAI-1, IL-10, IL-17a, IL-17e, IL-17f were determined in all blood by multiplex analysis. Statistical processing was carried out in the SPSS 13.0 program.

Results: Patients with hypertension had higher levels of IL-17a (1.64 times) and IL-6 (52.91%) compared to the control group. There was no difference in other indicators. The influence of AO on the level of the studied markers in the control group was not revealed. In the group with AH, a higher level of PAI-1 ($p<0.05$) was in the subgroup with AO. For the subgroups with AO, the difference between patients without AH and those with AH was manifested in a decrease in IL-17e and an increase in IL-6 in patients with AH ($p<0.05$). The relative probability of early arterial hypertension was associated with the presence of AO and an increase in IL-6 levels.

Conclusions: From the markers of inflammation studied by us, an increased level of IL-6 and IL-17a can serve as potential biomarkers indicating a high probability of developing early hypertension in people under 45 years of age. The work was carried out within the framework of program No. 122031700094-5 and grant No. 21-15-00022.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#824

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

EFFECTS OF TWO ISOCALORIC HEALTHY DIETS ON POSTPRANDIAL LIPID RESPONSE IN TYPE 2 DIABETES PATIENTS

VIRTUAL E-POSTER SESSION

Giuseppina Costabile, Giuseppe Della Pepa, Dominic Salamone, Roberta Testa, Marilena Vitale, Paola Ciciola, Alessandra Corrado, Angela Albarosa Rivellese, Giovanni Annuzzi, Lutgarda Bozzetto
Clinical Medicine And Surgery, Federico II University, Naples, Italy

Background and Aims: To investigate the effects of an isocaloric Multifactorial diet on postprandial lipid response in individuals with type 2 diabetes (T2D).

Methods: According to a randomized controlled parallel group design, 43(25M/18F) T2D patients, 35–75 years old, were assigned to an 8-week isocaloric intervention with a Multifactorial diet rich in MUFA, PUFA, fibre, polyphenols, and vitamins (n=21) or a MUFA rich diet (n=22). Before/after the intervention plasma triglycerides, total and HDL-cholesterol concentrations were measured at fasting and over a 4h test-meal with a similar composition as the assigned diet.

Results: Fasting plasma triglycerides and total cholesterol did not change after both diets; HDL-cholesterol significantly decreased after Multifactorial (42±10 vs 39±8 mg/dL, p=0.010), but not after MUFA diet (39±9 vs. 39±10 mg/dL, p=0.324), with no significant difference between groups (p=0.090). Postprandial triglycerides (iAUC) did not change significantly after Multifactorial (5790±5008 *vs.* 5661±6057, mg/dL*240 min, baseline *vs.* 8-week, p=0.370) and MUFA diet (7579±4424 *vs.* 8503±4382 mg/dL*240 min, p=0.194); with a significant difference between groups (p=0.018). Total cholesterol (iAUC) did not change after Multifactorial diet (-1866±1466 vs -1957±1218 mg/dL*240 min, p=0.725); while it tended to decrease less after MUFA diet (-1511±1324 vs -953±1109 mg/dL*240 min, p=0.077), with a significant difference between groups (p=0.013). Postprandial HDL-cholesterol did not change after Multifactorial diet (-708±399 vs -642±402 mg/dL*240 min, p=0.725); it decreased less after MUFA diet (-723±466 vs -431±440 mg/dL*240 min, p=0.014), with no difference between groups (p=0.066).

Conclusions: In T2D patients, a Multifactorial diet improved postprandial lipid profile especially in terms of triglycerides response.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#823

Topic: *AS04 Clinical Vascular Disease / AS04.11 Anti-inflammatory therapies*

EARLY STAGE ATHEROSCLEROSIS REGRESSION USING COMBINED ENCAPSULATED DOCETAXEL NANOPARTICLES- MEDIATED ULTRASOUND SONOPORATION THERAPY AND GOLD NANOPARTICLES- MEDIATED X- RAYS- BASED AUGER ELECTRON THERAPY

VIRTUAL E-POSTER SESSION

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Background and Aims: In atherosclerosis, local inflammation and associated macrophage activity can lead to foam cell- rich lesion formation. In this study, we developed an experimental ultrasound sonoporation therapy system, and investigated its effectiveness on early stage atherosclerosis regression in combination with X- rays- based Auger electron therapy, wherein diagnostic B- mode ultrasound is combined with ultrasound therapy system, with a goal of increased safety.

Methods: Briefly, Golden Syrian hamsters underwent primary balloon dilatation at the abdominal aorta 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 in the treatment group, treated using low level pulsed- focused ultrasound (F= 1.1 MHz, P= 24 W, PD= 100 ms)- mediated sonoporation therapy accompanied by intravenous lipid- based encapsulated docetaxel nanoparticles (10ml/kg) administration and lipid- based encapsulated gold nanoparticles- mediated X- rays (25 Gy)- based Auger electron therapy. Foam cells density were evaluated in the treatment group compared with the control group using ultrasonography and histopathology.

Results: from B-mode 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 control group ($p < 0.05$).

Conclusions: Enhanced sonoporation effect of ultrasound, induced by inertial cavitation effect of collapsed capsules, accompanied by enhanced apoptotic effect of electron therapy, induced by lipid- based encapsulated gold nanoparticles administration, can significanty cause to enhance apoptotic, anti-proliferative and toxicity effect of docetaxel and regress of the early stage atherosclerosis.

91ST EAS CONGRESS
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#266

Topic: *AS04 Clinical Vascular Disease / AS04.01 Coagulation and Thrombosis*

PREDICTIVE FACTORS FOR CARDIOVASCULAR INVOLVEMENT IN BEHCET DISEASE: A RETROSPECTIVE TUNISIAN COHORT

VIRTUAL E-POSTER SESSION

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Background and Aims: Cardiovascular involvement, also referred as angio Behçet Disease (BD), is frequent affecting veins and arteries as well as cardiac layers. We aimed in this work to describe clinical characteristics, predictive factors and management of angio BD in the Tunisian context

Methods: We retrospectively studied 213 records of all BD patients followed between January 2004 and May 2016 in the Internal Medicine Department and who fulfilled the ISGBD criteria. We described first clinical features of BD with cardiovascular involvement then predictive factors were studied in univariate then multivariate analysis.

Results: Among the 213 patients, 64 (30%) were diagnosed as having angio BD. The mean age at diagnosis was 31.5 years. About 81.25% of them were males and 18.75% females. Vascular involvement was found in 73 patients (34.27%). Deep venous thromboses are most common (62.5%) compared with superficial ones (23.4%), pulmonary arterial thrombosis (14.1%) or aneurysms (9.4%). Cardiac involvement can affect all layers ranging from pericarditis (1.6%) to intra cardiac thrombosis (3.1%) and myocardial infarction (1.6%). Predictive factors associated with cardiovascular involvement in BD are male gender **(OR=3.043, 95% CI= 1.436- 6.447, p=0.004)**, erythema nodosum **(OR= 4.134, 95% CI= 1.541- 11.091, p=0.005)** and neurologic involvement **(OR= 2.46, 95% CI= 1.02- 5.89, p=0.043)**.

Conclusions: Cardiovascular involvement in BD is frequent in the Tunisian context with a broad spectrum of manifestations ranging from vascular involvement to cardiac one. Male gender, patients with erythema nodosum or neurologic involvement are prone to develop cardiovascular features of BD needing therefore close monitoring.

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#271

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

MUTATION M.15059G>A IN CYTB GENE ASSOCIATED WITH MACROPHAGE PRO-INFLAMMATORY CYTOKINES PRODUCTION

VIRTUAL E-POSTER SESSION

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Background and Aims: There are some mtDNA mutations associated with atherosclerosis. Model cytoplasmic hybrid cell lines with mutations in mtDNA created from THP-1 monocyte line can be used for studying of this association. In this study we examined the association of cytokine production by macrophages with m.15059G>A mutation in mitochondrial CytB gene.

Methods: Human monocyte-like cell line THP-1 used as reference, cybrid line TCHSMAM1 with m.15059G>A mutation (CytB gene), and cybrid line TCHSMAM1 with eliminated m.15059G>A mutation (TCHSMAM1-Cas) by CRISPR/Cas9 editing. The production of cytokines was assessed by ELISA. The pro-inflammatory response was induced by bacterial lipopolysaccharide (LPS).

Results: It was found that in the cybrid lines TCHSMAM1 and TCHSMAM1-Cas have an increased basal level of IL-1β, IL-6, IL-8 and MCP-1, while the basal levels of TNFα has no differences compared to the control THP-1 cells ($p>0.05$). The cybrids TCHSMAM1 has an increased levels of IL1β, IL-6 and MCP-1, and reduced level of TNFα compared to the THP-1 cells after LPS stimulation, the IL-8 production has not differed from the THP-1 cells ($p>0.05$). The cybrids TCHSMAM1-Cas show an increased levels of IL1β, IL-6, IL-8 and MCP-1, and reduced level of TNFα compared to the THP-1 cells after LPS stimulation. Furthermore, TCHSMAM1-Cas cells show an increased production of IL-6, IL-8 and IL-1β compared to TCHSMAM1 after LPS stimulation.

Conclusions: Elimination of m.15059G>A mutation in CytB gene induced an increase in the production of pro-inflammatory cytokines after LPS stimulation in TCHSMAM1-Cas cells. This work was supported by Russian Science Foundation Grant #23-65-00002.

91ST EAS CONGRESS
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#817

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

ASSOCIATION OF HDL-C SUBFRACTION PROFILE WITH THE PROGRESSION OF INSULIN RESISTANCE

VIRTUAL E-POSTER SESSION

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Background and Aims: Type 2 diabetes mellitus (T2DM) is a rapidly growing public health problem globally. Development of T2DM is preceded by insulin resistance (IR), the progression of which can be assessed by the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index. Carbohydrate and lipid metabolism disorders are closely linked, but the role of HDL-C subfractions in these processes is poorly understood. The present study aimed to investigate the association between HOMA-IR and the profile of ten HDL-C subfractions on 377 samples (from 165 Hungarian general and 212 Roma).

Methods: Correlations were evaluated by linear and logistic regression analyses, and receiver operating characteristics (ROC) and Youden methods were used to estimate the discriminatory power of HDL subfractions. All analyses were adjusted for ethnicity, age, sex, BMI, current smoking, LDL level, and medication habits.

Results: The presence of IR (HOMA-IR>3.68) was significantly associated with decreased levels of HDL-1-6 subfractions in mmol/l, which in the lipid profile was related to a significant decrease in the proportion of HDL-2 and -3 and an increase in HDL-6 to 9 subfractions. Based on the result of ROC analyses, HDL-2 had the highest IR predictive ability ($AUC_{HDL-2} = 0.722$), with an optimal cut-off point of 0.1017. The risk of IR was 4.31 times higher (95%CI: 2.37 - 7.85, p<0.001) in those with HDL-2 levels above the established threshold.

Conclusions: Our results suggest that the HDL-2 subfraction is inversely associated with the risk of developing IR and may be a predictor and target molecule for interventions to prevent the development of T2DM in the future.

91ST EAS CONGRESS
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#416

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

EFFECT OF LDL DESIALYLATION ON THE DEVELOPMENT OF ATHEROSCLEROSIS IN MICE

VIRTUAL E-POSTER SESSION

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Background and Aims: One of the types of atherogenic LDL modification is desialylation. LDL desialylation facilitates the self-association of LDL, that stimulates phagocytosis and secretion of proinflammatory factors. It is believed that desialylation is an important atherogenic modification of LDL in the early stages of atherosclerosis. But there is limited understanding of the effect of LDL desialylation on the development of atherosclerosis *in vivo*.

Methods: The control group of *Apoe-/-* mice received by a single injection of saline, while the experimental group of *Apoe-/-* mice received 20 mU neuraminidase immobilized on mouse IgG. Both groups were fed with high fat diet (HFD) for 12 weeks and were terminated at the end of this period. The content of LDL sialic acid was measured according to Warren's method. Blood lipids were measured by commercial kits. Quantification of atherosclerotic burden in mouse aorta was determined by staining with Oil Red O.

Results: The experimental group had a reduced content of LDL sialic acid. But LDL desialylation didn't lead for significant changes in levels of blood lipids in experimental group compared with control group. It was shown that the experimental group had an increased area of atherosclerotic lesions by 42.7% compared with changes in the control group.

Conclusions: LDL desialylation don't directly affect levels of blood lipids, but it accelerates atherosclerosis by affecting the area of atherosclerotic lesions in *Apoe-/-* mice. These results can be considered a confirmation of the important role of LDL desialylation in the pathogenesis of atherosclerosis. This work was supported by the Russian Science Foundation (Grant № 22-25-00391).

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#650

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

THE LEUKOCYTE TELOMERE LENGTH, MTDNA COPY NUMBER AND ACUTE CORONARY SYNDROME IN A 15-YEAR FOLLOW-UP

VIRTUAL E-POSTER SESSION

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Background and Aims: We studied the relationship between leukocyte telomere length (LTL), mitochondrial DNA copy number (mtDNA-CN) and 15-year risk of acute coronary syndrome in an ageing population.

Methods: A random population sample was examined at baseline in 2003-2005 (n=9360, 45-69, Novosibirsk, the HAPIEE project) and followed-up for 15 years. In the frame of nested case-control, we selected all incident cases of myocardial infarction/acute coronary syndrome (MI/ACS) (n=256) among those free from baseline CVD, and sex- and age-stratified controls free from baseline CVD or cancer and alive by the end of follow-up (n=799). The baseline relative LTL and mtDNA-CN were assessed using qPCR. Logistic regression was used to estimate odds ratio of MI/ACS per 1 decile decrement of LTL or mtDNA-CN.

Results: The carriers of shorter baseline telomeres had increased risk of MI/ACS with adjusted OR=1.87 (95% CI 1.70-2.06) per 1 decile decrement of LTL independent of other factors. Similarly, smaller baseline mtDNA-CN was associated with increased risk of MI/ACS with adjusted OR=1.19 (95% CI 1.12-1.26) per 1 decile decrement of mtDNA-CN. In stepwise regression, the proportion of variance explained by the model and the percentage of correctly predicted outcomes were higher for LTL vs mtDNA-CN. All associations persisted after adjusting for sex, age, and CVD risk factors.

Conclusions: The baseline LTL and mtDNA-CN inversely associated with 15-year risk of MI/ACS in the middle-age and elderly Siberian (Caucasoid) population cohort. These findings may have practical implication and merit further elucidation of the mechanisms of these associations. Supported: RSF 20-15-00371.

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#812

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

CO-RELATION BETWEEN HIGH SENSITIVITY TROPONIN AND LIPOPROTEIN(A) IN PRIMARY PREVENTION POPULATION FROM A TERTIARY CARE CENTER IN INDIA

VIRTUAL E-POSTER SESSION

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Background and Aims: South-Asian population develop atherosclerotic cardiovascular disease (ASCVD) a decade earlier compared to the West, adversely affecting both health and economy. Elevated high sensitivity troponin (hs-cTn) levels reflect cardiac muscle injury and predict future cardiovascular (CV) events. Lipoprotein(a)[Lp(a)] is a low-density lipoprotein (LDL) particle with an added apolipoprotein(a) and is a CV risk enhancer. Our study aims to co-relate the association between hs-cTn and Lp(a) in primary prevention population at a tertiary care center in India.

Methods: Our study included 126 subjects above the age of 40 who visited the cardiology out-patient department for general evaluation and no clinical ASCVD (primary prevention). The study included 73% men and 26.9% women with 45.2% diabetic and 61.9% hypertensive subjects.

Results: Hs-cTnI was >3.5ng/ml in 30(23.8%) subjects and >6ng/ml in 18(14.2%) subjects. Lp(a) was greater than 30mg/dl in 45(35.7%) and >50mg/dl in 28(22.2%) subjects. Only 10(33.3%) subjects with Hs-cTnI> 3.5 had Lp(a)>30mg/dl and 7(23.3%) had Lp(a)>50mg/dl. On the other hand, 7(38.8%) subjects with Hs-cTnI> 6 had Lp(a)>30mg/dl and 5(27.7%) had Lp(a)>50mg/dl. There was no co-relation between elevated Hs-cTnI and Lp(a) levels.

Parameters	Hs-cTnI>3.5ng/ml	Hs-cTnI>6ng/ml
Lp(a) >30mg/dl	10(33.3%)	7(38.8%)
Lp(a) >50mg/dl	7(23.3%)	5(27.7%)

Conclusions: Hs-cTn and Lp(a) are both independent predictors of CV morbidity and mortality as proven by various studies. 35.7% subjects had Lp(a)>30mg/dl showing its high incidence in Indian population. However, our study did not show any co-relation between these two important bio-markers. Large scale studies are needed to further confirm this finding as individual predictive ability of these two tests cannot be underestimated.

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#811

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

MITOPHAGY-ENHANCING FATTY ACIDS ATTENUATE LPS-INDUCED INFLAMMATION IN THP1 CELLS

VIRTUAL E-POSTER SESSION

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Background and Aims: It is well known that mitochondria play an important role in the immune response. Defects in the elimination of dysfunctional mitochondria may alter their inflammatory state. We decided to find out whether it is possible to modulate the immune response of inflammatory cells by influencing their mitophagy.

Methods: We screened fatty acids to evaluate their effect on mitophagy and pro-inflammatory response in THP 1 cells. First, we incubated THP-1 cells with arachidonic (at a concentration of 125 μM), linoleic (30 μM), linolenic (30 μM), oleic (30 μM) and palmitic (125 μM) for 24h. Then the level of basal mitophagy was assessed by mitochondrial and lysosomal dye colocalization using confocal microscopy. In parallel, we stimulated cells with 1 μg/ml LPS for 24h. The secretion of pro-inflammatory cytokines was assessed by ELISA (TNFa, IL-1β, IL-6, IL-8, CCL2).

Results: None of the fatty acids we used elicited a pro-inflammatory response in the THP1 cell line. It turned out that oleic and arachidonic acids increased the level of basal mitophagy in THP1 cells and reduced the secretion of pro-inflammatory cytokines (TNFa, IL-1β, IL-6, IL-8, CCL2) by LPS-stimulated cells. Palmitic acid, in contrast, reduced mitophagy in THP1 cells and increased secretion of IL-1b and CCL2 by LPS-stimulated cells.

Conclusions: We suppose that the high pro-inflammatory activity of cells may be associated with the low efficiency of mitophagy. Increasing the intensity of mitophagy in inflammatory cells using natural lipid mediators may be a promising approach to target chronic inflammation. Supported by RSF (Grant № 20-15-00337)

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#277

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.05 Extracellular matrix and calcification*

ASSOCIATION OF MUTATION IN THE MTDNA CYTB GENE WITH MACROPHAGE PROLIFERATION AND SYNTHETIC ACTIVITY

VIRTUAL E-POSTER SESSION

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Background and Aims: The association of mutations in the mtDNA with atherogenesis was recently discovered. However, it remains unknown how these mutations affect the activity of macrophages. Model cytoplasmic hybrid cell lines with mutations in mtDNA created from THP-1 monocyte line can be used for studying of this association. We have studied the association of m.15059G>A mutation in mitochondrial CytB gene with proliferation and protein synthesis activity of macrophages.

Methods: Human monocyte-like cell line THP-1 used as reference, cybrid line TCHSMAM1 with m.15059G>A mutation (CytB gene), and cybrid line TCHSMAM1 with eliminated m.15059G>A mutation (TCHSMAM1-Cas) by CRISPR/Cas9 editing. Cyclin B1 (*CCNB1*) and cyclin D1 (*CCND1*) were used to assess macrophage proliferation. RNA Polymerase I Subunit A (*POLR1A*) and Collagen Type VI Alpha 1 Chain (*COL6A1*) were used to assess synthetic activity of macrophages. Expression of the genes was measured by qPCR.

Results: Proliferation was increased in both cybrid cell lines compared to THP-1 cells based on gene expression of *CCNB1* ($p<0.01$) and *CCND1* ($p<0.001$), but there was no difference in proliferation activity in TCHSMAM1-Cas cybrids compared to TCHSMAM1 cells ($p>0.05$). Increased expression of the *POLR1A* and *COL6A1* was observed in TCHSMAM1 cells compared to the THP-1 cells ($p<0.001$). Nevertheless, decreased expression of the *POLR1A* and *COL6A1* was found in TCHSMAM1-Cas cells compared to TCHSMAM1 cells ($p<0.01$).

Conclusions: The mutation m.15059G>A mutation does not affect the proliferation activity of macrophages. At the same time, this mutation may increase the synthetic activity of cells. This work was supported by Russian Science Foundation Grant #22-25-00393.

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MANNHEIM GERMANY | MAY 21-24, 2023

#283

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE ROLE OF THE MITOCHONDRIAL MEMBRANE POTENTIAL IN PRO-INFLAMMATORY ACTIVATION OF HUMAN MONOCYTE-MACROPHAGES.

VIRTUAL E-POSTER SESSION

Egor Chegodaev[1,2,3], Alexander Zhuravlev[1,4], Svetlana Verkhova[1,3], Alexander Orekhov[3,4], Mikhail Vysokikh[5], Maria Marey[6], Nikita Nikiforov[1,7]
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Background and Aims: The potential of the mitochondrial membrane is necessary for the synthesis of ATP, and its fall can be detected in violations of the respiratory chain. It was found that the pro-inflammatory activity of blood monocytes and pathogens of macrophages is covered by atherosclerosis in the carotid arteries. We decided whether there is a relationship between the mitochondrial membrane potential of circulating blood monocytes and stimulates the generation of a pro-inflammatory response.

Methods: CD14+ monocytes were isolated from the blood of 34 healthy individuals and stained with a potential-dependent Mitotracker Orange dye. Isolated cells were stimulated with 1 mcg/ml of LPS during the day. On day 6, LPS was added to unstimulated monocyte-macrophages during the day. The secretion of IL-1β, TNF-α, CCL2, IL-6, IL-8 and IL-10 was measured in the supernatants at each stage using ELISA.

Results: It turned out that there are individual differences in the level of mitochondrial membrane potential in circulating blood monocytes. The analysis showed direct correlations between the basal secretion of TNFa, IL-6, IL-10 by monocytes in culture with the mitochondrial potential of the cells. Moreover, inverse correlations were found between the secretion of TNFa and IL-6 by 7-day-old macrophages after LPS stimulation with the mitochondrial potential of the cells.

Conclusions: A decrease in the potential of the mitochondrial membrane in monocytes is associated with a reduced basal secretory activity of monocytes and increased pro-inflammatory activation of monocytes-macrophages differentiated from them. However, the molecular mechanisms of this relationship have not yet been studied. Supported by RSF (Grant No. 22-25-00650).

91ST EAS CONGRESS
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#802

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

ASSOCIATION OF VARIANTS OF THE RELATIVE LENGTH OF TELOMERIC REPEATS WITH CORONARY HEART DISEASE WITH OLD MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

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Background and Aims: Tandem telomere repeats serve to maintain the stability of the nuclear genome. Telomere shortening is associated with factors such as unfavorable environmental factors and various diseases; i.e. with states characterized by the intensification of oxidative stress. The aim of this work was to study the association of telomere repeat length variants with coronary heart disease with old myocardial infarction (CHD with old MI).

Methods: We analyzed relative telomeric repeat length (RTRL) variants in 150 DNA samples from samples of patients with CHD with old MI and 150 apparently healthy study participants by real-time PCR method on a BIO-RADCFX 96 Real-Time System amplifier. The results are presented as a percentage of the calibrator. DNA isolated from HeLa cell line was used as a calibrator. It should be noted that the RTRL variants have designations, depending on their relative length in percent to the calibrator.

Results: According to the obtained results, the mean value of RTRL was significantly lower in patients with coronary heart disease with old myocardial infarction (by 25.0%), compared to apparently healthy study participants. Correlation analysis revealed an association of CHD with old MI with 5 RTRL variants: RTRL-46, RTRL-49, RTRL-51, RTRL-53 and RTRL-56. At the same time, 6 RTRL variants have a protective effect in CHD with old MI: RTRL-63, RTRL-65, RTRL-68, RTRL-70, RTRL-71 and RTRL-73.

Conclusions: Five variants of RTRL are associated with CHD with old MI. This study was supported by Russian Science Foundation (Grant # 20-15-00364).

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#799

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

THE ASSOCIATION OF BLOOD LIPIDS LEVELS WITH MACROPHAGES ACTIVATION IN OBESE PATIENTS WITH ESTABLISHED ISCHEMIC HEART DISEASE

VIRTUAL E-POSTER SESSION

Yurgita Varaeva[1], Antonina Starodubova[1], Elena Livantsova[1], Natalia Shaposhnikova[1], Anzhela Mikaelyan[1], Natalya Pokidkina[1], Tatyana Kirichenko[2], Yuliya Markina[2], Taisiya Tolstik[2]
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Background and Aims: According to Global Burden of Diseases data, 16.17% of deaths are attributed to Ischemic Heart Disease (IHD) that is the first cause of deaths globally. Obesity is considered as a risk factor of IHD due to multiple pathological mechanisms, including the blood lipids changes, chronic low-grade inflammation. The aim of this study was to assess the relationship between blood lipids levels and LPS-induced proinflammatory cytokine (IL-1β) secretion in monocytes (CD14+) extracted from obese patients with established IHD.

Methods: 49 IHD patients with median BMI of 39.8[35.1;44.9] kg/m^2 and mean age of 63.4(5.9) were recruited. The plasma lipids (TCH, LDL-CH, HDL-CH, TG) were measured (by standard laboratory procedure). CD14+ leucocytes were extracted (by ficoll-gradient method) from blood samples and separated. IL-1β cell secretion were assessed (ELISA) in non-stimulated vs. LPS-stimulated cells with calculation of cytokine secretion ratio as macrophages activation (MA).

Results: Non-stimulated IL-1β median levels was higher (p=.000 Wilcoxon signed rank test) in LPS-stimulated cells (100.0[77.7;192.0] pg/ml and 1232.1[816.2;1719.8] pg/ml consequently) with median MA 9.1[6.2;17.3]. Pearson correlation revealed significant positive correlation of MA with TCH (r=0.355, p=.040) and LDL-CH (r=0.389, p=.023) levels. The association with HDL-CH and TG levels did not reach statistical significance.

Conclusions: The results present a reliable positive association of TCH and LDL-CH with LPS-induced monocyte activation in obese patients with established IHD. Further research is needed to compare the study population with patients without IHD and investigation of a panel of pro-inflammatory cytokines secretion. The study was supported by a grant from the Russian Science Foundation N22-25-00414, https://rscf.ru/project/22-25-00414/.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#829

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

ROLE OF INDOLE-3-PROPIONIC ACID, A GUT MICROBIOTA-DERIVED METABOLITE, IN ENDOTHELIAL DYSFUNCTION

VIRTUAL E-POSTER SESSION

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Background and Aims: Indole-3-propionic acid (IPA) is a molecule produced by the intestinal microbiota, after tryptophan ingestion. From the gut, IPA is absorbed through the intestinal barrier and enters the systemic circulation, where it plays several physiological roles, such as regulation of the intestinal barrier function, antioxidant and anti-inflammatory activity, anticancer potential, and protective role in neurodegenerative disease. Furthermore, the effect of IPA on cardiovascular disease has been investigated, with conflicting results. Aim of this research is to investigate the role of IPA in endothelial dysfunction, by studying the effects on the BAE-1 (bovine aortic endothelial) cell line.

Methods: IPA cytotoxicity was evaluated by MTS assay, while ROS and NO production were studied by fluorescent microscopy (with CellRox-Green and DAR4M-AM probes). Finally, immunoblotting analysis for eNOS phosphorylation were performed.

Results: MTS assays did not show any cytotoxic effect of IPA (from 10 nM to 5 mM) after 24h and 4h treatments, while after 48h a reduction in cell viability only at the highest concentration was observed. Furthermore, IPA treatments did not modify the intracellular production of reactive oxygen species, both in basal condition and in the presence of an oxidative stress inducer (menadione). On the other hand, 1μM IPA induced a significative reduction of the nitric oxide released by ATP-stimulated BAE-1 cells, suggesting a potential role of the molecule in altering the physiological vascular tone.

Conclusions: This research is a starting point to understand the mechanisms underlying the relationship between IPA and endothelial function, which further supports recent findings relating gut microbiota to cardiometabolic health.

91ST EAS CONGRESS
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#265

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

MYOCARDIAL INFARCTION AS A FIRST SYMPTOM OF ACTIVATED PROTEIN C RESISTANCE ASSOCIATED TO HYPERHOMOCYTEINEMIA

VIRTUAL E-POSTER SESSION

Melek Kechida[1], Walid Jomaa[2], Syrine Daadaa[1], Imene Chaabene[1], Ines Khochtali[1], Khaldoun Ben Hamda[2]
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Background and Aims: **Introduction:** Coagulopathy in myocardial infarction with normal coronary arteries can reach 36% of cases. We aimed to report a new case of a combined coagulopathy in a patient with myocardial infarction.

Methods: case report

Results: **Case report:** We report the case of a 62 year-old-male patient who was admitted for acute coronary syndrome without ST elevation and with high Troponin level. He had no history of diabetes, hypertension or tobacco. Coronary angiography revealed completely normal coronary arteries without narrowing. 1 week later he presented a second episode of myocardial infarction spontaneously reperfused. Coronary artery thrombosis was suspected and an extensive work-up for thrombophilia revealed hyperhomocysteinemia at 47 µmol/l associated to activated protein C resistance. The patient was treated with oral anticoagulation and susbtitutional treatment of folic acid with a good outcome 1 year after discharge. Controlled homocysteinemia was at 18 µmol/l.

Conclusions: **Conclusion:** Thrombophilia should be considered in patients with myocardial infarction with normal coronary arteries without apparent cardiovascular risk factors. Combined thrombophilia may expose to an increased risk for thrombosis.

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#285

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

ASSOCIATION OF MUTATION IN CYTB GENE WITH CASPASE-1 ACTIVATION AND IL-1B PRODUCTION IN MACROPHAGES

VIRTUAL E-POSTER SESSION

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Background and Aims: Several studies have shown that NLRP3 inflammasome activation and IL-1β production are involved in the pathogenesis of atherosclerosis. The presence of mtDNA mutations in the atherosclerotic plaque cells was recently showed. However, it remains unknown how these mutations affect the pro-inflammatory response of macrophages. We have studied the association of m.15059G>A mutation in mitochondrial CytB gene with the expression of IL-1β and caspase-1.

Methods: Human monocyte-like cell line THP-1 used as reference, cybrid line TCHSMAM1 with m.15059G>A mutation (CytB gene), and cybrid line TCHSMAM1 with eliminated m.15059G>A mutation (TCHSMAM1-Cas) by CRISPR/Cas9 editing. The expression of the caspase-1 (*CASP1*) and interleukin 1β (*IL1B*) genes were measured by qPCR. The pro-inflammatory response was induced by bacterial lipopolysaccharide (LPS).

Results: Increased basal expression of *CASP1* gene was observed in TCHSMAM1 cells compared to THP-1, while the expression of *CASP1* gene in TCHSMAM1-Cas cells was decreased compared to THP-1 and TCHSMAM1 cells. It was also found that *CASP1* expression did not differ between TCHSMAM1 and TCHSMAM1-Cas cells after LPS stimulation. Basal expression of *IL1B* genes was significantly increased in TCHSMAM1 and TCHSMAM1-Cas cells compared to the THP-1. Moreover, *IL1B* expression was decreased in TCHSMAM1-Cas cells compared to TCHSMAM1. It has been observed that LPS stimulation induced an increased *IL1B* expression in TCHSMAM1-Cas cells. Nevertheless, there was no difference in *IL1B* expression between TCHSMAM1 and TCHSMAM1-Cas cells after LPS stimulation.

Conclusions: The m.15059G>A mutation in CytB gene may be associated with increased pro-inflammatory response and inflammasome formation in macrophages. This work was supported by Russian Science Foundation Grant #22-25-00393.

91ST EAS CONGRESS
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#916

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

GENETIC TESTING ON LPA GENE VARIANTS IN THE PREVENTION OF CARDIOVASCULAR EVENTS

VIRTUAL E-POSTER SESSION

Rafael Knack[1], Renata Knack[2], Ricardo Egidio Knack[2], Thiago Omena[3], Nathalia Bittar[4], Katia Alessandra Lopes[4]
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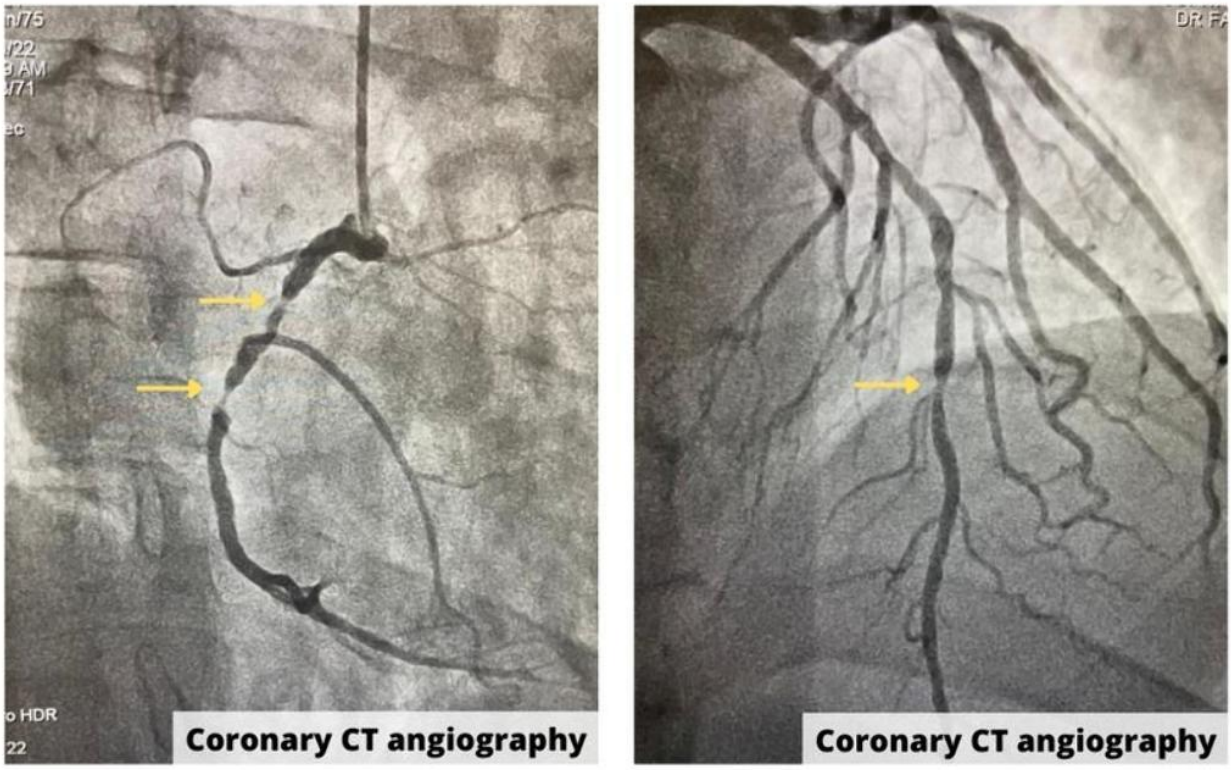
Background and Aims: Lp(a) can be deposited in the walls of blood vessels, and there are many problems caused by high Lp(a) concentrations, which can lead to an increased tendency to clot and form blood clots in blood vessels. In addition, Lp(a) promotes inflammation, which increases the likelihood of plaque rupture. High Lp(a) levels can also lead to aortic stenosis, which is a narrowing of the aortic valve. There is an urgent need to understand the genetic basis for variation in Lp(a) levels so that therapies can become more assertive. Genetic variation is thought to account for 75 to 95 percent of the variation in lipoprotein(a) levels. Because non-genetic factors such as diet and physical activity have little effect on lipoprotein(a) levels, genetic testing is well suited to identify individuals at high risk for cardiovascular disease.

Methods: Case report.

Results: We report the case of a male patient, 47 years old, nonsmoker, physically active, with a family history of heart disease. The patient underwent predictive genetic testing by Versa Gene Company, which indicated the presence of a risk allele in SNP rs3798220 in the LPA gene. Considering the increased cardiovascular risk, Lp(a) levels were examined, which showed a 3-fold increase in the reference value (194.3 nmol/L). Coronary CT angiography was performed and the patient underwent

angioplasty.



Conclusions: The expansion of Precision Medicine shows us that cardiovascular disease is hereditary and that information from family history combined with individual genetics is useful in predicting risk, especially when dealing with individuals who do not have clinical symptoms.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#935

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

LOW T-CELL CONTENT ASSOCIATED WITH HIGH RATE OF NEOVASCULARIZATION IN ATHEROSCLEROSIS OF CAROTID ARTERIES

VIRTUAL E-POSTER SESSION

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Background and Aims: Mature T cells differ genetically from other cell types due to T-cell receptor (TCR) gene rearrangements. This genetic dissimilarity can be exploited to quantify the T-cell fraction in DNA specimens. Intimal neovascularization is an almost ubiquitous feature of atherosclerotic disease, correlating with histologic grade and symptoms.

Methods: Carotid atherosclerotic plaque samples (n=42) were harvested at carotid endarterectomy surgery. Immunohistochemical analyses of atherosclerotic plaques were performed according to the AHA guidelines. We have developed a single triplex dPCR assay to quantify T cells by absolute quantification of the TCR β and δ chain genes and RPP30 (reference) by digital PCR.

Results: The average T-cell content level through atherosclerotic plaque samples was 12% ± 7%. Thirty-one atherosclerotic plaque samples were at stage VI, and 20 showed signs of neovascularization. We report that atherosclerotic plaques in stage VI without neovascularization have a high T-cell content (average 14%) compared with plaques in the same stage with neovascularization (average T-cell content 9.6%, p.value = 0.016, Mann–Whitney test).

Conclusions: This pilot study, using advanced approaches, revealed unexpected results. It is known that atherosclerotic plaque neovascularization correlates well with leukocyte levels and plaque destabilization. In this regard, one could assume a higher role for T-lymphocytes in plaque stabilization than before. This study paves the way for further research in this direction.

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#422

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

DYNAMICS OF MYOCARDIAL DEFORMATION PROPERTIES OF LEFT VENTRICLE AFTER REVASCULARIZATION IN PATIENTS OF CHRONIC CORONARY ARTERY DISEASE WITH PRESERVED EJECTION FRACTION.

VIRTUAL E-POSTER SESSION

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Background and Aims: The purpose of the research was to evaluate the property of left ventricular myocardial deformation in patients with chronic coronary artery disease (CAD).

Methods: 136 patients were selected with chronic coronary artery disease aged between 38 and 74 years. All participants underwent the following examinations and diagnostic tests: evaluation of risk factors, physical examination, laboratory blood tests, 12-lead ECG, 24-ABPM, TTE, two-dimensional speckle tracking echocardiography(STE), coronary angiography(CAG). Global Longitudinal Strain (GLS) was assessed within 48 hours and 30 days after percutaneous coronary intervention (PCI). The total number of candidates were divided into 2 groups. The first group with single-vessel CAD, with the average GLS -17,76±0.59%. The second group of patients consisted of two-vessel CAD, with GLS around -15,77±0.57%.

Results: In the first category of patients who underwent revascularization with PCI, the values of GLS within 48 hours and in 30 days were -17,81±0.69 and -18,12±0.63 respectively (P>0.05 and P=0.015). The second group had GLS -15.76±0,63 and -16,13±0.71 (P>0.05 and P=0.024), in the same specific periods.

Conclusions: The research findings indicate that after PCI, there is a significant increase of GLS index in patients with chronic coronary artery disease in 30 days.

91ST EAS CONGRESS
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#257

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

BLOOD TRANSFUSION AND ISCHEMIC HEART DISEASE, ONE OBSERVATIONAL STUDY BASED ON NHANES 2007–2018

VIRTUAL E-POSTER SESSION

Hao Jin, Wenbin Lu, Jiandong Ding
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Background and Aims: On the basis of The National Health and Nutrition Examination Survey (NHANES), our study was performed to evaluate the relationship between blood transfusion and risk of ischemic heart disease (IHD), including coronary heart disease (CHD), angina and myocardial infarction (MI).

Methods: Based on the NHANES between 2007 and 2018, we will conduct an observational study and extract relevant characteristics, including information related to blood transfusion and IHD. To evaluate the relationship between blood transfusion and IHD, logistic regression and propensity score-matched (PSM) analysis were performed in our analysis. Data were weighted and analyzed with R (version4.1.2). Based on PSM, covariates were matched with a 1:1 nearest-neighbor algorithm, together with a caliper width of 0.2.

Results: On the basis of PSM with 1:1 ratio, there were 1688 participants enrolled in our analysis, including 844 IHD patients. Distribution of propensity scores in participants with IHD and without was shown in Figure 1. Standardized difference after matching was close to 0 and SMD<10%, meaningfully, a good balance was achieved in IHD and non-IHD group. In propesity-score matched multivariable logistic regression analysis, blood transfusion remained associated with higher risk of IHD in comparison (OR:1.95; 95%CI: 1.56-

2.44).

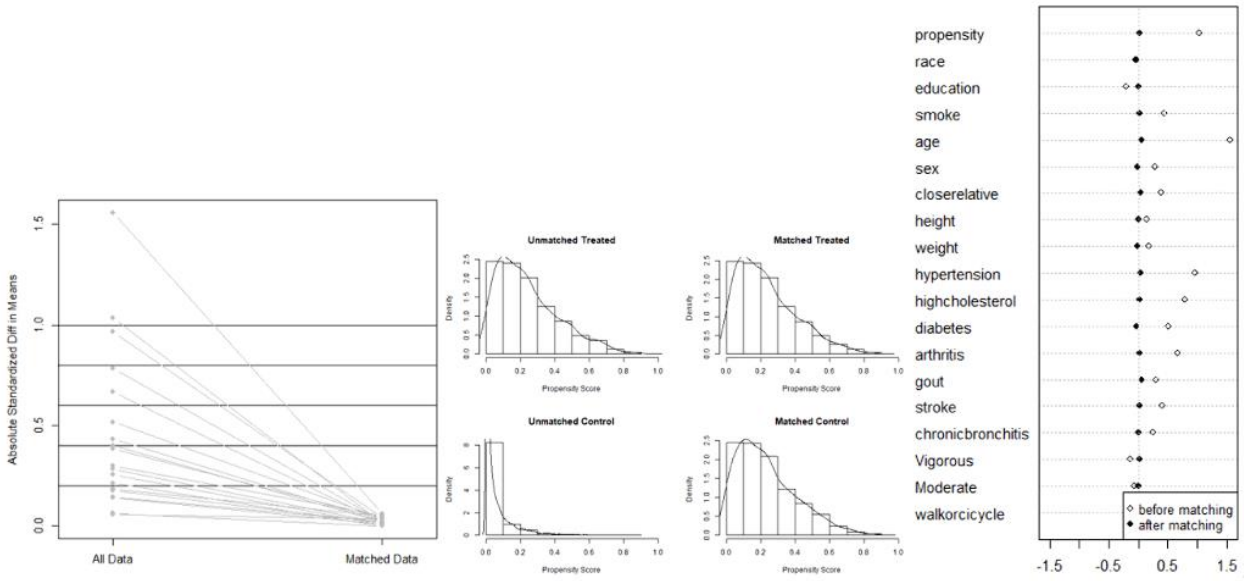

Figure 1: Distribution of propensity scores (1:1) in participants with IHD and without.

Conclusions: Patients treated with blood transfusion might take increased risk of IHD.

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#928

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

FIBRATE USE IS ASSOCIATED WITH A LOWER INCIDENCE OF HEART FAILURE: A REAL-WORLD STUDY AMONG PEOPLE WITH TYPE 2 DIABETES

VIRTUAL E-POSTER SESSION

Mario Luca Morieri[1], Mauro Rigato[1], Carlo Fagarazzi[1], Angelo Avogaro[2], Gian Paolo Fadini[2]
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Background and Aims: Fenofibrate has been recently shown to reduce the incidence of heart failure (HF), an effect found to be independent from fenofibrate's action on lipid profile. We aimed to validate such findings in a real-world setting.

Methods: This observational study included patients with type 2 diabetes (T2D) evaluated from 2008-to-2018. The association of fibrate prescription with the combined outcome of hospitalization for HF and cardiovascular mortality (HF-CVM) was tested with Cox models with time-dependent co-variates or Cox marginal structural models. A similar "falsification" analysis was run for omega-3 fatty acids, which have a similar indication as fibrates.

Results: We included 5419 patients, 41% women, with an average age of 66 and a diabetes duration of 7.6 years. During a median follow-up of 7.3 years, patients were seen 12 times, and we recorded 1710 events in 1136 patients. Around 5% of the population (n=265) was treated with fibrates (mainly fenofibrate). Fibrate use was associated with younger age, male sex, obesity, NAFLD, worst glycemic and lipid profile, but a lower prevalence of CVD and HF. After accounting extensively for these confounding factors, fibrate use was associated with a 35% lower risk of HF-CVM (HR 0.65; 95% CI 0.43-0.98; p=0.04). The effect of omega-3 FA on HF-CVM was neutral (HR 1.03; 95% CI 0.85-1.23; p=0.8).

Conclusions: Our findings support the possible beneficial effect of fibrates on HF in patients with T2D. Further studies are warranted to identify the mechanism of action and confirm whether fenofibrate might be considered a treatment option against the HF burden in diabetes.

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#926

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

INTERLEUKIN-33 RELATIONS WITH DECREASED ANKLE-BRACHIAL INDEX IN OBESE PATIENTS WITH CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: The recent investigations showed that interleukin 33 (IL33) can be an important player in atherosclerotic development. Herewith, there are lack of data about the association of IL 33 level and atherosclerosis disorder in obese patients with coexistent coronary artery disease (CAD).
The study's objective was to find out the association of IL33 with the ankle-brachial index (ABI) in obese patients with stable CAD.

Methods: 81 obese CAD patients were enrolled: 34 females (42%), mean age 51.83 ± 5.79 years. ABI which is an atherosclerosis indicator was measured by ratio of ankle artery blood pressure to arm artery blood pressure. The IL-33 - by ELISA.

Results: The median IL 33 level was 139.87 [101.35; 193.17] pg / ml among all enrolled patients. Two groups of patients were created accordingly to this median: the first group – those with over median IL33 concentration ≥ 139.87 pg/ml, n=42, females 18 (43%), and the second group with IL33 lower than median concentration, n=39, females – 16 (41%). The first group showed 29 (69.05%) patients, and group with low IL-33 revealed 16 (41.03%) subjects with ABI<0.9. Contingency table analysis showed significant association of the increased IL33 levels with atherosclerotic indicator ABI: odds ratio 3.207; 95 % CI: 1.286 to 7.997; p = 0.012.

Conclusions: Conclusion: The increased IL33 level can be considered as significant predictor for atherosclerosis development, indicated as decreased ABI in obese patients with coronary artery disease. It might be valuable for stratification of those patients' risks of cardiovascular morbidity and mortality.

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#917

Topic: *AS04 Clinical Vascular Disease / AS04.10 Anti-thrombotic therapies*

INERTIAL CAVITATION-MEDIATED CATHETER- BASED Q-SWITCHED ND: YAG LASER THERAPY IN COMBINATION WITH EXTRACORPOREAL ELECTROHYDRAULIC LOW- LEVEL FOCUSED SHOCK WAVE THERAPY FOR THROMBOLYSIS OF EMBOLIC ARTERY

VIRTUAL E-POSTER SESSION

Hossein Mehrad[1,2,3]
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Background and Aims: A plaque may rupture with high risk of subsequent thrombus mediated acute clinical events such as myocardial infarction and stroke. The aim of this study was to generate a rabbit model of carotid artery thromboembolic occlusion and the subsequent investigating the feasibility of catheter- based Q-switched Nd: YAG laser therapy accompanied by simultaneously extracorporeal shock wave therapy in this model.

Methods: Briefly, New Zealand White rabbits were submitted to thromboembolic occlusion by injecting autologous blood clots through carotid artery. Then treatment group underwent Q-switched Nd: YAG laser (Frequency= 532 nm, Power= 25 W, Pulse Duration= 15 ns) inertial cavitation therapy accompanied by simultaneously extracorporeal electrohydraulic low- level focused shock wave (V= 15 Kv, F= 0.5 Hz, Impulses= 100) therapy, wherein diagnostic B- mode ultrasound is combined with therapy system, with a goal of increased safety.

Results: from B-mode ultrasound imaging concurrent with combined catheter- based Q-switched Nd: YAG laser and shock wave therapy, showed the generation of collapsed bubbles, resulted in the inertial cavitation- based thrombolytic therapy in the carotid artery. Also, histopathology results, showed a significant reduction in the mean value for thrombus density at the embolic region in the treatment group compared with the other groups ($P < 0.05$).

Conclusions: Enhanced thrombolytic effect of Q-switched Nd: YAG laser, induced by shock waves can significantly cause to reduce the thrombus density and dilate the luminal cross-sectional area at the embolic region and lower treatment time and reduce total costs of treatment

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#907

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

PULSE PRESSURE AND MORTALITY IN THE 4D STUDY

VIRTUAL E-POSTER SESSION

Babak Yazdani[1], Aruscha Asgari[1], Marcus Kleber[1], Graciela Delgado[1], Gökhan Yücel[2], Faeq Husain-Syed[3], Thomas Kraemer[4], Andreas Gerken[5], Clara Daschner[1], Christiane Drechsler[6], Christoph Wanner[7], Bernhard Krämer[8]
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Background and Aims: Systolic (SBP), diastolic (DBP) and mean arterial pressure (MAP) are risk factors for cardiovascular mortality (CVM). Pulse pressure (PP) is an easily available parameter of vascular stiffness, but its impact on CVM in chronic dialysis patients is unclear.

Methods: Therefore, we have examined the predictive value of PP in the German Diabetes and Dialysis (4D) study, a prospective, randomized, double-blind trial enrolling 1255 patients with type 2 diabetes on hemodialysis in 178 dialysis centers.

Results: After dividing the cohort into corresponding tertiles, HRs were 1, 1.10 (95% CI, 0.847-1.42), 0.819 (95% CI, 0.62-1.08) for PP and 1, 1.05 (0.83-1.33), 1.06 (0.83- 1.35) for MAP regarding CVM and nonfatal CV events. HR for SBP were 1, 0.839 (0.66-1.06), 0.889 (0.70-1.12) and for DBP 1, 0.959 (0.77-1.19), 1.15 (0.88-1.5) for CVM and nonfatal CV events in the first, second and third corresponding tertile.

Conclusions: In a multivariate analysis, adjusted for age and sex, no blood pressure parameters showed a significant predictive value with regard to CVM or events in a diabetes/dialysis cohort.

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#263

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

INCREASED PRO-INFLAMMATORY RESPONSE OF THP-1-BASED CELLS WAS ASSOCIATED WITH DEFECTIVE MITOPHAGY

VIRTUAL E-POSTER SESSION

Alexander Zhuravlev[1,2], Svetlana Verkhova[1,2], Nikita Nikiforov[1,3], Maria Marey[4], Mikhail Vysokikh[4], Alexander Orekhov[1,5]
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Background and Aims: The functional activity of inflammatory cells depends on the work of mitochondria. Defective mitophagy can lead to an accumulation of dysfunctional mitochondria. We hypothesized that mitophagy may be associated with an immune response.

Methods: We investigated 13 inflammatory cell lines differ in mtDNA heteroplasmy profile (Cybrids). Cells were stimulated with 1 μg/ml of LPS for 20 and the secretion of TNF, IL-1β, IL-6, IL-8 and CCL2 was evaluated by ELISA. In parallel, we induced the mitophagy in cell lines with FCCP (5 μM) for 6 h. The level of mitophagy was assessed by colocalization of the mitochondrial and lysosomal dye using confocal microscopy.

Results: We found that the cell lines differed in their ability to generate a pro-inflammatory response. When evaluating FCCP-induced mitophagy in cells, we found that in some lines mitophagy is not induced, that is, it is defective. In addition, lines with defective mitophagy had increased secretory activity of cytokines IL-8, IL-1β and TNFα in response to LPS.

Conclusions: Mitophagy was weakly induced in cybrid lines with a high proinflammatory response. Possibly, defective mitophagy may be the reason for the high pro-inflammatory activity. Supported by RSF (Grant № 23-25-00339).

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#418

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

ENDOGENOUS NEURAMINIDASE ACTIVITY IN ATHEROSCLEROTIC LESIONS AS A FACTOR CONTRIBUTING TO LDL DESIALYLATION

VIRTUAL E-POSTER SESSION

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Background and Aims: Modified low density lipoproteins (LDL) play a significant role in atherosclerosis. Desialylated LDL has greater susceptibility to self-association and accumulation in the intima than native LDL. The main enzyme involved in LDL desialylation is neuraminidase (NEU). Studying of neuraminidase transcriptional activity will allow us to complement our understanding of LDL modification in atherosclerotic lesions.

Methods: Real-time qPCR was used to evaluate the expression of lysosomal (*NEU1*), cytosolic (*NEU2*), plasma (*NEU3*), and mitochondrial (*NEU4*) neuraminidase genes. Samples of fatty streaks, lipofibrous, fibrous plaques and unaffected areas of human aortic intima were collected from an autopsy aorta. RNA from the samples was isolated with ExtractRNA and digested with DNase I. Two-step RT-PCR was used to convert RNA to cDNA.

Results: The results of differential gene expression analysis of four neuraminidases in atherosclerotic lesions compared with healthy tissue samples were obtained. The level of *NEU1* gene transcripts in fatty streaks was increased compared to healthy tissue samples (2-fold, $p<0.05$). But there was a decrease in the level of *NEU1* mRNA in lipofibrous and fibrous plaques. *NEU2* and *NEU3* genes were reduced 5-fold in lipofibrous plaques compared to healthy tissues ($p<0.05$). In addition, a high level of *NEU4* gene was found in fibrous plaques (20-fold, $p=0.005$) compared with the control.

Conclusions: An increase in neuraminidase activity may indicate active disialylation of LDL in lysosomes of macrophages, which usually phagocytize LDL. We have demonstrated the transcriptional activity of NEU1-NEU4 genes, which indicates their active participation in the atherosclerosis progression. This work was supported by the Russian Science Foundation (Grant № 22-25-00391).

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#902

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

ASSESSMENT OF LDL-C CONTROL AFTER MYOCARDIAL INFARCTION WITH CDSS ANALYTICS

VIRTUAL E-POSTER SESSION

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Background and Aims: Aim was to assess LDL-C control in patients with history of myocardial infarction (MI) using analytics of Clinical decision support system (CDSS) MedicBK based on Electronic Health Records (EHRs).

Methods: MedicBK CDSS accumulated EHRs data from one of the regions of Russia for 2022, EHRs of 25496 patients were received. 6880 patients had a history of MI, 1297 patients underwent MI within one year (median age 63 [31-98] years, 435 women (33.5%)) and 709 patients underwent MI from one to two years ago (median age 64 [29-92] years, 245 women (34.6%)). The prevalence of comorbidities did not differ between the groups, except moderate eGFR decrease (4.5% and 7.3% in patients with MI from one to two years ago, p = 0.001).

Results: EHRs of 266 patients with MI within one year included information about LDL-C (20.5%). 34 patients had LDL-C less than 1.4 mmol/L (12.8% of patients with known LDL-C, 2.6% of patients with MI within one year). EHRs of 154 patients with MI from one to two years ago included information about LDL-C (21.7%). 27 patients had LDL-C less than 1.4 mmol/L (17.5% of patients with known LDL-C and 3.8% of patients with MI from one to two years ago). The mean level of LDL-C in patients underwent MI within one year was 2.5 mmol/L, in patients underwent MI from one to two years ago was 2.26 mmol/L (p = 0.018).

Conclusions: CDSS analytics should be used for LDL-C control assessment after MI. Further detailing of such kind of analytics is needed.

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#901

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

APOCIII AND PANCREATIC FAT ACCUMULATION IN INDIVIDUALS WITH TYPE 2 DIABETES: RESULTS FROM THE MEDEA RANDOMIZED CONTROLLED TRIAL.

VIRTUAL E-POSTER SESSION

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Background and Aims: To investigate the effects of an isocaloric multifactorial diet, previously shown to reduce pancreatic fat (PF), in patients with type 2 diabetes (T2D), on plasma ApoCIII that may have a role in the accumulation of ectopic fat.

Methods: In a randomized controlled parallel group study, forty-three T2D individuals (25 M/18 F), 35–75 years, were assigned to an 8-week isocaloric multifactorial diet rich in MUFA, PUFA, fibre, polyphenols, and vitamins (n=22) or a MUFA rich diet (n=21). Before/after the intervention plasma ApoCIII concentrations were measured at fasting and over a 3h test-meal with a similar composition as the assigned diet. Insulin secretion and sensitivity indices were calculated.

Results: Fasting plasma ApoCIII did not change after both diets. Postprandial ApoCIII response (AUC) did not change significantly after MUFA (2163±173 *vs.* 2323±233, mg/dL·180min, baseline *vs.* 8-week, mean±SEM, p=0.149) and Multifactorial diet (2252±247 vs. 2117±228); changes (8-week *minus* baseline) between diets were significantly different (Δ: +160±124 vs. -134±15, p= 0.043). Fasting ApoCIII changes directly correlated with PF changes (r=0.385, p=0.020). In individuals with higher levels of ApoCIII identified by a cluster analysis (n=22), changes in fasting ApoCIII indirectly correlated with HOMA- β (r=-0.484, p= 0.026), β-cell Function (r=-0.553, p=0.011) and OGIS changes (r=-0.526, p=0.014) and directly with PF changes (r=0.534, p=0.023). Postprandial ApoCIII indirectly correlated with β -cell Function changes (r=-0.474, p=0.035).

Conclusions: In T2D patients, the reduction of plasma ApoCIII levels, independently of type of diet, was associated with a reduction in PF and an improvement in β -cell function and insulin sensitivity.

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#898

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ULTRASOUND- GUIDED CATHETER- BASED YTTRIUM-90- MEDIATED BRACHYTHERAPY OF NEOINTIMAL HYPERPLASIA ACCOMPANIED BY 5- AMINOLEVULINIC ACID- MEDIATED PHOTODYNAMIC THERAPY

VIRTUAL E-POSTER SESSION

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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 developed an experimental combined β^- brachytherapy and photodynamic therapy protocol, and investigated its effectiveness on neointimal hyperplasia reduction, wherein diagnostic ultrasound system is adjuncted with treatment system, with a goal of increased safety.

Methods: Briefly, rats underwent perivascular severe cold injury at the abdominal aorta. After eight weeks, the histopathology results showed progressive smooth muscle cells proliferation in the intimal layer, resulted in vessel wall thickening. Then treatment group underwent catheter- based β^- brachytherapy (^{90}Y, 15 Gy) in combination with 5- Aminolevulinic Acid- mediated red diode laser (WL= 635 nm, E/A= 120 J/cm2) photodynamic therapy.

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 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 β^- brachytherapy in combination with anti- inflammatory and toxicity effect of red laser photodynamic therapy, can cause to reduce the immune cells and smooth muscle hyperplasia cells in intimal layer and significantly dilate the luminal cross-sectional area of stenosis. These findings provide the basis for developing of combined β^- brachytherapy and photodynamic therapy for a successful clinical application in the treatment of hyperplastic conditions such as restenosis.

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#837

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

INCIDENCE OF LIPOPROTEIN(A) IN PRIMARY PREVENTION POPULATION IN A TERTIARY CARE CENTER IN INDIA

VIRTUAL E-POSTER SESSION

Lavanya Narra, Abraham Oomman, Robert Mao, Refai Showkathali, Seshagiri Dondapati, Radhapriya Yalamanchi
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Background and Aims: Lipoprotein(a) is a liver derived lipoprotein consisting of low-density lipoprotein (LDL) particle with an added apolipoprotein(a). It has pro-atherogenic, pro-thrombotic and pro-inflammatory effects. Globally, 20% of the population are estimated to high elevated Lp(a) levels. Literature review supports the strong association of elevated Lp(a) with atherosclerotic cardiovascular disease (ASCVD), calcified aortic stenosis and cardiovascular(CV) mortality. The risk of CV events is higher at Lp(a)>50mg/dl even when LDL levels are <70mg/dl. Our aim is to study the incidence of elevated Lp(a) levels in primary prevention population in India.

Methods: Our study included 126 subjects above the age of 40 years who visited the cardiology out-patient department for general evaluation with no history of ASCVD (primary prevention population).

Results: The study included 92(73%) men and 34(26.9%) women. 57(45.2%) subjects were diabetic and 78(61.9%) were hypertensive. Lp(a) was greater than 30mg/dl in 45(35.7%) and >50mg/dl in 28 subjects (22.2%).

Conclusions: Lp(a) is an important risk stratifying biomarker which is not often included in the lipid panel. Routine treatment for dyslipidaemia does not significantly lower the levels of Lp(a), leaving patients with high levels of Lp(a) and residual CV risk. Our study showed that 22.2% subjects with no ASCVD had elevated Lp(a). This shows its high incidence in Indian population and the need for early testing and novel treatment options to reduce CV morbidity and mortality in primary prevention population.

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#262

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

NEXT-GENERATION SEQUENCING REVEALS GENETIC DIFFERENCES BETWEEN TWO DISTINCT ETIOLOGIES OF DILATED CARDIOMYOPATHY

VIRTUAL E-POSTER SESSION

Fernando Bonet[1], Elena Alonso Villa[1], Francisco Hernandez-Torres[2], Ismael Campanario[3], Carlos Perez-Perez[3], Anibal Bermudez[4], Tomás Daroca[4], Juan Antonio Ranea[5], Jose Cordoba Caballero[4], Alipio Mangas[3], Rocio Toro[3]
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Background and Aims: Dilated cardiomyopathy (DCM) entails a broad group of diseases, acquired or genetic, which result in a similar phenotype. In the era of precision medicine, genotype-directed therapies have started to emerge. MicroRNAs (miRNAs) are short sequences of non-coding RNA that play an important role in the regulation of gene expression. MiRNAs are crucial in the development of several cardiovascular diseases, including DCM. The aim of this study was to analyze the mRNA and miRNA transcriptome in human heart tissue to delineate DCM etiology-specific gene expression signatures.

Methods: We used miRNA and mRNA sequencing to identify differences between the transcriptome of human left vetricular (LV) tissue from patients with DCM caused by volume overload (DCMv) and ischemic DCM (ICM). Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses were performed on the differentially expressed genes. Diferentially expressed miRNAs were validated by qRT-PCR.

Results: MiRNome and transcriptome of human LV tissue showed 111 mRNAs and 5 miRNAs dysregulated in DCMv vs ICM, and unveiled 37 miRNA-mRNA interactions. GO analysis revealed extracellular matrix pathways among the most enriched GO terms. KEGG pathway revealed cardiac muscle contraction, calcium signaling, fatty acid and immune response among the most enriched pathways. Finally, qRT-PCR validation in all collected DCMv (n = 8) and ICM (n = 5) samples showed that miR-218-5p, miR-487b-3p and miR-494-3p are upregulated in DCMv as compared to ICM.

Conclusions: Our results suggest that transcriptome signatures may distinguish distinct etiologies of DCM, shedding light on underlying biological differences between DCMv and ICM.

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#405

Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

RELATIONSHIP OF EPICARDIAL FAT TISSUE THICKNESS AND ARTERIAL RIGIDITY IN PATIENTS WITH CHRONIC HEART FAILURE AND OBESITY

VIRTUAL E-POSTER SESSION

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Background and Aims: Aim. To study the relationship between the thickness of the epicardial adipose tissue and the stiffness of the main arteries in patients with chronic heart failure (CHF) and obesity

Methods: 156 patients with CHF I-III FK, 45-65 years were divided into 3 groups: group 1 – CHF normal weight, 2 —CHF overweight, 3 —CHF obesity. The tEAT, pulse wave propagation velocity through the vessels of muscular (PWVm) and elastic (PWVe) types, adipokines were evaluated

Results: tEAT was significantly higher in group 3 patients compared to group 1 patients. PWVe is higher in patients with CHF and obesity compared with patients with CHF and normal body weight (10.6 [9.1; 11.7] vs 9.1 [7.6; 8.9] m/s). Serum leptin levels were significantly lower in group 1 compared to groups 2 and 3 (12.3 [5.8; 23.6] vs 35.2 [7.1; 48.6] and 64.3 [24.1; 82.5] ng/ml, respectively). The concentration of serum adiponectin was statistically significantly higher in group 1 compared to groups 2 and 3 (44.6 [19.7; 48.5] vs 20.7 [13.6; 26.3] vs 15.6 [8.7; 21.6] ng/ml, respectively). Among patients with CHF and obesity, highly reliable correlations were established between PWVe and tEAT ($r=0.36$, $p<0.05$), PWVe and the concentration of leptin and ($r=0.36$), PWVe and the level of adiponectin ($r=-0.36$), the level of leptin and tEAT and ($r=0.52$, $p<0.05$), the level of adiponectin and tEAT ($r=-0.48$, $p<0.05$).

Conclusions: The relationship between EAT and arterial wall stiffness has been established, which indicates an important role in the progression of arterial stiffness in patients with CHF in combination with obesity.

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#293

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

A REAL-WORLD OBSERVATIONAL STUDY TO EVALUATE DYSLIPIDEMIA MANAGEMENT IN PATIENTS WITH FIRST ACUTE CORONARY EVENT IN INDIA

VIRTUAL E-POSTER SESSION

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Background and Aims: To describe the prescription patterns of lipid lowering drugs at the time of hospital discharge in the patients with first Acute coronary event. we also present comorbidities and adequacy of lipid lowering therapy in these patients.

Methods: Data of 61 patients hospitalized for first acute coronary event and received lipid lowering therapy was collected from a tertiary care hospital in India. Male and female patients who had prescription data for 12 months post-discharge were included in the final analysis. Data of detailed medical history, demographic data and associated risk factors was collected. Laboratory data of lipid profile was collected at discharge and 12 months after discharge.

Results: Data of 61 patients' (42 males, 19 females) with mean (SD) age of 72.93 (±12.25) years was analysed. Of the 61 patients 55 (90.2%) had dyslipidemia (baseline mean LDL-C = 147.4 mg/dl), 22 (36.1%) had hypertension. 27 (44.3%) patients never exercised. The most prescribed lipid lowering drug was rosuvastatin (55.7%), followed by atorvastatin (44.3%) for secondary prevention (figure 1). The dose of atorvastatin ranged from 10 mg (7.4%) to 80 mg (18.5%) with 40 mg being the most prescribed dose (59.3%), whereas the daily dose used for rosuvastatin was 20 mg (26.5%) and 40 mg (73.5%). Improvements were observed in lipid profile after 12 months of lipid lowering therapy (table-1) however statins were underdosed hence suboptimal in reaching guideline directed lipid goals.

Conclusions: In this Indian real-word practice of secondary prevention of ACS, Rosuvastatin was preferred over atorvastatin but both were under dosed in significant proportion of patients. Lipid-lowering intensification is required.

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#940

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

A RARE CAUSE OF SEVERE HYPERTRIGLYCERIDEMIA: CREB3L3 HETEROZYGOUS MUTATION

VIRTUAL E-POSTER SESSION

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Background and Aims: Acute pancreatitis is an essential manifestation of chylomicronemia syndrome characterized by severe hypertriglyceridemia(1). It can be divided into familial or monogenic (FCS) and multifactorial or polygenic (MCS)(2). Currently, there are new variants related to the development of this condition. This case report aims to present a CREB3L3 heterozygous nonsense mutation leading to recurrent pancreatitis secondary to hypertriglyceridemia.

Methods: A case report and literature review in MEDLINE with the MeSH terms "CREB3L3 protein, human" [Supplementary Concept] and "Hypertriglyceridemia" [Mesh]. Articles that reported an association between CREB3L3 mutation and hypertriglyceridemia are reviewed in table 1. Figure 1 represents the physiologic effects of
CREBH.

Table 1. Association between CREB3L3 mutation and hypertriglyceridemia

Author	Cases	Variant/ zygosis	Treatment	Associated comorbidity
Cefalù, et al(3).	3 related members	c.359delG Heterozygosis	EPA+DHA, 3 g/d Fenofibrate 200 mg/d	None
D'Erasmo L, et al. (2)	4 cases from 38 studied	L233V E239K E59G and V74L p.R241X Heterozygosis	No specific data	No specific data
Wòjcik C, et al.	1 case	Double heterozygosity: Pathogenic APOA5 nonsense variant (p.Q275X) and CREB3L3 nonsense variant (p.C296X)	Eicosapentaenoic acid ethyl ester and gemfibrozil	None
Dron, et al(4).	265 total 5 with CREB3L3 variants	c.724C>T c.732dupG 5'UTR to exon 2 Heterozygosis	No specific data	No specific data
Johansen, et al(5).	413 total 23 with CREB3L3 variants	No specific data	No specific data	No specific data

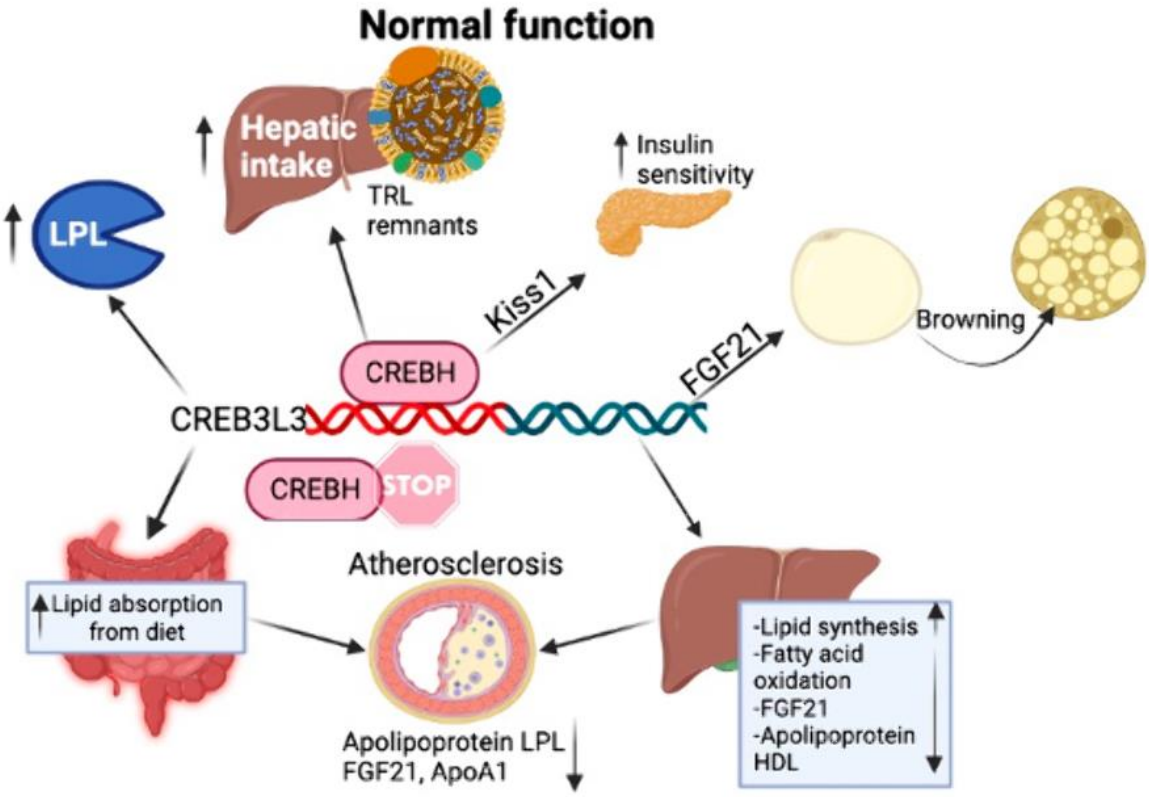

Figure 1. Function CREBH
Source: Authors. Adapted from(6-8)

Results: A 54-year-old male patient was evaluated at the Endocrinology Unit of the Clínica Universitaria Bolivariana in Medellin, Colombia, because of a pathological history of hypothyroidism and severe hypertriglyceridemia with levels as high as 3210 mg/dL (36.27 mmol/L) associated with recurrent pancreatitis since 2009. His family history is unremarkable. His blood pressure was normal; his body-mass index was 27. The Biochemical analyses were as follows- Fasting Glucose: 96mg/dL, Total Cholesterol: 180mg/dL, Triglycerides: 626mg/dL, High-density cholesterol: 24mg/dL, Low-density cholesterol: 27mg/dL. Genetic testing confirmed a heterozygous, probably pathogenic variant c.603C>A; p.Tyr201* in CREB3L3 and two variants of uncertain clinical significance in GCKR and APOA5. Currently, the patient is on fenofibrate 200 mg o.d., levothyroxine 200 mcg o.d., rosuvastatin 40 mg o.d., and icosapent ethyl 1g q.d.

Conclusions: Hypertriglyceridemia is a common condition worldwide. When suspecting a genetic cause, CREB3L3 gene mutations should be part of the primary genetic work-up.

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#677

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

REMNANT CHOLESTEROL IN PATIENTS WITH ESTABLISHED ATHEROSCLEROTIC CORONARY ARTERY DISEASE. OUR EXPERIENCES

VIRTUAL E-POSTER SESSION

Ivana Burazor[1], Petar Otasevic[1], Nebojsa Tasic[1], Vladimir Jakovljevic[2], Milovan Bojic[1]
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Background and Aims: Remnant cholesterol in triglyceride-rich lipoproteins is associated observationally and causally with increased risk of atherosclerotic cardiovascular disease. To evaluate attainment of guideline recommended targets for lipid lowering treatment, physical activity level in patients with documented atherosclerotic cardiovascular disease and its relation to SMART score and remnant cholesterol.

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. Remnant cholesterol was calculated as well as SMART risk score.

Results: Out of 1098, 102 CHD patients fulfilled 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%. Mean HDL cholesterol was 1.08mmol/l in males and 1.02mmol/l in females, mean LDL 2.86 mmol/L. Remnant cholesterol was< 0.5 mmol/l in 39% and between 0.5-0.99 mmol/l in 59% Majority of patients were taking statins – 96.1%, 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. Residual, SMART risk remained high

Conclusions: There is a huge and urgent need to continue to improve risk factor profile and optimize medical therapy and life style interventions to reduce high residual risk in patients with established atherosclortic coronary artery disease.

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#729

Topic: *AS02 Lipids and Lipoproteins / AS02.12 Adipose tissue biology and pathology*

EXPRESSION OF GENES FOR SPHINGOMYELINASE AND SPHINGOMYELIN SYNTHASE ENZYMES IN THE ADIPOSE TISSUE OF THE HEART OF PATIENTS WITH CARDIOVASCULAR DISEASES

VIRTUAL E-POSTER SESSION

Olga Gruzdeva[1], Yulia Dyleva[1], Ekaterina Belik[1], Evgenya Uchasova[1], Anastasia Ponasenko[2], Maxim Zinets[3], Aleksandr Stasev[3], Evgenia Gorbatovskaya[1], Olga Barbarash[4]
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Background and Aims: To study the expression of enzymes ceramide metabolism in the heart and blood vessels of patients with coronary artery disease and valvular heart disease.

Methods: Explore 60 patients with CAD and with acquired heart disease (aortic valve stenosis/insufficiency). During surgery, biopsies of adipose tissue (AT) of subcutaneous, epicardial and perivascular localization were obtained. In AT samples the enzymes of ceramide synthesis genes expression (acid sphingomyelinase *SMPD1*, neutral sphingomyelinase *SMPD3*) and ceramide utilization (sphingomyelin synthase: *SGMS1, SGMS2*) by qPCR. **Source of financing.**Russian Science Foundation grant No 22-15-20007.

Results: The gene of *SMPD1* was more expressed in cardiac AT than the gene of *SMPD3*. In the group of patients with CAD, the mRNA level of *SMPD1* was the highest in SAT and EAT compared to PVAT, in group of heart defects-in subcutaneous adipocytes compared to perivascular ($p \leq 0.05$). Gene expression of *SMPD2* had no tissue and group specificity. The mRNA level of *SMPD1* and *SMPD3* in AT did not differ between the studied groups. In the EAT of patients with CAD, the maximum gene expression of *SGMS1* gene was found, which was combined with a high gene expression of *SGMS2* in the SAT, PVAT. The mRNA level of *SGMS1* in EAT in the CAD group was higher and *SGMS2* in SAT, PVAT compared with patients with heart defects ($p \leq 0.05$).

Conclusions: The results obtained indicate the probable activation of this ceramide synthesis pathway in adipocytes of predominantly epicardial localization in CAD, which may contribute to the accumulation of ceramides associated with the pathophysiological aspects of atherosclerosis in EAT.

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#726

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

THE EFFECT OF DIFFEREN LIPID-LOWERING THERAPY REGIMES ON TRIGLYCERIDES LEVEL IN STEMI PATIENTS

VIRTUAL E-POSTER SESSION

Dmytro Bilyi, Anton Stepura, Oleg Irkin, Yaroslav Lutai, Alexander Parkhomenko
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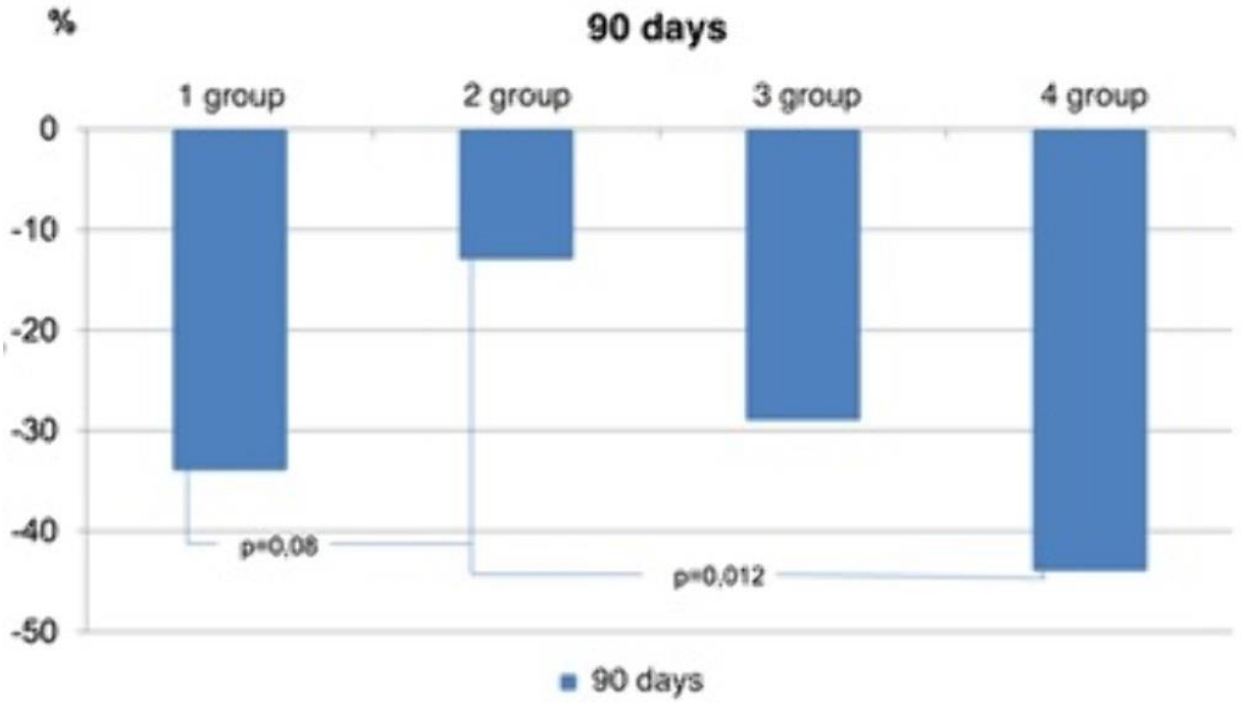
Background and Aims: Lipid-lowering therapy(LLT) with statins is essential for the treatment of STEMI.But many pts can't achieve novel lipids target levels with statin monotherapy and need a combined therapy.**The purpose** of the study was to evaluate the effect of combined high-intensity LLT with atorvastatin and ezetimibe on triglyceride(TG) level in STEMI patients.

Methods: The study included 135 patients admitted to the intensive care unit with a diagnosis of STEMI within the first 12 hours(on average (4.7±1.0) hours)from the onset of symptoms.Patients were randomly divided to one of four treatment groups with the prescription of a combination of atorvastatin 10mg and ezetimibe 10mg (the 1st group, 26pts),atorvastatin 40mg monotherapy(the 2nd group, 24pts),atorvastatin 80mg monotherapy (the 3rd group, 43pts) and a combination of atorvastatin in a dose of 40mg and ezetimibe 10mg(the 4th group, 42pts).LLT was initiated immediately upon admission, and before revascularization.There were no differences between groups in baseline characteristics and standards of treatment.TG levels were assessed at admission and after 90days of treatment.

Results: On day 90, TG levels decreased in all treatment groups. Minimal changes (a decrease of 13%) were observed in the 2nd group. Combined therapy was significantly more effective, while the greatest reduction in TG levels (44%) after 90 days of treatment was observed with the combination of atorvastatin 40mg and ezetimibe 10mg (p=0.012 compared to group2). Low dose combination also tended to be more effective in TG lowering than atorvastatin 40mg monotherapy (p=0.08)(Fig.

1).



Conclusions: Combined LLT in patients with STEMI was more effective in TG lowering than monotherapy of atorvastatin.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#724

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

GENE EXPRESSION OF DE NOVO CERAMIDE SYNTHESIS ENZYMES IN THE ADIPOSE TISSUE OF THE HEART AND LIPID SPECTRUM PARAMETERS IN PATIENTS WITH CARDIOVASCULAR DISEASES

VIRTUAL E-POSTER SESSION

Olga Gruzdeva[1], Yulia Dyleva[1], Ekaterina Belik[1], Evgenya Uchasova[1], Anastasia Ponasenko[2], Sergey Ivanov[3], Evgenia Gorbatovskaya[1], Olga Barbarash[4]
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Background and Aims: To determine the relationship between the expression of de novo ceramide synthesis enzymes in cardiac adipose tissue and serum cholesterol levels in patients with cardiovascular diseases

Methods: The study included 30 patients with CAD and 30 patients with acquired heart defects. Biopsies of subcutaneous, epicardial, perivascular AT (SAT, EAT, PVAT) were obtained during surgery. Expression of de novo ceramide synthesis enzyme genes (serine palmitoyltransferases C1 and C2 subunits*: SPTLC1*, *SPTLC2*; ceramide synthase 1-6: *CERS1-6*; dihydroceramide desaturase: *DEGS1*) was assessed by quantitative PCR. The lipid spectrum indicators (the level of total cholesterol (TC), cholesterol of low (C-LDL), very low (C-VLDL) and high density lipoproteins (C-HDL), triacylglycerides (TAG), atherogenic index (AI)) were determined on the Konelab 30i (Thermo Fisher Scientific, Finland)

Results: Patients with CAD were characterized by dyslipidemia, manifested by high levels of TC, C-LDL, TAG and AI in comparison with patients heart defects. High expression of SPTLC1, CERS2, CERS4, DEGS1 was revealed in EAT in patients with CAD. The *SPTLC1* expression in EAT correlates with the level of LDL cholesterol (r=0.83, p=0.039). Among the six isoforms of ceramide synthases evaluated, the mRNA level of ceramide synthase-1, -2, -4, and -5 was the highest. *CERS2* and *CERS4* expression in the EAT with the TAG in the blood serum (r=0.80, p=0.029; r=0.77, p=0.022), CERS4 expression in PVAT (r=0.71, p=0.046) with serum TAG. While among patients with heart defects no correlations were found

Conclusions: Thus, indicators of ceramide synthesis can be new biomarkers of atherosclerosis and therapeutic targets, regardless of cholesterol levels.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#722

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.06 Gender and cardiovascular risk*

RELATIONSHIP OF EXPRESSION DE NOVO CERAMIDE SYNTHESIS ENZYMES WITH GENDER AND AGE IN CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Olga Gruzdeva[1], Ekaterina Belik[1], Yulia Dyleva[1], Evgenya Uchasova[1], Anastasia Ponasenko[2], Kirill Kozyrin[3], Sergey Ivanov[3], Evgenia Gorbatovskaya[1], Olga Barbarash[4]
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Background and Aims: to study the relationship between expression de novo ceramide synthesis enzymes in adipose tissue (AT) and non-modifiable risk factors of cardiovascular disease (CVD) in coronary artery disease (CAD)

Methods: The study included 30 patients with CAD, undergoing coronary artery bypass grafting. Biopsies of subcutaneous, epicardial, perivascular AT (SAT, EAT, PVAT) were obtained during surgery. Expression of de novo ceramide synthesis enzyme genes (serine palmitoyltransferases C1 and C2 subunits SPTLC1, SPTLC2; ceramide synthase 1-6 CERS1-6; dihydroceramide desaturase DEGS1) was assessed by qPCR. Statistical analysis of results was performed using GraphPad Prism 8 (GraphPad Software)

Results: Men with CAD were characterized by higher levels of expression of de novo ceramide synthesis enzymes SPTLC1, CERS1, 5 and DEGS1 in EAT and PVAT than women. The expression of the studied enzymes in SAT did not differ statistically significantly depending on gender. In patients older than 60 years, the maximum expression levels SPTLC1, CERS1,2,6, DEGS1 in AT of cardiac localization were revealed in comparison with persons younger than 50 and 50-59 years ($p<0.005$). Correlation analysis revealed a direct correlation of SPTLC1, CERS1,2,6, DEGS1 in EAT and PVAT with age ($p<0.05$)

Conclusions: Close relationships were found between the expression of enzymes of the main pathway of ceramide synthesis in AT of cardiac localization and gender and age characteristics of patients with CAD. Determination of the expression of de novo ceramide biosynthesis enzymes plays an important role for risk stratification both in addition to traditional risk factors and independently, which is important for primary and secondary prevention of CVD

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#719

Topic: *AS02 Lipids and Lipoproteins / AS02.12 Adipose tissue biology and pathology*

EVALUATION OF EXPRESSION ENZYMES DE NOVO CERAMIDE SYNTHESIS PATHWAY IN THE CARDIAC ADIPOSE TISSUE AND BLOOD VESSELS IN PATIENTS WITH CARDIOVASCULAR DISEASES

VIRTUAL E-POSTER SESSION

Yulia Dyleva[1], Olga Gruzdeva[1], Ekaterina Belik[1], Evgenya Uchasova[1], Anastasia Ponasenko[2], Maxim Zinets[3], Aleksandr Stasev[3], Evgenia Gorbatovskaya[1], Olga Barbarash[4]
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Background and Aims: To evaluate in a comparative aspect the expression of enzymes of ceramide biosynthesis along the *de novo* pathway in the AT of the heart and blood vessels of patients with CAD and acquired heart diseases

Methods: The study included 60 patients with CAD and aortic stenosis/insufficiency. Biopsies of subcutaneous, epicardial, perivascular AT were obtained during surgery. Expression of *de novo* ceramide synthesis enzyme genes (serine palmitoyltransferases C1 and C2 subunits: *SPTLC1*, *SPTLC2*; ceramide synthase 1-6:*CERS1-6*; dihydroceramide desaturase: *DEGS1*) was assessed by quantitative PCR.**Source of financing.** Russian Science Foundation grant No.22-15-20007.

Results: Patients with CAD were characterized by a higher level of mRNA*SPTLC1* in SAT and EAT, *SPTLC2*, *CERS1*, producing ceramides C18, *CERS5* and *CERS6*, generating ceramides C14-C16 in EAT, *CERS2*-in SAT, producing long-chain ceramides C20-C24, *CERS4*, synthesizing very long chain cepamids C18-C20. In PVAT, a high expression of *CERS4* and *CERS3*, which synthesizes very long-chain ceramides C26 and higher, was revealed. *DEGS1* expression was maximal in SAT and EAT. In patients with heart defects, there was a high expression of *CERS3* in PVAT, *CERS4* in EAT and PVAT, *DEGS1* in EAT. The mRNA level of *SPTLC1* in SAT and EAT, *SPTLC2* in EAT, *CERS2* in all studied AT, *CERS4* and *5* in EAT, *DEGS1* in SAT and EAT among patients with CAD was higher than in the comparison group.

Conclusions: The results obtained indicate the activation of ceramide synthesis along this pathway in adipocytes of predominantly epicardial localization in coronarogenic pathology, which may contribute to the accumulation of long-chain ceramides in the AT.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#673

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.06 Vascular biology of the arterial wall: Miscellaneous*

PERICYTIC MARKERS OF CELLS OF THE SUBENDOTHELIAL LAYER OF THE INTIMA OF THE HUMAN AORTA

VIRTUAL E-POSTER SESSION

Alexander Markin[1,2], Yuliya Markina[1,3], Anastasia Bogatyreva[1], Taisiya Tolstik[1], Ulyana Zotova[1], Vadim Cherednichenko[1], Anton Postnov[1], Alexander Orekhov[1,3,4]
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Background and Aims: The aim of our work was to screen the expression profile and surface markers of primary cell culture and tissue samples of the subendothelial layer of the human aorta

Methods: Primary cells were isolated from samples of the subendothelial layer of the aortic intima. This biological material was collected in compliance with the principles of medical ethics during surgical procedures, based on the informed consent of patients. The obtained tissue samples were treated with a cocktail of proteolytic enzymes (collagenase and elastase) to separate the tissue into individual cells. The cells were cultured in DMEM/F12 medium in the presence of 5% FBS, glutamine and streptomycin/penicillin. The isolated cells were subjected to immunophenotyping procedure. Also, RNA was isolated from samples of cells and tissue of the subendothelial layer of the aorta for expression analysis.

Results: Our study showed that from 15 to 30% of isolated cells have pericytic markers: CD146, aSMA, NG2, Desmin, CD13; and don't have: CD31, CD34, CD45, CD56. Analysis of the gene expression of tissue samples showed a wide representation of pericytic markers in the subendothelial layer. Samples of 18 people have been analyzed

Conclusions: Our data indicate that the cells of the subendothelial layer are in dynamic equilibrium, which can change under the influence of damaging factors. The next step will be the immortalization of isolated cells and the creation of a cellular model to study the processes of atherogenesis in the subendothelial layer. This work was supported by the Russian Science Foundation (Petrovsky National Research Center of Surgery Grant №22-65-00089).

91ST EAS CONGRESS
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#395

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

FOUR YEARS OF APPLICATION EXPERIENCE IPCSK9

VIRTUAL E-POSTER SESSION

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Background and Aims: The aim of the study was to evaluate the results of four-years use of iPCSK9 in Karelia Republic, Russia.

Methods: the observation group consisted of 94 patients (52.1% with familial hypercholesterolemia (FH), 57.4% with the history of myocardial infarction), mean age 52.1± 4.3 years, 64 (68%) men, follow-up duration from one year to four years, 66.6% received therapy for more than two years, 49 received alirocumab and 45 received evolocumab. Before the start of therapy, the majority received maximally tolerated statin therapy, 85% received statin therapy in combination with ezetemibe, three patients - ezetemibe monotherapy due to statin intolerance. The target LDL levels were considered for very high risk patients <1.4 mmol /L, high risk <1.8 mmol/L, extreme risk <1 mmol/L.

Results: the LDL reduction on iPCSK9 was 58%; target LDL levels were achieved in 71.3% (62% patients with FH and 82% patients without FH). The level of LDL decrease less than 50% was noted only in 7.4% cases. Patients requiring a large dose of the drug were classified as very high risk, had higher cholesterol and LDL levels. The Lp(a) level decreased on 29.7% by 6-12 months. No destabilization of coronary heart disease, new cases of stroke were registered

Conclusions: the iPSK9 inclusion in the treatment regimen contributed to the stable course of atherosclerosis-associated diseases, the achievement of LDL cholesterol targets in 71.3% of patients, was not accompanied by side effects during 4 years therapy.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#671

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

HDL - LOADED PESDA MICROBUBBLES- MEDIATED FOCUSED ULTRASOUND SONOPORATION THERAPY OF ADVANCED ATHEROSCLEROSIS WITH VULNERABLE ATHEROMATOUS PLAQUE: EVALUATION WITH MAGNETIC RESONANCE IMAGING (MRI) AND HISTOPATHOLOGY

VIRTUAL E-POSTER SESSION

Hossein Mehrad[1,2,3]
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Background and Aims: Mature or immature atheroma within a thin- fibrous cap, accompanied by foam cells, extracellular lipid- laden cells and a few calcified crystals, is called vulnerable atheromatous plaque. In this study, we investigated the feasibility of imaging of vulnerable atheromatous plaque, using Magnetic Resonance Imaging (MRI) technique.

Methods: Vulnerable atheromatous plaque with thin fibrous cap was induced in the right common carotid artery of White New Zealand rabbits. The animals treated by extracorporeal pulsed- focused ultrasound (F= 1.1 MHz, I= 24W/cm^2, PD= 350 ms), accompanied by intravenous high-density lipoprotein (HDL) (80 mg/Kg)- loaded PESDA microbubbles (100 µl/kg, 2–5×10^5 bubbles/ml) administration. The lipidic and fibrotic tissue densities of plaques were measured by MRI and histopathology. 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 plaque lipidic tissue density and significant increase in the mean value for plaque fibrotic tissue density, in the treatment group compared with the other groups ($P < 0.05$).

Conclusions: Enhanced sonoporation effect of ultrasound, induced by collapsed microbubbles, can cause to enhance the Reverse Cholesterol Transport (RCT) and anti- inflammatory effects of HDL, and significantly lead to atheromatous plaque stabilization. Furthermore, MRI technique is a reliable method for evaluation of this treatment protocol.

91ST EAS CONGRESS
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#710

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

RELATIONSHIP BETWEEN SMOKING AND EXPRESSION OF DE NOVO CERAMIDE SYNTHESIS ENZYMES IN LOCAL FAT DEPOTS IN PATIENTS WITH CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Ekaterina Belik[1], Olga Gruzdeva[1], Yulia Dyleva[1], Evgenya Uchasova[1], Anastasia Ponasenko[2], Maxim Zinets[3], Aleksandr Stasev[3], Evgenia Gorbatovskaya[1], Olga Barbarash[4]
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Background and Aims: to study the relationship between the expression of *de novo* ceramide synthesis enzymes in adipose tissue (AT) and smoking in coronary heart disease (CAD).

Methods: The study included 30 patients with CAD, undergoing coronary artery bypass grafting. Biopsies of subcutaneous, epicardial, perivascular AT (SAT, EAT, PVAT, respectively) were obtained during surgery. Expression of de novo ceramide synthesis enzyme genes (serine palmitoyltransferases C1 and C2 subunits SPTLC1, SPTLC2; ceramide synthase 1-6 CERS1-6; dihydroceramide desaturase DEGS1) was assessed by quantitative real-time polymerase chain reaction (qPCR) using TaqManTM in a ViiA 7 Real-Time PCR system (Applied Biosystems, USA). Smoking is classified as current (at least one cigarette per day within the past year) or former smokers. Statistical analysis of the results was performed using GraphPad Prism 8 (GraphPad Software)

Results: Among the examined patients with coronary artery disease, 17 were smokers, 13 were not. Analysis of the studied parameters depending on the fact of smoking in patients with CAD showed that smokers were characterized by increased expression of SPTLC1, SPTLC2, CERS1, 2, 4, 6 and DEGS1 in adipocytes of subcutaneous, epicardial and perivascular localization ($p<0.005$)

Conclusions: In patients with CAD smoking revealed an increase in the expression of most enzymes of the main pathway for the synthesis of ceramides in all types AT. The data obtained indicate a close relationship between the expression of enzymes of the main ceramide synthesis pathway in AT and smoking in patients with CAD. One of the reasons for this may be the development of hypoxia, which activates de novo ceramide biosynthesis.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#709

Topic: *AS02 Lipids and Lipoproteins / AS02.12 Adipose tissue biology and pathology*

RELATIONSHIP OF THE DEGREE OF CORONARY LESION AND EXPRESSION OF DE NOVO CERAMIDE SYNTHESIS ENZYMES IN THE CARDIAC ADIPOSE TISSUE IN CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Yulia Dyleva[1], Olga Gruzdeva[1], Ekaterina Belik[1], Evgenya Uchasova[1], Anastasia Ponasenko[2], Aleksandr Stasev[3], Maxim Zinets[3], Olga Barbarash[4]
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Background and Aims: To study the relationship between coronary artery disease and the levels of de novo ceramide synthesis enzyme expression in the adipose tissue of the heart in coronary artery disease

Methods: The study included 30 patients with coronary artery disease (CAD) (65.5 (61.1-71.5) years). During coronary bypass grafting samples of subcutaneous (SAT), epicardial (EAT) and perivascular (PVAT) adipose tissue were obtained. Patients were divided into 3 groups: moderate coronary lesion (CL) (≤ 22 SYNTAX Score), severe CL (23-31 SYNTAX Score), and extremely severe CL (≥32 SYNTAX Score). *SPTLC1*, *SPTLC2, CERS1-6, DEGS1* expression was assessed by quantitative PCR

Results: The patients with moderate coronary lesion were lowest of *SPTLC1, CERS2, CERS4, CERS5, DEGS1* expression in EAT. In severe coronary lesion, an increase the mRNA level of *CERS2* and *CERS4* in EAT and PVAT was observed in comparison with the moderate coronary lesion group. Patients with extremely severe coronary lesion were characterized by maximum of *SPTLC1*, *CERS2*, *CERS4, CERS5, DEGS1* expression in EAT and *CERS2* and *CERS4* in PVAT compared with moderate and severe coronary lesion. The most significant predictors of severe/extremely severe coronary injury in CAD are: *SPTLC1* expression in EAT (OR 1.28, 95% CI 0.45-0.87, p =0.011), *CERS2* expression in EAT (OR 1.49, 95% CI 1.27-1.78, p=0.014), *CERS4* expression in EAT (OR 1.56, 95% CI 1.37-1.81, p=0.014)

Conclusions: The data obtained indicate the presence of a relationship between the degree of coronary lesion and the level of expression of de novo ceramide synthesis enzymes in the EAT of the heart in patients with CAD

91ST EAS CONGRESS
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#705

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

IMMUNOPHENOTYPE OF STEM CELLS FROM SUBCUTANEOUS, EPICARDIAL AND PERIVASCULAR ADIPOSE TISSUE IN PATIENTS WITH ACQUIRED HEART DEFECTS

VIRTUAL E-POSTER SESSION

Evgenya Uchasova[1], Olga Gruzdeva[1], Yulia Dyleva[1], Ekaterina Belik[1], Vera Matveeva[2], Aleksandr Stasev[3], Olga Barbarash[4]
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Background and Aims: To describe the immunophenotype of ADSCs isolated from subcutaneous, epicardial and perivascular fat depots in patients with AHD.

Methods: The study included 5 patients with AHD. The average age is 65.5±5.5 years. Patients had indications for open intervention on the heart. ADSCs from biopsy samples of subcutaneous, epicardial and perivascular AT that were obtained from patients during surgery and isolated according to the method of Zeng G (2013). When cells grew to 80–90% confluence, they were digested with 0.25% trypsin and they were transferred to 75 cm culture flasks and cultured to 80-90% cell confluence Flow cytometry analysis was performed on passage 2.

Results: In the SAT cell culture, the joint level of expression of CD90-CD105 was found in 72.3%, and CD73-CD90 in almost 99% of cells. Expression of CD34 was not observed, but there was a high percent of joint expression of CD34-CD90-72.3%. SAT was dominated by cells with stem cell phenotype CD90+CD105+CD73+CD34-. In EAT cell culture, CD 90-CD105 were simultaneously expressed by about 61%, and CD90-CD73-59%. The level of CD34 was 32.3%, and the combined level of CD90-CD34 was 47.3%. In EAT, 3 populations of cells were found with a dominance of the main one similar in phenotype to MSCs. PVAT, high levels of co-expression of CD90-CD105-78.4% and CD90-CD73-90.5%. Co-expression of CD34 and CD90 was only in 37% of the cells.

Conclusions: In all studied fat depots, as in patients with AHD, the population with the CD90+, CD105+, CD73+ CD34- stem cell phenotype dominated with a low level expression of CD34.

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MANNHEIM GERMANY | MAY 21-24, 2023

#388

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

ONE MONTH CHANGES OF LDL-C IN PATIENTS WITH ACS ON HIGH-DOSE STATIN THERAPY. PRELIMINARY RESULTS OF THE COMBI-LLT ACS STUDY.

VIRTUAL E-POSTER SESSION

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Background and Aims: to study the effect of high-dose combined lipid-lowering therapy on the vulnerability of atherosclerotic plaques, assessed using CCTA, as well as biomarkers in patients with ACS (Combi-LLT ACS. NCT05624658)

Methods: The open, prospective, randomized, single-center study includes 120 patients admitted with ACS. All patients will undergo IRA-PCI, as well as CCTA later. During hospital stay patients will receive statins at a maximum dosage - atorvastatin 80 mg/rosuvastatin 40 mg/day. Patients who showed high compliance and did not reach the target LDL-C level (≤1.4 mmol/l) after 1 month at the 2nd visit will be randomized into two groups (statins + ezetimibe vs statins + iPCSK9). At the 2nd and final visit (12 months), patients will undergo CCTA, CAVI, laboratory tests - blood count (NLR), lipid profile, ALT, AST, Troponin I, Galectin-3, CRPhs, MMP-9, TIMP-1, NGAL. The total duration of follow-up will be 52 weeks.

Results: During September-November 2022, 46 patients (M76%, average age 56,2±11,6 years) were screened. Average dosage of atorvastatin was 80 mg / rosuvastatin 40 mg/day. Only 8/46 patients (15 %, M100%, average age 47,8± 13,5 years) reached the target level of LDL-C (1,24 ± 0,15 mmol/l). 38 patients (M71%, average age 57,8±10,6 years) were randomized into the study. The dynamics of lipids within 1 month is shown on the

table.

Parameters	Enrolled (n=38)		% reduction	Screen-failures (n=8)		% reduction
	Visit 1	Visit 2		Visit 1	Visit 2	
Total cholesterol (mmol/l)	5,87 ± 1,35	3,93±0,76	33%	5,02 ± 0,56	2,62 ± 0,4	48%
LDL-C (mmol/l)	3,59±0,94	2,25±0,5	37%	2,74 ± 0,67	1,24 ± 0,15	54%
HDL-C (mmol/l)	1,28±0,39	1,15±0,29	10%	1,34 ± 0,35	0,93 ± 0,18	30%
TG (mmol/l)	1,67±1,74	1,14±0,3	32%	1,35 ± 0,37	1,02 ± 0,30	24%
ALT AST	30,7±18,0 42,4±29,1	30,6±16,9 22,7±5,97	0,32% 46%	60,5±68,5 86,9±121,5	44±37,4 47,6±54,4	27% 45%

Conclusions: Target level of LDL-C was reached in only 15% of patients with ACS within 1 month on the maximum dosage of statins. Combined lipid-lowering therapy may be required since the first days after ACS in the vast majority of patients.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#696

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

IMMUNOPHENOTYPE OF STEM CELLS FROM EPICARDIAL AND PERIVASCULAR ADIPOSE TISSUE IN PATIENTS WITH CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Olga Gruzdeva[1], Evgenya Uchasova[1], Yulia Dyleva[1], Ekaterina Belik[1], Vera Matveeva[2], Maxim Zinets[3], Olga Barbarash[4]
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Background and Aims: To describe the immunophenotype of adipose-derived stem cells isolated from epicardial and perivascular fat depots in patients with coronary artery disease.

Methods: The study included 5 patients with CAD. The average age is 65.5±5.5 years. Patients had indications for open intervention on the heart - direct myocardial revascularization by CABG. ADSCs from biopsy samples of epicardial and perivascular AT that were obtained from patients during surgery (CABG) and isolated according to the method of Zeng G (2013). When cells grew to 80–90% confluence, they were digested with 0.25% trypsin and proliferation for subsequent experimental analyses.

Results: On the 29th day of cultivation (pas.2), it was shown that CD105 and CD90 were present in the EAT of a patient with CAD on 79.71%, while one antigenic marker CD105 was present in 17.54% of the cells. Membrane proteins CD73 and CD90 were present in 79.47%, only one CD73 in 18.26%, while CD34 was present in only 3.76%. Thus, the phenotype of the resulting culture of cells isolated from EAT CD73+, CD90+, CD105+, CD34-. In addition to the main population, 2 minor: 1-CD90-, CD105+, CD34-, CD73+ CD45- presumably endothelial population, 2-CD90+, CD105-, CD34-, CD73-, CD45- presumably hematopoietic population. In PVAT, a high (over 90%) expression of membrane proteins characteristic of stem cells. CD34 was expressed by 3.46%. In PVAT, we observe 3 populations, as in EAT.

Conclusions: At the early stages of cultivation, SVF PVAT and EAT contain cells that carry markers inherent in both stem cells and markers of hematopoietic and endothelial populations.

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#372

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

FAMILIAL HYPERCHOLESTEROLEMIA IN CHILDREN AND ADOLESCENTS: MANAGEMENT AND CONTROL BY SEX. A LONGITUDINAL ANALYSIS FROM THE NATIONAL DYSLIPIDEMIA REGISTRY OF THE SPANISH ATHEROSCLEROSIS SOCIETY.

VIRTUAL E-POSTER SESSION

Clara Viñals[1], Amanda Jiménez[1,2,3], Gemma Yago[1], Monica Domenech[1,3], Núria Plana[4], Emilio Ortega-Martínez De Victoria[1,2,3]
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Background and Aims: Familial hypercholesterolemia (FH) is a frequent genetic cause of premature cardiovascular disease(CVD). Early detection and treatment from childhood is critical for reducing events. Our objective was to describe the grade of lipidic control, the use of treatment, and to evaluate the differences between sex, in a population with FH under 18 years old.

Methods: Multicentric and retrospective study based on the national registry of the Spanish atherosclerosis society. We included all the patients under 18 years old with a genetic or clinical diagnose of FH. The goals of lipid control were LDL-cholesterol <130 mg/dL or a relative reduction of LDL-cholesterol without treatment ≥50%(RR≥50%).

Results: 238 patients were included, 52,1% female, mean age 12.9±3.7 years. The lipid profile in the diagnosis was total cholesterol (TC) 295.1±83.2mg/dl, LDL-Cholesterol 222.9±82.1mg/dl, without sex differences. 49.4% were receiving treatment with statins (59.1% male vs 36.3% female;p=0.045), 7.1% ezetimibe, 4.2% resins and 39.3% wasn't on treatment, being the lipid profile (TC 239.5±54.9 mg/dl, LDL-Cholesterol 169.7±52.5 mg/dl) similar between sexes. In a multivariant analysis the probability of receiving treatment with statins was lower in females (OR 0.38;95%CI:0.16-0.92), and higher in those with higher LDL-Cholesterol (OR 1.02;95%CI:1.01-1.03). During the follow-up (2.1±1.7 years), 55.2% achieved an LDL-Cholesterol <130 mg/dl and only 12.1% a RR≥50%, without sex differences.

Conclusions: The achievement of LDL-Cholesterol goals in children and adolescents with FH is scarce and there are disparities by sex in the prescription. Strategies to improve control and studies that explore the factors potentially involved in these differences are required.

91ST EAS CONGRESS
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#333

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

THE ROLE OF AUTONOMIC REGULATION OF CARDIAC ACTIVITY IN PATIENT WITH NON-OBSTRUCTIVE CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Kristina Kopeva[1], Elena Grakova[1], Anna Gusakova[2], Alina Maltseva[3], Andrey Mochula[3], Konstantin Zavadovsky[3], Andrew Smorgon[2]
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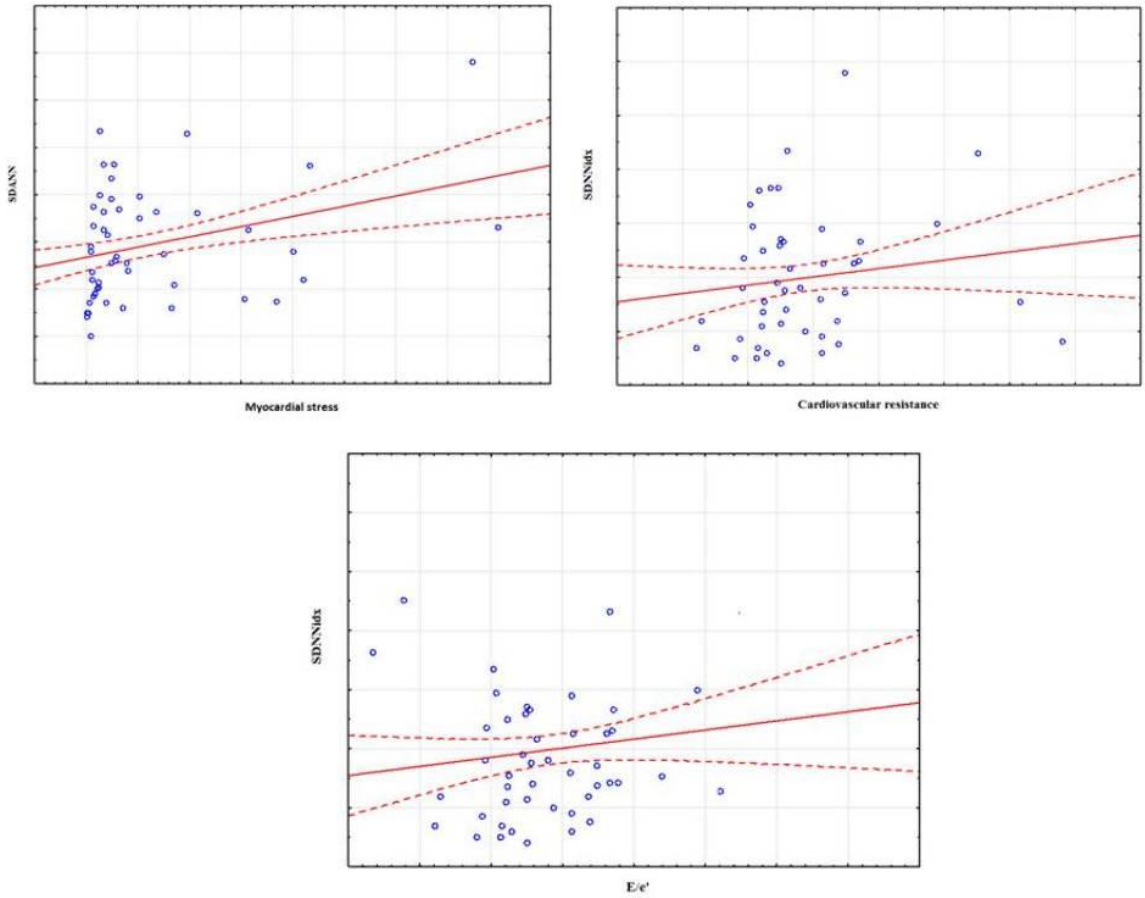
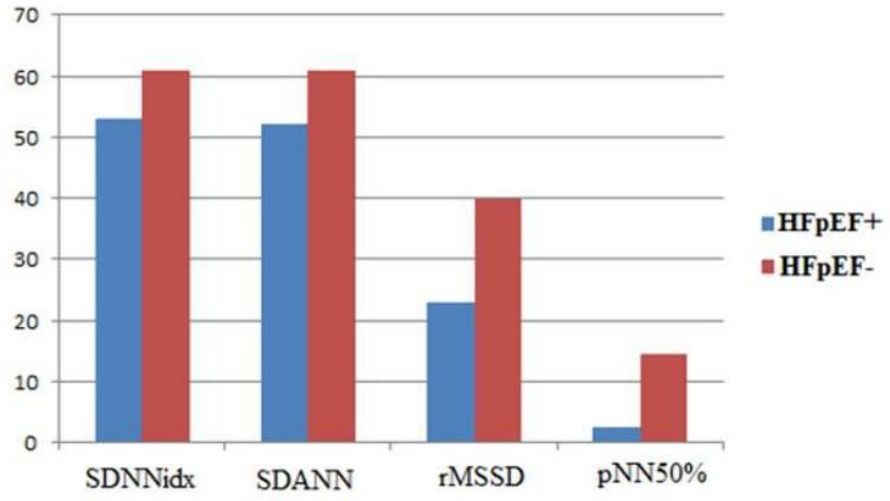
Background and Aims: To study the role of autonomic regulation of cardiac activity in patients with non-obstructive coronary artery disease (CAD) depending on the presence of heart failure with preserved ejection fraction (HFpEF).

Methods: Group 1 included 48 patients with newly diagnosed HFpEF, group 2-17 patients without HFpEF. Non-obstructive CAD was confirmed by computed coronary angiography. NT-proBNP concentrations were determined by ELISA. Heart rate variability was assessed by 24-hour ECG monitoring. LV function parameters were assessed using echocardiography.

Results: SDANN correlated with myocardial stress in diastole (r=0.345; p=0.006), and SDNNidx correlated with cardiovascular resistance (r=0.301; r=0.045) and E/e' (r=0.256; r=0.032) (Fig.1).

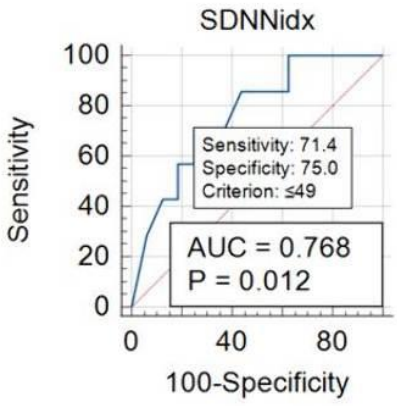


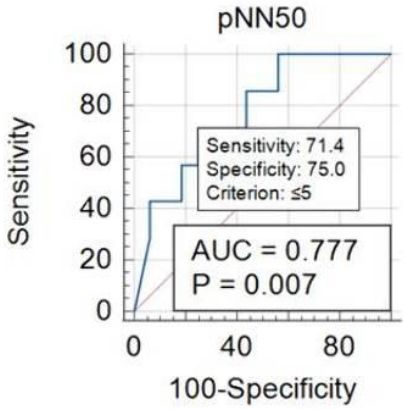
In group 1, SDANN values (p=0.006) were 13.1% lower than in group 2. In group 1, SDNNidx values (p=0.012) were 14.8% higher than in patients of group 2. At night, group 1 showed a decrease in rMSSD by 42.5% (p=0.007) compared with group 2. In group 1 pNN50% values were 2.6 (1.7; 11.5), and in group 2 - 14.6 (6.2; 67.5) ms (p=0.009) (Fig.2).



Based on ROC analysis, SDNNidx ≤49 ms (AUS=0.768; p=0.012) and pNN50 ≤5 ms (AUS=0.777; p=0.007) were defined as threshold values associated with the presence of HFpEF in patients with non-

obstructive coronary artery disease (Fig.3).





Conclusions: Patients with non-obstructive CAD and HFpEF showed a decrease in parasympathetic effects on the heart at night with a parallel increase in the activity of the sympathoadrenal nervous system. SDNNidx and pNN50 values can be used as a marker for diagnosing HFpEF. Funding: Russian Science Foundation No. 22-25-20019 https://rscf.ru/project/22-25-20019/ and funds from the Administration of Tomsk Region”

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#331

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

THE ASSOCIATIONS OF ADIPOKINES WITH PROINFLAMMATORY CYTOKINES IN MEN WITH ATHEROSCLEROSIS OF THE CORONARY ARTERIES AND OVERWEIGHT

VIRTUAL E-POSTER SESSION

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Background and Aims: To study adipokines and their associations with proinflammatory cytokines in men with atherosclerosis of the coronary arteries and overweight.

Methods: Funding information: Rissian Government budget theme: 122031700094-5; grant of the President of the Russian Federation: MK-1641.2022.3. The 79 men with coronary angiographically verified atherosclerosis of coronary arteries, after histological analysis of fragments of intima-media were divided into two subgroups: 43 people-without unstable plaques in the coronary arteries; 36 people - with unstable atherosclerotic plaques. The control group consisted of 40 men of comparable age and body mass index who did not have clinical manifestations of coronary heart disease. The content of adipokines in serum were determined in all patients by multiplex analysis using the MILLIPLEX MAP Human Adipokine Panel 1.

Results: The blood concentration of lipocalin-2 in patients with atherosclerosis of the coronary arteries was higher than in the control group ($p<0.01$). Among the studied adipocytokines, both subgroups of men with coronary atherosclerosis showed significant differences from the values in the control group in the content of TNF-α ($p<0.05$), CRP and IL-6 ($p<0.01$).The most significant direct associations were found between the content of adipokines with: TNF-α, IL-6 and CRP ($p<0.01$).The results of logistic regression analysis showed that an increase in the content of lipocalin-2 and IL-6 in the blood is associated with a relative chance of significant coronary artery stenosis.

Conclusions: Changes in blood adipokines associated with an increase in pro-inflammatory cytokines may be a factor that increases the likelihood of clinically significant coronary artery stenosis in overweight men with coronary atherosclerosis.

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#658

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

METABOLIC SYNDROME IS A DETERMINANT OF SERUM APOLIPOPROTEIN E RESPONSE TO SLEEVE GASTRECTOMY

VIRTUAL E-POSTER SESSION

Sílvia Paredes[1], Jonatas Garcez[2], Fernando Mota-Garcia[3], Maria Lopes Pereira[4], Laura Ribeiro[5]
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Background and Aims: Metabolic syndrome (MetS) patients have high risk of developing cardiovascular disease (CVD). Apolipoprotein E (ApoE) plays a role in triglyceride-rich lipoproteins metabolism and may contribute to residual CVD risk. This study aims to determine the effect of sleeve gastrectomy (SG) on ApoE, in patients with and without MetS.

Methods: Anthropometric and metabolic parameters of patients submitted to SG between January 2011 and July 2015 were recorded, before and 12 months after surgery. Univariate and multivariate analysis of ApoE, anthropometric and metabolic parameters were performed.

Results: We studied 258 individuals with mean age 39.95 ± 9.4 years-old, mean body mass index 43.6 ± 5.6 kg/m^2 and mean ApoE concentration 3.932 ±0.96 mg/dL. Patients with MetS exhibited higher ApoE baseline levels (4.243 ±0.99 vs. 3.724 ±0.88, $p < 0.001$) and there was a positive correlation with the number of MetS diagnostic criteria. At 12 months after surgery, only patients without MetS displayed a statistically significant ApoE serum concentration increase (3.781 ± 0.83 vs 3.954 ± 0.91, p=0.019). The number of MetS diagnostic criteria, ApoE baseline level and low-density lipoprotein cholesterol change were found to predict ApoE increase.

Conclusions: Only patients without MetS exhibited a significant increase in ApoE concentration after SG. These results expand the literature on ApoE metabolism by demonstrating that MetS impacts ApoE response to SG.

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#308

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

PBMC EXPRESSION OF GENES RELATED TO HDL METABOLISM AND ATHEROGENESIS IS INVOLVED IN MODULATING PLASMA HDL-CHOLESTEROL IN CAD PATIENTS

VIRTUAL E-POSTER SESSION

Alexander Dergunov[1], Mikhail Popov[2], Elena Nosova[3], Veronika Baserova[1], Alexandra Rozhkova[3], Margarita Vinogradina[3], Liudmila Dergunova[3]
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Background and Aims: To reveal the predictors of plasma HDL-cholesterol variability in CAD patients at transcriptome subset level.

Methods: 77 male patients 40-60 years old with CAD diagnosed by angiography were enrolled in the study. Two sets of genes related to HDL metabolism (HDL-cluster with 23 genes) and atherosclerosis-prone (atherogen-cluster with 41 genes) were selected. Transcript levels in RNA isolated from peripheral blood mononuclear cells (PBMC) were measured by real-time RT-PCR.

Results: For HDL-cluster by bivariate correlation, HDL-C was positively associated with *ABCG1*, *ALB*, *CUBN*, *HDLBP*, *PRKACG* transcripts. However, HDL-C was negatively associated with *BMP1*, *LCAT*, *PRKACB* transcripts. Importantly, HDL-C was negatively associated with *HMGCR* transcript. For atherogen-cluster, HDL-C was positively associated with *IL18RAP*, *PRKCQ*, and *SREBF1* transcripts, while negatively with the following fourteen transcripts: *CD14*, *CD36*, *CYBA*, *F5*, *MGST1*, *NPC2*, *OLR1*, *S100A12*, *S100A8*, *S100A9*, *SLP1*, *TLR5*, *TLR8*, and *VEGFA*. The contribution of gene transcripts into variability of HDL-C was explored also with multiple linear regression. Only transcripts from both gene clusters with significant correlations with HDL-C were included as independent variables, together with plasma TG and non-HDL-C. *IL18RAP* and *SREBF1* transcripts were positive predictors, while *BMP1* and *LCAT* transcripts were negative predictors of HDL-C variability, totally explaining 81% variation of HDL-C.

Conclusions: The decrease of BMP1 activity that cleaves proA-I to the mature apoA-I active in cholesterol efflux, with the decrease of large HDL due to low LCAT activity, may underlie the negative association of *BMP1* and *LCAT* transcripts with HDL-C level. SREBP1-IL18RAP axis seems to link intracellular lipid metabolism to the innate immune response.

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#791

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

LOWER LDL-C TARGET-GOAL ACHIEVEMENTS IN PATIENTS WITH ACUTE CEREBRAL INFARCTION COMBINED WITH TYPE 2 DIABETES

VIRTUAL E-POSTER SESSION

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Background and Aims: Acute cerebral infarction (ACI) belongs to fatal arteriosclerotic cardiovascular disease with high morbidity and mortality in most developing and developed countries. Low-density lipoprotein cholesterol (LDL-C) control is one of those key target goals among ACI patients. This study aimed to evaluate LDL-C target-goal achievement in patients with acute cerebral infarction (ACI) combined with or without type 2 diabetes (T2DM) at a tertiary hospital in department of Neurology at a tertiary hospital in Shanghai, China.

Methods: ACI diagnosis was established by clinical manifestation and cranial computerized tomography or magnetic resonance imaging. The baseline anthropological data, in-hospital biochemistry results including LDL-C levels were collected and analyzed and LDL-C target-goal achievement was calculated using recent ESC (2019), American (2017) and Chinese (2019) guidelines.

Results: 830 consecutive patients were enrolled including 458 ACI, 341 ACI combined with T2DM and 31 T2DM alone between January 2020 and December 2021. At baseline, ACI patients had higher levels of homocysteine, HDL-C and creatinine (all $p<0.01$). ACI+T2DM patients had higher levels of fasting blood sugar, hemoglobin A1C, triglyceride and LDL-C (all $p<0.01$). Both ACI and ACI+T2DM patients had lower LDL-C target-goal achievement than T2DM patients regarding ESC (5.1%, 5.5%, 16.1% respectively, $p<0.05$), American (5.4%, 5.8%, 32.3% respectively, $p<0.001$) and Chinese guidelines (14.3%, 14.3%, 45.2% respectively, $p<0.001$).

Conclusions: There exist clinical and biochemistry differences among ACI, ACI+T2DM and T2DM patients and very lower LDL-C target-goal achievement for secondary prevention in patients with ACI with or without T2DM in department of Neurology which deserves multiple active intervention.

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#659

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

INTERMEDIATE STAGE ATHEROSCLEROTIC PLAQUE REGRESSION, USING HIGH- DOSE ATORVASTATIN- LOADED MICROBUBBLES- MEDIATED FOCUSED ULTRASOUND SONOPORATION THERAPY: EVALUATION WITH POSITRON EMISSION TOMOGRAPHY (PET) IMAGING AND HISTOPATHOLOGY

VIRTUAL E-POSTER SESSION

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Background and Aims: Intermediate stage atherosclerosis is highlighted by infiltration of low-density lipoproteins (LDL) into the arterial intima layer and the formation of foam cells and extracellular lipid droplets- rich plaque. In the present study, we developed an extracorporeal focused ultrasound sonoporation therapy system and investigated its effect on intermediate stage atherosclerosis regression using Positron Emission Tomography (PET) imaging.

Methods: Briefly, Golden Syrian hamsters underwent endothelial denaturation using ballooning at the abdominal aorta, before being fed a 1.5% cholesterol-rich diet. After four weeks, the histopathology results showed the formation of macrophages foam cells-rich plaque, resulting in vessel wall thickening and intermediate stage atherosclerosis formation in all of the hamsters' arteries. Then treatment group underwent pulsed- focused ultrasound (F= 1.1 MHz, P= 24 W, I= 24 W/cm2, PD= 200 ms) sonoporation therapy accompanied by simultaneously intravenous high- dose atorvastatin (5 mg/Kg/day)- loaded PESDA (Perfluorocarbon- Exposed Sonicated Dextrose Albumin) microbubbles (100ml/kg, 2-5 ×105 bubbles/ml) administration. Then, 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, lipidic tissue and 18F- FDG density in the treatment group compared with the other groups ($P < 0.05$).

Conclusions: Enhanced sonoporation effect of pulsed-focused ultrasound, induced by collapsed microbubbles, can significantly lead to enhance the anti- inflammatory, lipophilic and pleiotropic effects of high- dose atorvastatin therapy, and can cause to reduce the inflammation and lipidic tissue density within the plaque. Furthermore, we conclude the PET imaging is reliable to accurate and repeated evaluation of inflammation in this model.

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#776

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

PM2.5-INDUCED CYTOTOXICITY EXACERBATES FOAM CELLS FORMATION IN MACROPHAGES, BY PROMOTING AN OXIDATIVE AND INFLAMMATORY PHENOTYPE

VIRTUAL E-POSTER SESSION

Lílian Costa-Beber, Hémelin Farias, Jessica Obelar Ramos, Rafael Moraes, Jade De Oliveira, Fátima Guma
Department Of Biochemistry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil

Background and Aims: Fine particulate matter ($PM_{2.5}$), an air pollutant, enhances the susceptibility to atherosclerosis. The phagocytosis of oxLDL by macrophages is a fundamental trigger for foam cells generation. Besides, macrophages apoptosis aggravates the thrombus formation and inflammation. In this context, 70 kDa-heat shock proteins (HSP70) are powerful anti-senescence chaperones, related to cell survival and anti-inflammatory signaling. We investigated if the atherogenic effect of $PM_{2.5}$ could be related to cytotoxicity, through an impairment in oxidative, inflammatory and HSP signaling in macrophages.

Methods: $PM_{2.5}$ retained in filters was partially extracted in PBS and centrifuged at 1000g. This solution (1 g filter/125 mL PBS) was diluted in DMEM 10% FBS ten times. We exposed RAW264.7 macrophages cell line to $PM_{2.5}$ for 48 h, and used PBS as Control. Nitric oxide was verified by Griess method; Triglycerides intracellular accumulation by AdipoRed staining; Cell death by Annexin and PI kit; cell proliferation by Ki-67 immune-content; HSP70 and iNOS levels by immunocytochemistry in flow cytometer.

Results: First, we established an *in vitro* model of foam cells, by exposing macrophages to $PM_{2.5}$ for 48 h, and adding native LDL (50 µg/mL) at the last 24 h. As expected, LDL induced intracellular accumulation of lipids, which was exacerbated by the pollutant. $PM_{2.5}$ promoted cytotoxicity by inducing apoptosis, and reducing the proliferating cells. The surviving macrophages increased their production of iNOS-dependent nitric oxide. Curiously, the pollutant enhanced HSP70 levels, as a countermeasure to cytotoxicity

(Fig1).

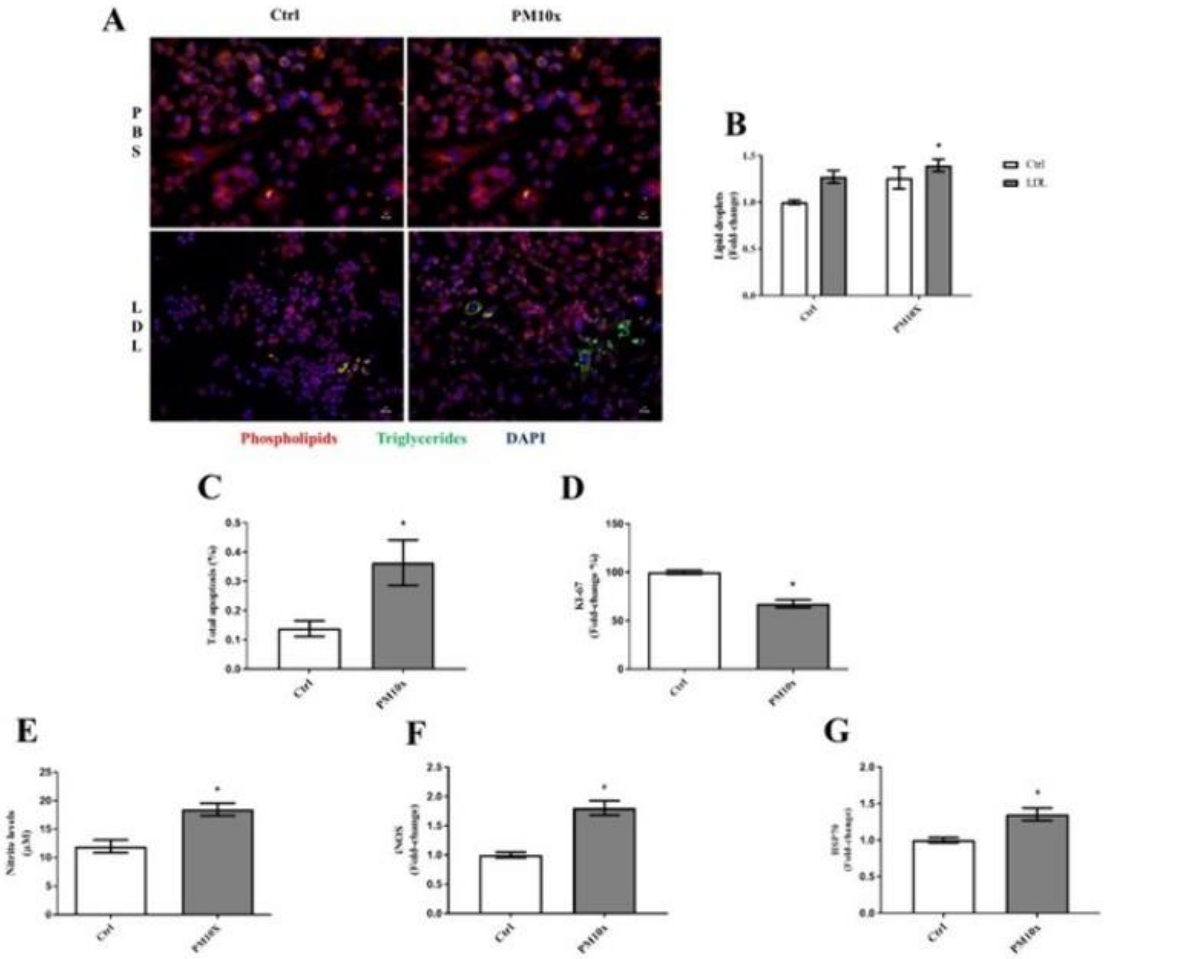

Figure 1: $PM_{2.5}$ exposure exacerbates foam cells formation by inducing cytotoxicity, oxidative and inflammatory phenotype. A. AdipoRed staining. B. Lipid droplets (Triglycerides). Two-way ANOVA, followed by Tukey. Pollutant: P = 0.013; LDL: 0.009; Interaction: 0.342. **C. Total apoptosis.** T-test P = 0.032. **D. Proliferating cells.** T-test P < 0.0001. **E. Nitrite levels.** T-test P = 0.0002. **F. iNOS levels.** T-test P = 0.0012. **G. HSP70 levels.** T-test P = 0.0021. * vs Ctrl.

Conclusions: $PM_{2.5}$-induced cytotoxicity exacerbates foam cells formation in macrophages, by promoting an oxidative and inflammatory phenotype.

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#661

Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

ROLE OF CIRCULATING MIR-217 IN STABLE CORONARY ARTERY DISEASE PATIENTS AND ASSOCIATING WITH AGING

VIRTUAL E-POSTER SESSION

Md Sayed Ali Sheikh[1], A Alduraywish[1], Basil Mohammed Alomair[1], Umme Salma[2], Li Fei[3], Tl Yang[3]
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Background and Aims: Aging has a major impact on the coronary atherosclerosis process. The aim of this study was to investigate the clinical significance of plasma miR-217 in stable coronary artery disease patients (CAD) and its relationship with aging.

Methods: Angiographically documented 122 multivessel stenosed CAD, 90 double vessel occluded CAD, 55 single vessel blocked CAD patients and 75 healthy subjects were included in this study.

Results: The expressions of plasma miR-217 levels were significantly up-regulated in the multivessel, double vessel, and single vessel blocked CAD patients as compared with healthy participants ($p<0.001$). Single, double, and multivessel occluded CAD subjects were remarkably distinguished from healthy subjects with AUC of 0.957, 0.952, and 0.914 respectively. Moreover, circulatory plasma miR-217 expressions in the multivessel, dual vessel, and single vessel elderly (61-76 years) subjects were greatly higher as compared with fairly younger CAD subjects (30-45 years) and (46-60 years) ($p<0.001$). Furthermore, plasma miR-217 levels were comparatively higher in elderly healthy participants (61-76 years) groups than in relatively younger (30-45 years) and (46-60 years) groups.

Conclusions: Elevated plasma miR-217 may be considered a major risk factor for atherosclerotic CAD patients and acts as a novel clinical biomarker for the early evaluation of CAD patients and it has a strong correlation with aging.

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#296

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

BIG DATA IN LDL-C MANAGEMENT ASSESSMENT

VIRTUAL E-POSTER SESSION

Kseniya Benimetskaya[1], Igor Mikheenko[1], Andrey Ponomarenko[1], Yury Krivosheev[1], Artem Gavrilko[1], Elena Semenova[1], Denis Losik[1], Anna Shangina[2]
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Background and Aims: The rapid development of digital technology in Healthcare systems led to the big data era of analytics. Electronic Health Records (EHRs) have a lot of data, but it is difficult to analyze all of them. Our aim is to provide real-world data on LDL-C management in two regions of Russia using Clinical decision support system (CDSS) MedicBK analytics based on EHRs.

Methods: MedicBK CDSS is a software that is able to detect patient parameters and specific disease characteristics from EHRs. In addition to suggesting therapeutic strategies on the basis of clinical guidelines and high-quality randomized clinical trials data it collects big data from EHRs available for analysis. MedicBK CDSS accumulated EHR data from Lipetsk and Voronezh regions (Russia) for 2021-2022. EHRs of patients with arterial hypertension, coronary artery disease, dyslipidemia, atrial fibrillation and heart failure were received.

Results: EHR of 41775 patients were analyzed (24684 in Lipetsk, 17091 in Voronezh). Very high and high cardiovascular risk were defined in 27776 (66.5%) and 3340 (8%) patients, respectively. Obesity was found in 19868 (47.6%) of the patients. Information about LDL-C level was found in EHRs of 3894 (9.3%) patients in the whole and in EHRs of 2697 very high risk patients (9.7% of very high risk patients). Only 1861 of very high risk patients had LDL-C level less than 1.4 mmol/L that is 6.7% of all very high risk patients and 69% of very high risk patients with known LDL-C levels.

Conclusions: CDSS analytics should be used for target lipid goals achievement and treatment corrections.

91ST EAS CONGRESS
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#663

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

FEATURES OF ALA-INDUCED METABOLISM OF PROTOPORPHYRIN IX IN CYTOPLASMIC HYBRID CELLS.

VIRTUAL E-POSTER SESSION

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Background and Aims: We continued our work on the study of the features of protoporphyrin IX (PpIX) metabolism in cultures of cytoplasmic hybrids. The accumulation of PpIX was induced by exposure to 5-aminolevulinic acid (5-ALA) in mitochondria in a cascade of heme synthesis reactions. Increased intake of 5-ALA from the outside leads to excessive accumulation of PpIX in cells, which cannot be quickly utilized by the ferrochelatase enzyme in heme.

Methods: We examined ten cybrid lines and a control (THP-1 cells). Using MitoTrackerGreen (Thermo Fisher Scientific), the functional state of the mitochondria of individual cells was evaluated. CLARIOstar Plus and MACSQuant Analyzer 10 were used to register the fluorescent signal in cells.

Results: The data obtained indicate that the accumulation of PpIX depends on the functional state of mitochondria, whose activity apparently depends on a different set of SNVs in the mitochondrial genome of the studied cells. Six of the nine cybrid lines showed a significant increase in the accumulation of PpIX in comparison with the control. It should be noted that all cybrid lines differ in the set of mitochondrial SNVs. Also, we observed a signal association between PpIX in the cell and the mitochondrial potential.

Conclusions: This can become the basis for the development of a method for the selective elimination of dysfunctional mitochondria using the photodynamic effect. As a result of such an impact, normally functioning mitochondria and the cell will not be destroyed. This work was supported by the Russian Science Foundation (Petrovsky National Research Center of Surgery Grant №22-25-00190).

91ST EAS CONGRESS
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#757

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

EXTRACELLULAR VESICLES SECRETED BY ADIPOSE TISSUE DURING OBESITY AND TYPE 2 DIABETES MELLITUS INFLUENCE CHOLESTEROL METABOLISM GENE EXPRESSION IN HUMAN MACROPHAGES

VIRTUAL E-POSTER SESSION

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Background and Aims: Obesity is associated with adipose tissue (AT) dysfunction and subsequent changes of extracellular vesicles (EVs) biogenesis and composition that could play a key role in the development of obesity related pathologies. We hypothesised EVs secreted by obese AT can affect arterial wall macrophages facilitating progression of cardiovascular disease. Aim of the study was to investigate the effect of AT EVs on cellular cholesterol metabolism gene expression in macrophages.

Methods: Subcutaneous and visceral AT (SAT and VAT) explants were cultured to generate EVs from subjects: 1) obese with type 2 diabetes mellitus (DM2) (n=26), 2) obese without DM2 (n=27), 3) without obesity (n=15). Macrophages of healthy blood donors were differentiated from the peripheral blood mononuclear cells for 5 days and exposed to SAT and VAT EVs. Cholesterol metabolism key gene expression was estimated by real-time PCR.

Results: *ABCA1* and *ABCG1* cholesterol transporters gene expression in macrophages was induced via addition of AT EVs from patients with DM2. *ABCA1* gene expression also was elevated via all types of VAT EVs. It was accompanied by opposite effects of obese AT EVs on gene expression of nuclear receptors LXRs. *LXRβ (NR1H2)* gene expression was elevated via AT EVs of patients with obesity as well as DM2. *LXRa (NR1H3)* as well as *PPARG* gene expression was reduced by addition of AT EVs of patients with obesity and DM2.

Conclusions: EVs secreted by SAT and VAT during obesity and DM2 influence cholesterol metabolism gene expression in human macrophages. Supported by the Russian Foundation for Basic Research (a 20-015-00502).

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#398

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

OBESITY AND THE RISK OF ISCHEMIC STROKE IN PATIENTS WITH ATRIAL FIBRILLATION: FINDINGS FROM A BIG DATA ANALYSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: The use of big data analysis makes it easier to assess the contribution of individual risk factors to the prognoses, compared with large-scale epidemiological studies.

Methods: At the Medical Institute of PetrSU, in the educational process the complex «Multicomponent software and hardware system for automated collection, storage, markup of research and clinical biomedical data, their unification and analysis based on Data Center with Artificial Intelligence technologies» is applied (it was financially supported by the Ministry of Science and Higher Education of the Russian Federation Theme № 075-15-2021-665). Data from electronic health records of 4.9 million patients were analyzed. Cases of atrial fibrillation (AF) were selected (56,003) patients. The frequency of ischemic stroke (IS) was estimated. Pearson's chi-squared test was used to compare subgroups.

Results: The average age of patients was 67.4±14.5 years, men 41%. Obesity was diagnosed with 44% of cases. The frequency of IS was 6.6%, among men 6.9%, women 6.4% ($p<0.05$). The following body mass index (BMI, kg/m2) ranges were identified: 18.5-21.9 (n=3558), 22.0-24.9 (n=8014) (was taken as a reference), 25.0-29.9 (n=19565), 30.0-34.9 (n=14591), 35.0-39.9 (n=6711), 40.0-60.0 (n=3564). Statistically significant differences in the incidence of IS were noted between the BMI reference range and BMI 25.0-29.9 and 30.0-34.9 (6.1% vs. 6.8% ($p<0.05$) and 6.1% vs. 6.8% ($p<0.05$), respectively).

Conclusions: When analyzing big data with information from electronic health records of 56,003 patients with atrial fibrillation, a significant relationship between the frequency of IS in patients with AF with overweight and obesity was proved.

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#315

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

LNCRNAS SIGNATURE OF HUMAN CAROTID ATHEROSCLEROTIC PLAQUES: DIFFERENCES BETWEEN HIGH- AND LOW-GRADE LESIONS

VIRTUAL E-POSTER SESSION

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Background and Aims: Long non-coding RNAs (lncRNAs) are emerging as regulatory molecules involved in the pathogenesis of an increasing number of diseases. To date, their association with atherosclerosis is still poorly investigated. Thus, we carried out a comprehensive RNAseq investigation to evaluate lncRNAs stage-specific expression with the aim to find novel therapeutic and/or diagnostic biomarkers.

Methods: Human carotid atherosclerotic plaques and their adjacent regions (lower grade lesions) from 15 patients undergoing endarterectomy were collected (30 samples). All samples were homogenized and processed for RNA extraction, by a Trizol and MirVana kit combined protocol. After quality check, NGS libraries were prepared using the Illumina Stranded Total RNA Prep kit and sequenced using the Illumina NextSeq550Dx instrument. Dragen RNA bioinformatic tool (Illumina) was used for quality check. Differential expression analysis was carried out by using the iDEP.96 web-based pipeline.

Results: Two hundred fourteen downregulated and 756 upregulated genes were identified in the plaques respect to the adjacent regions by clustering analysis. Among these, 108 upregulated and 42 downregulated lncRNAs were identified. Interestingly, a few of these have been already described and associated to cardiovascular diseases. In particular, SAMMSON and LINC00670 have been already reported as downregulated, whereas HAGLR, LINC01480, LINC00528, IFNG-AS1, and HAGLROS as upregulated. The others, being novel findings, should be further studied to assess their potential role in atherosclerosis.

Conclusions: Our data, even if preliminary, show a differential lncRNAs signature in the plaque respect to the adjacent region and highlight several potential novel biomarkers to be assessed by functional studies.

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#754

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.03 Macrophages in lipid metabolism and atherosclerosis*

ASSOCIATION OF CAROTID INTIMA-MEDIA THICKNESS WITH MONOCYTE ACTIVATION IN OBESE PATIENTS

VIRTUAL E-POSTER SESSION

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Background and Aims: Today, obesity is considered as a multifactorial disease in which systemic inflammation plays a leading role. Obesity leads to defeat many organism systems, in particular the cardiovascular system, and the development of atherosclerosis. This study was aimed to assess the relationship of carotid intima-media thickness (cIMT), one of the main surrogate markers of atherosclerosis, with pro-inflammatory activation of monocytes in obese patients.

Methods: Totally 30 patients with mean BMI of 41.4(7.9) kg/m^2 and mean age of 60.5(5.8) were included in the study. The cIMT was measured using ultrasound duplex scanning of carotid arteries. CD14+ leukocytes were extracted from whole blood by the standard ficoll-gradient method followed by magnetic cell separation. Secretion of the pro-inflammatory cytokines TNF-α and IL-1β was measured by ELISA. Monocyte activation was calculated as the ratio of stimulated LPS and non-stimulated secretion of the cytokines.

Results: Correlation analysis of the relationship between the cIMT and monocyte activation showed a significant level of association with IL-1β - Pearson correlation coefficient 0.486, p = 0.007. The relationship between the cIMT and the activation of monocytes by TNF-α was not significant: the Pearson correlation coefficient was 0.344, p = 0.063.

Conclusions: This study showed an association of carotid intima-media thickness with IL-1β monocyte activation but not TNF-α in obese patients. Further research is needed to investigate the role of pro-inflammatory monocyte activation in obese patients, study groups, and a panel of cytokines should be expanded. This work was supported by the Russian Science Foundation (Grant № 22-15-00252).

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#402

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

THE ANALYSIS OF NON-LIPID RISK FACTORS INFLUENCES ON TENDON XANTHOMAS APPEARANCE IN FAMILIAL HYPERCHOLESTEROLEMIA

VIRTUAL E-POSTER SESSION

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Background and Aims: to analyze the influence of non-lipid risk factors on tendon xanthomas appearance in patients with familial hypercholesterolemia (FH).

Methods: from 351 FH patients we selected 61 patients (group 1) with tendon xanthomas (17.4%) and compared it with the group 2 without tendon xanthomas (290). Some clinical aspects and several non-lipid risk factors were analyzed (heredity for cardiac heart disease, hypertension, male sex, smoking, glucose level, the presence of LDLR mutation).

Results: heredity increased the probability of xanthomas in four times (OR 4,129 [1,18;14,96], p=0,027), age over 45 years in three times (OR 3.39 [1.20; 9.60], p=0.022). The number of smokers was higher in the group 2, the probability of detecting xanthomas in smokers was low (OR 0.16 [0.064; 0.396], p=0.0001). The presence of hypertension did not significantly differ (27% and 14%, p=0,096). The presence of LDLR mutation increased the probability of xanthomas nearly in five times (OR 4.74 [1.44; 15.57], p=0.01). The presence of aortic stenosis increased the probability of xanthomas in 50 times (OR 50 [6.04; 414.0], p=0.0003). Ischemic heart disease (IHD) was diagnosed in 31.1% and 13.5% respectively (p=0,019). The history of myocardial infarction (MI) was 32.7% and 16.9% respectively (p=0,049). The combine point (the history of MI and stroke) was 36% and 15% (p=0,02).

Conclusions: tendon xanthoma is rare FH symptom, it's appearance was depended from heredity, age over 45 years, and the presence of LDLR mutation, xanthoma was the marker of aortic stenosis, IHD, MI and stroke.

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#401

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

THE ASSOCIATION OF TENDON XANTHOMAS IN FAMILIAL HYPERCHOLESTEROLEMIA WITH LIPID PARAMETERS

VIRTUAL E-POSTER SESSION

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Background and Aims: to analyze the relationship between tendon xanthomas in familial hypercholesterolemia (FH) and lipid spectrum indicators.

Methods: from 351 FH patients we selected 61 patients (group 1) with tendon xanthomas (17.4%) and compared with the group 2 without tendon xanthomas (290). We analyzed the following parameters: total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), non-HDL, triglycerides (TG), lipoproteins (a) (Lp (a)), cumulative (cum) levels (cum LDL (non-HDL) was calculated as LDL (non-HDL) max × (age at initiating of hypolipidemic therapy) + LDL (non-HDL) at inclusion age at initiation/correction therapy). Cum LDL (non-HDL)/age" was calculated as the ratio cum LDL (non-HDL) to age. Statistical analysis was performed by Statistica.10

Results: the average level of TC in all FH patients was 10.4±1.9 mmol/l. The obtained parameters in the groups 1 and 2 was: TC 10.94 ±1.8 and 9.68±1.49 mmol/l; LDL 8.14±1.33 and 7.11±1.40 mmol/l; non-HDL 9.32±1.88 and 8.16±1.59 mmol/l; Lp(a) 0.95±0.47 and 0.29±0.34g/l ($p<0.05$); HDL 1.59 ±0.51 and 1.64±0.60 mmol/L; TG 1.51±0.45 and 1.66±0.71mmol/l ($p>0.05$). Cum LDL level was 418.97±120.81 and 347.97±144.18, for cum non-HDL 495.51±154.22 mmol/l* years and 403.56 ±161.26, $p<0.05$. The cumulative LDL index accumulated over a year of life was 7.71±1.20 mmol/l* years and 6.99±1.38 ($p=0.011$), for non-HDL - 9.12±1.86 and 8.02±1.56 mmol/l/years, $p=0.015$.

Conclusions: tendon xanthomas were diagnosed in 17.4% in FH patients, it occurrence was associated with the levels of TC, LDL, Lp (a), cumulative LDL and non-HDL, but not with HDL and TG.

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#748

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

LDL-C TARGET-GOAL ACHIEVEMENTS IN PATIENTS WITH ACUTE CEREBRAL INFARCTION, OLD CEREBRAL INFARCTION AND TRANSIENT ISCHEMIC ATTACK, GAPS DO EXIST AND A LONG WAY TO GO

VIRTUAL E-POSTER SESSION

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Background and Aims: Low-density lipoprotein cholesterol (LDL-C) plays an important role in the formation of arteriosclerotic cardiovascular disease and LDL-C control is the first target goal. This study aimed to evaluate LDL-C target-goal achievement in patients with acute cerebral infarction (ACI), old cerebral infarction (OCI) and transient ischemic attack (TIA) at a tertiary hospital in department of Neurology at a tertiary hospital in Shanghai, China.

Methods: ACI, OCI and TIA diagnosis were established by medical history, clinical manifestation and cranial CT or MRI. In-hospital clinical data and biochemistry results were collected and LDL-C target-goal achievement was analyzed using updated ESC (2019), American (2017) and Chinese (2019) guidelines.

Results: 991 consecutive patients including 799 ACI, 128 OCI and 64 TIA between January 2020 and December 2021 were enrolled. At admission, ACI patients had higher levels of white blood cells, homocysteine, fasting blood sugar (FBS), TC, LDL-C (all $p<0.01$); OCI patients had higher ratio of smoking, diabetes and peripheral atherosclerosis and lower levels of TC and LDL-C while TIA patients had lower levels of FBS, ratio of diabetes and peripheral atherosclerosis (all $p<0.01$). Ratio of LDL-C target-goal achievement among ACI patients was lower regarding ESC, American and Chinese guidelines (5.3%, 5.3%, 14.9% respectively; $p<0.05$). Meanwhile, OCI patients had relatively higher LDL-C target-goal achievement referring American and Chinese guidelines (32.3%, 40.9%) and 11.0% concerning ESC guideline ($p<0.001$).

Conclusions: There are different clinical and biochemistry characteristics among ACI, OCI and TIA patients and very lower LDL-C target-goal achievement in patients with ACI which should attract more attention.

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#399

Topic: *AS02 Lipids and Lipoproteins / AS02.10 Modified lipoproteins*

SIALIDASE ACTIVITY CAUSING ATHEROGENIC IODIFICATION OF LDL IN THE BLOOD

VIRTUAL E-POSTER SESSION

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Background and Aims: In earlier studies we have found that human serum contained the *trans*-sialidase activity. This enzyme may be responsible for the desialylation of low density lipoprotein (LDL) in the blood. We have shown that desialylation is an atherogenic modification of LDL that makes the lipoprotein capable of inducing lipid accumulation in arterial wall cells, turning them into foam cells. In this work, we studied the properties of sialidase activity in the blood and tried to identify it.

Methods: Terminal sialic acid binding protein(s) were isolated from lipoprotein-deficient serum using affinity chromatography carried out with Neu5Acα2-8Neu5Ac-sepharose FF-6. Mass spectra were recorded on an Ultraflex TOF/TOF MALDI mass spectrometer (Bruker Daltonics, Germany) equipped with a 337 nm nitrogen laser.

Results: Optimal pH values for the *trans*-sialidase were 3.0, 5.0 and 7.0. Calcium and magnesium ions stimulated the enzyme activity at millimolar concentrations. Isolated enzyme can remove sialic acid from LDL, IDL, VLDL, and HDL particles (in decreasing rate order). Serum *trans*-sialidase transferred sialic acid from glycoconjugates of plasma proteins (fetuin, transferrin) and gangliosides (GM3, GD3, GM1, GD1a, GD1b). Sialylated glycoconjugates of human blood erythrocytes also served as substrate for serum *trans*-sialidase. Using mass spectrometry, we did not identify any sialidases among proteins isolated from serum by affinity chromatography. Additional experiments led to the following conclusion.

Conclusions: An unidentified protein with sialidase activity circulates in the blood both in free form and non-covalently bound to the membrane of extracellular vesicles (exosomes?). This work was supported by the Russian Science Foundation (Grant # 22-65-00005).

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#939

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

DIFFERENCES IN LIPID AND CARBOHYDRATE PROFILES IN PATIENTS WITH ARTERIAL HYPERTENSION AND SUBCLINICAL HYPOTHYROIDISM DEPENDING ON THE SIRT1 RS7069102 POLYMORPHISM

VIRTUAL E-POSTER SESSION

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Background and Aims: Sirtuin 1 (*SIRT1*) *rs7069102* has been associated with the risk of atherosclerosis, but it is still unknown if this risk is even greater in patients with subclinical hypothyroidism (SH). The aim of our study was to assess metabolic profile of patients with arterial hypertension (AH) and SH depending on *SIRT1* polymorphic variant.

Methods: The study included 70 patients with AH and SH and 50 patients with AH without SH. *SIRT1* polymorphism was analyzed using polymerase chain reaction.

Results: Among patients with isolated AH, differences were observed only in low density cholesterol (LDL-C) levels between CG and GG-carriers (p=0.038). CC-carriers with AH and SH compared to CG and GG-carriers had significantly lower levels of triglycerides (p=0.002 and p=0.001), very low density cholesterol (p=0.006 and p=0.002), LDL-C (p=0.029 and p=0.003), insulin (p=0.016 and p=0.013) and HOMA-IR (p=0.001 and p=0.011), respectively. Patients with GG genotype also had lower levels of total cholesterol (TC) compared to CC-carriers and higher levels of LDL-C compared to CG-carriers. Associations between the *SIRT1* polymorphic variants and levels of TC (p=0.009), LDL-C (p=0.001) were found among patients with AH and SH. Hyper-LDL cholesterolemia ($\chi 2=14.961$, $p = 0.001$) was more frequent in GG compared with CC-carriers.

Conclusions: *SIRT1* (rs7069102) G allele, especially GG genotype, carriers among patients with AH and concomitant SH, are characterized by more profound changes in the "metabolic portrait" with a pronounced deterioration in lipid and carbohydrate profile compared to CC-carriers, which is necessary to take into account when choosing further treatment.

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#248

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

METABOLIC AND SPHINGOLIPID CHANGES ASSOCIATED WITH THE ADIPONECTIN MEDIATED PROTECTION FROM ENDOTHELIAL DYSFUNCTION: AN IN VITRO STUDY

VIRTUAL E-POSTER SESSION

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Background and Aims: Endothelial dysfunction is one of the earliest manifestations of atherosclerosis. Adiponectin, an insulin-sensitizing and anti-inflammatory hormone secreted from the adipose tissue, protects from atherosclerosis. This study explored the metabolic and sphingolipid changes in endothelial cells associated with adiponectin-mediated protection from endothelial dysfunction.

Methods: Human umbilical vein endothelial cells (HUVECs) were used as the model endothelial cells. HUVECs were treated with tumour necrosis factor-alpha (TNF-α, 5ng/mL) to induce endothelial dysfunction. AdipoRon (5μM), an agonist of the adiponectin receptor 1 and 2, was used to study the effects of adiponectin. Agilent Seahorse extracellular flux analyser and Liquid chromatography-tandem mass spectrometry (LC-MS/MS) were used to study metabolism and sphingolipid alterations, respectively. Unpaired t-test was used to estimate statistical significance.

Results: TNF-α treatment induced endothelial dysfunction in HUVECs, demonstrated by the increased adhesion molecule expression and reactive oxygen species. TNF-α treatment significantly upregulated glycolysis while down-regulating long-chain fatty acid (LCFA) oxidation and mitochondrial ATP production. In HUVECs, TNF-α treatment significantly increased C16 and C18 ceramides and sphingosine 1-phosphate (S1P) intracellularly while S1P in the extracellular compartment decreased. Co-treatment of AdipoRon partially reversed the metabolic and sphingolipid changes associated with TNF-α. Compared to TNF-α, AdipoRon co-treatment decreased glycolysis and increased LCFA oxidation and mitochondrial ATP production. AdipoRon co-treatment decreased C16 and C18 ceramides and S1P intracellularly while increasing the S1P levels extracellularly.

Conclusions: Adiponectin-mediated protection from endothelial dysfunction could be mediated by reversing specific metabolic and sphingolipid changes. Targeting the endothelial metabolism could be a novel therapeutic avenue for the prevention of atherosclerosis.

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#1171

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

SUBCLINICAL ATHEROSCLEROSIS OF THE CAROTID ARTERIES IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH LOW CARDIOVASCULAR RISK

VIRTUAL E-POSTER SESSION

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Background and Aims: To evaluate the detection rate of subclinical carotid atherosclerosis and clinical significance of immunoinflammatory markers in rheumatoid arthritis (RA) patients (pts) with low cardiovascular risk (CVR).

Methods: The study included 182 RApts with low CVR (mSCORE<1%) and control group (n=100).

Results: Carotid atherosclerotic plaque (ASP) were observed more frequently in RApts with low CVR than in the control group (24% versus 13%, p=0,02). In RA, the detection of subclinical atherosclerosis was associated with traditional RF: carotid ASP were detected more frequently in men than in women (50% versus 24%, p<0,01), carotid IMT correlated with age (R=0,45), BMI (R=0,16), LDL-C level (R=0,19), systolic blood pressure (R=0,16), p<0,05 in all cases. According to a multivariate model, in RA, the risk of developing ASP increased in the presence of dyslipidemia (OR–2,97;95%CI:1,36-6,49; p=0,006) and arterial hypertension (OR–2,16;95%CI:1,03-4,54;p=0,04). No correlation between carotid IMT and blood concentrations of sCD40L, sVCAM, and sICAM was found in RApts or controls. In RApts with carotid ASP, sCD40L level was associated with carotid IMT (R=0,32,p=0,04) and cholesterol concentration (R=0,39,p=0.01).

Conclusions: Carotid ASP were observed in 24% of RApts with low CVR and were detected at a significantly more frequent rate compared to the control group. The risk of developing carotid ASP increased by 2-3 times with concomitant hypertension and dyslipidemia. The carotid IMT was associated with traditional RF - age, gender, lipid levels and blood pressure indicators, in cases of detection of ASP - with an immunoinflammatory marker - sCD40L.

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#1090

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.04 Adipose tissue homeostasis*

THE ASSOCIATIONS OF FATTY ACID PROFILE WITH WEIGHT IN MEN

VIRTUAL E-POSTER SESSION

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Background and Aims: The people with an excessive amount of adipose tissue have elevated levels of fatty acids (FA) in the blood, which ultimately leads to disorders of lipid metabolism and insulin resistance, which are the main factors in the development of diabetes mellitus. The aim to study the content of FA in blood, as well as their association with weight in men.

Methods: The study included 250 men. Selected participants were divided into Groups according to their body mass index (BMI): (1)–62 people with BMI≤24.9 kg/m^2, (2)–101 people with BMI 25.0–29.9 kg/m^2, (3)–87 people with BMI≥30.0 kg/m^2. Further, obese men were divided into: (4)–62 people with BMI 30.0–34.9 kg/m^2, (5)–19 people with BMI 35.0–39.9 kg/m^2, (6)–6 people with BMI≥40.0 kg/m^2.The content of FA was determined in the blood.

Results: The content of docosatetraenoic acid was higher in groups(2) and (5), when compared with group(1) (p=0.002,p=0.003,respectively). The content of gamma-linolenic acid was higher in group(3) than in group(1) (p=0.041). Concentration of oleic; linoleic; arachidonic; eicosapentaenoic FA were higher in group(5) than in group(1) (p=0.007,p=0.023,p=0.006,p=0.001,respectively). On the contrary, the content of nervonic acid is noted higher in groups(1) and (2) than in group(4) (p=0.029,p=0.012,respectively). The relative chance of obesity is associated with an increase in the level of gamma-linolenic (1.030;1.006-1.056;p=0.015) and eicosapentaenoic FA (1.061;1.000-1.125;p=0.045), and a decrease in the level of nervonic acid (0.953;0.913-0.994;p=0.027).

Conclusions: We determined that an increase in the level of gamma-linolenic and eicosapentaenoic FA, and a decrease in the level of nervonic acid are associated with obesity, regardless of the age of men.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#184

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

POTENTIAL ROLE OF RADIOMIC ANALYSIS OF EPICARDIAL ADIPOSE TISSUE IN THE PROGNOSIS OF ACUTE CORONARY SYNDROME

VIRTUAL E-POSTER SESSION

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[1]Laboratory Of Nuclear Medicine, Cardiology research institute of Tomsk National Research Medical Center, Tomsk, Russian Federation, [2]Department Of General Clinical Cardiology And Cardiovascular Epidemiology, Cardiology research institute of Tomsk National Research Medical Center, Tomsk, Russian Federation

Background and Aims: Relation of radiological parameters of epicardial adipose tissue to the development of ACS.

Methods: A retrospective study included 100 CT images of patients undergoing CTA to exclude atherosclerotic lesions of the coronary arteries (CA). For further analysis, 39 patients were selected who had signs of CAD from 30 to 90% and were listed in the ACS registry. The follow-up period was 5 years. Radiomic image analysis was performed for 39 images. Epicardial adipose tissue (EAT) volume was assessed on the images and 837 radiomic characteristics were calculated, including first-order statistics, GLCM, GLDM, GLRLM, GLSZM, and NGTDM parameters.

Results: Patients were divided into 2 groups without ACS (group 1; n=27 (69%)) and with ACS (group 2; n=12 (31%)). When comparing the 2 groups, there were no significant differences in the volume and density of EAT ($p>0.05$). 8 out of 837 radiomic parameters had significant differences ($p>0.05$), which indicates a specific radiomic phenotype of EAT in patients with ACS; correlation analysis of radiomic parameters with the degree of coronary artery stenosis and calcium index did not reveal significant correlations. Multiple regression analysis demonstrated that only Size zone nonuniformity (SZN(GLZM)) and Gray Level Variance (GLV GLCM) parameters were independent predictors of ACS. ROC-curve analysis showed that SZN ≤8025.7 (sensitivity 96%, specificity 75%, AUC: 0.806; $p=0.005$) and GLV ≤4.08; specificity 93%, sensitivity 83%, AUC=0.861, $p<0.001$ indicate a high risk of ACS.

Conclusions: The radiomic characteristics of EAT can serve as predictors of the development of ACS. Patients with ACS have a particular radiomic phenotype of EAT.

91ST EAS CONGRESS
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#1116

Topic: *AS04 Clinical Vascular Disease / AS04.03 NASH and other ectopic lipid diseases*

THE ROLE OF ATHEROGENIC DYSLIPIDEMIA, ENDOTHELIAL DYSFUNCTION AND SYSTEMIC INFLAMMATION IN THE DEVELOPMENT OF VASCULAR COMPLICATIONS IN PATIENTS WITH NAFLD

VIRTUAL E-POSTER SESSION

Kateryna Pivtorak, Iryna Fedzhaga, Oleksandr Marchuk, Natalia Pivtorak
Internal Medicine And Clinical Pharmacology, National Pirogov Memorial Medical University, Vinnytsia, Ukraine

Background and Aims: Patients with NAFLD are at high risk of coronary heart disease and stroke, but the mechanisms are not yet fully understood. Aim is to determine the relationship between atherogenic dyslipidemia, systemic inflammation, endothelial dysfunction as causes of cardiovascular complications in patients with NAFLD.

Methods: 152 NAFLD patients participated in the study. Cardiovascular risk stratification was performed using the traditional version of the SCORE scale.The level of inflammatory mediators (TNF-α, IL-1, IL-6), markers (C-reactive protein, fibrinogen), endothelin (ET-1), Willebrand Factor (vWF) activity, thickness of the intima-media complex, presence of atherosclerotic plaques and carotid artery stenosis, HOMA-IR index in all subjects. AST, ALT levels, the degree of liver fibrosis using elastography.

Results: In patients with NAFLD due to obesity, a decrease in endothelium-dependent vasodilatation was observed, indicating the presence of endothelial dysfunction. The concentration of pro-inflammatory cytokines in patients with NAFLD was 3-7 times higher than similar parameters of patients with a similar degree of obesity, but without signs of NAFLD. The concentration of ET-1 in the blood plasma of patients with NAFLD has a strong direct correlation with the degree of cardiovascular risk of the examined patients. Many inflammatory mediators (TNF-α, IL-1, IL-6) and markers (C-reactive protein, fibrinogen) highly correlate with the degree of obesity, the concentration of ET-1, vWF and markers of insulin resistance, a predictor for cardiovascular risk.

Conclusions: The presence of atherogenic dyslipidemia and endothelial dysfunction in patients with NAFLD contributes to myocardial remodeling and cognitive deficits. Violation of endothelium-dependent vasodilatation, inflammatory mediators are highly correlated with the degree of cardiovascular risk.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1098

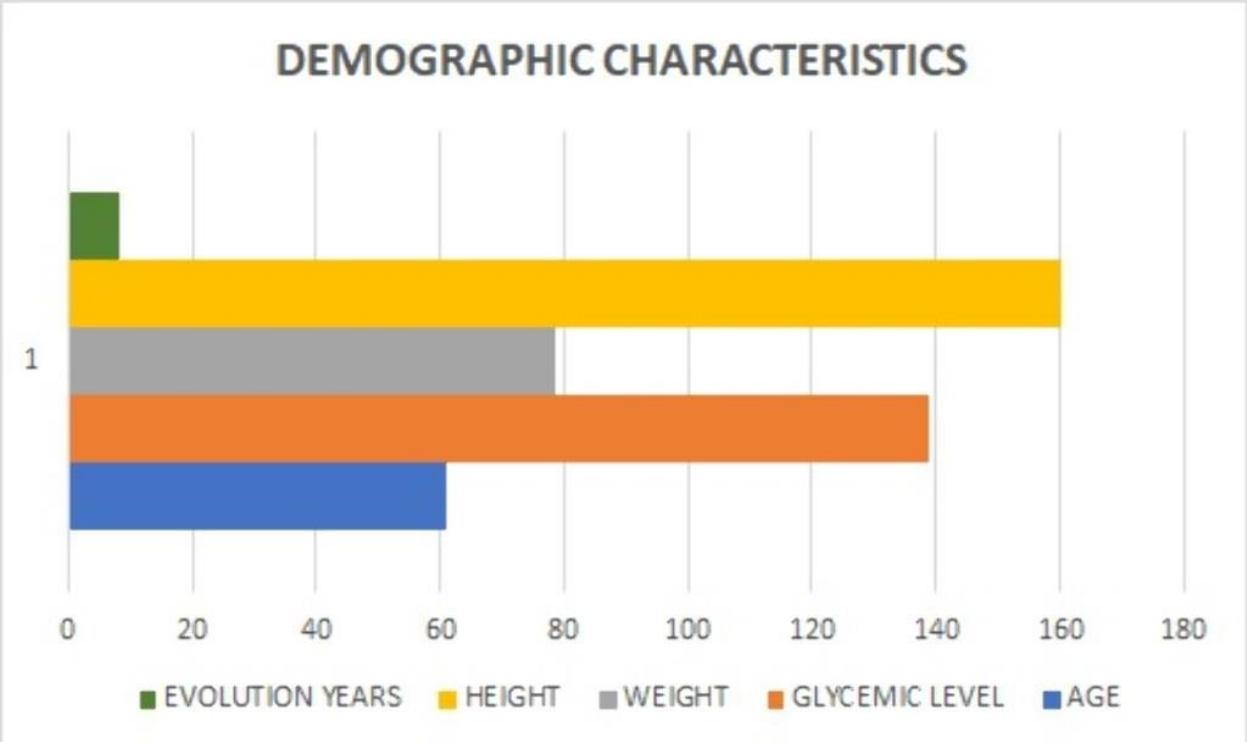
Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

SPANISH TRANSLATION, ADAPTATION, AND VALIDATION OF THE DIABETES KNOWLEDGE TEST (DKT) IN ADULTS WITH TYPE 2 DIABETES IN MEXICAN POPULATION.

VIRTUAL E-POSTER SESSION

Daniel Mendoza
Umf03, IMSS, JARDINES ALCALDE, Mexico

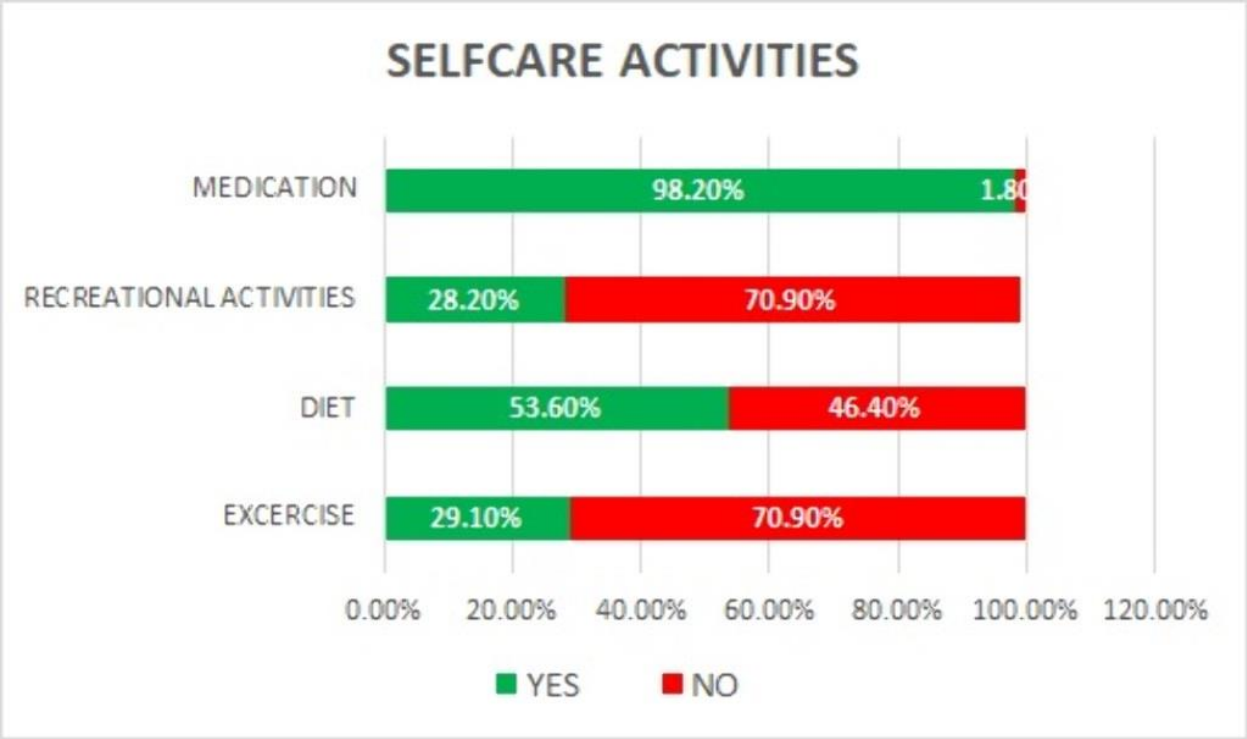
Background and Aims: Objective: The feasibility to evaluate patients' knowledge related to diabetes, lifestyle and glycemic control is achieved by using the Diabetes Knowledge Test, a simple 20 item tool. Translate, adapt, and validate the Spanish version of this test to facilitate the evaluation of diabetes educational
programs.



Methods: Methods: The translation process was using a two-way method, the English version was translated into Spanish by a certified translator, and then the same instrument was translated back into English by a group of physicians. Grammar and comprehension were tested in 10 patients focus group.

Results: Results: The final version was applied among 110 patients, 101 (91%) were women and 9 (9%) were men. The mean age was 61 (+7) years. The mean duration of diabetes was 8.18 (+2) years. 47% of

the participants had elementary education, and the mean blood glucose was 138(+15) mg/dl. Validation, Cronbach's alpha was used to test the reliability of the items. The criterion for accepting Cronbach's alpha was a score between 0.303 and 0.883. All analyses were conducted using the Statistical Package for Social Sciences (SPSS), version 29.0 (IBM Corp.) The data given indicate that the Spanish version of DKT received high internal consistency scores with coefficient alpha (95% confidence interval), These values were within the recommended range of Cronbach's alpha tests for 17 items and showed highly significant statistical
correlation.



Conclusions: Conclusion: Spanish version of the DKT is a valid and feasible tool to assess patients' knowledge related to diabetes and facilitate the evaluation of diabetes educational programs.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1096

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

SUICIDAL IDEATION LEADS TO DIABETES AND CORONARY HEART DISEASE-RELATED MORTALITY

VIRTUAL E-POSTER SESSION

Sri Banerjee, Gary Szirony
Department Of Public Health And Policy, Walden University, Leola, United States of America

Background and Aims: Suicidal Ideation is a part of a constellation of mental health conditions. Understanding the connection with cardiovascular disease is especially important and may be counterintuitive when thinking of suicidal ideation. We tried to determine if there was a relationship between diabetes and Coronary Heart Disease (CHD)-related mortality.

Methods: Our study population comprised of adults (> 20 years) from the 1999- 2010 with a positive history of suicidal ideation (from PHQ-9). National Health and Nutrition Examination Survey. Participants had completed a medical examination and interview and had results for CHD and Diabetes Status. Complex Samples Cox Regression was used to assess if diabetes influenced the relationship between coronary heart disease and mortality.

Results: The percentage with CHD levels was higher among males than females. For all-cause mortality, the overall adjusted hazard ratio (HR) for CHD to no CHD was 1.32 (95% confidence interval [CI], 0.53-3.25, p=0.54). The adjusted HR with CHD *was* elevated 2.52 (CI 0.83-7.68, p=0.10) and those without diabetes which was closer to 1 (CI 0.83-7.68, p=0.37) with diabetes. Similar patterns were not observed in the general population.

Conclusions: Through this study, we found this was the first time anyone has determined that both of the unadjusted and adjusted that coronary heart from a nationally representative sample this has been tested and in order to show that cardiovascular disease can lead to poorer outcomes. In this study we were able to show the relationship beteen mental health and physical health.

91ST EAS CONGRESS
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#1093

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE EFFECT OF ANGINA PECTORIS AND OBESITY ON OVERALL MORTALITY

VIRTUAL E-POSTER SESSION

Sri Banerjee
College Of Health Sciences, Walden University, Leola, United States of America

Background and Aims: Cardiovascular Disease has been known directly linked from diabetes. This is the number one cause of death in the United States. In this paper, we explored if the Angina modifies effect of obesity on mortality status.

Methods: The National Health and Nutrition Examination Survey (NHANES) is a survey completed by non-institutionalized population of the United States. All respondents from the NHANES survey, who were 20 years or older between the years 1999-2010 were included in the analysis with follow-up through 2015. Self-reported information was used for diagnosis of obesity and assessment of angina. Analysis was performed using complex samples Cox regression to determine if angina modifies the relationship of diabetes on Obesity-related mortality.

Results: Out of the multi-ethnic group, more females than males die from cardiovascular disease. During the 8.6-year follow-up, the adjusted hazard ratio (HR) of obesity to no obesity was (HR=1.01 CI 0.92-1.10). The adjusted HR was elevated, 1.35 (CI 1.002-7.46, p = 0.048), among angina with obesity individuals but closer to 1.0 (1.03 CI 0.93 -1.13, p=0.59) among individuals who were obese but did not have angina, after controlling for medical and demographic risk factors.

Conclusions: This study demonstrates that certain cardiovascular diseases may cause 35% higher mortality than individual without both angina and obesity. Understanding the ultimate chronic conditions combined to better address this condition is needed. Diabesity which demonstrate the need to take whole constellation for preventative measures.

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#1092

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

CONGESTIVE HEART FAILURE MODIFIES EFFECT OF DIABETES ON OVERALL MORTALITY AMONG MALE AGING POPULATION

VIRTUAL E-POSTER SESSION

Sri Banerjee
Department Of Public Health And Policy, Walden University, Leola, United States of America

Background and Aims: Readmissions and high cost of care continue to rise due to many factors including increased prevalence of the disease, lack of guideline directed therapy, and lack of patient adherence contributes to this relationship. The precise contributory relationship of diabetes and congestive heart failure (CHF) is poorly understood especially for males.

Methods: The National Health and Nutrition Examination Survey (NHANES) is a survey administered to non-institutionalized populations within the United States. Male respondents of the NHANES survey aged 65 or older and between the years 1999-2010 were included in the analysis, with follow-up through 2015. Analysis was performed using complex samples Cox regression to determine the relationship of diabetes on all-cause mortality and the influence, if any, of CHF status.

Results: Percent mortality among individuals with CHF was more in males than females, with mean follow-up of 10.4 years. For all-cause mortality, the overall unadjusted hazard ratio (HR) for CHF to no CHF was 1.44 (95% confidence interval [CI], 1.19-1.73, $p < 0.001$). The adjusted HR was elevated, 1.83 (CI 1.24-2.71, $p = 0.003$), among individuals who had CHF and diabetes but closer to 1.0 (1.28 CI 1.05-1.55, $p = 0.02$) among individuals who had diabetes to no diabetes, after adjusting for medical and demographic risk factors. Significant similar patterns were not among the general population.

Conclusions: Analysis of the data suggests that male adults with Diabetes causes increased mortality; we found that combination of positive diabetes and CHF status experience higher mortality rates than those adults with CHF alone. Conclusions include the need for diabetes education and health promotion addressing CHF factors improving diabetes.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#185

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

THE ASSOCIATION OF MONOMERIC C-REACTIVE PROTEIN PLASMA LEVEL WITH THE INCREASE IN PLAQUES NUMBER AND HEIGHT IN PATIENTS WITH LOW-GRADE CAROTID STENOSES AND HSCRP LEVEL

VIRTUAL E-POSTER SESSION

Ivan Melnikov[1], Sergey Kozlov[2], Olga Pogorelola[3], Maria Tripoten[3], Leyla Khamchieva[3], Tatiana Balakhonova[3], Olga Saburova[1], Yuliya Avtaeva[1], Maria Zvereva[1], Tatiana Kuznetsova[4], Konstantin Guria[1], Lyudmila Prokofieva[5], Zufar Gabbasov[1]
[1]Laboratory Of Cellular Hemostasis, National Medical Research Center of Cardiology of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [2]Department Of Problems Of Atherosclerosis, National Medical Research Center of Cardiology of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [3]Department Of Vascular Ultrasonography Diagnostic Methods, National Medical Research Center of Cardiology of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [4]Department Of Neurohumoral And Immunologic Diagnostics, National Medical Research Center of Cardiology of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [5]Laboratory Of Stem Cells, National Medical Research Center of Cardiology of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

Background and Aims: Monomeric C-reactive protein (mCRP) is a form of CRP associated with local inflammation. We studied whether mCRP level is associated with the increase in plaques number (PN) and height (PH) in patients with initially moderate SCORE risk and asymptomatic low-grade carotid atherosclerosis (CA) on statin treatment.

Methods: The initial study cohort comprised 80 patients 53±6 years old with initially moderate SCORE risk, LDL-C 2.7-4.8 mmol/L and asymptomatic low-grade CA. All patients were prescribed statins and followed up for 7 years. At the completion of the follow-up, carotid ultrasonography, high-sensitivity CRP (hsCRP) and mCRP measurements were performed. For the final analysis, a cohort of 54 patients (33 male/21 female) with hsCRP level <2,0 mg/L was selected.

Results: The level of LDL-C was 2.3 (2.0; 2.4) mmol/L, hsCRP 0.8 (0.5; 1.1) mg/L, mCRP 5.0 (3.1; 7.6) µg/L. The patients were divided by the median mCRP level. The increase in PN was 0.0 (0.0; 1.0) vs. 1.0 (0.0; 1.0) and PH 0.2 (-0.3; 2.0) mm vs. 1.7 (0.3; 2.8) mm in patients with the mCRP level <5.0 µg/L and in patients with the mCRP level ≥5.0 µg/L, respectively. The adjusted odds ratio for the increase in PN was 4.1 (95% CI 1.3; 13.7, p=0.02) for the patients with the mCRP level ≥5.0 µg/L.

Conclusions: The higher mCRP level was associated with the more pronounced increase in PN and PH in patients with hsCRP level <2.0 mg/L.

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#1129

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

DOES THE TRIGLYCERIDES-GLUCOSE INDEX PREDICT OUTCOMES IN A COHORT OF PATIENTS IN CARDIAC REHABILITATION?

VIRTUAL E-POSTER SESSION

Ricardo Martinez Gonzalez, Jesus Saldaña Garcia, Ana Torremocha Lopez, Lucia Cobarro, Clara Ugueto Rodrigo, Cristina Contreras Lorenzo, Almudena Castro Conde
Cardiology, Hospital La Paz, Madrid, Spain

Background and Aims: The Triglyceride-glucose index is a novel marker of insulin resistance. We wonder if the was related it to cardiovascular events.

Methods: An unicenter, retrospective and observational study recruited patients who attended to a cardiac rehabilitation program. The TyG index was estimated according to the first blood sample at admission, we considered it abnormal above 8.8. The severity of CAD was measured using coronariography and stratified as single-vessel or multi-vessel. MACCE was defined as myocardial infarction, stroke or cardiovascular death. We also calculated TG/HDL, TC/HDL and remant cholesterol. Statistical analyses were performed using R project.

Results:

	Non-CAD	CAD	p
Age	61.7 ± 12.8	60.3 ± 11	0.48
Basal Glycemia	96.7 ± 14.5	114.6 ± 49.4	<0.001
Triglycerides (mg/dL)	115.7 ± 64.3	145.7 ± 75.4	0.005
TyG index	8.5 ± 0.5	8.9 ± 0.6	<0.001
Total cholesterol (mg/dL)	159.1 ± 42.6	167.1 ± 43.5	0.24
LDL (mg/dL)	95.3 ± 32.2	102.1 ± 39.1	0.21
HDL (mg/dL)	43 ± 14.4	39.6 ± 13.9	0.14
Non-HDL (mg/dL)	116.1 ± 36.9	127.4 ± 40.8	0.06
TG/HDL	3.1 ± 2.1	4.2 ± 2.8	0.003
VLDL (mg/dL)	8.6 ± 2.9	7.9 ± 2.8	0.14
Remnants (mg/dL)	20.8 ± 9.1	25.4 ± 11.3	0.003
TC/HDL	3.9 ± 1	4.5 ± 1.3	0.001
Hba1c (%)	5.8 ± 0.6	6 ± 1.1	0.06
BMI	29.5 ± 6.4	27.3 ± 3.3	0.05
perimetro	101.9 ± 16.7	99.9 ± 10.4	0.55

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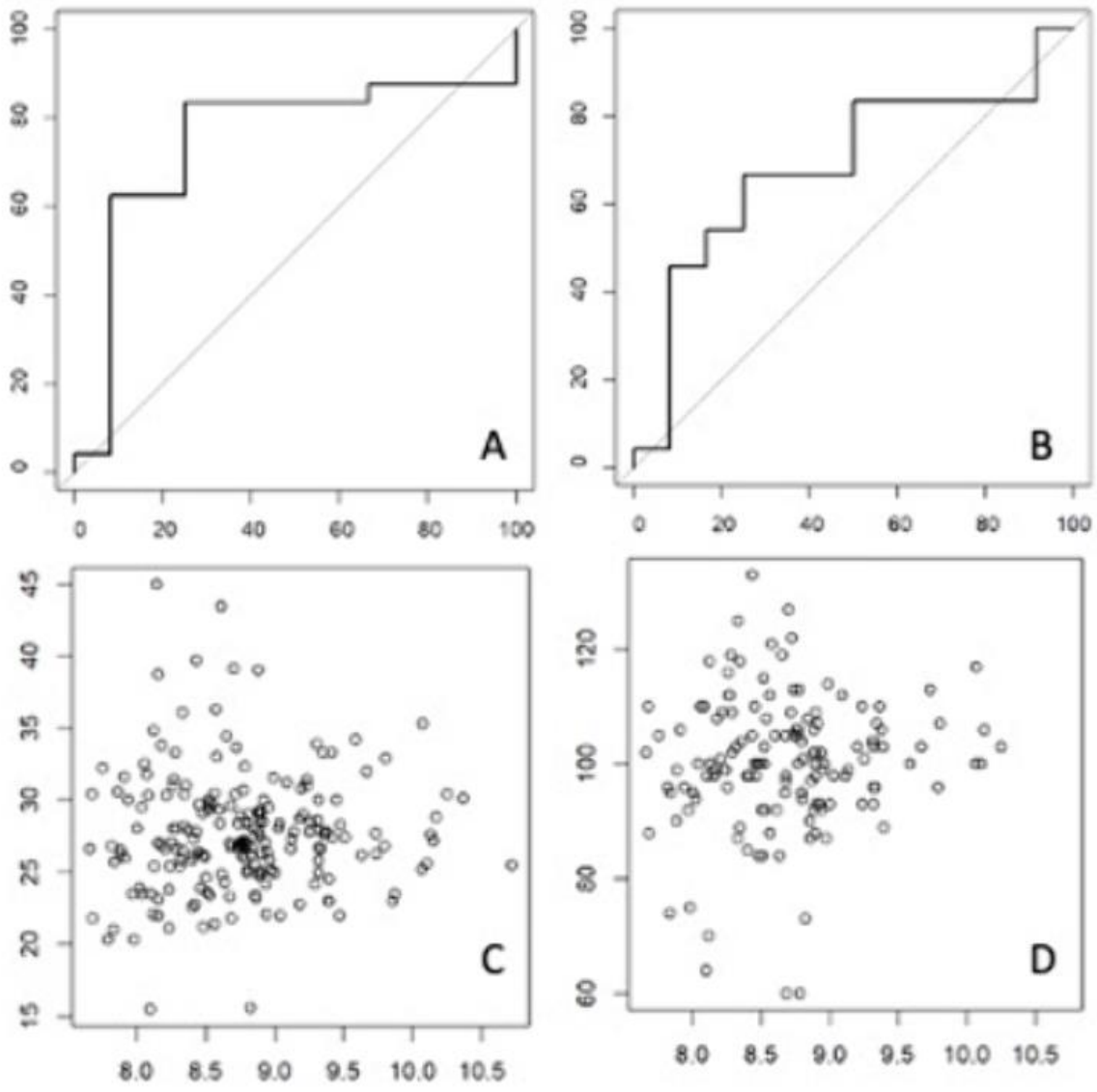

A total of 238 patients were enrolled, 190 were men, mean age 60.5. PCI was done in 175 patients and CABG in 9; 36 individuals had suffered MACCE previously. During the follow up, 12 underwent another MACCE. The TyG index was statistically higher between patients who suffered MACCE (8.9±0.6, $p<0.01$). This connection was also found with TG/HDL, TC/HDL and remnant (Figure1). As for our cutoff of 8.8 the TyG index established a specificity of 72.5% and positive predictive value of 86.9% for MACCE. TyG index predicted better a second event (AUC=74.6%)(Figure2A) than TC/HDL (AUC=59.03%)(Figure 2B). There was no statistical relationship between TyG index with body mass index nor abdominal circumference (Figure 2C, 2D)

Conclusions: TyG index is an easy and early sign of diabetic dyslipemia. In association with others indicators, it can help us to focus on those patients at high cardiovascular risk or with higher residual risk, specially nowadays that new non-statin therapies are about to come.

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#1070

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

INCREASED ALBUMINURIA IN PATIENTS WITH POLYVASCULAR DISEASE: PREVALENCE, ASSOCIATION WITH ATHEROSCLEROSIS BURDEN AND COMPLICATIONS

VIRTUAL E-POSTER SESSION

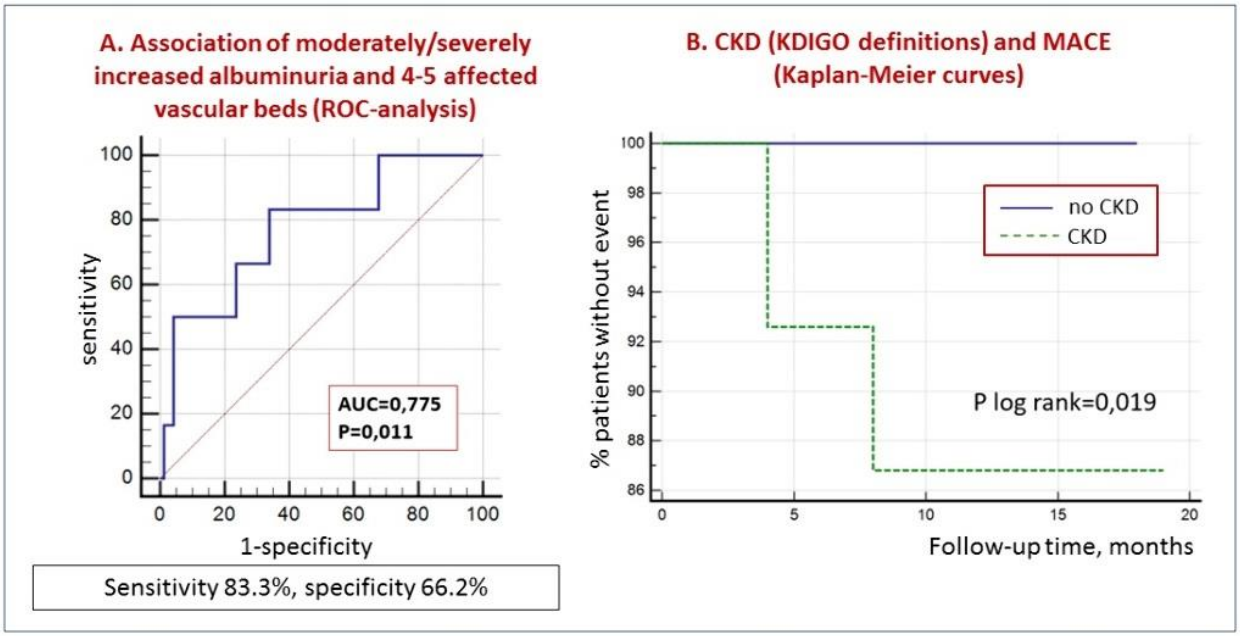
Olga Shakhmatova, Elena Krivosheeva, Andrey Komarov, Anatoly Dobrovolsky, Elizaveta Panchenko
Atherothrombosis, CHAZOV NATIONAL MEDICAL RESEARCH CENTER OF CARDIOLOGY, Moscow, Russian Federation

Background and Aims: Albuminuria is known as predictor for atherosclerosis and thrombotic complications. The role of this marker in patients with polyvascular disease (PD) receiving a new variant of antithrombotic therapy, the combination of aspirin and rivaroxaban 2.5 mg, has been little studied. We aimed to evaluate the relation of albuminuria to atherosclerotic burden, development of thrombotic and bleeding outcomes in such patients.

Methods: The data was obtained from the prospective registry REGATA-1 (NCT04347200). 74 patients (75.7% males, median age 67 [61-69] years) with PD (CAD and *peripheral arterial disease*) were enrolled. Urine albumin-to-creatinine ratio (UACR) and eGFR (CKD-EPI) were analyzed at inclusion.

Results: Median UACR was 16.5 [13.2 - 26.1] mg/g. High-normal UACR (10-29.9 mg/g) was observed in 45.9% of patients, moderately/severely increased albuminuria (≥30 mg/g) – in 29.7%. Chronic kidney disease (CKD) according to KDIGO definition (eGFR<60 ml/min and/or moderate/severe albuminuria as a sign of kidney damage) had 39.2% of patients. Moderate/severe albuminuria associated with numbers of affected vascular beds (picture 1A). During the follow-up (12 [8-18] months) 3 patients developed MACE, 11 – BARC 2-3 bleedings. Not UACR or eGFR but CKD (KDIGO) was independent predictor of MACE (in significant multiple regression model beta – coefficient for CKD was 0.097, p=0.042). UACR, eGFR and CKD (KDIGO) were not independent predictors of

bleeding.



Conclusions: Moderate/severe albuminuria is a marker of more generalized atherosclerosis. The use of extended criteria for CKD, considering moderate/severe albuminuria, increases the predictive value of this feature in relation to MACE but not to bleedings in patients with PD.

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#187

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.02 Epidemiology of dyslipidemias*

AGE- AND GENDER-SPECIFIC LIPID AND LIPOPROTEIN LEVELS AND PERCENTILES FROM THE THAI NATIONAL HEALTH EXAMINATION SURVEY (NHES-VI) IN THAILAND

VIRTUAL E-POSTER SESSION

Poranee Ganokroj[1], Wichai Aekplakorn[2], Weerapan Khovidhunkit[3]
[1]Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [2]Department Of Community Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, [3]Division Of Endocrinology And Metabolism, Department Of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Background and Aims: The reference values of lipoprotein level which are age-, gender- and country-specific are important in identification of lipoprotein disorders, such as familial hypercholesterolemia (FH).

Methods: During the nationwide NHES-VI in 2019, plasma lipid and lipoprotein levels were measured after a 12-hour overnight fast and the data were examined according to age and gender.

Results: The total of 25,169 participants (10,760 men and 14,409 women) were included. Among those aged 10-20 years, the median and 95th percentile values of total cholesterol (TC) were 183 and 246 mg/dL and of LDL-cholesterol (LDL-C) were 109 and 161 mg/dL, respectively. Participants aged ≥20 years had the median and 95th percentile values of 210 and 292 mg/dL for TC and 126 and 195 mg/dL for LDL-C, respectively. Both TC and LDL-C levels increased with age. The maximum levels were found in men aged 35- 45 years (median TC 216, median LDL-C 129 mg/dL) and in women aged 45-60 years (median TC 224, median LDL-C 137 mg/dL). Women tended to have higher TC and LDL-C levels than men among those <20 years and >45 years until ≥80 years.

Conclusions: In Thai adults aged ≥20 years, the 95th percentile level of TC and LDL-C were 292 and 195 mg/dL, respectively. Our data are crucial in determining appropriate cut-off points for making a diagnosis of FH in our population.

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#189

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

M1 MONOCYTES AS A PREDICTOR OF SHORT-TERM PROGRESSION OF CAROTID ATHEROSCLEROSIS IN ASYMPTOMATIC MIDDLE-AGED PATIENTS

VIRTUAL E-POSTER SESSION

Vadim Genkel[1], Ilya Dolgushin[2], Albina Savochkina[2], Irina Baturina[2], Karina Nikushkina[2], Anna Minasova[2], Alla Kuznetsova[3], Igor Shaposhnik[1]
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Background and Aims: Monocytes play a crucial role in the initiation and progression of atherosclerosis. Circulating monocytes with a pro-inflammatory M1 phenotype may be biomarkers of subclinical atherosclerosis and predict atherosclerosis progression. The aim of this study was to investigate the prognostic value of M1 monocytes in relation to the short-term carotid atherosclerosis progression.

Methods: The study included patients aged 40–64 years without established atherosclerotic CVDs who underwent a duplex ultrasound scanning at the first visit and at a second visit 12-24 months later. The presence of plaque was assessed according to Mannheim consensus. The criterion for progression of subclinical carotid atherosclerosis was the onset of a novel atherosclerotic plaque. Monocyte subpopulations were phenotyped by flow cytometry, based on CD68 and CD163 expression (M1 monocytes – $CD14^{+}CD68^{+}CD163^{-}$).

Results: The study included 92 patients, median age was 49.5 (44.0; 55.0) years. 62 (67.4%) patients had carotid plaques at the first visit. Follow-up duplex ultrasound scanning were performed at an interval of 15.4 (12.4; 20.6) months. Novel atherosclerotic plaques were detected in 25 (27.2%) patients. Furthermore, an ROC analysis was performed to determine the possible prognostic value of M1 monocyte in relation to the carotid atherosclerosis progression (Figure 1).

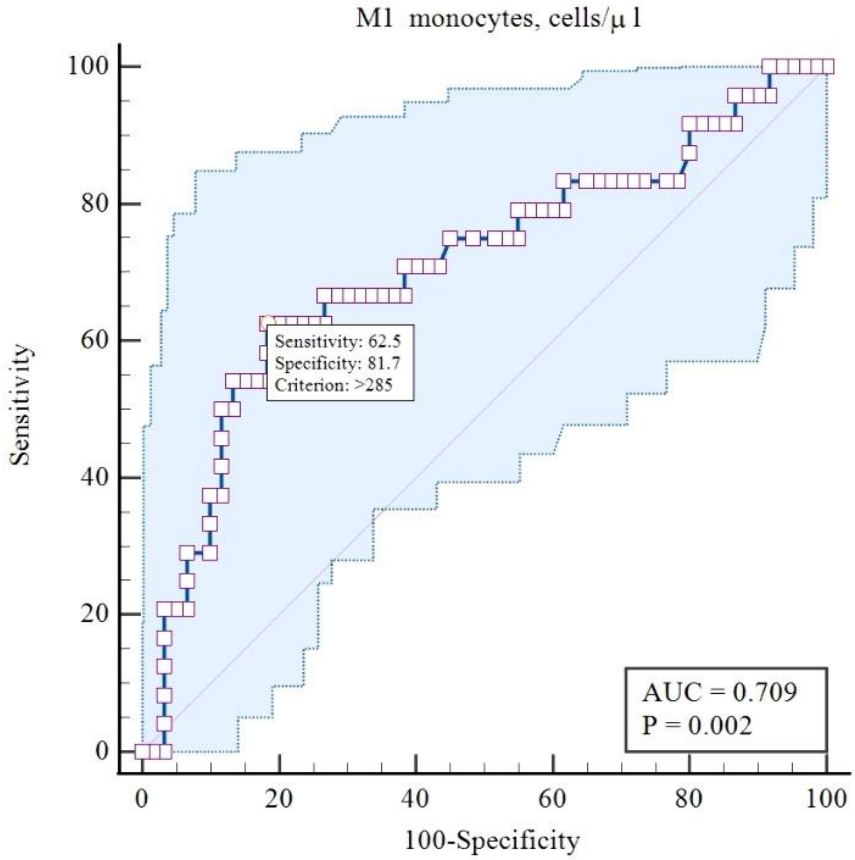

Figure 1. ROC curve for M1 monocytes According to Cox regression analysis, the number of circulating M1 monocytes greater than 285 cells/μL was associated with a 2.99-fold increase in relative risk of carotid atherosclerosis progression (95% CI 1.26-7.12; p=0.013).

Conclusions: In middle-aged patients without established atherosclerotic CVDs circulating M1 monocytes are a predictor of short-term progression of carotid atherosclerosis.

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#602

Topic: *AS02 Lipids and Lipoproteins / AS02.03 HDL*

INCREASED EXPRESSION OF MIR-223-3P AND MIR-375-3P IN HDL TOGETHER WITH A HIGH ANTI-INFLAMMATORY CAPACITY OF HDL IN BREAST CANCER

VIRTUAL E-POSTER SESSION

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Background and Aims: HDL has anti-inflammatory actions and transports microRNAs that may be involved in the pathogenesis of breast cancer (BC). It was determined the expression of miRNAs and the anti-inflammatory activity of HDL isolated from newly diagnosed, naïve-treatment BC women (n=40) in comparison to age and body mass index paired control women (n=10).

Methods: HDL was isolated from plasma by ultracentrifugation and its composition in lipids(total cholesterol, triglycerides, and phospholipids) was determined by enzymatic techniques, and apoA-I, by immunoturbidimetry. miRs were determined by RT-qPCR. Cholesterol-overloaded macrophages were incubated with HDL from BC and control women (24h).Then, cells were challenged with lipopolysaccharide (24h), and the secretion of interleukin6 (IL6) and tumor necrosis factor (TNF) were determined by ELISA. Comparisons were done by the Mann-Whitney and Kruskal-Wallis tests

Results: HDL composition in lipids and apoA-I was similar between the control and BC groups. IL6 and TNF secretion were, respectively,47% (p=0.0009) and 34% (p=0.0378) lower in cells treated with HDL from BC as compared to controls, especially in advanced stages of BC (stages III and IV; p=<0.0001;58%) in comparison to initial stages (I and II; p=0.0095;35%). miR-17-5p, miR-138-1-3p, miR-223-3p, and miR-275-3p were found in the HDL particle but only miR-223-3p and miR-375-3p were, respectively, 5.6x (p=<0.0001) and 2.2x(p=0.0224) more expressed in HDL from BC presenting a high discriminating capacity with the control group (respectively, AUC=1.000; p=0.0003 and AUC=0.8105; p=0.0254)

Conclusions: The increased anti-inflammatory capacity of HDL and differential expression of inflammation-related miRs in the HDL particle may contribute to BC pathophysiology and clinical outcome.

91ST EAS CONGRESS
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#193

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.13 Other*

ASSOCIATION OF FIBULIN-1, COAGULATION FACTORS AND PLASMINOGEN IN THE BLOOD WITH THE PRESENCE OF UNSTABLE ATHEROSCLEROTIC PLAQUES IN CORONARY ATHEROSCLEROSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the associations of blood proteins with the presence of unstable atherosclerotic plaques in the arteries in coronary atherosclerosis.

Methods: The study involved patients with coronary heart disease and coronary atherosclerosis (n=40), the average age of patients is 58±7 years. Protein concentrations in serum samples were determined using the PeptiQuant Plus Proteomics Kit. The identification of protein fractions was carried out by monitoring multiple reactions on a Q-TRAP 6500 mass spectrometer combined with a liquid chromatograph.

Results: Mass spectrometric identification revealed an increased concentration of proteins: fibrinogen, fibulin-1 and complement factor H in blood serum samples from patients with unstable atherosclerotic plaques. With a simultaneous decrease in the level of proteins: α-2-antiplasmin, heparin cofactor 2, coagulation factor XII, plasminogen, prothrombin, vitronectin, complement proteins (C1, C3, C7, C9) and complement factor B. The differences were considered significant at $p<0,05$. In addition, multivariate logistic regression analysis showed that the instability of atherosclerotic plaques is associated with the concentration of fibulin-1 (Exp(B) = 1,008; 95% CI 1,000-1,015; p = 0,05), plasminogen (Exp(B) = 0,995; 95% CI 0,990-0,999; p = 0,027) and coagulation factor X (Exp(B) = 0,973; 95% CI 0,949-0,998; p = 0,037).

Conclusions: The increased concentration of fibulin-1 can be considered as a potential biomarker of atherosclerotic plaque instability in coronary atherosclerosis. The possibility of using the studied proteins as biomarkers of atherosclerotic plaque instability requires further studies. *This study was conducted within the budget theme on the state task №122031700094-5 and within the framework of the RSF grant №21-15-00022*.

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#606

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

PATHOGENICITY CLASSIFICATION OF VARIANTS ASSOCIATED WITH FAMILIAL HYPERCHOLESTEROLEMIA: COMPARISON BETWEEN GUIDELINES

VIRTUAL E-POSTER SESSION

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Background and Aims: Familial Hypercholesterolemia (FH) is a genetic dyslipidemia caused by pathogenic variants several genes (mainly *LDLR*, *APOB* and *PCSK9*). The presence of one or two pathogenic variants determine different disease form, the heterozygous (HeFH) and the homozygous one (HoFH). We aimed to perform a systematic reevaluation of all variants identified in 717 index patients.

Methods: All identified variants (193) were classified according to the ACMG's guidelines (Richards et al. 2015) and the most recent FH-specific suggestions (Chora et al. 2018 for *APOB* and *PCSK9* and ClinGen – Chora et al. 2022 - for *LDLR*).

Results: The most recent guidelines led to an increased number of *LDLR* variants classified as uncertain significance (VUS) respect to the general ones (38 vs 18 variants) and, conversely, a decreased number of pathogenic/likely pathogenic ones (92 vs 113 variants). The criteria most impacting the difference in classification are related with the functional characterization, the number of unrelated patients with the variant and the consideration of missense variants in *LDLR*. Four HoFH patients resulted reclassified as HeFH+USV, despite a clear variant/phenotype segregation among relatives. No differences were observed about 45 variants in *APOB* and 11 variants in *PCSK9*.

Conclusions: New guidelines suggested FH-specific criteria useful for standardization of pathogenicity evaluation worldwide, although several variants resulted reclassified as USV. For rarest variants, guidelines could be improved giving more strength to the few available evidence, when no benignity criteria are present. The dissemination of frequency and segregation data present in molecular laboratory databases could improve the classification.

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#1128

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.04 Inflammation, immunity and infection in atherosclerosis*

SMOKING STATUS LEADS TO INCREASE IN FOOD INSECURITY AND CARDIOVASCULAR DISEASE IN THE UNITED STATES

VIRTUAL E-POSTER SESSION

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Background and Aims: Smoking is one of the few modifiable risk factors which leads to increased chances of lung cancer. Smoking status can also lead to Chronic Obstructive Pulmonary Disease (COPD). In this study we will look for the relationship between Food insecurity, cardiovascular mortality, and smoking status.

Methods: The National Health and Nutrition Examination Survey (NHANES) is a survey administered to non-institutionalized populations within the United States. Respondents of the NHANES survey aged 20 or older and between the years 1999-2010 were included in the analysis, with follow-up through 2015. Complex samples Cox regression to determine the relationship of food insecurity on cardiovascular-related mortality and the influence, if any, of smoking status.

Results: Percent mortality among individuals with CRP was more in males than females,. For cardiovascular mortality, the overall adjusted hazard ratio (HR) for food insecurity to no food insecurity was 1.66 (95% confidence interval [CI], 1.14-2.41, $p < 0.01$). The adjusted HR was elevated, 2.22 (CI 1.09-4.52, $p < .05$), among individuals who had CRS and diabetes but closer to 1.60 (CI 0.88-2.92, $p = 0.12$) among individuals who had cardiorenal syndrome only, after adjusting for medical and demographic risk factors.

Conclusions: While we were expecting the food insecurity is individually was related to mortality, however this is the first time anyone has shown that there is intersectionality between food insecurity and smoking status.

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#597

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.05 Extracellular matrix and calcification*

CITRULLINATION CONTRIBUTES TO THE DEVELOPMENT OF CAROTID ATHEROSCLEROSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: Citrullination is considered as a pivotal feature of autoimmune disorders (e.g., rheumatoid arthritis), yet anti-citrullinated protein antibodies are also associated with cardiovascular death and 3-fold more frequently detected in the serum of patients with coronary artery disease, even without rheumatoid arthritis, as compared to healthy blood donors. Here we investigated the role of citrullination in the development of carotid atherosclerosis.

Methods: The study included carotid atherosclerotic plaques excised during the carotid endarterectomy (n = 12) and adjacent intact arterial segments (n = 12). The levels of peptidylarginine deiminase (PAD) 2 and 4, as well as peptidylcitrulline, were measured by immunofluorescence staining and Western blotting. In addition, we also examined these proteins in plaque-derived extracellular vesicles isolated upon plaque homogenisation, filtration (1.0 μm), and ultracentrifugation at 200,000×g.

Results: The levels of peptidylcitrulline and PAD4, but not PAD2, were higher in carotid plaques as compared with adjacent intact segments. In keeping with these findings, plaques were characterised by a higher PAD4/PAD2 ratio. Both peptidylcitrulline and PAD2 were co-localised with neointimal cells whereas tunica media was devoid of these molecules. In contrast to peptidylcitrulline, PAD2 was highly (70-90% of the enzyme amount) co-localised with the extracellular vesicles within the neointima.

Conclusions: Citrullination is a frequent phenomenon in carotid atherosclerotic plaques, as adjacent tunica media is devoid of peptidylcitrulline and PAD4 and intact arterial segments contain significantly lower amounts of these molecules. This study was supported by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities), grant number 0419-2021-001 (https://www.rosrid.ru/ikrbs/detail/V7B4FOKSN5NU0QCFLCPK75S1).

91ST EAS CONGRESS
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#1049

Topic: *AS02 Lipids and Lipoproteins / AS02.06 Cholesterol efflux and reverse cholesterol transport*

ALTERATIONS IN HIGH-DENSITY LIPOPROTEIN PROTEOME AND LIPIDOME ASSOCIATED WITH THE IMPROVEMENT IN CHOLESTEROL EFFLUX CAPACITY IN INDIVIDUALS WITH ACUTE MYOCARDIAL INFARCTION: A LONGITUDINAL STUDY

VIRTUAL E-POSTER SESSION

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Background and Aims: Individuals with acute myocardial infarction (AMI) remain at high risk for recurrent cardiovascular (CV) events. Improving the cholesterol efflux capacity (CEC) of high-density lipoprotein (HDL) may reduce these CV events early after an AMI. In this study, we explored the changes in HDL composition associated with improvement in CEC in individuals with AMI

Methods: We recruited 100 individuals with AMI and followed them up for six months. CEC was quantified in the baseline and follow-up blood samples using THP-1 macrophages as cholesterol donors and apoB-depleted serum as the acceptor. We selected four individuals who showed maximum improvement in CEC. HDL proteome and lipidome of these individuals were analysed using liquid chromatography-tandem mass spectrometry. Paired t-test with a p-value adjusted for multiple comparisons was used to identify significantly altered proteins and lipids associated with improvement in CEC.

Results: Among the 247 proteins identified in the HDL, improved CEC was associated with a significant increase in phosphatidylcholine-sterol acyltransferase, apolipoprotein A-I, apolipoprotein A-II, and phospholipid transfer protein. Among the acute phase proteins associated with HDL, leucine-rich alpha-2-glycoprotein and serum amyloid A-4 increased as CEC improved, while C-reactive protein, serum amyloid A-1, complement C-2, complement factor 1, and protein S100 decreased. Seven hundred sixty-five unique lipid species were identified in HDL. Improvement in CEC was associated with significant alterations in 58 lipid species.

Conclusions: Improvement in CEC is associated with characteristic changes in HDL proteome and lipidome.

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#167

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

MIR-130B-3P ALLEVIATES PALMITATE-INDUCED LIPOTOXICITY VIA THE PPARϒ SIGNALING PATHWAY IN CARDIOMYOCYTES

VIRTUAL E-POSTER SESSION

Elena Alonso Villa[1,2], Fernando Bonet[1,2], Maribel Quezada-Feijoo[3], Monica Ramos[3], Maria Dolores Fernandez De Córdoba[2], Carlos Perez-Perez[1], Ismael Campanario[1], Alipio Mangas[1], Rocio Toro[1]
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Background and Aims: The heart is the most energy-demanding tissue of the body and utilizes fatty acids (FAs) for ATP generation. However, excess lipid accumulation in adult cardiomyocytes conduces to lipotoxicity, accompanied by overproduction of reactive oxygen species (ROS), and to cardiac dysfunction. It is well documented that peroxisome proliferator-activated receptor gamma (PPARϒ) modulates genes expression involved in uptake, storage, oxidation and synthesis of FA. Cardiomyocyte-specific overexpression of PPARϒ causes dilated cardiomyopathy associated to lipotoxicity in mice. In this context, we have previously demonstrated that miR-130b-30 is downregulated in plasma of idiopathic DCM patients. Analysis *in silico* show PPARϒ as potential target of miR-130b-3p, however whether miR-130b-3p may modulate lipotoxicity via PPARϒ is still unknown.

Methods: AC16 cells were transfected with miR-130b-3p *mimic* and supplemented with Palmitate (PA), as *in vitro* lipotoxicity model. PPARϒ and downstream PPARϒ expression levels were estimated by qRT-PCR. Mitochondrial oxidated stress status was assessed by MitoTracker Green together with Redox-Sensor.

Results: Our results showed that overexpression of miR-130b-3p rescued PA-induced PPARϒ expression. *CD36*, *PLIN2*, *FASN* and *CPT1B* expression were upregulated in PA condition but miR-130b-3p *mimic* presence significantly reverted the increased levels of CD36, PLIN2 and CPT1B. In agreement, the oxidative stress intensity was higher upon PA treatment and alleviated with miR-130b-3p overexpression.

Conclusions: These findings suggest that miR-130b-3p may exert a protector role against PA-induced lipotoxicity and associated damage in human cardiomyocytes through modulation of PPARϒ signaling pathway.

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#444

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

PREDICTORS OF REPEATED CARDIOVASCULAR EVENTS IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

Valentin Oleynikov, Elena Averyanova, Yulia Barmenkova, Anastasia Tonkoglaz, Marina Lukyanova
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Background and Aims: Search for predictors of recurrent cardiovascular events (CVE) in people after myocardial infarction with ST-segment elevation (STEMI).

Methods: 151 patients after STEMI were included, mean age 51 (95%CI 41-61) years, the majority are men (88%). All patients were treated according to guidelines (ESC, 2017) and high-dose atorvastatin therapy. As part of pharmacoinvasive strategy, the pain-to-stent interval was 8.9 hours (95%CI 7.5-12.3). Endpoints were hospitalization, PCI or coronary artery bypass graft due to damage to another coronary artery or restenosis, repeated MI, cardiovascular death. 2 groups were defined: "RE" - 26 (17.2%) - persons, who have undergone repeated CVE; "WE" - without them - 125 (82.8%). Patients of the "RE" group were 2.4 times more likely to have a history of coronary artery disease - 30.7% (p=0.048). Patients on the 7th-9th day of STEMI underwent: (1) 2D echocardiography with measurement of left ventricle end-systolic (LVESV) and end-diastolic volume (LVEDV), LV end-systolic (LVESD) and end-diastolic diameter (LVEDD); (2) daily ECG monitoring with analysis of chronotropic load parameters (Ta and Sa); (3) brain natriuretic peptide level (BNP); (4) measurement of height, weight, body mass index (BMI). The contribution of parameters to the development of the endpoint was assessed by the method of one-way regression analysis with determination of relative risk (RR).

Results: According to the results of one-way regression analysis, factors for the occurrence of repeated CVE
were:

Factor	RR (95%CI)	p
Weight	RR 1,21 (95%CI 1,01-1,46)	P=0,03
BMI	RR 0,56 (95%CI 0,325-0,96)	p=0,046
Parameter Ta	RR 1,03 (95%CI 1,02-1,12)	p=0,04
BNP	RR 1,012 (95%CI 1,003-1,08)	p=0,01
LVESD	RR 1,04 (95%CI 1,01-1,13)	p=0,036

Conclusions: Early independent predictors of recurrent CVE in STEMI patients are anthropometric indicators, Ta, BNP and LVESD.

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#1167

Topic: *AS04 Clinical Vascular Disease / AS04.02 Endothelial dysfunction; Clinical assessment*

ASSESSMENT OF THE GLOBAL, SEGMENTAL LEFT VENTRICLE STAIN IN CHILDREN WITH FAMILY HYPERCHOLESTEROLEMIA

VIRTUAL E-POSTER SESSION

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Background and Aims: Aim of the study: to assess the global, segmental longitudinal deformation of the left ventricle in children with familial hypercholesterolemia.

Methods: . The study was conducted on the basis of the Children's Lipidology Center at the Children's Republican Clinical Hospital (Kazan) from July to September 2022. The study involved 59 children, of which 25 healthy children made up the control group (mean age 10.1 (7.3–14.1) years) and 34 children diagnosed with heterozygous familial hypercholesterolemia included in the main group (mean age 10.5 (7.0–14.3) years). Echocardiographic study was carried out on the ultrasound scaner "Philips Epiq Elite" (USA) using the sector sensor S5-1 according to the standard method. The assessment of global and segmental longitudinal deformation of the left ventricle was carried out in 4-chamber apical, 3-chamber and 2-chamber projections using the automated measurement tool TOMTEC Autostrain LV.

Results: . There were no statistically significant differences in global longitudinal strain (GLS) between children in the control group and FH (-22.5(2.5)% and -21.2(2.9)%, respectively, p=0.072). An individual analysis showed that in 2 patients with FH, there was a decrease in GLS to -14.7% and -17.7%, respectively. Analysis of segmental longitudinal deformity revealed a statistically significant decrease in parameters in patients with FH at the level of the basal and apical anterior-septal, basal lower segments (-17.5(1.8)%, -17.8(2.7)% and -16 .4(3.1)%, respectively, $p<0.05$).

Conclusions: Conclusion. The use of speckle-tracking echocardiography made it possible to identify patients with a decrease in longitudinal deformation of left ventricle among children with FH, in absence of pathological abnormalities during standard echocardiography.

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#585

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.11 Plaque remodelling*

PROTEOMIC PROFILING OF CAROTID ATHEROSCLEROTIC PLAQUES AND ADJACENT INTACT ARTERIAL SEGMENTS

VIRTUAL E-POSTER SESSION

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Background and Aims: Although proteomic profiling studies become frequent in atherosclerosis research, there is still dearth of those investigating molecular signatures of advanced carotid atherosclerosis as compared with adjacent intact arterial segments.

Methods: Here we carried out a data-independent proteomic profiling of atherosclerotic plaques excised during the carotid endarterectomy (n = 12) and adjacent intact arterial segments (n = 12). Upon the extraction of total protein through tissue homogenisation, samples were enriched by ultracentrifugation at 200,000×g. Shotgun proteomics analysis was performed by ultra-high performance liquid chromatography–tandem mass spectrometry with ion mobility.

Results: We found 213 proteins upregulated in plaques and 111 proteins overexpressed in intact arterial tissues. Among the top 20 proteins overrrepresented in plaques were PON1, TREM2, haptoglobin, ApoB-100, fetuin-A, angiotensinogen, ApoD, and MMP-9. Both plaques and intact arterial segments showed molecular signatures of activated immune response, complement activaton, defense response to bacteria, phagocytosis, and extracellular vesicles secretion. Opposite to intact arterial segments, plaques beared signatures of positively regulated innate immune response, oxidative stress, macromolecule biosynthesis, coagulation, and programmed cell death. Signatures of adaptive immune response, including B cell activation, were unique for intact arterial segments.

Conclusions: Carotid plaques and adjacent arterial segments share a number of molecular signatures. Whereas plaques displayed activated innate immunity, intact segments showed upregulated B cell response. This study was supported by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities), grant number 0419-2021-001 (https://www.rosrid.ru/ikrbs/detail/V7B4FOKSN5NU0QCFLCPK75S1). Proteomics analysis have been conducted in the Centre for Molecular and Cell Technologies, Saint Petersburg State University Research Park.

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#443

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

SPECT-DERIVED MYOCARDIAL VIABILITY IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE AND LEFT VENTRICULAR DYSFUNCTION SELECTED FOR SURGICAL REVASCULARIZATION

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the interrelation between left ventricular (LV) systolic function and myocardial viability in patients with stable coronary artery disease (SCAD) and LV dysfunction (LVD) selected for coronary artery bypass grafting (CABG).

Methods: The cross-sectional study enrolled 21 SCAD patients with LVD selected for CABG (mean age 58±8 years; 18 males). Among them, 9 patients were selected for isolated CABG, and 12 patients – CABG with adjunct LV aneurism and/or valve surgery. The extent (%) of LV viable myocardium (VM) was assessed by single-photon emission computed tomography (SPECT). LV ejection fraction (EF) was measured by both transthoracic echocardiography (TTE) and SPECT.

Results: The extent of LVVM in the whole sample of patients was (hereinafter – median, interquartile range) 56 % (49-64 %) (min-max 40-70 %) (n=21). SPECT-derived LVEF was 24 % (17-28 %) (min-max 10-34 %) (n=19). At the same time, TTE-derived LVEF was 34 % (27-38 %) (min-max 11-44 %) (n=21). Both SPECT- and TTE-derived LVEF correlated significantly with each other (ρ = 0,490; p=0,033) (n=19). However, we did not reveal significant correlations of LVVM extent with both SPECT- and TTE-derived LVEF.

Conclusions: Among the enrolled SCAD patients with LVD undergoing CABG, both SPECT- and TTE-derived LVEF, generally, correlated with each other. At the same time, the SPECT-derived percentage of LVVM didn't correlate with LVEF evaluated by both methods. Higher levels of LVVM might be considered as an important additional criterion to perform surgical revascularization.

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#1157

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

THE MORNING BLOOD PRESSURE SURGE IN DIABETIC HYPERTENSIVE PATIENTS WITH DIFFERENT DIPPER PATTERNS.

VIRTUAL E-POSTER SESSION

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Background and Aims: This study aims the increase of morning blood pressure surge (MBPS) on the different dipper profiles of diabetic hypertensive patients, established by ambulatory blood pressure monitoring (ABPM).

Methods: 166 consecutive hypertensive patients with diabetes mellitus (DM) have performed 24 hours' ABPM. We follow MBPS, mean heart rate (MHR), mean arterial pressure (MAP) and the correlations of dipper profiles with the high blood pressure (HBP) treatment.

Results: There were: 80 non-dippers, 57 dippers, 22 reverse-dippers and 7 extreme-dippers. Non-dippers had MBPS: 12.871±11.152 mmHg, dippers: 17.370±12.594, p=0.0291, reverse-dippers: 13.318±7.498, p=0.860 and extreme-dippers: 25.142±12.482, p=0.0069. Non-dippers with beta-blockers (BB) in treatment (54) have MBPS 13.211±11.144 mmHg, those without BB (26) have 12.192±11.356. Dippers with BB (34) have MBPS 17.062±14.169 and those without BB (23) have 17.818±10.177. Non-dippers with angiotensin converting enzyme inhibitors (ACEI) (49) have MBPS 12.958± 10.112 and those without ACEI (31) have 12.733±12.824. Dippers with ACEI (36) have MBPS 15.818±12.312 and those without ACEI (21) have 19.809±12.944, p=0.251. Non-dippers and reverse-dippers (102) have MBPS 12.97±10.425 compared to dippers and extreme-dippers (64) have 18.262±12.725, p=0.004.

Conclusions: The dippers diabetics and extreme-dippers have grown MBPS compared to non-dippers and reverse-dippers. The non-dippers treatment with BB and ACEI does not significantly influence MBPS, as well the treatment of dipper with BB, but instead the treatment of dippers with ACEI leads to a decrease MBPS. The increasing MBPS is an important cardiovascular risk factor especially on the extreme-dipper profile.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1156

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

ATHEROSCLEROTIC LESIONS OF THE CORONARY AND CAROTID ARTERIES IN PATIENTS WITH RHEUMATOID ARTHRITIS.

VIRTUAL E-POSTER SESSION

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Background and Aims: To determine the frequency of atherosclerotic lesions of the carotid and coronary arteries in rheumatoid arthritis (RA) patients (pts).

Methods: To study 64 RApts with suspected CAD (male/female 25/38, mean age 58[52;63] years, with a long history of the disease (9[3;15] years).

Results: Carotid ASP was detected in 26% of RApts (Group I). In 74% pts are defined intact carotid arteries (Group II). Groups were comparable in terms of age, disease duration and DAS28. Males prevailed in Group I: 67% vs 33% in Group 2 (p<0,05). The prevalence of traditional risk factors was similar in both groups. Serum HDL-C concentrations in Group I (1,2[1,0;1,5]mmol/l) was lower, than in Group II (1,55 [1,3;2,0]mmol/l, *p*=0,03). CA stenosis was detected in 34% of pts: in 40% of the Group I (50% - single vessel, 50% - three-vessel damage), and in 33% of the Group II (75% - single vessel, 25% - three-vessel damage). The multiple regression analysis did not established a direct association between CA stenosis and gender, age, activity RA, cholesterol and LDL-C concentrations. The biggest, but not significant value for predicting stenosis spacecraft showed age (OR 0,85;95%CI[0,72-1,0], p=0,05) and HDL-C <1,2mmol/L for women and <1,0mmol/L for men (OR 0.82;95%CI[0,64-0,90], p=0,09).

Conclusions: Carotid ASP were diagnosed in 26% and CA stenosis - in 34% in RApts with suspected CAD. Only a third of RApts have a combined lesion of the carotid and coronary arteries. Male gender, low HDL-C seem to increase the risk of atherosclerotic lesions of the carotid and coronary arteries in RApts.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#440

Topic: *AS04 Clinical Vascular Disease / AS04.09 Lipid-lowering therapies*

EFFECT OF POLYPILL THERAPY ON LIPID PROFILE AND ARTERIAL STIFFNESS IN PATIENTS WITH DYSLIPIDEMIA, ARTERIAL HYPERTENSION AND COVID-19 IN DIFFERENT AGE GROUPS

VIRTUAL E-POSTER SESSION

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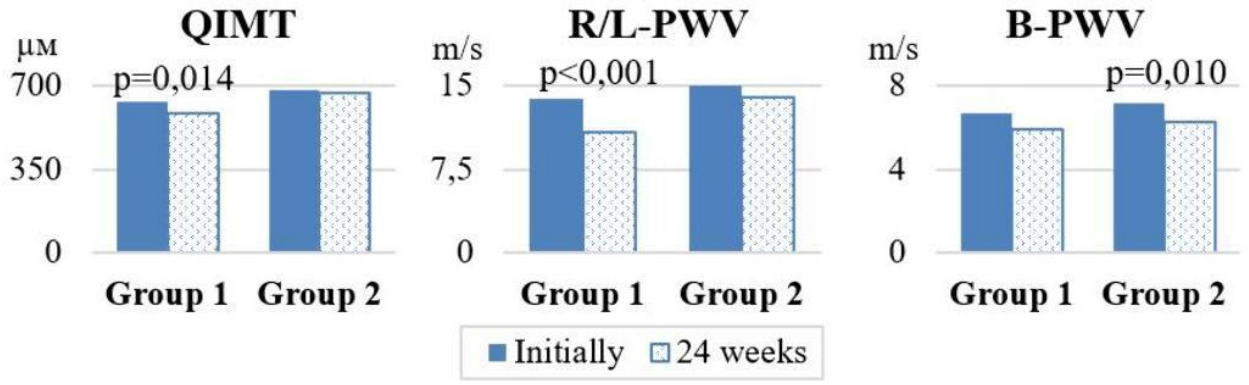
Background and Aims: To study the dynamics of lipid profile indicators, arterial stiffness during 12-week polypill therapy in patients younger and older than 50 years with dyslipidemia+arterial hypertension who underwent COVID-19.

Methods: 35 patients were included, who were divided into groups: group 1 (n=15) - under 50 years old, group 2 (n=20) - over 50 years old. Within 12 weeks patients took polypill (perindopril 4/8mg, indapamide 1.5/2.5mg, rosuvastatin 20mg). Initially and after 12 weeks total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were determined. Intima-media complex thickness (QIMT) of the carotid arteries was recorded using RF technology. Volume sphygmography was used to determine the pulse wave velocity in the arteries of predominantly elastic (R/L-PWV) and muscular types (B-PWV).

Results: In group 1, TC decreased from 5.9±1.1 to 3.5±1mmol/l (p<0.001), LDL-C cholesterol decreased from 3.8±1 to 1.8±0.8mmol/l (p<0.001). In the 2nd group, TC decreased from 6.7±1.2 to 4.1±0.7mmol/l (p<0.001), LDL cholesterol - from 4.4±0.8 to 2.3±0.6mmol /l (p<0.001). According to ultrasound of the carotid arteries, QIMT in the 1st group decreased by 7.9% (p=0.014). In the 2nd group, QIMT did not change. According to volume sphygmography, in group 1 R/L-PWV decreased by 21% (p<0.001); B-PWV has not changed. In group 2, B-PWV decreased by 12.5% (p=0.010); R/L-PWV has not changed.



Conclusions: 12-week polypill therapy in persons younger than 50 years contributed to the improvement of stiffness in the elastic type arteries, in the group older than 50 years - in the arteries of the muscular type with comparable dynamics of the lipid profile.

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MANNHEIM GERMANY | MAY 21-24, 2023

#1137

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

PROGNOSTIC VALUE OF ANGIOGRAPHY-DERIVED IMR IN PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING ROTATIONAL ATHERECTOMY

VIRTUAL E-POSTER SESSION

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Background and Aims: Rotational atherectomy(RA) is the major tool used to treat severely calcified lesions in patients with coronary artery disease (CAD). The relationship between coronary microvascular dysfunction and RA remains unknown. Therefore, we attempted to explore the predictive implications of the coronary angiography-derived index of microcirculatory resistance (angio-IMR) in CAD patients undergoing RA.

Methods: The study retrospectively included 118 patients with severe coronary calcification who underwent a successful RA procedure from January 2018 to June 2021. The angio-IMR was calculated based on computed flow and pressure dynamics principles to assess coronary microcirculatory function. In addition, follow-up was performed on all patients for major adverse cardiovascular events (MACEs), including all-cause death, non-fatal myocardial infarction, target vessel revascularization (TVR), and stroke.

Results: The mean angio-IMR for all patients was 25.58 ± 7.93. Fifty-four (45.8%) patients had angio-IMR ≥ 25. The logistic regression analysis showed that clinical factors and coronary physiological indicators were not significantly associated with coronary microvascular dysfunction. After median follow-up 21.7(15.1 - 24.0) months, MACEs (30.6%) occurred, including 12.5% all-cause deaths, 6.4% non-fatal myocardial infarction, 14.5% TVR, and 0.9% stroke. Kaplan-Meier analysis demonstrated that patients with angio-IMR ≥ 25 had greater cumulative MACEs (41.6%) and TVR (20.7%) than patients with preserved angio-IMR. Cox regression analysis indicated that angio-IMR ≥ 25 and reduced left ventricular ejection fraction were independent predictors of MACEs. In addition, angio-IMR ≥ 25 and lowered minimum luminal area independently predicted TVR occurrence.

Conclusions: In CAD patients undergoing RA procedure, angio-IMR ≥ 25 was an independent and significant predictor of MACEs and TVR.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1150

Topic: *AS04 Clinical Vascular Disease / AS04.11 Anti-inflammatory therapies*

THE DIAGNOSTIC AND PROGNOSTIC RELEVANCE OF THE CYTOKINE IL-17A IN OLDER PATIENTS WITH TYPE 2 DIABETES

VIRTUAL E-POSTER SESSION

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Background and Aims: Type 2 diabetes (T2D) is an age-related complex chronic disease associated with chronic inflammation. The cytokine IL-17A is emerging as a marker of chronic inflammation in cardio-metabolic conditions. The aim was to critically evaluate the diagnostic and prognostic utility of this biomarker in diabetic patients.

Methods: A total of 170 older (>50) patients diagnosed with T2D, attenders in primary care, were selected by the consecutive selection method. Independent associations of groups of variables indicating socio-demographic and clinical characteristics of patients with increasing values (quartiles) of IL-17A were determined by using multinomial regression models. The diagnostic value of IL-17A and its comparison with classical inflammatory markers (CRP, Neutrophil-Lymphocyte Ratio, and heamoglobin) were assessed using the c-statistics (ROC).

Results: The regression models showed that frailty and treatments with some oral hypoglycemic drugs, which interfere with IL-17A-related metabolic pathways, act to decrease IL-17A values, while some chronic diseases with inflammation in the background, such as osteoporosis, act to increase IL-17A values. A gender bias is significant to acknowledge when assessing inflammatory markers.

Conclusions: The discriminatory ability of IL-17A is best when it is used in combination with CRP in discerning diabetic patients based on the dichotomy “obese/not obese.” To take advantage of the diagnostic potential of inflammatory markers in complex chronic diseases, new clustering techniques and different types of variables should be used.

91ST EAS CONGRESS
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#1147

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

BILIVERDIN REDUCTASE B IS A PLASMA BIOMARKER FOR INTRAPLAQUE HEMORRHAGE AND A PREDICTOR OF ISCHEMIC STROKE IN SYMPTOMATIC CAROTID STENOSIS

VIRTUAL E-POSTER SESSION

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Background and Aims: Intraplaque hemorrhage (IPH) is a hallmark of atherosclerotic plaque instability. Biliverdin reductase B (BLVRB) is enriched in plasma and plaques from patients with symptomatic carotid atherosclerosis and functionally associated with plaque IPH. We explored the biomarker potential of plasma BLVRB through 1) its correlation with IPH in carotid plaques assessed by magnetic resonance imaging (MRI) and with recurrent ischemic stroke; and 2) its use for monitoring pharmacotherapy targeting IPH in a preclinical setting.

Methods: Plasma BLVRB levels were measured in symptomatic patients from the PARISK study (n=177, 5-year follow-up) with and without IPH upon MRI quantification. Plasma BLVRB levels were also measured in a mouse vein graft model of IPH at baseline and following anti-angiogenic therapy targeting vascular endothelial growth factor receptor 2 (VEGFR-2).

Results: Plasma BLVRB levels were significantly higher in patients with IPH (737.32 ± 693.21 vs 520.94 ± 499.43 mean fluorescent intensity (MFI), p=0.033), with no association to baseline clinical and biological parameters. Baseline plasma BLVRB levels were significantly higher in patients who developed recurrent ischemic stroke (1099.34 ± 928.49 vs 582.07 ± 545.34 MFI, HR = 1.600, CI [1.092- 2.344]; p=0.016). Plasma BLVRB levels were significantly reduced following prevention of IPH by anti-VEGFR-2 therapy in mouse vein grafts (1189 ± 258.73 vs 1752 ± 366.84 MFI; p<0.004).

Conclusions: Plasma BLVRB is a viable biomarker for IPH and plaque instability based on its 1) association with carotid plaque IPH, 2) higher levels in patients with recurrent ischemic stroke, and 3) capacity to monitor the efficacy of pharmacotherapy for IPH reduction.

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#1144

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

MONITORING OF PLASMA CIRCULATING DONOR DNA REFLECTS CARDIAC GRAFT INJURY

VIRTUAL E-POSTER SESSION

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Background and Aims: The current standard for graft rejection surveillance is endomyocardial biopsy (EMB), an invasive procedure with rare but potentially serious complications. Detection of circulating donor-derived cell-free DNA (ddcfDNA) is an option for noninvasive monitoring of graft injury and rejection.

Methods: Two patients (a 63-year-old man and a 65-year-old woman) were monitored (EMB) for allograft rejection. Forty-eight single-nucleotide polymorphisms (SNPs; with minor allele frequency (MAF) range 0.4-0.5) were screened to distinguish donor and recipient DNA based on homozygosity, and digital droplet PCR (ddPCR) was used to analyze ddcfDNA concentrations.

Results: Both subjects suffered rejection within the first 6 months after transplantation. The maximal ddcfDNA level (270 cp/mL) during EMB-confirmed acute cellular rejection (ACR; low grade 1R/2, patient 1), and the maximal concentration 1846 cp/mL in case of EMB-confirmed antibody-mediated rejection (AMR; grade 1+; patient 2) was detected.

Conclusions: Individual monitoring of ddcfDNA dynamics from the 1st to the 6th- month posttransplant (post-Tx) reflected cardiac graft injury in patients suffering ACR or AMR, meaning ddcfDNA could serve as a noninvasive biomarker.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#182

Topic: *AS04 Clinical Vascular Disease / AS04.10 Anti-thrombotic therapies*

THE ASSOCIATION OF CHADS-P2A2RC RISK SCORE WITH OUTCOMES IN PATIENTS TAKING P2Y12 INHIBITOR MONOTHERAPY AFTER 3 MONTHS OF DUAL ANTIPLATELET THERAPY FOLLOWING PERCUTANEOUS CORONARY INTERVENTION

VIRTUAL E-POSTER SESSION

Pil-Sang Song, Jin-Ok Jeong
Cardiology, Chungnam National University Hospital, Daejeon, Korea, Republic of

Background and Aims: The predictive value of the ischemic risk score and the appropriate antiplatelet regimen based on its stratum remains unclear. This study aimed to assess the predictive ability of the CHADS-P2A2RC in patients undergoing percutaneous coronary intervention (PCI) and its association with antiplatelet strategies.

Methods: This was a post-hoc sub-study of the SMART-CHOICE trial that compared P2Y12 inhibitor monotherapy after 3-months of dual antiplatelet therapy (DAPT) with prolonged DAPT (12 months or longer) in patients who underwent PCI. The randomized antiplatelet effect was assessed in three CHADS-P2A2RC risk groups. The primary outcome was a major adverse cardiac cerebral event (MACCE), a composite of all-cause death, recurrent myocardial infarction, or stroke.

Results: At three years, the high CHADS-P2A2RC risk group had the highest incidence of MACCE (105 (12.1%), adjusted hazard ratio (HR), 2.927; 95% confidence interval (CI), 1.358-6.309; *P*=0.006) followed by moderate-risk (40 (1.4%), adjusted HR, 1.786; 95% CI, 0.868-3.674; *P*=0.115) and low-risk (9 (0.5%), reference) (*P*=0.006). In sensitivity analyses, P2Y12 inhibitor monotherapy reduced the Bleeding Academic Research Consortium (BARC) types 2, 3, or 5 bleeding without increasing the risk of MACCE as compared with prolonged DAPT across the three CHADS-P2A2RC risk strata without significant interaction term (interaction *P* for MACCE = 0.705 and interaction *P* for BARC types 2, 3, or 5 bleeding = 0.055).

Conclusions: The CHADS-P2A2RC risk score is valuable in discriminating high ischemic risk patients undergoing PCI. Even in such patients, P2Y12 inhibitor monotherapy was associated with a lower incidence of bleeding without increased risk of ischemic events.

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#183

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

PREVALENCE AND PROGNOSTIC IMPLICATIONS OF WORSENING RENAL FUNCTION AFTER ACUTE MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

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Background and Aims: To investigate the relationship between worsening renal function (WRF) at one-year follow-up and clinical outcomes at three years after acute myocardial infarction (AMI).

Methods: We analyzed data from 13,104 patients enrolled in the national AMI registry from November 2011 to December 2015. Patients with all-cause death, recurrent myocardial infarction (re-MI), and re-hospitalization for heart failure (rHHF) at one-year follow-up after AMI were excluded. A total of 6,235 patients were extracted and divided into WRF and non-WRF groups. WRF was defined as a ≥25% decrease in estimated glomerular filtration rate (eGFR) from baseline to one-year follow-up. The primary outcome was three-year major adverse cardiac events (MACE), a composite of all-cause death, re-MI, and rHHF.

Results: On average, a -1.5 ml/min/1.73 m^2/year rate of decline in eGFR was exhibited, and 575 (9.2%) patients exhibited WRF at one-year follow-up. After multiple adjustments, WRF at one-year follow-up was independently associated with increased risks of MACEs (adjusted hazard ratio: 1.498, 95% confidence interval: 1.113-2.016, *P*=.01), all-cause death, and re-MI at three-year follow-up. Older age, female, diabetes, hypertension, non-ST segment elevation AMI, anterior AMI, anemia, left ventricular ejection fraction <35%, and baseline eGFR <30 ml/min/1.73 m^2 were identified as independent predictors of WRF after AMI.

Conclusions: At one-year follow-up after AMI, WRF was significantly associated with future adverse outcomes, and certain conditions may predict the development of WRF. These data highlight the need for follow-up assessment of renal function and appropriate secondary prevention for patients with risk factors for WRF after AMI.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1138

Topic: *AS04 Clinical Vascular Disease / AS04.11 Anti-inflammatory therapies*

BLACK CUMIN ETHANOLIC EXTRACT REDUCE AORTIC INTIMA MEDIA THICKNESS DUE TO CIGARETTE SMOKE EXPOSURE IN EXPERIMENTAL RATS

VIRTUAL E-POSTER SESSION

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Background and Aims: Cigarette smoking could induce pro-atherogenic changes seen in endothelial cells and increase inflammation markers due to oxidative stress. This can lead to increased intima media thickness of blood vessel and accelerate atherosclerosis. Black cumin (*Nigella sativa*) may inhibit oxidative stress. Aim of this study is to explore the link between cigarette smoking exposure to endothelial-nitric oxide synthase and vascular cell adhesion molecule-1 as well as the protective effects of black cumin in reducing aortic intima media thickness caused by cigarette smoking.

Methods: An experimental study with post-test only controlled group design was used in this study. Fifty Wistar rats (*Rattus norvegicus*) were divided into five groups: negative control (K(-)); positive control (K)+)) which exposed to 40 cigarettes/day for 4 weeks; and three groups exposed to cigarette smoke with the administration of black cumin ethanolic extract for four weeks at different doses: 0.3 g/kg/day (P1); 0.6 g/kg/day (P2); and 1.2 g/kg/day (P3). After interventions, aorta was removed and examined to measure the level of e-NOS, VCAM-1, and IMT.

Results: Using linear regression model, we found that black cumin ethanolic extract decreased VCAM-1 expression. VCAM-1 was positively correlated with aortic IMT ($r^2 = 0.102$, $\beta = 0.319$, $p = 0.038$). Black cumin ethanolic extract also increase e-NOS levels, however e-NOS did not correlate with aortic IMT ($r^2 = 0.165$, $p = 0.094$).There were significant correlations between black cumin ethanolic extract with increased e-NOS, decreased VCAM-1, and decreased aortic IMT.

Conclusions: Increased e-NOS and decreased VCAM-1 expression following black cumin ethanolic extract administration in rats exposed to cigarette smoke showed that black cumin may prevent endothelial dysfunction.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#197

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

GENERALIZED ATHEROSCLEROSIS: PATHOGENETIC MECHANISMS AND IT`S PHARMACOTHERAPY

VIRTUAL E-POSTER SESSION

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Background and Aims: An important place in the progression of generalized atherosclerosis (GAS) belongs to disorders of the neurotransmitter pool - serotonin(S), histamine(H) and dophamine(D). **The aim** is to investigate a complex of drugs aimed at reducing the degree of progression of atherosclerosis on the basis of the study of violations of S, H and D in patients with GAS.

Methods: We examined 54 patients with GAS (67.8±5.7) years with coronary, cerebral, peripheral atherosclerosis. The control group(CG) - 18 men (66.5±4.9) years. The level of S, H and D in blood serum (by ELISA). Volumetric blood flow(FV) in the cerebral, mesenteric and femoral vascular territories, Holter ECG monitoring and cognitive function were studied. The treatment: cilostazol(C) (100 mg/day) and aminalon(250 mg/day) were given during 12 weeks

Results: The initial examination of patients showed higher levels of S, H and D ($p<0.001$), compared to CG, in 4.3; 2.1 and 1.9 times, respectively. After 12 weeks of treatment, the level of S and H decreased by 37.9% and 16.4% ($p<0.05$), respectively, the level of D didn`t change significantly. An increase in FV was observed in all studied arteries, which was confirmed by a decrease in episodes of myocardial ischemia (by 21.6%; $p<0.05$), an improvement in cognitive function.

Conclusions: In patients with GAS, high levels of S, H and D were found, and the appointment of additional drugs led to a decrease in ultra-high levels of S and H without changing the level of D, which was reflected in the improvement of the clinical picture of patients and hemodynamic indicators.

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#1047

Topic: *AS02 Lipids and Lipoproteins / AS02.14 Other*

ADVANCED GLYCATION PRODUCTS MAY BE A GOOD PREDICTOR OF DECREASED COGNITION IN ELDERLY PEOPLE WITH DIABETES

VIRTUAL E-POSTER SESSION

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Background and Aims: The aging process can cause a series of changes in the body. In this phase of life there is a high incidence of the development of non-transmissible chronic diseases such as diabetes mellitus. The aim of this study was to assess the cognitive ability of diabetic elderly and correlate it with plasma lipids and skin autofluorescence (indicative of advanced glycation products - AGEs).

Methods: Our cross-sectional, quantitative study included 57 elderly men with a mean age of 70±3.9 (years) was approved by the local Ethics Committee (55683822.5.0000.0089). The global cognitive state was tested with Mini Mental State Examination. Serum total cholesterol, high-density lipoprotein cholesterol, and triglyceride levels were determined at the initial assessment using standard enzymatic colorimetric techniques. Low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol levels were calculated. Data were analysed by Graph Prism 9.0.

Results: The results showed a cognitive state below the cut-off point and high blood glucose values. As expected, a negative correlation was observed between age and cognitive status, surprisingly we observed that older individuals had lower plasma triglyceride values. Even though the individuals were diabetic, the average values of Triglycerides, non-HDL cholesterol, HDL-c, LDL-c were within the reference values. On the other hand, the values of fructosamine and skin autofluorescence (indicators that reflect the formation of AGEs) were positively correlated with age.

Conclusions: These data may indicate that in the diabetic population, plasma lipids are not a good predictor of cognitive impairment. Therefore, fructosamine and skin autofluorescence may be important for predicting cognitive impairment in this population.

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#944

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

STRUCTURAL AND FUNCTIONAL CHANGES IN ARTERIES IN PATIENTS WITH DIABETES MELLITUS AND CHRONIC KIDNEY DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: Chronic kidney disease (CKD) with diabetes mellitus (DM) is a major public health problem, resulting in significant cardiovascular and kidney adverse outcomes worldwide. **We aimed** to evaluate the structural and functional changes in arteries in patients with DM and chronic kidney disease (CKD).

Methods: A total of 449 patients with DT2 and DT1, aged 34 to 84 years (60 [60;72]), were examined. All patients underwent clinical and laboratory examination, ultrasound examination of the vessels of the lower extremities and brachiocephalic arteries (BCA).

Results: The thickness of the intima-media complex increased with an increase of cystatin C level in the right carotid artery (CA) (from 0.80 [0.70; 0.90] mm to 0.97 [0.90; 1.02] mm) and in the left CA (from 0.90 [0.80; 0.94] mm to 0.92 [0.90; 1.10] mm). Logistic regression analysis demonstrated that an increase of cystatin C level > 0.93 mg/l raises the risk of intima-media thickening by 2.5 times (OR 2.505, p=0.042) and by 5 times when increase of cystatin C>1.38 mg/l (OR 4.718, p=0.001). At the same time, the association with homocysteine was unreliable (p=0.058). The level of cystatin C ≥0.82 mg/l with a sensitivity of 72 % and a specificity of 52 % allowed to predict the development of subclinical atherosclerosis in patients with DM and CKD (ROC AUC – 0.739).

Conclusions: Cystatin C is not only a highly sensitive and accurate indicator of GFR, capable of detecting early stages of renal dysfunction, but also a highly effective predictive marker of atherosclerotic process in patients with DM and CKD.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#977

Topic: *AS04 Clinical Vascular Disease / AS04.10 Anti-thrombotic therapies*

CHARACTERISTICS OF CHANGES IN THE FUNCTIONAL ACTIVITY OF PLATELETS IN PATIENTS WITH ACS USING DIFFERENT REGIMES OF ANTIPLATELET TREATMENT.

VIRTUAL E-POSTER SESSION

Nataliia Kozachyshyn, Vasyl Netiazhenko, Olga Plenova
Department Of Propaedeutics Of Internal Medicine № 1, Bogomolets National Medical University, Kyiv, Ukraine

Background and Aims: Platelets play a leading role in the pathogenesis of atherosclerosis.The use of dual antiplatelet therapy (DAPT) avoid the development of ischemic events.The aim was to compare the effect of different regimens of antiplatelet treatment on the functional activity of platelets in patients with ACS at the time of hospitalization.

Methods: The 43 patients had a history of CAD and at the time of examination were taking DAPT:1 group (24pts) ASA 75 -100 mg and clopidogrel 75 mg/day), 2 group(19 pts) ASA 75-100 mg and ticargelor 180 mg/day.The control group consisted of 19 practically healthy persons.The state of functional activity of thrombocytes was studied using laser aggregometry by light transmission curves with evaluation of spontaneous aggregation and aggregation induced by arachidonic acid (AA),adenosine diphosphate(ADP),collagen,ristocetin and epinephrine in low doses.Statistical analyses perfomed by MedStat v.5.1

Results: The use of both regimens of DAPT led to suppression of platelet activity.The indicators of induced aggregation were significantly lower than the control ones.In the ticagrelor group we observed a more effective reduction in platelet aggregation AA (2.94[1.72;10.5]vs.6.37[4.33;15.0]p=0.031), ADP (34.4[9, 23; 41.5] vs. 50.3[30.7; 66.25]p=0.031) and epinephrine(20.9[3.76; 30] vs. 29.9[25.6; 40.7] p=0.036).The response of platelets to collagen and ristocetin did not differ between the groups.Application of DAPT did not lead to inhibition of spontaneous aggregation(0.43 [0.2;1.25] vs 3.85[1.2; 6.65]p=0.023), in the 1 group and (0.43[0.2;1.25] vs 1.64[0.79; 2.12] p=0.032) in the 2 group

Conclusions: DAPT results in a significant reduction in induced platelet aggregation,which is more effective in the ticagrelor group. But spontaneous aggregation remains at a high level.

91ST EAS CONGRESS
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#227

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

TARGETING INFLAMMATION IN PATIENTS WITH MYOCARDIAL INFARCTION, A NETWORK META-ANALYSIS

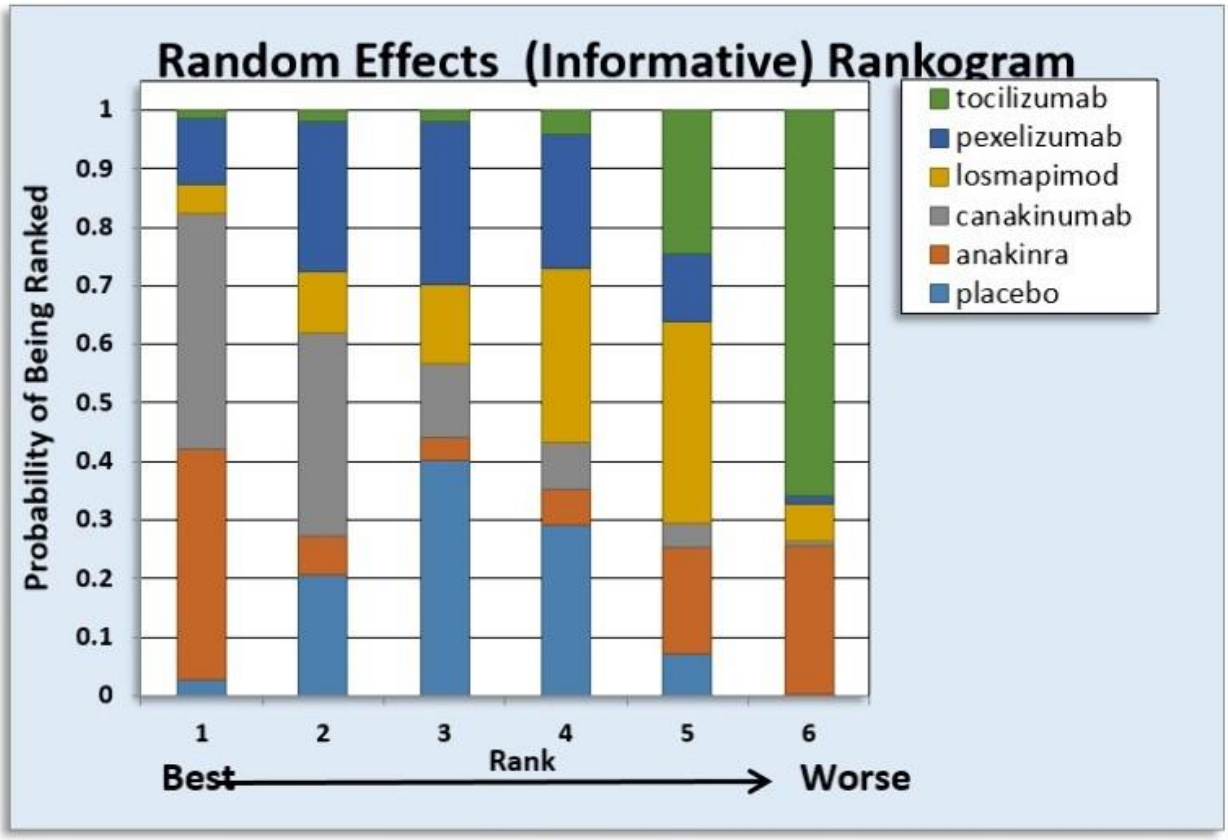
VIRTUAL E-POSTER SESSION

Hao Jin[1], Jiandong Ding[2], Wenbin Lu[2]
[1]Southeast University, southeast university, nanjing, China, [2]Zhongda Hospital, Southeast University, Zhongda Hospital, Southeast University, nanjing, China

Background and Aims: We performed a network meta-analysis to compare different medications targeting inflammation in myocardial infarction (MI) patients.

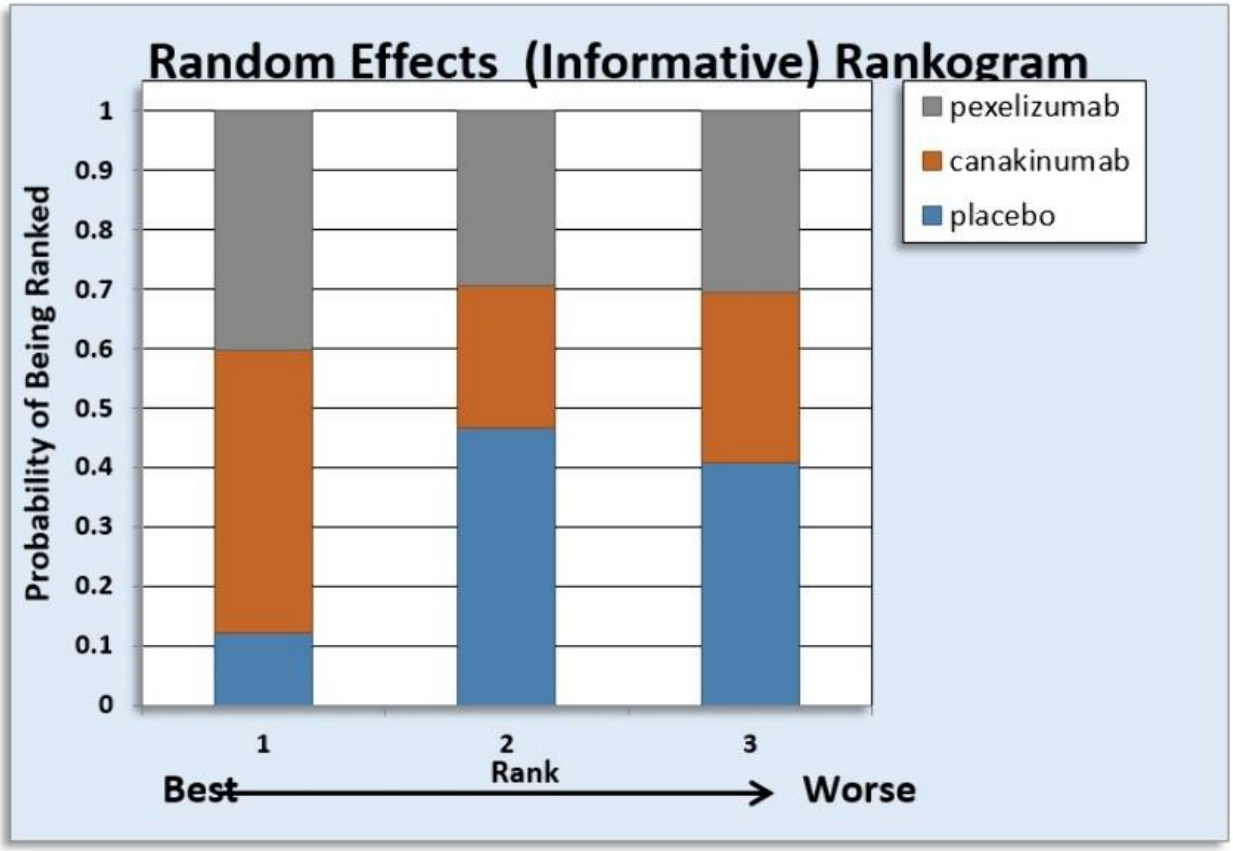
Methods: We searched PubMed, EMBASE and Cochrane Library with the items:" anakinra, canakinumab, tocilizumab, pexelizumab, losmapimod, myocardial infarction and acute coronary syndrome" through March 5, 2022, focusing on the randomized controlled trials (RCTs) evaluating the effect of drugs targeting inflammation in patients suffering from MI. The conventional meta-analysis was performed with Stata (version 12.0). Additionally, the network meta-analysis (NMA) would be performed with R (version3.5.1) and JAGS (version4.3.0) on the basis of gemtc package. Moreover, NetMetaXL (version1.6.1) and winBUGS (version1.4.3) would be employed to obtain the surface under the cumulative ranking curve area (SUCRA) of different medications.

Results: There was a high probability that canakinumab (SUCRA 0.79) would rank the first for preventing the incidence of MACE, followed by pexelizumab (SUCRA 0.60) and anakinra (SUCRA 0.53) (Figure 1). In addition, probability of ranking the first for preventing all-cause mortality was canakinumab (SUCRA 0.60), followed by pexelizumab (SUCRA 0.55) (Figure 2).With respect to reducing the risk of recurrent MI, tocilizumab (SUCRA 0.96) would rank the first, followed by canakinumab (SUCRA 0.71) (Figu



Treatment	SUCRA
canakinumab	0.7939
pexelizumab	0.5983
placebo	0.5627
anakinra	0.5348
losmapimod	0.4035
tocilizumab	0.1068

Figure 1: Ranking plots for the comparison on MACE in patients with MI.



Treatment	SUCRA
canakinumab	0. 596
pexelizumab	0. 5479
placebo	0. 356

Figure 2: Ranking plots for the comparison on all-cause mortality in patients with MI.

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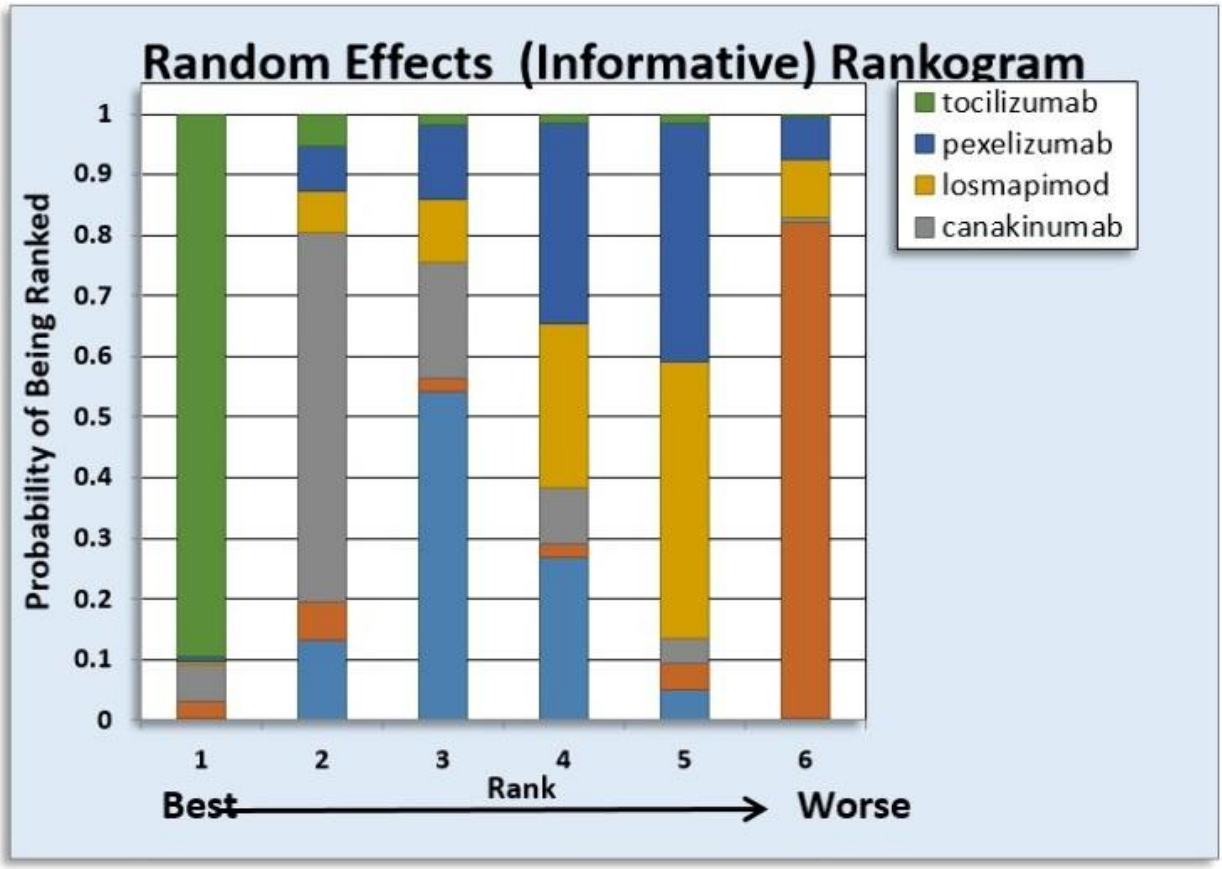

Treatment	SUCRA
tocilizumab	0.9575
canakinumab	0.7065
placebo	0.552
pexelizumab	0.3513
losmapimod	0.3218
anakinra	0.1109

Figure 3: Ranking plots for the comparison on recurrent MI in patients with MI.

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Conclusions: In patients with MI, canakinumab would be better choice for preventing the risk of negative incidence, including MACE, recurrent MI and all-cause mortality.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#630

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

EFFECT OF EPICARDIAL ADIPOSE TISSUE THICKNESS ON QT INTERVAL PROLONGATION IN PATIENTS WITH ARTERIAL HYPERTENSION AND NON-ALCOHOLIC FATTY LIVER DISEASE.

VIRTUAL E-POSTER SESSION

Irina Starodubtseva[1,2], Marya Derevyanchenko[1], Anastasia Streltsova[1]
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Background and Aims: To evaluate the effect of epicardial adipose tissue thickness (EATT) on corrected QT prolongation in patients with arterial hypertension (AH) and non-alcoholic fatty liver disease (NAFLD).

Methods: A cross-sectional comparative study was conducted, which involved 107 patients, aged 45 to 65, of both sexes with AH of I-II degrees, stages 1-2 (with NAFLD(FLI> 60) and without it).During the examination,a clinical examination was carried out: analysis of anthropometric parameters,ECG with the calculation of corrected QT (cQT) (the norm-450 ms for men and 460 ms for women),echocardiography with the definition of EATT.

Results: In comorbid patients, EATT was significantly higher (4.5[4.0;5.2] vs 3.5[2.5;3.5],p<0.001). It was found that in patients with hypertension and NAFLD, compared with patients with AH,cQT prolongation is more common (16(31.4)% vs 8(14.3)%,p=0.039),which indicates a greater risk of developing arrhythmias and sudden cardiovascular death in this category of patients. The regression analysis performed showed that when evaluating the dependence of cQT on EATT,a statistically significant direct correlation of moderate tightness was obtained:YcQT=299.3+28.9*XEATT,(ρ = 0.518;p=0.040).Based on the regression coefficient, a 1 mm increase in EATT was accompanied by a 28.9 ms increase in cQT.

Conclusions: This study showed that patients with AH and NAFLD had a statistically significantly higher incidence of QT prolongation on the ECG compared with patients with isolated hypertension. It was also found that an increase in EATT in patients with AH and NAFLD by 1 mm was accompanied by an increase in cQT by 28.9 ms, which may indicate a greater risk of cardiovascular events among this category of patients.

91ST EAS CONGRESS
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#632

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

REAL-LIFE ACHIEVEMENT OF LDL-C TARGETS IN PATIENTS WHO HAD EXPERIENCED ACUTE CORONARY SYNDROME.

VIRTUAL E-POSTER SESSION

Svetlana Bliznyuk[1], Natalia Lyahova[1], Anna Komarova[1], Marat Ezhov[2]
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Background and Aims: European guidelines set low-density lipoprotein cholesterol (LDL-C) goals <1.4 mmol/L after acute coronary syndrome (ACS). Many ACS patients do not achieve these goals. The study is aimed to assess lipid levels after hospitalization with ACS.

Methods: Botkin Hospital ACS Registry is recruited patients hospitalized with ACS and successfully treated.

Results: A total of 216 patients were included in registry. At follow up 191 (88%) patients were alive, 21 (10%) subjects died (5 patients died from cardiovascular causes) and 4 (5%) persons lost to follow-up. A total of 191 patients were included in final analysis (median age 64,5 [IQR 56; 74] years; 70% males, median follow-up 12 months). Patients' medical history included myocardial infarction (MI) (33.5%), percutaneous coronary intervention (46%) and coronary artery bypass grafting (8%). Comorbidities included hypertension (93%) and type 2 diabetes (19%); 32% subjects received statin therapy before hospital with ACS. At follow-up 181 (95%) persons were on a lipid-lowering therapy: 17% on a moderate-intensity statin, 73% were on high-intensity statin, 8% were on high-intensity statin plus ezetimibe, 2% were on proprotein convertase subtilisin/kexin type 9 inhibitor plus statin and/or ezetimibe. Median LDL-C level decreased significantly from baseline (from 3.5 to 1.9 mmol/L, $p < 0.001$). Proportion of patients with LDL-C level < 1.4 mmol/L was 16%. MI occurred in 4% of patients; 3% subjects suffered unstable angina and 3% - stroke.

Conclusions: Despite lipid-lowering therapy, many patients did not achieve LDL-C target by 12 months after an ACS event.

91ST EAS CONGRESS
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#633

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

STRUCTURAL CHANGES IN THE KIDNEYS IN PSORIATIC ERYTHRODERMA

VIRTUAL E-POSTER SESSION

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

Background and Aims: Psoriatic erythroderma is diagnosed in 2-3% of patients with psoriasis. This is a rare and severe generalized form of psoriasis that affects the skin of all parts of the body, but the visceral pathology determines the severity of the course and the prognosis of the disease. Kidney pathology or psoriatic nephropathy represents a heterogeneous group of diseases pathogenetically associated with psoriasis. Our aim was to examine the structural changes of the kidneys in patients with psoriatic erythroderma.

Methods: We have performed a clinical-morphological studies of outpatient cards data, disease histories and autopsy reports of 9 cases with psoriatic erythroderma at the life. Morphological changes in the kidneys in psoriatic erythroderma have been studied in all cases. The histological specimens of kidneys were stained by Hematoxylin–Eosin, Congo Red, performed a morphometric study.

Results: The main changes were characterized by mesangioproliferative (5 cases), membranoproliferative (1 case), mesangioproliferative in combination with amyloidosis (1 case), diffuse fibroplastic (2 cases) glomerulonephritis. Mesangioproliferative glomerulonephritis was focal and segmental. The specific volume of the nuclei of the vascular glomerulus was 22.29±10.5, which is 4 times more than the specific volume of the nuclei (4.49±2.02) of the unchanged kidney glomerulus. The specific volume in mesangiocapillary glomerulonephritis was smaller than in mesangioproliferative glomerulonephritis and was 16.96±10.34 because of a high degree of ischemia of the capillary loops and sclerosis of some loops of the glomerulus.

Conclusions: The extracapillary component, amyloid deposition in the glomeruli indicates the severity of psoriatic nephropathy. A morphological feature of nephropathy in psoriatic erythroderma is the polymorphism of structural changes.

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#982

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

BLOOD LIPID PROFILE AND ECG SIGNS OF LEFT VENTRICLE HYPERTROPHY IN PATIENTS WITH HYSTORY OF MYOCARDIAL INFARCTION

VIRTUAL E-POSTER SESSION

Ergashali Tursunov, Amayak Kevorkov, Nodir Zakirov, Alisher Rasulov
Cardiac Arrhythmias, Republican Specialized Scientific Practical Medical Center of Cardiology, Tashkent, Uzbekistan

Background and Aims: Purpose: Assessment of relationship between ECG signs of left ventricle hypertrophy (LVH) and blood lipid profile in patients with history of myocardial infarction and preserved left ventricle ejection fraction (LVEF).

Methods: Methods: study enrolled 525 patients with a history of MI (median age 63 [57; 69] years) and preserved LVEF. All patients underwent lipid profile determination and 12-lead ECG. In blood lipid profile total cholesterol (TC), triglycerides (TG), high density (HDL-C), very low density (VLDL-C), low density lipoprotein cholesterol (LDL-C) were determined. Also, non-high density lipoprotein cholesterol (non-HDL-C), TC/HDL-C ratio and plasma cholesterol coefficient (PCC) were calculated. As ECG signs of left ventricle hypertrophy (LVH) Cornell voltage (S in V3 + R in aVL), Cornell product ((Cornell voltage + 0.6 mV for females) × QRS duration) an Sokolow-Lyon Criteria (S in V1 (or V2) + R in V5 (or V6)) were calculated.

Results:

Table 1. Blood lipid profile and ECG signs of left ventricle hypertrophy

Blood lipid profile	Sokolow-Lyon	Cornell voltage	Cornell Product
TC	0,251*	0,190*	0,152
TG	0,041	-0,028	-0,029
HDL-C	0,155	-0,032	-0,060
VLDL-C	0,043	-0,031	-0,033
LDL-C	0,267*	0,271*	0,240*
nonHDL-C	0,224*	0,205*	0,168
TC/HDL-C	0,118	0,226*	0,232*
PCC	-0,094	-0,017	-0,011
All data presented as Spearmen correlation coefficient (R); * - p<0.05			

Results: The results obtained are presented in the table 1. Our data indicate the presence of a positive correlation between the most atherogenic fraction of the lipid profile – LDL-C and all three studied ECG signs of LVH. Both TC and nonHDL-C have positive correlation with Sokolow-Lyon and Cornell voltage criteria. TC/HDL-C ratio is demonstrated positive correlation with both Cornell voltage and product signs.

Conclusions: Conclusion: In patients with history of MI and preserved LVEF there is a significant relationship between ECG signs of LVH and blood lipid profile parameters. The most pronounced correlation with LVH signs was noted between LDL-C, TC, nonHDL-C fractions and TC/HDL-C ratio.

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#636

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.14 Epigenetics and microRNA*

DIFFERENT EFFECTS OF ATORVASTATIN AND ROSUVASTATIN ON CIRCULATING MICRORNAS-126 AND 146A LEVELS IN PATIENTS WITH CORONARY ARTERY DISEASE WITH TYPE 2 DIABETES MELLITUS

VIRTUAL E-POSTER SESSION

Serhii Serik[1], Vladyslav Riabukha[1], Natalia Mavrycheva[1], Viktoriia Malko[1], Tetiana Bondar[2]
[1]Department Of Ischemic Heart Disease, Metabolic And Cardiopulmonary Disorders, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine, [2]Laboratory Of Immuno-biochemical And Molecular-genetics Researches, L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine

Background and Aims: The lipid-lowering and pleiotropic effects of statins might be mediated by microRNAs. The purpose of the study was to investigate the effects of atorvastatin and rosuvastatin on circulating anti-inflammatory microRNAs-126 and 146a levels in patients with coronary artery disease (CAD) with type 2 diabetes mellitus (T2DM).

Methods: The study included 49 patients with CAD with T2DM with statin treatment at least 3 months (atorvastatin 20-40 mg/day – 23 patients, rosuvastatin 10-20 mg/day – 26 patients), 18 statin-naive CAD patients with T2DM. Circulating microRNAs-126-3p and 146a-5p were determined in blood plasma by real time PCR. Results expressed in relative units.

Results: In atorvastatin-treated CAD patients with T2DM microRNA-126 level (52,02 [23,10; 94,03]) was increased in comparison with non-statin-treated patients (21,65 [10,86; 55,51]) with borderline significance (p=0,062). In rosuvastatin-treated patients microRNA-126 level (60,39 [26,52; 100,58]) was higher than in statin-naive patients (p=0,010). MicroRNA-146a level in atorvastatin-treated patients (15,34 [30,20; 58,58]) was increased in comparison with statin-naive patients (4,24 [14,16; 23,85], p=0,012). In rosuvastatin-treated patients microRNA-146a level (12,60 [19,14; 40,99]) was higher than in non-statin-treated patients with borderline significance (p=0,096). The Kruskal-Wallis test proved a significant difference in both microRNA-126 and 146a levels between three groups (p=0,034, p=0,028). LDL-C and Non-HDL-C levels in both statin-treated groups were significantly lower than in statin-naive patients.

Conclusions: In CAD patients with T2DM atorvastatin and rosuvastatin may affect microRNAs-mediated epigenetic mechanism. Treatment with atorvastatin contributed to the more pronounced elevation of circulating microRNA-146a level and the use of rosuvastatin was associated with the greater increase of microRNA-126 expression.

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#236

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.01 Epidemiology of cardiovascular diseases and risk factors*

INFLAMMATION AND DYSLIPIDAEMIA AS THE ADDITIONAL RISK FOR STROKE IN PATIENTS WITH ATRIAL FIBRILLATION

VIRTUAL E-POSTER SESSION

Svetlana Grigoryan[1], Arthur Stepanyan[2], Parunak Zelveian[3], Lusine Hazarapetyan[1]
[1]Chair Of Cardiology, Yerevan State Medical University, Yerevan, Armenia, [2]Cardiology Chair, Yerevan State Medical University, Yerevan, Armenia, [3]Arrhythmia, Yerevan State Medical University, Yerevan, Armenia

Background and Aims: Atrial fibrillation (AF) is often accompanied by complications, especially ischemic stroke. AF is associated with atrial structural changes that may have an inflammatory basis. Dyslipidemia is the basis for the development of atherosclerotic diseases, their role in the development of AF is not entirely clear, and previous studies suggest a "cholesterol paradox". The aim of this study is to investigate the relationship between inflammation markers and dyslipidemia risk in patients with AF and stroke

Methods: . We observed 441 patients with AF during 5 years. In addition to general clinical examination, total cholesterol (TC), low density lipoproteins (LDL), triglycerides (TG), as well as C reactive protein (hsCRP) and Interleukin-6 (IL-6) were determined in patients. All of blood tests were determined by ELISA .

Results: Among 441 patients with AF in 137 patients ischemic stroke was detected. In these patients there was increase in inflammatory markers compared with other patients with AF. The significant differences between the levels of hsCRP are 6, 7± 1.8 vs 3.2±0.6 p = 0.002 and level of IL-6 is 4.2± 0.8 vs. 2.6± 1.1 p = 0.043. The levels of TC and TG were higher than normal in both groups, but LDL was significantly higher in patients with stroke 4.21 ± 0.6 vs 3.99 ± 0.4 mml/l p = 0.043.

Conclusions: Conclusion: We have demonstrated that in patients with AF and stroke the increase inflammation markers and LDL level.

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#996

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.05 Extracellular matrix and calcification*

A1A ADRENOCEPTOR BLOCKADE ATTENUATES CARDIAC HYPERTROPHY VIA MODULATION OF INTEGRIN-LINKED KINASE: POSSIBLE UNDERLYING MECHANISMS

VIRTUAL E-POSTER SESSION

Nouf Alrasheed, Sara Altalasi, Nouf Almutairi, Hatun Alomar, Maha Alamin, Haya Alrajeh, Iman Hasan, Hana Alajmi, Lama Alkhader, Nouf Al-Damry, Asma Alonazi, Anfal Bin Dayel, Tahani Alshammari, Wedad Sarawi, Nawal Alrasheed
Pharmacology And Toxicology, King Saud University, RIYADH, Saudi Arabia

Background and Aims: There is no clear evidence indicating an α_{1A} adrenoceptor blockade's ability to attenuate cardiac hypertrophy by modulating ILK-related angiogenesis. Thus, we hypothesize that inhibition of α_{1A} adrenoceptors using tamsulosin attenuates cardiac hypertrophy via ILK-related angiogenesis.

Methods: Twenty-four male Wistar rats (150–250 g) were randomly divided into four groups: a healthy control group receiving 0.9% NaCl orally for 14 days; isoproterenol (ISO)-treated group receiving 0.9% NaCl for seven days, followed by ISO (5 mg/kg/day, i.p) for seven consecutive days beginning on day seven; tamsulosin-treated healthy group receiving tamsulosin (0.4 mg/kg/day, orally) for 14 days; and tamsulosin+ISO-treated group treated with tamsulosin for 14 days, and injected daily with ISO for seven consecutive days beginning on day seven. The heart/body weight ratios and cardiac and angiogenic biomarkers were assessed. The protein expression levels of ILK, eNOS, p-PI3K, p-Akt, Flt-1, PECAM-1, and VEGF were detected and a histopathological examination of fixed-heart sections was performed.

Results: Tamsulosin significantly attenuated the cardiac hypertrophy index (4.20 ± 0.24 vs. 5.20 ±0.31 mg/g, $p<0.05$) and cardiac biomarkers such as troponin I and CK-MB (54.54 ± 24.78 vs 162.7.75 ± 29.69 pg/ml, $p<0.001$; 1.09 ± 0.24 vs 2.22 ± 0.76 ng/ml, $p<0.01$, respectively) compared to ISO-control group. Moreover, tamsulosin reversed histopathological changes in cardiac tissues and mediated significant increase protein expression levels of VEGF, eNOS, ILK, p-PI3K, p-Akt, Flt-1, and PECAM-1 compared to the ISO-control group.

Conclusions: Targeting α_{1A} adrenoceptors by inhibition offers a promising therapeutic approach for preventing cardiac hypertrophy via signal-transduction pathways including ILK-related VEGF/eNOS/PI3K/Akt.

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#638

Topic: *AS04 Clinical Vascular Disease / AS04.01 Coagulation and Thrombosis*

THROMBOINFLAMMATION PREVENTION IN COVID-19 HOSPITALISED PATIENTS: A RETROSPECTIVE STUDY

VIRTUAL E-POSTER SESSION

Georgios Chatzis[1], Maria Vlachopoulou[2], Konstantinos Koronios[3], Eleni Stratigaki[1], Dimitra Fellouri[1], Giorgos Aleiferis[1], Pantelis Koulouris[1], Maria Gasparaki[1], Panagiotis Nikolinakos[1], Sofoclis Bakidis[1]
[1]Internal Medicine, General hospital of Lakonia, Molaoi Lakonias, Greece, [2]Cardiology, General hospital of Lakonia, Molaoi Lakonias, Greece, [3]Administration, General hospital of Lakonia, Molaoi Lakonias, Greece

Background and Aims: Thrombotic complications of SARS-CoV-2 infection were recognized early in the pandemic, when infected patients often presented with abnormal coagulation findings and acute macrovascular obstruction. Our aim in these study is to determine if with thromvoinflammation prevention we can avoid these complications in hospitalised patients with COVID-19

Methods: We recorded all patients that were hospitalised from January 2022 to April 2022, in Molaoi COVID -19 unit, with PCR confirmed SARS - CoV-2 respiratory inflammation. Patients were recorded for existing comorbidities and clinical outcome during their hospitalisation. Also patients were recorded for the use of Low Molecular Weight Heparin (LMWH) or other thrombolitic agents during and after their hospitalisation, use of anakinra (Kineret), and corticosteroids as anti inflammatory agents.The raw data was statistically corellated using the SPSS statistical package

Demographics

Sex	42 female - 21 male
Age range	9 patients <60, 54 patients >60
Mortality	11 patients
LMWH	40 patients

Results: Of the 53 patients that they were recorded, LMWH was used in 40 of them. Mortality was statisticaly significant reduced in thath group, and statistically important (p<005) was the rduced number of thrombotic event and rehospitalisations in that group. Use of Anakinra also was statisticaly significant for the reduced mortality. Not statistical significant findings between the Delta and Omicron Variants. Diabetic patiens had incread mortality (18%) in contrast to the non diabetic patients. Patient that received corticosteroids after discharge had reduced prevalence of rehospitalisation.

Conclusions: All hospitalized patients with COVID-19 and low risk of bleeding should receive at least prophylactic-dose anticoagulation with a heparin anticoagulant

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#966

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

BODY SURFACE AREA AND GENDER-RELATED DIFFERENCES IN OUTCOMES OF PATIENTS WITH PERIPHERAL ARTERY DISEASE

VIRTUAL E-POSTER SESSION

Qiaoqing Zhong, Rayaan Yunus, Adnan Khan, Feroze Mahmood, Aidan Sharkey, Mahad Sohail, Taha Abdul Rehman, Yifan Bu, Robina Matyal
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Background and Aims: Peripheral artery disease (PAD) is a major atherosclerotic disease commonly associated with significant morbidity and mortality. Prior studies have found that the prognosis of PAD is inversely proportional to BMI, however, BMI is limited in differentiating excess from lean body mass and does not account for height within its calculation. Given doubts on the role of BMI as an assessment tool for cardiovascular risk, we investigated the gender-specific influence of body surface area (BSA) on outcomes following peripheral arterial interventions to determine whether BSA is a better indicator of atherosclerotic risk.

Methods: We conducted a retrospective review using data from the Vascular Quality Initiative database for patients who underwent peripheral arterial interventions between 2009 and 2020. The relationship between gender and 30-day post-operative outcomes was calculated using multivariable analysis.

Results: A total of 130,428 patients were included, 35% of which were female. Female patients were more commonly older and hypertensive, and presented with decreased preoperative drug use as compared to males. BMI<30 kg/m^2 and BSA>2.1 m^2 were key predictors for all-cause morbidity in both genders, however, BSA>2.1 m^2 had a stronger bearing on outcomes in women. Female patients had a significantly higher post-operative risk of all-cause morbidity, mortality, cardiac complications and

pulmonary complications.

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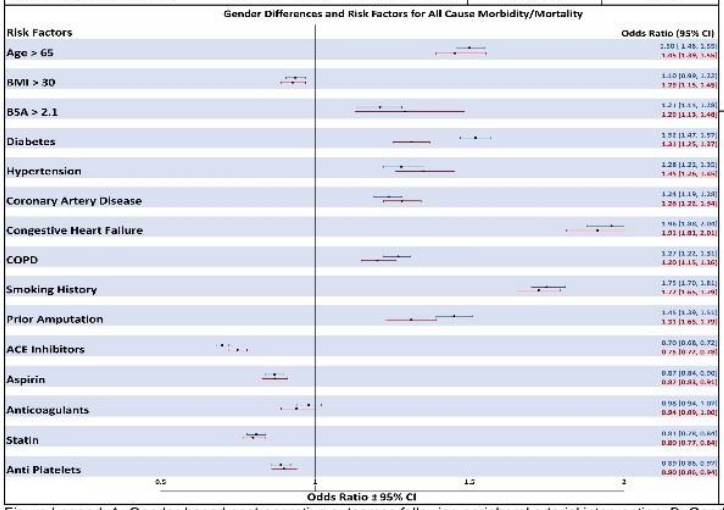
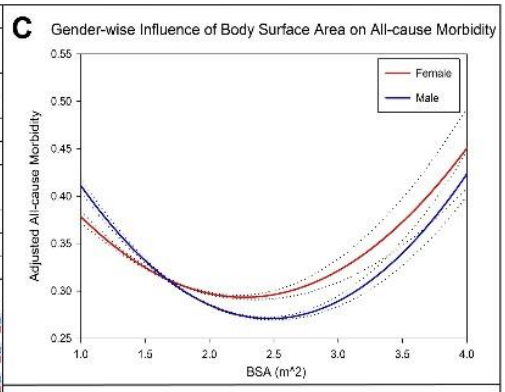
Primary Outcome	Male (n=85,394)	Female (n=45,034)	Adjusted Analysis	
			Odds Ratio (95% CI)	Bonferroni Adjusted p-value
Post-operative Complications	24,564 (28.8)	13,950 (31.0)	1.08 (1.06, 1.11)	**<0.001**
Mortality	16,295 (19.1)	9,622 (21.4)	1.11 (1.08, 1.13)	**<0.001**
Cardiac Complications	2,599 (3.0)	1,576 (3.5)	1.15 (1.09, 1.21)	**<0.001**
Pulmonary Complications	2,113 (2.5)	1,356 (3.0)	1.20 (1.13, 1.27)	**<0.001**
Renal Complications	3,916 (4.6)	1,877 (4.2)	0.89 (0.85, 0.93)	**<0.001**
Surgical Site Complications	1,776 (2.1)	1,021 (2.3)	1.09 (1.02, 1.16)	0.054
Return to the Operating Room	7,907 (9.3)	3,811 (8.5)	0.92 (0.89, 0.95)	**<0.001**
Hospital Length of Stay	5.00 (2.00 – 10.00)	5.00 (2.00 – 10.00)	0.00 (0.20)	0.63
Post-operative Length of Stay	4.00 (2.00 – 7.00)	5.00 (3.00 – 8.00)	0.01 (0.09)	**0.048**

B



C



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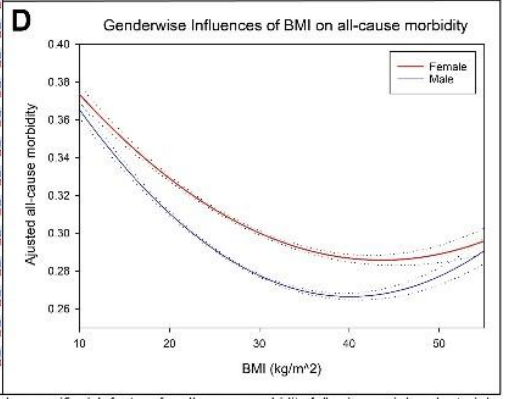

Figure Legend: A: Gender-based post-operative outcomes following peripheral arterial intervention; B: Gender-specific risk factors for all-cause morbidity following peripheral arterial intervention; C: Gender-wise influence of body surface area on all-cause morbidity; D: Gender-wise influence of body mass index on all-cause morbidity

Conclusions: High BSA is associated with adverse outcomes in a gender-neutral fashion and may be a better indicator of atherosclerotic risk than BMI. However, increasing BSA has a stronger bearing on PAD outcomes in women; future studies should investigate underlying gender-based mechanisms to personalize treatment in patients with PAD.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#957

Topic: *AS04 Clinical Vascular Disease / AS04.04 Chronic kidney disease and nephropathies*

PREDICTIVE POSSIBILITIES OF BLOOD INDICES IN ELDERLY AND SENILE PATIENTS WITH CARDIOVASCULAR COMORBIDITY AND CHRONIC KIDNEY DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: Chronic kidney disease (CKD) requires complex and comprehensive examination in patients with cardiovascular disease. There are no data to evaluate the predictive ability of blood indices in elderly and senile patients with cardiovascular comorbidity and chronic kidney disease

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).The ratio of neutrophils to lymphocytes (N/L ratio), eosinophils to leukocytes (Eo/Leu ratio), and monocytes to lymphocytes (M/L ratio) were calculated. Follow-up period was 1 year, primary endpoint - all-cause mortality.

Results: A lower Eo/Leu ratio was observed in patients with CKD compared with patients without CKD: 0.02 (0.01; 0.10) and 03 (0.01; 0.17), p=0.04.
When evaluating the prognostic value of laboratory parameters, it was found that the N/L ratio more than 3.88 is associated with mortality within a year in elderly and senile patients with CKD (sensitivity - 50%, specificity - 83.5% (AUC = 0.67); p=0.002). The M/L ratio more than 0.23 determined mortality within a year in elderly and senile patients with CKD (sensitivity - 92.9%, specificity - 52.2% (AUC=0.71); p<0.0001). Logistic regression analysis showed that an increase in the M/L ratio more than 0.23 in elderly and senile patients with CKD was associated with a significant risk of death (RR 9.8; 95% CI 2.83-33.97; p=0.0004).

Conclusions: The highest predictive value with a sensitivity (92.9%) and a specificity of 52.2% was found for the ratio of monocytes to lymphocytes (M/L ratio).

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#423

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

LOW HIGH-DENSITY LIPOPROTEIN LEVEL IS A RISK FACTOR FOR POSTVACCINATION COVID-19 IN HEMODIALYSIS PATIENTS

VIRTUAL E-POSTER SESSION

Natalia Stepanova[1], Andriy Rysyev[2], Lyudmila Snisar[1]
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Background and Aims: The association between baseline HDL levels and postvaccination COVID-19 in hemodialysis (HD) patients has never been investigated. The present study aimed to investigate the association between baseline HDL levels and postvaccination COVID-19 in HD patients.

Methods: A total of 170 HD patients aged 56 (44-63.2) years with a dialysis vintage of 44 (21-76.6) months were enrolled in this prospective observational cohort study. Baseline HDL was defined as the last measurement before the vaccination date. For statistical analysis, the Mann-Whitney and χ^2 tests, receiver operating characteristic (ROC), and Cox regression analyses were performed.

Results: Of the 170 HD patients enrolled in the study, 67 (39.4%) had received complete vaccination against COVID-19 with mRNA vaccines, and 103 (60.6%) patients had not been vaccinated for various reasons. During the 12-month follow-up period, 83/170 (48.8%) were infected with COVID-19, including 18/67 (26.7%) vaccinated patients and 65/103 (63.1%) patients who were not vaccinated (χ^2=10.8; p=0.001) Baseline HDL was significantly lower in HD patients with postvaccination COVID-19 compared to uninfected patients: 1.07 (0.88-1.16) vs. 1.8 (1.6-2.08) mmol/L, p <0.0001. The ROC analysis showed that the most appropriate cut-off point for baseline HDL level to predict postvaccination COVID-19 was ≤1.22mmol/L, with a sensitivity of 93.7% and specificity of 94.7% (Fig. 1).

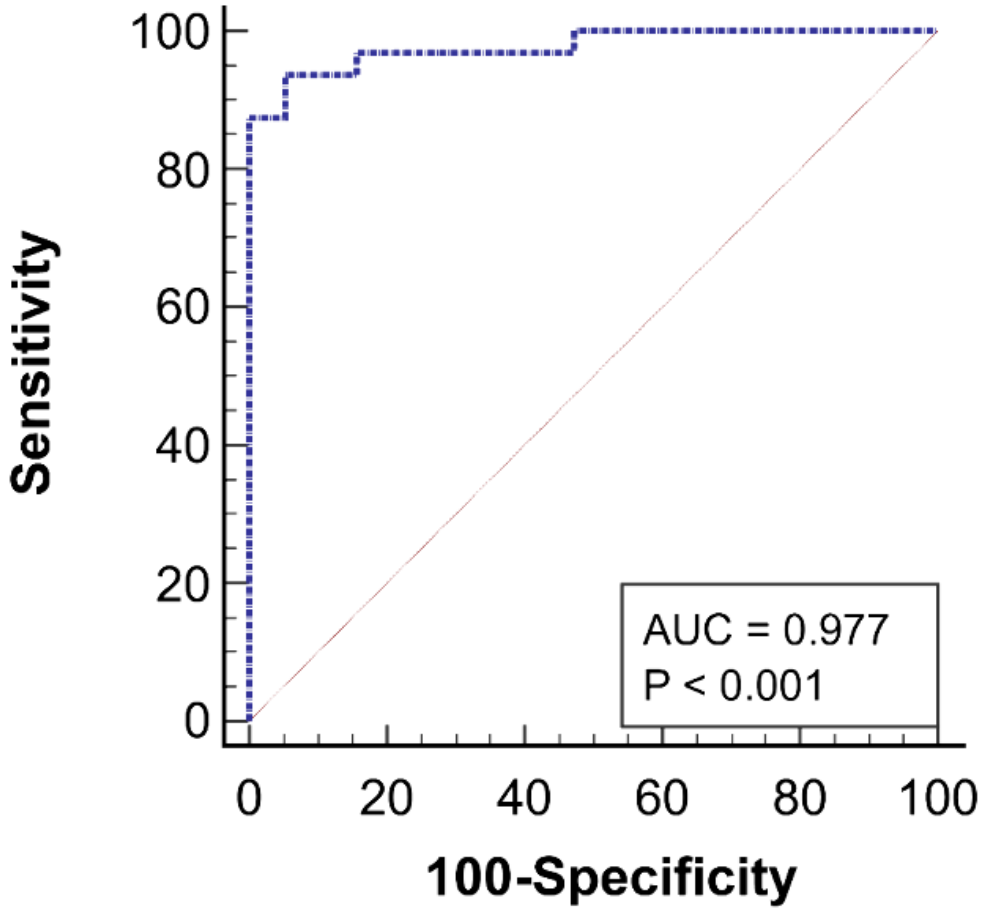

Fig. 1. The ROC curve for the cut-off value of HDL level for predicting postvaccination COVID-19 in HD patients

Cox regression analysis adjusted for age, sex, diabetes, and dialysis vintage showed that HDL level <1.22 mmol/L was associated with postvaccination COVID-19 in HD patients (Fig

2).

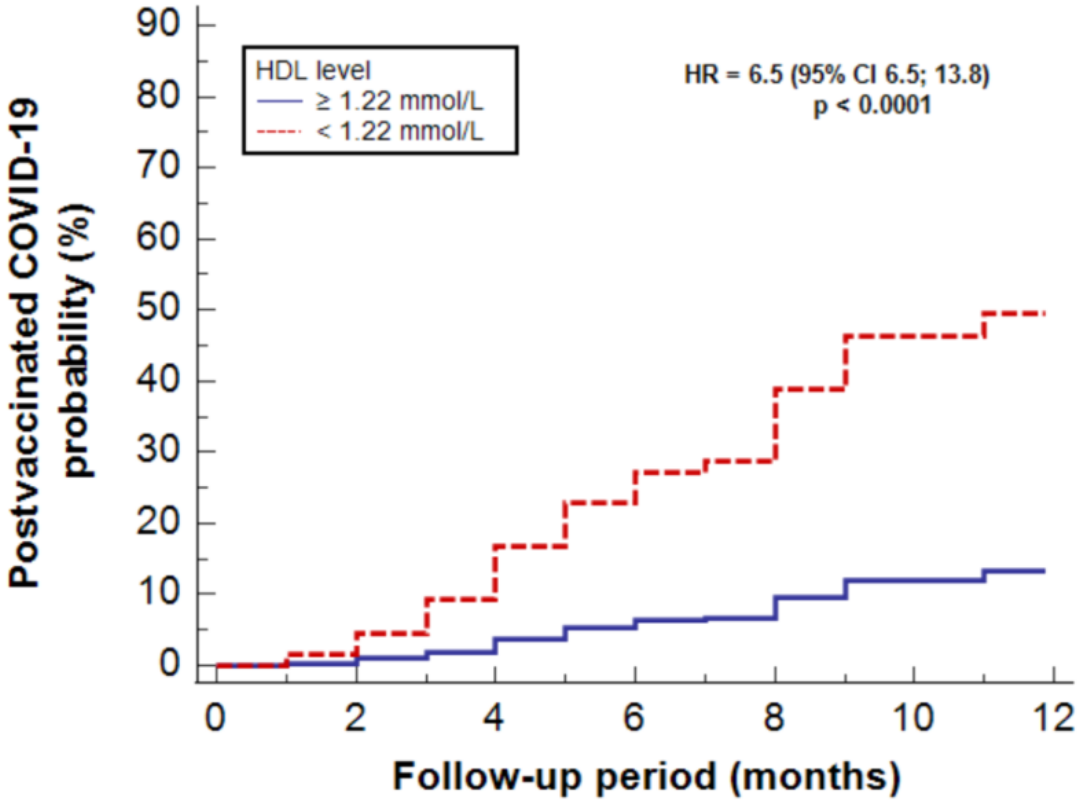

Fig. 2. Probability curves of postvaccination COVID-19 in HD patients stratified by baseline HDL values (adjusted for age, sex, diabetes, and dialysis vintage)

Conclusions: Baseline HDL level <1.22 mmol/L was independently associated with COVID-19 infection in fully mRNA-vaccinated HD patients.

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#641

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.07 Imaging technology*

CORONARY ARTERY CALCIFICATION SCORING AND VITAMIN D3 LEVELS IN PATIENTS WITH AORTIC VALVE SCLEROSIS

VIRTUAL E-POSTER SESSION

Symeon Evangelos Mavroudeas[1], G Papagiannis[2], C Betsis[2], C Mantis[3], A Gkogkos[3], G Matthaiopoulos[3], M Stasinopoulou[4], I Feskou[5], K Sotirakou[6], G Benetos[1], M Drakopoulou[1], G Synetos[1], N Kafkas[3], Costas Tsioufis[1], K Toutouzas[1]
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Background and Aims: Coronary artery calcification (CAC) is an important perspective indicator for patients with coronary artery disease. Two different types of CAC have been recognized, the intimal and medial calcification, each of them with different risk factors. Vitamin D as a calcium blood regulator affects vascular smooth muscle cells with direct cardiovascular effects. The aim of this study was to evaluate and associate the effect of vitamin D3 levels on CAC progress in individuals with aortic valve sclerosis (AVSc).

Methods: We present the preliminary results of a prospective study of 65 patients with AVSc, who underwent non-contrast ECG-guided multi-slice computed tomography (MSCT) to quantify the calcium score by Agatston units (AU) and blood sampling for biochemical analysis. Primary endpoints were the quantification of (1)aortic valve calcification (AVC) score; (2)CAC score; and (3)vitamin D3 blood levels. The study took place between 4 tertiary hospitals in Greece.

Results: The median age of all participants was 75.3 years old (IR=7.4),with median vitamin D3 levels being 27.4ng/dl (IR 13.0).Median AVC and CAC scores were 673.5 AU (IR=878.2) and 242.7 AU (IR=298.1) respectively.According to the results of a bivariate analysis, a statistically significant relationship between vitamin D3 levels and right coronary artery (RCA) calcification is noted. Decreased vitamin D3 levels were correlated with increased RCA calcification score (p=0.036).

Conclusions: A significant inverse relationship between blood vitamin D3 levels and RCA calcification score was confirmed in individuals with AVSc.The above result raises great interest in further research on the use of vitamin D3 levels for CAC evaluation in cardiovascular risk prevention.

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#643

Topic: *AS04 Clinical Vascular Disease / AS04.05 Diabetes; macro- and microangiopathies*

TYPE 2 DIABETES MELLITUS, ATHEROSCLEROSIS, AND ISCHEMIC STROKE: HISTOPATHOLOGICAL CHANGES OF THE BRAIN

VIRTUAL E-POSTER 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: Type 2 diabetes mellitus is associated with a marked increase in the risk of atherosclerotic diseases, including cerebrovascular disease. Atherosclerosis and ischemic stroke in diabetic patients occur 4 times more often than in the general population. Our aim was to investigate the brain tissue of patients with type 2 diabetes mellitus who died from ischemic stroke.

Methods: The 31 patients with type 2 diabetes mellitus died in Lviv regional and city hospitals during 2020-2021 from ischemic stroke and we selected all cases from the archive of Pathological Anatomy Department. General information obtained from the autopsy protocol included clinical data, clinical and morphological conclusion, macroscopic characteristics, status of intracranial arteries and autopsy findings. We studied macroscopic and microscopic changes of brain with use common histological methods and IHC for GFAP, CD68 and CD3.

Results: In patients with type 2 diabetes mellitus were atherosclerosis arteries and thrombus formation, calcification of the middle tunica of arteria, including large areas of calcification and many small areas. 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.

Conclusions: The morphological changes of the brain associated with atherosclerosis and type 2 diabetes mellitus include pathology of the macro- and microvasculature, ischemic infarction with encephalolysis, astrogliosis with positive GFAP, microgliosis, perivascular infiltration by CD3 in different regions of the brain.

91ST EAS CONGRESS
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#995

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

POLYMORPHISM OF DNA REPAIR GENES (APEX1 T444G RS1130409) IN OBESE GOUT PATIENTS IN THE MALE POPULATION OF THE TRANS-BAIKAL TERRITORY IN RUSSIA

VIRTUAL E-POSTER SESSION

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[1]Cardiovascular Surgery, Moscow State Budgetary Institution of Health Care, Moscow, Russian Federation, [2]Department Of Internal Diseases Of The Pediatric And Dental Faculties, Chita State Medical Academy of the Ministry of health of the Russian Federation, Chita, Russian Federation, [3]Department Of Children's Infections, Chita State Medical Academy of the Ministry of health of the Russian Federation, Chita, Russian Federation, [4]The Laboratory Of Clinical And Experimental Biochemistry And Immunology Of The Research Institute Of Molecular Medicine Of The Chita State Medical Academy, Chita State Medical Academy of the Ministry of health of the Russian Federation, Chita, Russian Federation

Background and Aims: The aim of the study was to analyze the frequency distribution of alleles and genotypes of polymorphic locus rs1130409 in the DNA repair gene APEX 1 in gout patients with obesity and assess their association with risks of the disease development.

Methods: 80 men with gout and obese (mean BMI, 33.5+/-1.3) subjects were examined. The material for the study was DNA extracted from leukocytes of whole peripheral blood samples by a set of reagents "DNA-Express Blood" ("Litech", Russia). All patients were genotyped to detect polymorphism of T444G (rs1130409) locus of the gene APEX1.

Results: The study of T444G polymorphism of the gene APEX1 in patients with gout and obese showed a tendency to the increase in frequency of allele G mutations compared to the control group (53.1% vs. 40.2%; $\chi 2=3.89$; p=0.04; OR=1.68; CI 95%: 1.00-2.83) and a statistically significant increase in the frequency of homozygous genotype G/G (27.5% vs. 9%; $\chi 2=6.3$; p=0.01; OR=3.98; CI 95%:1.28-12.4). T allele carriage was associated with a decreased risk of gout without obesity development (46.9% vs 59.8%; $\chi 2=3.89$; p=0.04; OR=0.59; CI 95%:0.35-0.99).

Conclusions: Differences in the frequency distribution of alleles and genotypes of polymorphic locus APEX 1 T444G (rs1130409) in patients with gout and obesity and healthy subjects were found. G/G genotype and minor allele G increase the risk of gout development by 3.9 and 1.7 times, respectively. Wild-type allele carriage (T) has a protective effect.

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#498

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

SIX-MONTH ORAL INTAKE OF MAGNESIUM CITRATE REDUCES TOTAL AND IONISED CALCIUM IN APOE-KNOCKOUT MICE

VIRTUAL E-POSTER SESSION

Daria Shishkova, Olga Gruzdeva, Anastasia Kanonykina, Victoria Markova, Anastasia Lazebnaya, Alyona Poddubnyak, Yulia Dyleva, Anton Kutikhin
Laboratory Of Molecular, Translational, And Digital Medicine, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Background and Aims: Increased serum calcium is associated with a higher risk of major adverse cardiovascular events and cardiovascular death. Here we tested whether magnesium citrate, a drug combining chelate effect with Mg^{2+} ions (Ca^{2+} antagonist), is able to reduce serum calcium and ameliorate atherosclerosis and cardiovascular calcification in elderly ApoE-knockout mice.

Methods: The study included 68 ApoE-knockout mice (12-month-old) which were divided into equal groups (n=34 per each) receiving either oral magnesium citrate (animal equivalent dose 1.845 mg/day, corresponding to the human equivalent dose 450 mg/day) or placebo. After 6 months, animals were sacrificed with the following biochemical profiling and lipid/calcium staining of aortas and aortic valves.

Results: Aortic valves of magnesium citrate- and placebo-treated mice showed similar extent of lipid retention (7.04% and 7.11% Oil Red-positive area, respectively) and calcium deposition (4.98 and 4.27% Alizarin Red-positive area, respectively). Both groups also had similar atherosclerotic burden within the aorta (27% and 20%, respectively) indicative that magnesium citrate does not inhibit atherosclerosis progression when applied to the elderly ApoE-knockout mice. Yet, total and ionised calcium were reduced in magnesium citrate group as compared with placebo (total: 2.24 vs 2.44 mmol/L; ionised: 1.04 mmol/L vs 1.09 mmol/L, respectively).

Conclusions: Oral magnesium citrate reduces total and ionised calcium in ApoE-knockout mice. Further studies should elicit its efficiency in reduction of atherosclerotic or calcification burden in aortas and aortic valves of young hyperlipidemic mice. This study was supported by the Ministry of Science and Higher Education of the Russian Federation (National Project Science and Universities), grant number 0419-2021-001 (https://www.rosrid.ru/ikrbs/detail/V7B4FOKSN5NU0QCFLCPK75S1).

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#1036

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.11 Gut microbiome*

ORAL MICROBIOTA IN PATIENTS WITH FH AND VERY-HIGH CV RISK: WHAT LINK?

VIRTUAL E-POSTER SESSION

Damiano D'Ardes[1], Maria Cristina Curia[2], Pamela Pignatelli[2], Domenica D'Antonio[2], Elena Olmastroni[3], Luca Scorpiglione[1], Francesco Cipollone[1], Alberico Catapano[3], Adriano Piattelli[4], Marco Bucci[1], Paolo Magni[5]
[1]Medicine And Aging Science, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy, [2]Medical, Oral And Biotechnological Sciences, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy, [3]Epidemiology And Preventive Pharmacology Service (sefap), Department Of Pharmacological And Biomolecular Sciences, Università degli Studi di Milano, Milan, Italy, [4]Health Sciences, Saint Camillus International University for Health Sciences (Unicamillus), 00131 Rome, Italy., Rome, Italy, [5]Pharmacological And Biomolecular Sciences, University of Milan, Milan, Italy

Background and Aims: Low-grade chronic inflammation, mediated by microbiota, contributes to CV disease. Studies have shown that *Porphyromonas gingivalis* (*Pg*) and *Fusobacterium nucleatum (Fn)* concentrations have been associated with atherosclerosis. We decided to study oral *Pg* and *Fn* abundance in very high-risk patients with previously cardiovascular events, with or without HeFH, and in subjects with HeFH in primary prevention. We compared the results with healthy subjects.

Methods: We studied 97 patients who were selected to assess oral health status and to quantify oral *Pg* and *Fn* abundance (through qPCR). In particular we included: - 40 patients with previously diagnosed cardiovascular events (10 with genetically proven HeFH and 30 without FH); - 26 subjects with HeFH in primary prevention; - 31 healthy subjects.

Results: Patients with previously diagnosed CV events showed greater *Pg* abundance (1101.3 vs. 192.4, $p = 0.03$), but a similar *Fn* abundance if compared to healthy subjects. HeFH patients with CV events had an even greater *Pg* abundance than did non-HeFH patients and healthy subjects (1770.6 vs. 758.4 vs. 192.4, respectively; $p = 0.048$). In HeFH subjects in primary prevention no differences were found in the levels of *Pg* and *Fn* abundance if compared to healthy subjects.

Conclusions: Higher oral *Pg* abundance is present in very high-risk patients with previously diagnosed CV events suggesting a potential relationship with CV events. Future studies will have the aim to discover the predictive value of *Pg* abundance measurement in CV risk stratification and will reveal a possible role of causality between microbiota and CV events in patients at consistent CV risk such as FH patients.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#614

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.03 Diabetes, insulin sensitivity and resistance*

OMEGA-3 POLYUNSATURATED FATTY ACIDS: EFFECTS ON THE ARTERIAL STIFFNESS AND HEART RATE VARIABILITY IN PATIENTS WITH DIABETIC CARDIAC AUTONOMIC NEUROPATHY

VIRTUAL E-POSTER SESSION

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[1]Endocrinology, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine, [2]Medical Biology, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Background and Aims: Cardiac autonomic neuropathy (CAN) in type 2 diabetes mellitus T2DM is one of the independent risk factors for cardiovascular mortality. We evaluated the effect of omega-3 polyunsaturated fatty acids (omega-3 PUFAs) on the heart rate variability (HRV) and arterial stiffness indices in T2DM patients with confirmed CAN.

Methods: 36 patients with T2DM and confirmed CAN were involved. The study was carried out on two separate arms: traditional therapy (n=15, control) and one capsule/day omega-3 PUFAs (n=21). The duration of the study was three months. Artery stiffness parameters (aorta augmentation index (AIxao), brachial augmentation index (AIxbr) and pulse wave velocity (PWV) were assessed using the device TensioMedTM Arteriograph. We performed Holter-ECG (ECG 'EC-3H' ['Labtech,' Hungary]) analysis including measurement of 24-h ECG and HRV parameters. Statistics: ANOVA (MicroCal Origin v. 8.0).

Results: Omega-3 PUFAs was contributed to the decrease of the PWV [-11.6%±2.09% ($p<0.05$)] and AIxao [-16.2%±3.12% ($p<0.01$)] during the active; PWV [-18.9%±3.9% ($p<0.01$)], AIxao [-11.2%±4.2% ($p<0.05$)] and AIxbr [-98.0%±18.1% ($p<0.05$)] during the passive period (compared to the control). Prescription of omega-3 PUFAs promoted an increase in low-frequency component (LF) [Δ=+30.2±6.42% ($p<0.01$)], high-frequency (HF) [Δ=+18.1±6.02% ($p<0.05$)] and in LF/HF ratio [Δ =+14.42±7.16% ($p<0.05$) during the active period of the day. Omega-3 PUFAs promotes increase in LF [Δ=+30.8%±4.95% ($p<0.01$)], HF [Δ=+18.9%±4.72% ($p<0.05$)], LF/HF ratio [Δ=+10.5%±2.1% ($p<0.05$)] during the passive period.

Conclusions: In patients with T2DM and CAN treatment with omega-3 PUFAs improved HRV and arterial stiffness parameters. However, further randomized, double-blind, placebo-controlled trials may provide evidence for the hidden therapeutic capacity of omega-3 PUFAs therapy.

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#1029

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

THE EFFECTS OF PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) INHIBITORS ON THE LEVEL OF DNA DAMAGE IN HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLAEMIA (HEFH)

VIRTUAL E-POSTER SESSION

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[1]Department Of Internal Diseases And Clinical Pharmacology, Medical University in Lodz, Lodz, Poland, [2]Department Of Internal Diseases And Clinical Pharmacology, Medical University Of Lodz, Medical University of Lodz, Lodz, Poland, [3]Department Of Biophysics Of Environmental Pollution, Faculty Of Biology And Environmental Protection, University in Lodz, Lodz, Poland

Background and Aims: Cellular damage in cardiovascular diseases is mainly due to lipid peroxidation caused by the action of ROS. The end-products of lipid peroxidation induce formation of DNA bulky adducts, leading to genome instability. Patients with Heterozygous familial hypercholesterolemia (HeFH) are exposed to elevated levels of LDL from birth and ox-LDL may will be induce oxidation pathways leading to atherosclerosis and cardiovascular disorders. The aim of the study was to determine the effects of PCSK9i on the level of DNA damage and the level of 8-oxo-2'-deoxyguanosine (8-oxodG) in HeFH.

Methods: The material for the study were PBMCs and serum collected from patients with HeFH (n=27) who were qualified for the iPCSK9 treatment. The control group consisted of patients with normolipidemia (n=26), not subjected to lipid-lowering therapy The level of DNA single-strand breaks (SSBs) was determined using the alkaline version of the comet assay. Detection of 8-OHdG serum was used enzyme immunoassay. Analyzes were made for both before and after 6 months treatment with iPCSK9.

Results: DNA damage was occur at the level of about 20% in HeFH patients, and the 6-month lipid-lowering therapy with PCSK9i was reduce the damage to 12%. The level of 8-OHdG was higher in HeFH patients compared to control group and decreased after treatment with PCSK9i.

Conclusions: Observed changes strongly suggest that PCSK9i induced indirect repair of DNA by inhibiting oxidative DNA damage and probably reduced ROS production.

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#1027

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.08 Platelets, thrombosis and atherosclerosis*

PLAQUE-STABILIZING EFFECT OF SAFFRON EXTRACT IN EARLY AND ADVANCED ATHEROSCLEROTIC NEW ZEALAND WHITE RABBITS

VIRTUAL E-POSTER SESSION

Noor Alicezah Mohd Kasim[1], Iman Nabilah Abd Rahim[2], Effat Omar[2], Suhaila Abdul Muid[2], Hapizah Mohd Nawawi[2]
[1]Department Of Pathology, Universiti Teknologi MARA (UiTM), Sungai Buloh, Malaysia, [2]Institute Of Pathology, Laboratory And Forensic Medicine (i-pperform), Universiti Teknologi MARA (UiTM), Sungai Buloh, Malaysia

Background and Aims: Vulnerable plaques are the major cause of acute coronary syndrome (ACS) and sudden death. Studies have shown that 75% of ACS cases are caused by plaque rupture. Recent studies have highlighted the anti-atherogenic effects of saffron. However, studies on the plaque-stabilizing effect of saffron have not been completely established. This study aims to investigate the plaque-stabilizing effect of saffron ethanolic extract (SEE) via the expression of matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1) in the aortic plaques of New Zealand White rabbits (NZWR).

Methods: Forty-five male NZWR were kept on 4 and 8-week high-cholesterol diets to induce early and advanced atherosclerosis respectively. They were randomized to the following groups: (i)baseline; (ii)treatments, given 50 and 100mg/kg/day SEE for 8 weeks; (iii)control, given distilled water. At the end of the study, rabbits were euthanized and the aortas were obtained for immunohistochemical detection of MMP-9 and TIMP-1.

Results: 100mg/kg/day SEE treatment for 8 weeks decreased the expression of MMP-9 ($p<0.01$) in the plaques and increased the positive expression of TIMP-1 ($p<0.05$) compared with the control group in early atherosclerotic rabbits. Decreased MMP-9/TIMP-1 ratio by 26.8% was observed post-treatment with 100mg/kg/day SEE compared to baseline ($p<0.05$), while 20% reduction of MMP-9/TIMP-1 ratio was observed post-treatment with 50mg/kg/day SEE compared to control ($p<0.05$) in early atherosclerotic rabbits. MMP-9/TIMP-1 mean ratio was significantly lower in the aorta of rabbits which received 100mg/kg/day SEE compared to 50mg/kg/day SEE in early and established atherosclerosis groups ($p<0.05$).

Conclusions: SEE exerts plaque-stabilizing effects in atherosclerotic NZWR in a dose-dependent manner.

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#1025

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

THE ROLE OF METABOLIC FACTORS IN ACCELERATING AGEING

VIRTUAL E-POSTER SESSION

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Background and Aims: Background: Biological age (BA) may be a more accurate metric for the risk of cardiovascular disease (CVD) and prediction of early vascular ageing, and atherosclerosis. **The aim** of this study was to assess the impact of metabolic disorders on BA in patients with low/moderate cardiovascular risk and the significance of the development of accelerating ageing.

Methods: The study included 120 patients with low/moderate CVR aged from 32 to 59 years (women n=65, 54.17%): the main group (n= 67) with metabolic disorders (overweight/obesity, insulin resistance, dyslipidaemia) and a control group (n=53). All subjects underwent anthropometric measurements and clinical and biochemical analysis. The Leukocyte telomere length (LTL) of blood leukocytes was determined by real-time PCR. The BA was calculated using the DNAm PhenoAge epigenetic clock.

Results: The obese patients had an accelerated ageing rate in patients of the main group. The increase in body mass index and waist circumference, hyperinsulinemia, hyperuricemia, and high levels of proatherogenic lipids are associated with an increase in BA. The presence of overweight and obesity is associated with a decrease in LTL and an increase in BA.

Conclusions: The acceleration of ageing processes is associated with both metabolic and molecular genetic factors, Assessment of premature ageing allows to identify of persons with a high risk of developing age-related diseases at a time when there are no clinical symptoms yet, and to develop measures for timely and effective prevention.

91ST EAS CONGRESS
MANNHEIM GERMANY | MAY 21-24, 2023

#1023

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

ANALYSIS OF GOUT- PREDISPOSING INTERGENIC INTERACTIONS

VIRTUAL E-POSTER SESSION

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Background and Aims: To study the frequency distribution of alleles and genotypes of polymorphic loci of genes of folate cycle (MTHFR C677T, MTHFR A1298C, A2756G MTR, MTRR A66G), locus C421A (rs2231142) of the ABCG2 gene in patients with gout, to identify their association with the risk of the disease development and to assess the combined effect of these genes on the development of gout.

Methods: 80 men and women with gout (mean age 54.8±12.4 years) were examined. The control group consisted of 46 healthy respondents of the corresponding age group. The material for the study was DNA extracted from leukocytes of whole peripheral blood using a set of reagents "DNA-Express Blood" (LLC NPF "Litekh", Russia). The analysis of intergenic interactions was performed using Generalized Multifactor Dimensionality Reduction program.

Results: ABCG2 gene and allele C421A (p=0.018;OR=3.5;CI95%:1.16-1.52), the genotype of ABCG2 421C/A (χ2=5.03;p=0.024;OR=3.5; CI95%:1.11-10.98), and the genotype of the MTHFR 677T/T (χ2=4.48;p=0.03;OR=3.86;CI95%:1,03-14,43) were identified to increase the risk of gout development. Carriage of the C allele of the gene ABCG2 C421A (χ2=5.58;p=0.018;OR=0.29;CI95%:0.09-0.86), genotype ABCG2 421 S/S (χ2=5.65;p=0.017;OR=0.27;CI95%:0.08-0.84) and genotype MTR2756A/A (χ2=3.826;p=0.045;OR=0.408;CI95%:0.16-1.04) was found to have the protective effect. In the analysis of gout - predisposing intergenic interactions 3 combinations were considered to be the most significant ones: interaction of two polymorphic genes MTR A2756G×ABCG2 C421A;interaction of three genes – MTHFR C677T×MTR A2756G× ABCG2 C421A; interaction of four genes MTHFR C677T×MTR A2756G×MTRR A66G×ABCG2 C421A.

Conclusions: Alleles and genotypes increasing the risk of gout development were identified. Analysis of intergenic interactions allowed to establish combinations of gout - predisposing candidate genes.

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#208

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.08 Novel risk factors and biomarkers*

ASSESSMENT OF VON WILLEBRAND FACTOR-MEDIATED PLATELET ADHESION IN PATIENTS WITH PREMATURE CORONARY ARTERY DISEASE

VIRTUAL E-POSTER SESSION

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Background and Aims: Premature coronary artery disease (CAD) is an aggressive disease which often manifests with acute atherothrombotic events. We suggest that excessive von Willebrand factor (VWF)-platelet interactions through glycoprotein Ib (GPIb) receptors following endothelial damage may contribute to the development of these events. We studied VWF-mediated platelet adhesion to collagen surfaces at high shear rates in patients with premature CAD.

Methods: The study enrolled 58 patients with premature CAD (45 men and 13 women). The control group comprised 33 age-matched patients (13 men and 20 women) without CAD. Whole blood samples were placed into the microfluidic device with the pump. Blood was perfused over surface coated with collagen at shear rate of 1300 s^{-1} through the cell. The platelet adhesion was characterized by measuring the intensity of scattered laser light after 15-minute blood circulation. Measurements were performed before and after addition of monoclonal antibodies (mAb) to GPIb into blood samples and then compared between the two groups.

Results: After addition of mAb to GPIb into blood samples platelet adhesion decreased by 75 (56; 83)% in patient with premature CAD and by 29 (10; 51)% in patients of the control group (p=0.0001). In logistic regression models, patients with platelet adhesion decrease by ≥43% were more likely to have CAD (adjusted odds ratio 22.2, 95% confidence interval 5.7 to 87.2, p <0.001) than patients with fewer platelet adhesion decrease.

Conclusions: The degree of platelets adhesion mediated by the interaction of GPIb receptors and VWF at high shear rates may be associated with the premature development of CAD.

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#613

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.14 Epigenetics and microRNA*

THE ASSOCIATION OF CIRCULATING MICRORNA-126 WITH INFLAMMATION AND INSULIN RESISTANCE IN PATIENTS WITH CORONARY ARTERY DISEASE WITH TYPE 2 DIABETES MELLITUS

VIRTUAL E-POSTER SESSION

Serhii Serik[1], Natalia Mavrycheva[1], Vladyslav Riabukha[1], Viktoriia Malko[1], Tetiana Bondar[2], Tetiana Chenchik[2]
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Background and Aims: Circulating microRNAs were suggested as biomarkers as well as modulators of coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM). The purpose of the study was to investigate the relationship of circulating microRNA-126-3p with pro-inflammatory interleukin-6 (IL-6) and glucometabolic parameters in patients with CAD with T2DM.

Methods: The study included 68 patients with stable CAD with T2DM, 25 CAD patients without diabetes and 18 healthy individuals as control. MicroRNA-126-3p was determined in blood plasma by real time PCR. Results expressed in relative units. IL-6 and insulin levels were measured in serum by ELISA.

Results: Circulating microRNA-126 levels in CAD patients with and without T2DM (50,32 [19,54; 93,82]; 109,46 [49,52; 211,11]) were increased in comparison with the controls (17,95 [13,74; 35,01]) (p=0,018; p=0,00002). But in diabetic patients microRNA-126 level was significantly lower than in patients without diabetes (p=0,0005). IL-6 level in CAD patients with T2DM (4,51 [2,63; 7,35] pg/ml) was increased compared with the controls (2,14 [1,89; 2,98] pg/ml, p=0,0001) and with patients without diabetes (3,26 [2,29; 4,01] pg/ml, p=0,001). In diabetic patients lower miRNA-126 level (the 1st tertile) was associated with the significant increase in IL-6, blood glucose levels and HOMA-IR in comparison with the 3rd tertile (p=0,006, p=0,011 and p=0,041).

Conclusions: Circulating microRNA-126-3p level in CAD patients with T2DM was increased compared to the controls but decreased in comparison with CAD patients without diabetes. The lowest microRNA-126-3p level in CAD patients with T2DM was associated with the significant elevation of IL-6, insulin resistance and blood glucose.

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#1019

Topic: *AS02 Lipids and Lipoproteins / AS02.02 TG rich lipoproteins metabolism and lipases*

AWERENESS OF THE PREVALENCE OF HIGH TRIGLYCERIDES IN AN SPONTANEOUS SURVEY IN ALL OF BRAZILIAN REGIONS

VIRTUAL E-POSTER SESSION

Tania Martinez[1], Anita Saldanha[2], Abel Pereira[2], Marileia Scartezini[2], Bernardo Almeida[1,2]
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Background and Aims: Introduction: Attention has recently increased to triglycerides, in particular, specially for its possible relation with remanescent chylomicrons and even Familial Hyperchylomicronemia Syndrome.

Aims: To evaluate how triglycerides are distributed in the five regions of Brazil, according to categories such as sex and age groups ranges, namely children, adults and elderlies in spontaneous and non fasting conditions.

Methods: The total sample analized consisted of 14.927 people, both sexes and ages starting at 20 yr old and over 80 yr, classified per two decades of life. The five regions were: Center West (CW), North East (NE), North (N), South Weast (SW) and South (S).

Results: Sex: Female (F)=51.3%; Age Groups: 20 to 39-21(1)=55%, 40 to 59 (2)=32.32%, 60 to 79 (3)= 22.80%, over 80 yr (4)=2.68% and not informed 20.65%. Triglycerides Mean of the total of sample: 272,11 mg/dl(Tg). Interpretation as to groups of results: concentration Less than 175(L), interval 175 to 400 - High (H) and over 400 as Very High (VH). As to participation in regions: CW=7.5%, NE=34.72%, N=14.88%, SE=23,65% and S=19.25%. By ranges in total by %: L=30.65, H=52.85 and VH=16.5. Means by sex: F=251.7 and male 292,16. Means by age group: 1-262,86, group 2 : 296,19, group 3: 287,22 and group 4: 246,9. Tg 269,18. Means by region: CW: 269.16, NE: 283,18, N: 286,06, SE: 262 and S: 254,93

Conclusions: Conclusion: As to Brazilians controlling triglycerides levels, either by treatment or not ,spontaneously, in all sexes, age groups and regions, results in Means are too abnormal. Lifestyle changes and health policies needed.

91ST EAS CONGRESS
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#226

Topic: *AS04 Clinical Vascular Disease / AS04.12 Prevention and treatment of cardiovasculardisease; miscellaneous*

THE HIGH-RISK INTERSECTION OF ATRIAL FIBRILLATION AND CORONARY ARTERY DISEASE IN A MIDDLE EASTERN COHORT. ANALYSIS FROM THE JORDAN ATRIAL FIBRILLATION STUDY

VIRTUAL E-POSTER SESSION

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Background and Aims: Clinical studies on the impact of coronary artery disease (CAD) on the outcome in patients with atrial fibrillation (AF) in the Middle East (ME) are scarce. The aim of this study is to evaluate baseline clinical profiles and one-year prognosis in AF patients with coexisting CAD in a ME cohort.

Methods: Consecutive AF patients evaluated in 29 centers were enrolled in the Jordan AF Study (May 2019 - December 2020). Clinical features, use of medications, and 1-year outcomes in patients with AF/CAD were compared with AF/no CAD patients.

Results: Of 2020 AF patients enrolled; 216 (10.7%) had CAD. CAD patients were more likely to be men and had higher prevalence of hypertension, diabetes, dyslipidemia, and heart failure (all p<0.007) compared with the AF/no CAD patients. Mean CHA2DS2-VASc and HAS-BLED scores were higher in AF/CAD patients than those with AF/no CAD (4.3±1.7 vs. 3.6±1.8, p<0.0001), and (2.0±1.1 vs. 1.6±1.1, p<0.0001), respectively. Use of oral anticoagulant agents was similar in the two groups (83.8% vs. 82.9%, p=81), but more patients with AF/CAD were prescribed antiplatelet agents (73.7% vs. 41.5%, p<0.0001) compared to patients with AF/no CAD. At one year, AF/CAD patients, compared to AF/no CAD patients had higher all-cause hospital admissions (39.4% vs. 29.2%, p=0.003), admission for acute coronary syndrome and coronary revascularization (6.9% vs. 2.4%, p=0.004), and all-cause mortality (18.5% vs. 10.9%, p=0.002).

Conclusions: In this cohort of Middle Eastern patients with AF, one in 10 patients had CAD. The coexistence of AF and CAD was associated with a worse baseline clinical profile and one-year outcome.

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#615

Topic: *AS03 Dyslipidemia and Risk Factors / AS03.05 Inherited dyslipidemias*

DUAL THERAPY WITH INCLISIRAN AND EVOLOCUMAB IN A HETEROZYGOUS FH PATIENT WHILE ON MAXIMUM STATIN AND EZETIMIBE DOSE TO ACHIEVE LDL TARGETS.

VIRTUAL E-POSTER SESSION

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Background and Aims: In 2019, a morbidly obese 51 year old lady was referred to lipid clinic. Treated lipid profile (while on Atorvastatin 80mg od) at the time of referral showed a total cholesterol 13.9, triglyceride 5.3, HDL 1.2. Baseline untreated lipid levels (when Atorvastatin was temporarily stopped) confirmed total cholesterol 18.7, triglyceride 6.6, HDL 0.7. She is a smoker and known to have a history of IHD (myocardial infarction, with PCI – whilst living in another locality aged 45). Four months later, patient suffered further NSTEMI - angiogram confirmed diffuse in-stent neoatherosclerosis, requiring drug eluting balloon. Familial hypercholesterolaemia genotyping confirmed heterozygous PCSK9:c.1120G>T variant. Evolocumab 140mg (PCSK9 inhibitor) was added to her Atorvastatin. Resulting lipids showed total cholesterol 7.1, triglyceride 3.9, HDL 1.2, LDL 4.1. Following the recent availability of Inclisiran, this was added to treatment to maximise CVD risk reduction in September 2022.

Methods: We postulated that using a combination of PCSK9 inhibitors, which will block the binding of PCSK9 to the LDL receptors together with Inclisiran, which reduces the overall hepatic synthesis of PCSK9 will provide a better LDL reduction compared to using either PCSK9i or Inclisiran on its own when combined with Atorvastatin.

Results: Lipid profile on Atorvastatin 80mg, Ezetimibe 10mg, Evolocumab 140mg and Inclisiran 284mg gave total cholesterol 3.7, triglyceride 2.8, HDL 1.7, LDL 0.7.

Conclusions: Combining two new injectable PCSK9i with maximum oral agents ensured lipid lowering levels within current guideline recommendations despite significantly elevated baseline levels.

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#214

Topic: *AS04 Clinical Vascular Disease / AS04.15 Other*

EFFICACY AND SAFETY OF EBRONUCIMAB, IN PATIENTS WITH PRIMARY HYPERCHOLESTEROLEMIA AND MIXED HYPERLIPIDEMIA: RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III CLINICAL STUDY

VIRTUAL E-POSTER SESSION

Yong Huo[1], Bo Zheng[1], Yu Xia[2], Max Wang[2], Baiyong Li[2], Xiang Ni[2], Guoqin Wang[2], Binge Yu[2]
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Background and Aims: Inhibiting PCSK9 activity results in lowering LDL-C levels and further reducing the risk of cardiovascular events. Ebronucimab (AK102) is a novel fully human immunoglobulin G1 monoclonal antibody against PCSK9. This study aimed to evaluate the safety and efficacy of Ebronucimab in subjects with primary hypercholesterolemia and mixed hyperlipidemia.

Methods: A total of 450 patients (male and female) with age ranging from 18 to 80 years were planned to enrolled. There were 4 cohorts (Q2W: 150mg, placebo; Q4W: 450mg , placebo) in this study. In each cohort, subjects were enrolled and randomized in a 2:1:2:1 ratio to receive either Ebdarokimab or matching

placebo.

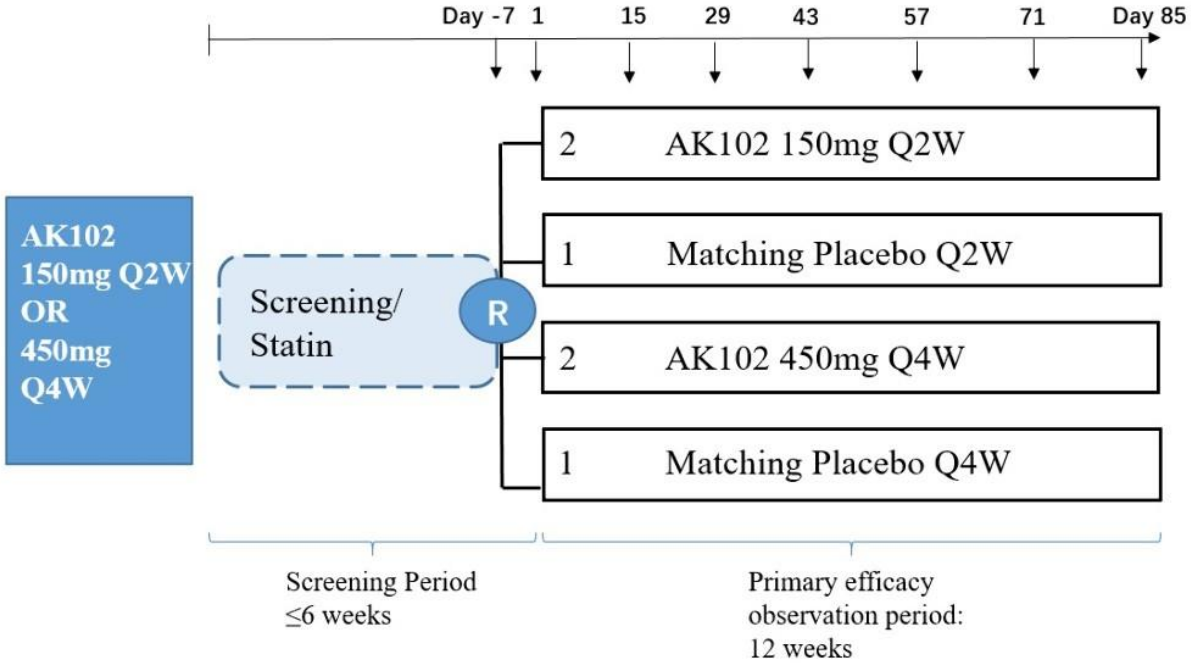

Figure 1 Study Design

Results: Both cohorts (450mg Q4W, 150mg Q2W) can effectively reduce fasting serum LDL-C and keep it stable up to week 12. The percentage change of fasting LDL-C relative to the baseline was 64.90% in 450 mg Q4W group, 59.13% lower than the placebo group. 66.21% in 150 mg Q2W group, and 60.43% lower than the placebo group after
treatment.

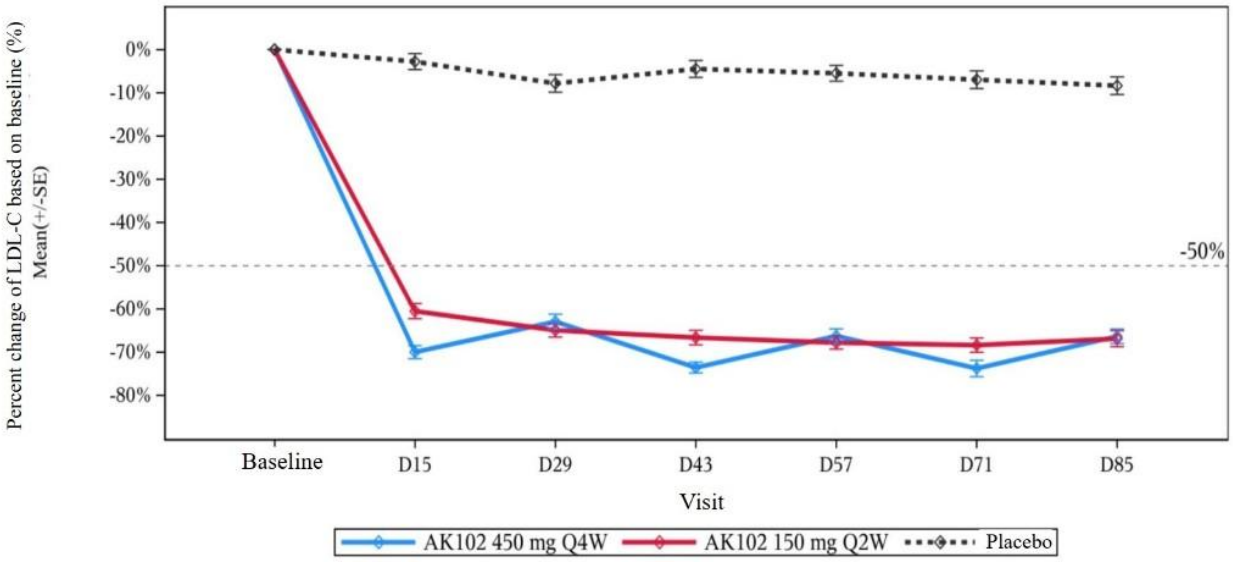

Figure 2 Percent change of fasting LDL-C relative to baseline at different visits during the study

461 subjects enrolled in safety set. 200(43.4%) subjects experienced at least one treatment-emergent adverse event (TEAE), 143 subjects receiving Ebronucimab and 57 subjects receiving placebo. 64(13.9%) subjects had TEAE (TRAE) related to study drug, including 54(17.5%) jubjects in Ebronucimab group and 10(6.6%) subjects in the placebo group. 14(3.0%) subjects experienced serious adverse event (SAE). Investigators assessed the SAEs were non-related to study drug. No death was reported.

Conclusions: Ebronucimab was generally safe and able to lowering serum levels of LDL-C in subjects with primary hypercholesterolemia and mixed hyperlipidemia.

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#623

Topic: *AS01 Pathogenesis of Atherosclerosis / AS01.01 Endothelial cell function and biology*

EFFECT OF VISCERAL OBESITY ON THE ELASTICITY OF THE MAIN ARTERIES IN PATIENTS WITH ARTERIAL HYPERTENSION, OBESITY AND TYPE 2 DIABETES MELLITUS.

VIRTUAL E-POSTER SESSION

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Background and Aims: to evaluate the effect of visceral obesity on the elasticity of the main arteries in patients with arterial hypertension (AH), obesity, type 2 diabetes mellitus (DM).

Methods: 320 patients with II-III AH 45-70 years old were divided into 4 groups: "isolated" AH (Group 1), AH and obesity (Group 2), AH, obesity and 2 DM (Group 3), AH and DM 2 without obesity (Group 4). The clinical status, parameters of visceral obesity, elasticity of the main arteries were assessed.

Results: At least 50% of all patients had visceral obesity, despite the absence of obesity in terms of 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 ($p<0.0001$). A higher percentage of individuals with adipose tissue dysfunction was noted in groups 2 and 3 compared to groups 1 and 4 (75% vs 81.1% vs 41.5% vs 53.4%, respectively, p1-2 <0.001, p1-3<0.001, p2 -4 = 0.023, p3-4 = 0.002). The percentage of persons with a pulse wave propagation velocity (PWVE) >10 m/s was more common among patients of group 3 compared with patients of groups 1 and 2 (77.0 vs 57.9 and 55.3%, p1-3= 0.004, p2-3=0.006). It was revealed the relationship between indicators of visceral obesity, the elasticity of the main arteries and the 5-year risk of cardiovascular complications.

Conclusions: The features of the influence of visceral obesity on the elasticity of the main arteries in patients with AH were revealed as obesity and type 2 diabetes were added to it.

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#1002

Topic: *AS02 Lipids and Lipoproteins / AS02.09 Lipid and lipoprotein metabolism*

ONLY THIRTY PERCENT (30%) OF PATIENTS ON PCSK9 INHIBITORS ACHIEVE ESC/EAS LDL-CHOLESTEROL GUIDELINE TREATMENT TARGETS IN A LIPID CLINIC: REAL WORLD DATA

VIRTUAL E-POSTER SESSION

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Background and Aims: Background: PCSK9 inhibitors have been introduced into our armamentarium of lipid lowering treatments in getting our patients towards optimal treatment targets. We started initiating PCSK9 inhibitors in the clinic in March 2017 and recently carried out an audit to determine how many of our patients have been able to achieve ESC/EAS LDL-C treatment targets of < 1.4 mmol/L and < 1.8 mmol/L.

Methods: Method: Clinic based audit using retrospective case note review of adults prescribed PCSK9 inhibitors from March 2017 – July 2022 and their most recent LDL-Cholesterol measurement.

Results: One hundred and fifty-one patients' files were reviewed, the most recent LDL-cholesterol was compiled from 89 patients, 41 (47%) males and 47 (53%) females with ages ranging from 30 – 82 years, with a mean age of 62.4 years. Median duration of PCSK9 inhibitor treatment was 2.5 years. The LDL-cholesterol ranged between 0.4 – 8.8 mmol/L, with an average of 2.5 mmol/L. The overall percentage of patients who achieved the ESC/EAS guideline recommended LDL-cholesterol levels of <1.4 mmol/L and <1.8 mmol/L after addition of PCSK9 inhibitors were 18% and 30%, respectively.

Conclusions: Conclusion: This present audit-based evaluation on treatment attainment in a real-world setting showed that only about a third of the patients attending a specialist lipid clinic treated with PCSK9 inhibitors achieved the recent LDL-C targets recommended ESC/EAS guidelines. There is going to be a need for the use of multiple lipid lowering medications in order to get a large proportion of patients to achieve the EAS/ESC guideline.

91ST EAS CONGRESS
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#225

Topic: *AS04 Clinical Vascular Disease / AS04.01 Coagulation and Thrombosis*

CLINICAL PROFILES AND ONE-YEAR OUTCOME IN MIDDLE EASTERN PATIENTS WITH ATRIAL FIBRILLATION AND MAJOR BLEEDING EVENTS. THE JORDAN ATRIAL FIBRILLATION STUDY

VIRTUAL E-POSTER SESSION

Ayman Hammoudeh[1], Yousef Khader[2], Yahya Badaineh[1], Ramzi Tabbalat[3], Sukaina Rawashdeh[4], Mustafa Jammal[5], Sadan Abrumman[6], Imad Alhaddad[7]
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Background and Aims: Oral anticoagulant agents (OACs) reduce the risk of stroke and systemic embolism (SE) in patients with atrial fibrillation (AF) but may increase the risk of major bleeding (MB) events. There is a scarcity of studies that address the incidence, predictors, and outcomes of bleeding events in AF patients in the Middle East. This contemporary multicenter study sought to evaluate in detail the bleeding events and predictors of these events

Methods: The Jordan AF Study enrolled patients in 29 centers (May/2019-December/2020) and followed them for one year. We compared the demographics and one-year events in patients with an MB and clinically relevant non-major (CRNM) bleeding compared with patients who did not have bleeding.

Results: Of 2018 patients; 166 (8.2%) sustained MB or CRNM bleeding, including 47 (2.3%) patients who had MB. Compared with 1852 (91.8%) patients with no bleeding, MB patients were older and had more hypertension, diabetes, heart failure, active malignancy, and higher mean HAS-BLED score (2.1±1.1 vs. 1.6±1.6, p=0.002). More patients with MB used OACs (93.6% vs. 78.9%, p=0.02). Patients with MB events had higher one-year rates of stroke/SE (23.4% vs. 3.6%, p<0.0001), and all-cause mortality (31.9% vs 11.6%, p=0.001) than nonbleeders. Independent predictors of MB were stroke/SE (OR 10.8, 95% CI 5.3-21.9, p<0.0001), malignancy (3.4, 1.3-8.5, p=0.01), OACs use (4.4, 1.3-14.7, p=0.02) and DM (1.9, 1.0-3.5, p=0.04).

Conclusions: Major and non-major bleeding occurred in ≈8% of Middle Eastern patients with AF at one year. Patients with MB (≈2%) had worse baseline clinical profiles and one-year outcomes compared with those with no bleeding events.

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#999

Topic: *AS02 Lipids and Lipoproteins / AS02.01 Lp(a)*

CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH ELEVATED LP (A) IN THE CZECH REPUBLIC

VIRTUAL E-POSTER SESSION

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Center Of Preventive Cardiology 3rd Department Of Internal Medicine, General University Hospital in Prague, Prague, Czech Republic

Background and Aims: The main purpose of this study is to identify and describe common characteristics of patients with elevated Lp (a), to identify and describe subgroup of patients with the highest risk of cardiovascular complications in the population of patients with elevated Lp (a) and to determine relationship between elevated Lp (a) and other parameters of lipid metabolism.

Methods: A descriptive, non-interventional, retrospective cohort study of 458 patients from Center of Preventive Cardiology 3rd Department of Internal medicine 1st Faculty of Medicine and VFN in Prague, with elevated Lp (a) was conducted. A database of patients with lipid metabolism disorders and elevated Lp (a) level was created with relevant data about patients' age, weight and height, smoking status, selected parameters of lipid metabolism, comorbidities (such as diabetes mellitus, ischemic heart disease, chronic kidney disease..) and therapy.

Results: The results based on the retrospective cohort indicated that Lp (a) did not correlate with other parameters of lipid metabolism in the study group. So far atherosclerotic cardiovascular disease was manifested in 20% of patients. The association Lp (a) with a higher risk of diabetes mellitus is not evident in the available results.

Conclusions: It should be added that the complete results are not currently available as the study is still ongoing. The plan is to expand the cohort size, complete data and to perform a more comprehensive statistical evaluation.

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Topic: *AS03 Dyslipidemia and Risk Factors / AS03.17 Other*

ASSOCIATION BETWEEN HYPERCHOLESTEROLEMIA AND OXALATE HOMEOSTASIS IN A RATS

VIRTUAL E-POSTER SESSION

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Background and Aims: Hypercholesterolemia is closely related to impaired kidney function and, consequently, increased plasma oxalic acid (POx) concentrations. However, whether hypercholesterolemia per se is associated with impaired oxalate homeostasis remains unknown. In this experimental study, we compared the association between hypercholesterolemia and POx concentrations and urine oxalate (UOx) excretion in rats with and without acute kidney injury (AKI).

Methods: Male Wistar rats (200-300 g, n=20) were randomly divided into 2 groups. After 24 hours of water deprivation, rats in group 1 (n=10) received an intramuscular injection of 50% glycerol (10 ml/kg body weight), while group 2 (n=10) served as the control group. During the 10-week experimental period, POx concentration, UOx excretion, serum creatinine, and total cholesterol levels were measured in each group of rats. Data analysis and all graphs were generated using MedCalc software.

Results: At 10 weeks following AKI initiation, significantly lower UOx and higher concentrations of serum creatinine, total cholesterol, and POx were observed in the experimental group compared with the control group (Fig.
1).

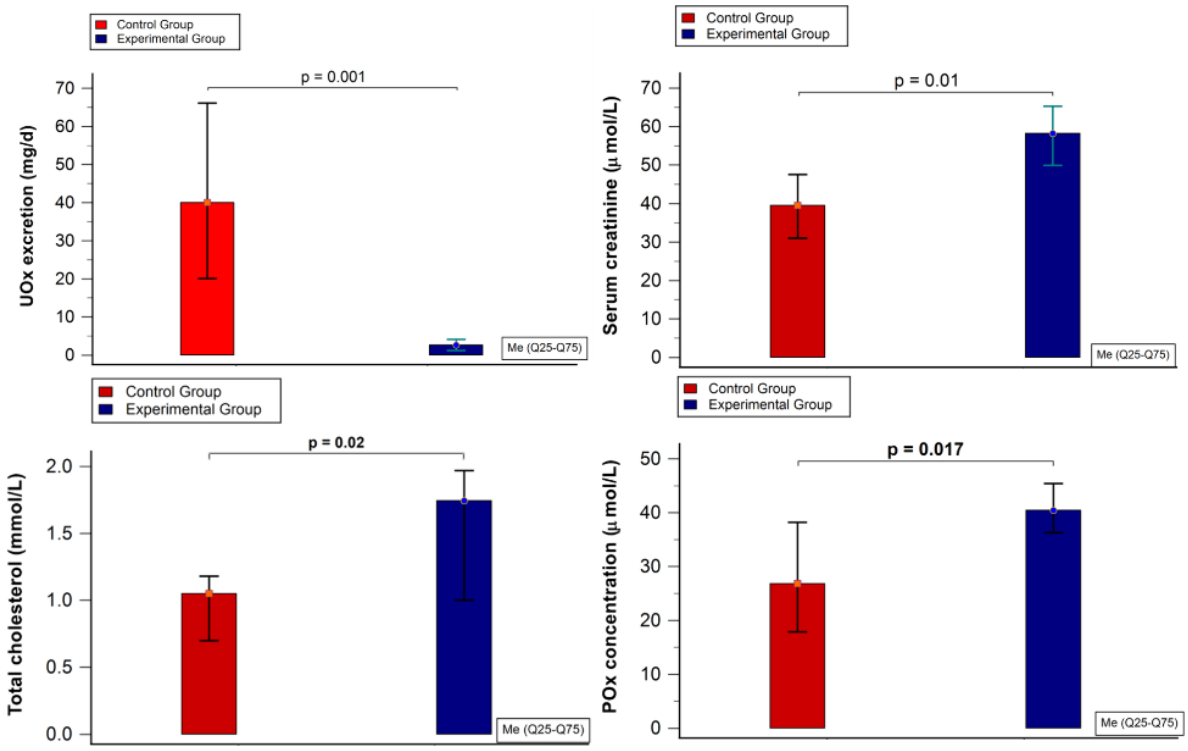

Fig. 1. Daily UOx, serum creatinine, total cholesterol and POx concentrations in the experimental and control rats

Obviously, serum creatinine level was directly associated with total cholesterol (r=0.57, p=0.03) and POx (r=0.55, p=0.002) concentrations, and showed an inverse correlation with UOx excretion (r=0.37, p=0.04) in the experimental group. However, a direct strong correlation between cholesterol and POx levels was also observed in the control group (Fig.
2).

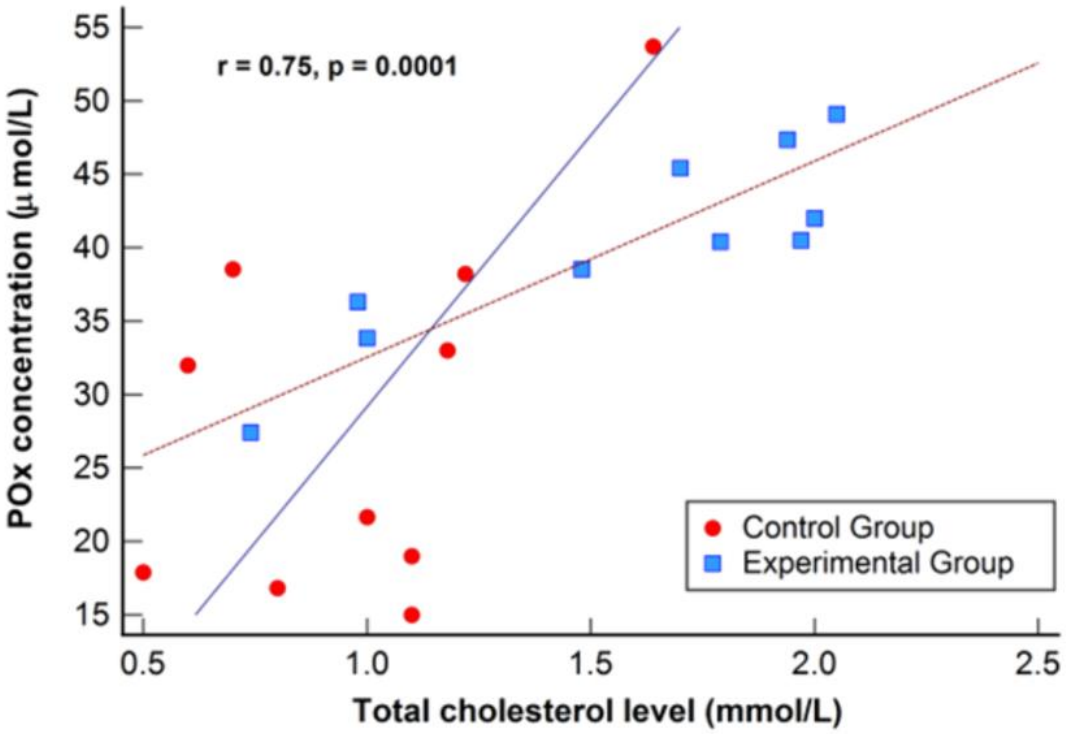

Fig. 2. The association between total cholesterol and POx concentrations in rats

In the partial correlation analysis, total cholesterol level was significantly associated with POx concentration independently of creatinine level (r=0.53, p=0.03).

Conclusions: Hypercholesterolemia is associated with increased POx concentration in rats independent of kidney function.