

MALNUTRITION AND CACHEXIA IN CANCER

CLINICAL CASE DISCUSSION

Jann Arends

Universitätsklinikum Freiburg, Klinik für Innere Medizin I Freiburg, Germany

DISCLOSURE

JA has received honoraria for an advisory role or lectures for Baxter, B. Braun, Chugai, Falk, Fresenius, Helsinn, Nutricia, Roche, Seca



Cancer Cachexia in Adult Patients: ESMO Clinical Practice Guidelines

F. Bozzetti⁺¹, F. Strasser⁺², J. Arends^{+3,4}, S. Gonella^{5,6,7}, T. Skeidsvoll-Solheim^{8,9}, C. Madeddu¹⁰, P. Ravasco^{11,12}, L. Buonaccorso¹³, M.A.E. de van der Schueren^{14,15}, C. Baldwin¹⁶, M. Chasen^{17,18} & C. Ripamonti¹⁹ on behalf of the ESMO Guidelines Committee*

⁺contributed equally

¹University of Milan, Milan, Italy; ²Kantonsspital St. Gallen, St. Gallen, Switzerland; ³Department of Medicine I, Medical Center - University of Freiburg; ⁴Faculty of Medicine, University of Freiburg, Freiburg, Germany; 5A.O.U. Città della Salute e della Scienza of Turin, Turin; ⁶University of Turin, Turin; ⁷University of Verona, Verona, Italy; ⁸European Palliative Care Research Centre (PRC), Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, NTNU, Norwegian University of Science and Technology and St. Olav's University Hospital, Trondheim; 9Cancer Clinic, St. Olav's University Hospital, Trondheim, Norway; 10 Medical Oncology Unit, Department of Internal Medicine and Public Health, University of Cagliari, Cagliari, Italy; 11University Hospital of Santa Maria, Lisbon; 12Centre of Interdisciplinary Research in Health (CIIS), UCP Universidade Católica Portuguesa, Lisbon, Portugal; 13Psycho-Oncology Unit, Scientific Direction, Azienda USL di Reggio Emilia – IRCCS, Reggio Emilia, Italy; ¹⁴Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam; ¹⁵Department of Nutrition and Health, Faculty of Health and Social Studies, HAN University of Applied Sciences, Nijmegen, the Netherlands; 16Diabetes and Nutritional Sciences Division, School of Medicine, King's College London, London, UK; ¹⁷William Osler Health Services, University of Toronto, Toronto; 18McMaster University, Hamilton, Canada; ¹⁹Department Onco-Haematology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy.

Updated 2018 ESMO Clinical Practice Guidelines to be published later

Malnutrition/Cachexia

Prevalence in hospitalised patients: 20-70%, depending on setting

Impact:

Quality of life
Treatment tolerance

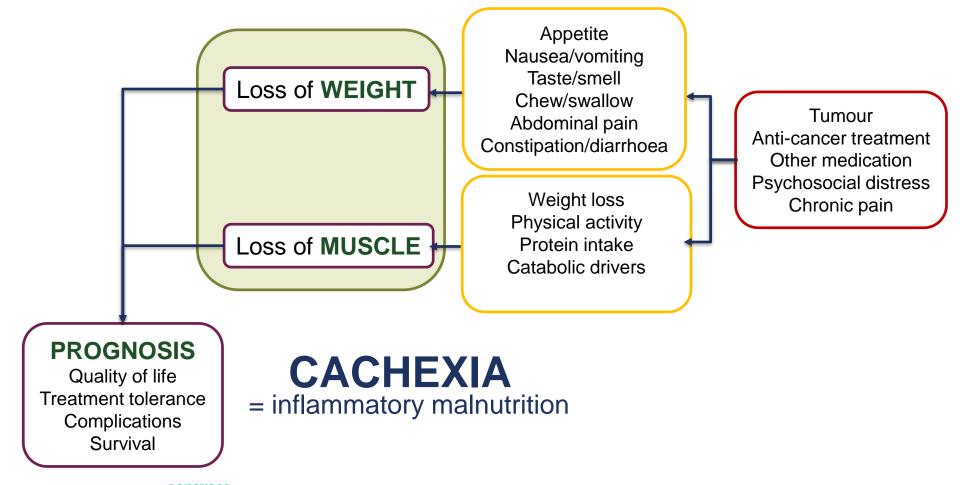
Complications

Survival

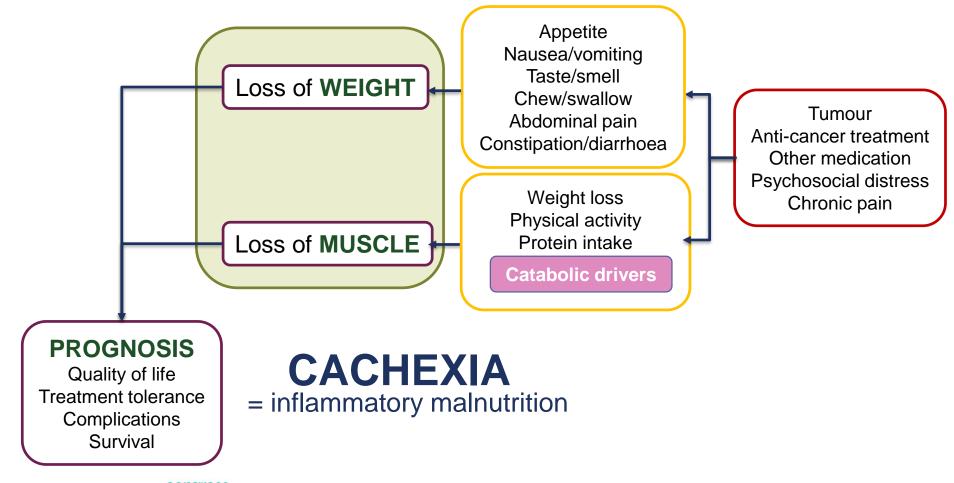
Reports of malnutrition prevalence in hospitalized patients with cancer.

Study, country	Cancer type	Malnutrition prevalence
Attar et al., 2016 [6]	Upper	52% of patients on
France	gastrointestinal	chemotherapy
Planas et al., 2016 [5]	Multiple types	34% at hospital admission,
Spain		36% at discharge
Fukuda et al., 2015 [20]	Gastric	19% of those hospitalized
Japan		for gastrectomy
Maasberg et al., 2015 [21]	Neuroendocrine	25% at risk or actually
Germany		malnourished
Silva et al., 2015 [17]	Multiple types	71%, with 35% moderate
Brazil		and 36% severe
Hebuteme et al., 2014 [4]	Multiple types	39% overall prevalence,
France		varying by cancer type
Aaldriks et al., 2013 [19]	Advanced	39% in patients >70 years,
Netherlands	colorectal	prior to chemotherapy
Freijer et al., 2013 [18]	Multiple types	30% in patients >18
Netherlands		and <60 years old
		39% in patients ≥60 years
Pressoir et al., 2010 [1]	Multiple types	31%, with 12% rated as
France		severely malnourished
Wie et al., 2010	Multiple	61% of all patients, varying
Korea [2]		by cancer type and stage

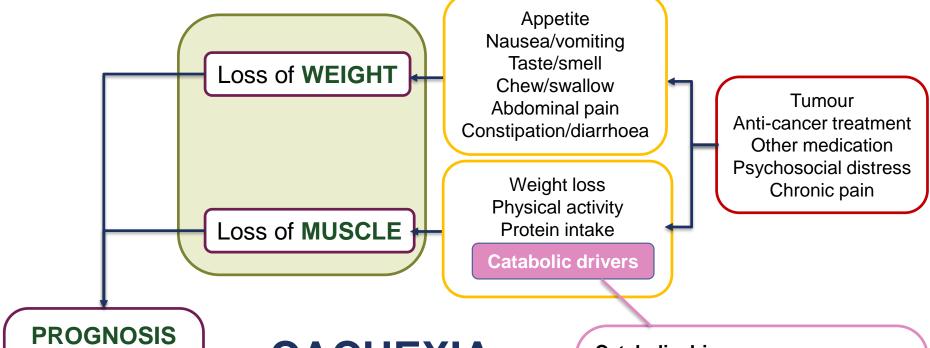












Quality of life
Treatment tolerance
Complications
Survival

CACHEXIA

= inflammatory malnutrition

Catabolic drivers

Acute phase proteins: CRP, albumin

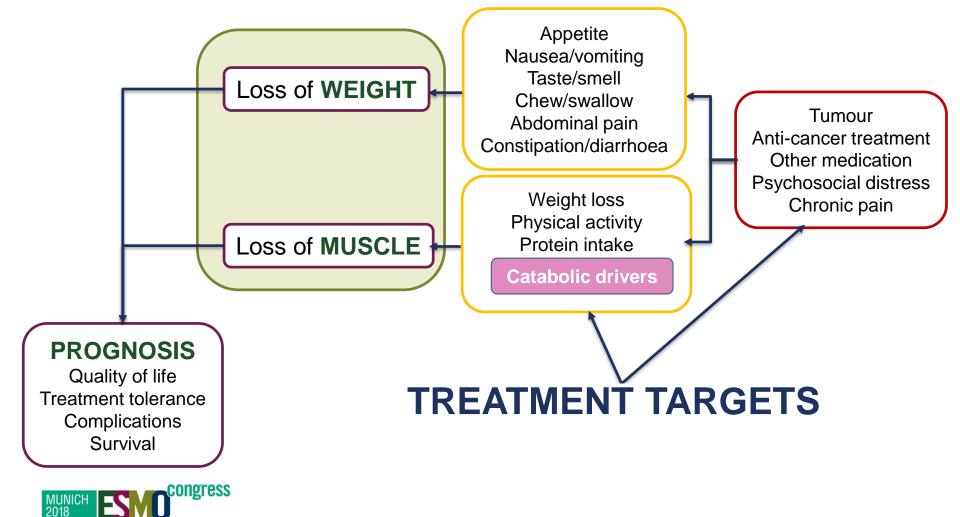
Cytokines: IL6, IL1, TNFα

Hormones: corticosteroids, glucagon, insulin

Eicosanoids: Prostaglandins, leukotrienes

Transcription factors: NFkB, STAT3 Chemokines: CCL2, CCL5, CXCL8 Radical oxygen/nitrogen species





What is malnutrition: up-to-date definition 2018*

Global Leadership Initiative on Malnutrition (GLIM)

Malnutrition Risk Screening: positive

WEIGHT LOSS

- > 5% in 6 M or > 10%**
- > 10% in 6 M or > 20%***

<50% for >1 week any reduction > 2 weeks chronic impaired absorption

LOW FOOD INTAKE

LOW BMI < 20 (< 70y) or < 22 (> 70y)

Asia: < 18.5 (< 70y) or < 20 (> 70y)

acute inflammation chronic inflammation

SYSTEMIC INFLAMMATION

LOW MUSCLE MASS

appendicular skeletal muscle index appendicular lean mass

MUNICH 2018 Congress

*Cederholm T et al. Clin Nutr 2018

**Moderate

***Severe malnutrition

Malnutrition screening

Screen:

all patients undergoing active anti-cancer treatment and all patients with life expectancy of at least a few months using a validated screening tool

NRS 2002 Nutrition risk screening

MUST Malnutrition universal screening tool

SGA Subjective global assessment

MNA Mini Nutritional Assessment

Criteria

Weight

Weight loss

Food intake

Metabolic stress



Malnutrition assessment

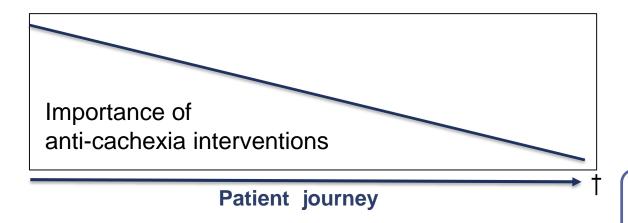
Repeat at regular intervals to guide treatment

If "at-risk", assess:

- nutritional status (weight, weight loss, body composition)
- metabolic status (inflammatory state)
- physical activity
- nutrition impact symptoms (e.g. nausea, dysphagia)
- gastrointestinal dysfunction
- chronic pain
- psycho-social distress



- Provide adequate energy and nutrients
- Alleviate gastrointestinal defects and other impact symptoms
- Decrease catabolic drivers and increase anabolic stimuli



Scores to predict overall survival Good for cohorts

Inadequate for individuals



- Treat if inadequate intake for more than a few days
- Use multi-targeted multi-professional approach
- Offer dietary advice if able to eat; emphasis on protein and at least 5 meals/day
- Treat conditions which interfere with food intake
- Offer nutritional supplements
- If oral intake is inadequate, offer tube feeding; if this is inadequate offer parenteral feeding

<u>But:</u> Offer PN or EN with NGT or PEG only if on anti-cancer treatment <u>or</u> if expected survival is at least several weeks



Estimated requirements

ENERGY: With enteral or parenteral nutrition aim for 25-30 kcal/kg/day

PROTEIN: Provide 1.0-1.5 g/kg/day

SUBSTRATES: In cachexia supply fat to account for 50% of non-protein calories



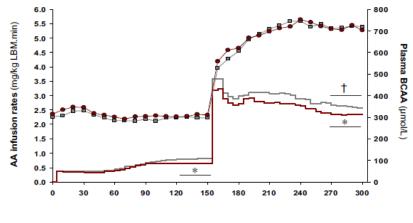
Estimated requirements

ENERGY: With enteral or parenteral nutrition aim for 25-30 kcal/kg/day

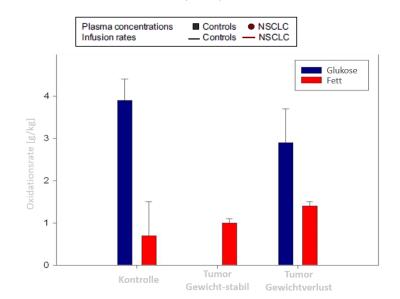
PROTEIN: Provide 1.0-1.5 g/kg/day

SUBSTRATES: In cachexia supply fat to account for 50% of non-protein calories









Pharmaco-nutrients

Supplements enriched in ...

- N-3 fatty acids (EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid)
 - → inadequate evidence
- Leucine, arginine, glutamine
 - → inadequate evidence

Supplements
enriched in N-3 fatty
acids + protein*
→ potential benefit on
Body weight
Lean body mass
Quality of life



Tube feeding, parenteral nutrition (PN)

Use tube feeding to maintain stable weight or reduce losses in malnourished and dysphagic patients with head-neck or upper gastrointestinal cancers on anti-cancer treatment

Insert PEG if requiring 4 weeks or more of enteral feeding

Consider PN if enteral feeding is inadequate to improve nutritional status, physical function and QoL



Pharmacologic agents

A. The following agents may be considered:

Metoclopramide

Consider to treat anorexia or early satiety

Corticosteroids

Consider to use for up to 3 weeks to treat anorexia Consider unwanted effects

Progestins

Consider to treat anorexia, body weight loss

No proven effects on muscle mass, quality of life, physical function

Consider unwanted effects: thromboembolism, oedema, adrenal insufficiency, hypogonadism in males

Pharmacologic agents

B. Insufficient evidence or proven ineffective

Insufficient evidence

Androgens

Cannabinoids

Olanzapine

Cyproheptadine

NSAIDs

Adenosine

Ginseng

Carnitine

Creatine

Proven ineffective

Thalidomide

Melatonin

Pentoxifylline



Physical exercise

Moderate physical exercise

- is safe in patients with cancer cachexia
- is recommended to maintain and improve muscle mass

Grand et al. J Cach Sarc Muscle/Cochrane 2015

Exercise training in cachexia

Systematic review: no RCT found!



Communicative interventions

Consider a psychosocial, educational and communicative intervention, to benefit both patients and their family carers

HCP should:

- empower patients and families to understand the nature and typical course of cachexia, thus promoting patient's hope in the care relationship
- address nutritional concerns of both patients and their family carers and provide tailored information about the role of nutritional support according to the disease stage
- routinely assess patients and their carers for a timely identification of any emotional distress

Multi-modal/combination therapy

We recommend offering multimodal treatment to improve weight loss, anorexia, reduced physical performance and QoL

This is, combining efforts to:

- normalise energy and nutrient intake
- physical activity
- metabolic balance between anabolism and catabolism
- alleviate psychosocial distress

