MALNUTRITION AND CACHEXIA IN CANCER

CLINICAL CASE DISCUSSION

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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

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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

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

Loss of MUSCLE

Appetite
Nausea/vomiting
Taste/smell
Chew/swallow
Abdominal pain
Constipation/diarrhoea

Weight loss
Physical activity
Protein intake
Catabolic drivers

Tumour
Anti-cancer treatment
Other medication
Psychosocial distress
Chronic pain

PROGNOSIS

Quality of life
Treatment tolerance
Complications
Survival

CACHEXIA
= inflammatory malnutrition
Cachexia = inflammatory malnutrition
Loss of WEIGHT
- Appetite
- Nausea/vomiting
- Taste/smell
- Chew/swallow
- Abdominal pain
- Constipation/diarrhoea

Loss of MUSCLE
- Weight loss
- Physical activity
- Protein intake
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Tumour
- Anti-cancer treatment
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CACHEXIA = inflammatory malnutrition

PROGNOSIS
- Quality of life
- Treatment tolerance
- Complications
- Survival

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)

<table>
<thead>
<tr>
<th>Malnutrition Risk Screening: positive</th>
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<tbody>
<tr>
<td>WEIGHT LOSS</td>
</tr>
<tr>
<td>&gt; 5% in 6 M or &gt; 10%**</td>
</tr>
<tr>
<td>&gt; 10% in 6 M or &gt; 20%***</td>
</tr>
<tr>
<td>LOW BMI</td>
</tr>
<tr>
<td>&lt; 20 (&lt; 70y) or &lt; 22 (&gt; 70y)</td>
</tr>
<tr>
<td>Asia: &lt; 18.5 (&lt; 70y) or &lt; 20 (&gt; 70y)</td>
</tr>
<tr>
<td>LOW MUSCLE MASS</td>
</tr>
<tr>
<td>appendicular skeletal muscle index</td>
</tr>
<tr>
<td>appendicular lean mass</td>
</tr>
<tr>
<td>LOW FOOD INTAKE</td>
</tr>
<tr>
<td>&lt;50% for &gt;1 week</td>
</tr>
<tr>
<td>any reduction &gt; 2 weeks</td>
</tr>
<tr>
<td>chronic impaired absorption</td>
</tr>
<tr>
<td>SYSTEMIC INFLAMMATION</td>
</tr>
<tr>
<td>acute inflammation</td>
</tr>
<tr>
<td>chronic inflammation</td>
</tr>
</tbody>
</table>

1 phenotypic criteria + 1 etiologic criteria

*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
Treatment strategy

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

Importance of anti-cachexia interventions

Scores to predict overall survival
Good for cohorts
Inadequate for individuals
Treatment strategy

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

_But:_ Offer PN or EN with NGT or PEG only if on anti-cancer treatment
_or_ if expected survival is at least several weeks

EN, enteral nutrition; NGT, nasogastric tube; PEG, percutaneous endoscopic gastrostomy; PN, parenteral nutrition
Treatment strategy

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
Treatment strategy

Estimated requirements

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

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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

De van der Schueren MAE et al. Ann Oncol 2018
Use tube feeding to maintain stable weight or reduce losses in malnourished and dysphagia 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

NSAIDs, non-steroidal anti-inflammatory drugs
Physical exercise

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

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

HCP, health care provider
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