Cachexia and Nutrition SG

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Definition of Cancer Cachexia

- Multi-factorial syndrome
  - Characterized by ongoing loss of skeletal muscle mass ± loss of fat mass
  - Cannot be reversed fully by conventional nutritional support
  - Leads to progressive functional impairment

**Weight loss >5% over 6 mo** that cannot be attributed to simple starvation
  or

**BMI <20 + weight loss >2%**
  or

Appendicular skeletal muscle mass index consistent with **sarcopenia + weight loss >2%**

*BMI*, body mass index.
Prognostic value of Anorexia-Cachexia

Relationship between Prognosis

- Weight
- Appetite
- Nutritional Impact Symptoms
- Body Composition
- Multiple Domains of cachexia
Reduced survival = a function of body mass index & percent weight loss

Panels A to C represent a 5 × 5 matrix analysis of the five categories of BMI and five categories of %WL for a total of 25 possible combinations. The (A) sample size, (B) median overall survival (months), and (C) unadjusted estimated hazard ratios (HRs; HR, 1.0) are presented for each cell. (*) Reference categories are BMI ≥ 28.0 kg/m² and weight stable ± 2.4%. Different colors represent significant differences (P < .05) in median overall survival and HRs within and between cells of the matrix. Panel D represents the BMI-adjusted WL grading system (grades 0 to 4).

Median survival by grade
0 = 20.9 months
1 = 14.6
2 = 10.8
3 = 7.6
4 = 4.3

Lisa Martin; Pierre Senesse; Ioannis Gioulbasanis; Sami Antoun; Federico Bozzetti; Chris Deans; Florian Strasser; Lene Thoresen; R. Thomas Jagoe; Martin Chasen; Kent Lundholm; Ingvar Bosaeus; Kenneth H. Fearon; Vickie E. Baracos; JCO 2015, 33, 90-99.

<table>
<thead>
<tr>
<th>Panel</th>
<th>BMI (kg/m²)</th>
<th>Weight Loss (%)</th>
<th>Sample Size</th>
<th>Median Survival (months)</th>
<th>HR (1.0)</th>
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<tbody>
<tr>
<td>A</td>
<td>28 25 22 20</td>
<td>2.5 6 11 15</td>
<td>1,848</td>
<td>665 467 400 192 124</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1,384</td>
<td>381 321 368 167 147</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1,737</td>
<td>333 373 498 282 251</td>
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<td>1,182</td>
<td>184 198 339 221 240</td>
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<td>1,987</td>
<td>181 253 430 369 754</td>
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<td>1,744</td>
<td>1,612 2,035 1,231 1,516</td>
<td>Overall</td>
</tr>
<tr>
<td>B</td>
<td>28 25 22 20</td>
<td>2.5 6 11 15</td>
<td>21.6 19.9 15.7 13.5 8.4</td>
<td>17.3</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14.2 11.9 10.5 10.6 7.8</td>
<td>11.3</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10.7 9.2 6.8 6.7 4.7 2.7</td>
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</tr>
<tr>
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<td></td>
<td>8.1 8.1 6.2 5.4 4.4 2.1</td>
<td>6.2</td>
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</tr>
<tr>
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<td></td>
<td>7.1 4.8 4.7 3.7 4.1 1.8</td>
<td>4.4</td>
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</tr>
<tr>
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<td></td>
<td></td>
<td>13.1 10.2 8.1 6.1 4.7 2.1</td>
<td>Overall</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>28 25 22 20</td>
<td>2.5 6 11 15</td>
<td>1.0* 0.9 1.2 1.3 1.8 1.8</td>
<td>1.0</td>
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<td>1.3 1.4 1.6 1.5 1.5 1.8</td>
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<td>1.6 1.9 2.1 2.2 3.1 3.1</td>
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<td>1.9 1.9 2.1 3.1 3.1 3.1</td>
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<td></td>
<td>1.9 3.2 2.8 3.1 3.1 3.1</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.0 1.2 1.4 1.6 2.1 2.1</td>
<td>Overall</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>28 25 22 20</td>
<td>2.5 6 11 15</td>
<td>0 0 1 1 3 3</td>
<td>1 2 2 2 3 3</td>
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<td></td>
<td></td>
<td></td>
<td>1 2 3 3 3 3 4</td>
<td>2 3 3 3 4 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 3 3 3 4 4 4</td>
<td>3 4 4 4 4 4</td>
<td></td>
</tr>
</tbody>
</table>

Reduced survival = a function of body mass index & percent weight loss.
Identifying progression or reversibility

Figure 4  Bar charts for each baseline weight loss grade (0–4) showing the likelihood of improvement to preceding or progress to subsequent grades or death at 1, 2, and 3 months of follow-up.
Variation between skeletal muscle index (SMI) and body mass index (BMI) for females (n = 645)

Patients with cancer cachexia by the conventional criterion (involuntary weight loss) and by two additional criteria (muscle depletion and low muscle attenuation) share a poor prognosis, regardless of overall body weight.
Baseline quality of life as prognostic indicator of survival: Meta-analysis of individual patient data EORTC clinical trials

Overall survival curves stratified by QLQ-C30 appetite loss score. QLQ-C30 = the European Organisation for Research and Treatment of Cancer quality-of-life core questionnaire.

Chantal Quinten, Corneel Coens, Murielle Mauer, Sylvie Comte, Mirjam AG Sprangers, Charles Cleeland, David Osoba, Kristin Bjordal, Andrew Bottomley

Lancet Oncol Volume 10, Issue 9, 2009, 865–871
Cumulative hazard plots of survival (days) for total symptom score quintiles.

Nutrition impact symptoms in a population cohort of head & neck cancer patients: Multivariate regression analysis of symptoms on oral intake, weight loss and survival.

Arazm Farhangfar, Marcin Makarewicz, Sunita Ghosh, Naresh Jha, Rufus Scrimger, Leah Gramlich, Vickie Baracos
Development and validation of a clinically applicable score to classify cachexia stages in advanced cancer patients

Log-rank test p<0.001

Zhou T.J Cachexia Sarcopenia Muscle. 2018
# Pharmacological Management of Nutritional Impact Symptoms

<table>
<thead>
<tr>
<th>Nutritional Impact Symptom</th>
<th>Pharmacological Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early satiety; bloating; GERD</td>
<td>Metoclopramide 10mg qid to q4h po</td>
</tr>
<tr>
<td>Constipation</td>
<td>Laxatives e.g. polyethylene glycol, senna</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>Metoclopramide for non-CINV Olanzapine 5mg qhs if possibly CINV, depression Mirtazapine 15mg qhs if depression, insomnia, anxiety</td>
</tr>
<tr>
<td>Depressed mood or anxiety</td>
<td>Mirtazapine first choice Duloxetine if neuropathic pain</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>Zinc supplement trial for 2 weeks</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Testosterone replacement in males Vitamin D replacement</td>
</tr>
<tr>
<td>Severe pain e.g. Mucositis</td>
<td>Opioid, topical mouthwash</td>
</tr>
</tbody>
</table>

*CINV = chemotherapy-induced nausea or vomiting*
Goals

- Identify those at increased risk
- Identify patients early
- Monitor relevant outcomes
- Incorporate a multidisciplinary approach

Assessment Tool

- Symptom severity assessment including appetite (e.g. ESAS)
- Checklist of nutritional impact factors and weight loss
- Abbreviated PG-SGA, ESAS or other
- Physical performance (e.g. SPPB, handgrip) dynamometer

Multidisciplinary* Management

- Physician = Pharmacological symptom management, education
- Dietitian = Nutritional counseling, protein and calorie goal
- Physical Therapist = resistance and aerobic exercise, fall prevention
- Psychologist = reframing eating, conscious control, body image
- Nurse = education, reinforcement of management plan, phone contact

Monitor Key Outcomes

- Weight change, BMI
- Appetite
- Fatigue, Nutritional impact symptoms and overall symptom burden
- Physical performance
- Body composition
2019
21-23 June
San Francisco
Supportive Care Makes Excellent Cancer Care Possible

SAVE THE DATE
MASCC/IS00
Annual Meeting on Supportive Care in Cancer
www.mascc.org/meeting

Follow us on Twitter: @CancerCareMASCC #MASCC19
Weight-Related Outcomes in Patients with Cancer

- Increased risk for complications, death\(^1\)
- Decreased treatment response \(^2\)
- Greater failure to complete cycles of therapy\(^2,6\)
- Increased toxicity\(^3\)
- Increased fatigue\(^4\)
- Lower QoL\(^5,8\)
- Decreased Performance status
- Low testsosterone

Stages of Cancer Cachexia

Pre-cachexia
- Weight loss ≤5%
- Metabolic/endocrine change

Cachexia
- Weight loss >5%
- Reduced food intake/systemic inflammation

Refractory cachexia
- Low performance score
- Immunocompromise, <3-mo expected survival

“In the beginning of the malady it is easy to cure but difficult to detect, but in the course of time, not having been either detected or treated in the beginning, it becomes easy to detect but difficult to cure.”

Niccolo Machiavelli
Summary

• Consensus Cancer Cachexia definition updated
• Core criterion = weight loss
  Weight loss criteria modified by initial BMI
• Validated by large study resulting in grading system 0-4
• Additional domains may enhance the system
• Importance of appetite and NIS
• Body composition throughout trajectory
• Identify patients in clinical practice, prognosticate, design and inclusion of subjects in clinical trials
Survival analyses (Kaplan-Meier) with comparisons of curves. Survival of male patients with testosterone levels ≤185 ng/dL (blue) was decreased.

**Associations Among Hypogonadism, C-Reactive Protein, and Survival in Male Cancer Patients with Cachexia**

Egidio Del Fabbro, David Hui, Zohra I. Nooruddin, Shalini Dalal, Rony Dev, Gina Freer, Lynn Roberts, J. Lynn Palmer, Eduardo Bruera

# Nutritional Impact Symptoms and treatment

## In a Cancer Cachexia Clinic


<table>
<thead>
<tr>
<th>Nutrition Impact Symptoms</th>
<th>Number Affected (%)</th>
<th>Corresponding Intervention</th>
<th>Number Treated Among Affected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early satiety</td>
<td>94 (62)</td>
<td>Metoclopramide</td>
<td>74 (79)</td>
</tr>
<tr>
<td>Constipation</td>
<td>78 (52)</td>
<td>Laxative</td>
<td>68 (87)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>67 (44)</td>
<td>Antiemetic (metoclopramide)</td>
<td>54 (81)</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>63 (42)</td>
<td>Antidepressant (mirtazapine)</td>
<td>51 (81)</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>42 (28)</td>
<td>Zinc supplement</td>
<td>20 (48)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>21 (14)</td>
<td>GI/speech therapy</td>
<td>5 (24)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>14 (9)</td>
<td>Artificial saliva</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Mucositis pain</td>
<td>11 (7)</td>
<td>Opioid, topical mouthwash</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Dental issues</td>
<td>8 (5)</td>
<td>Dental referral</td>
<td>2 (25)</td>
</tr>
</tbody>
</table>
Fig 1. Line graphs representing the relationships between deciles of (A) body mass index (BMI) and (B) percent weight loss (%WL) to overall survival. Decile 1 represents (A) the lowest BMI and (B) the highest %WL. Decile 10 represents (A) the highest BMI and (B) the lowest %WL. Blue lines represent unadjusted estimated hazard ratios (HRs) associated with reduced overall survival. Reference categories are BMI decile 10 (BMI > 30.9 kg/m²; HR, 1.0) and weight stable (WS; ± 2.4%; HR, 1.0). Risk of reduced survival increases with decreasing BMI and increasing %WL. Gold lines represent the estimated median overall survival in months. Median survival decreases with decreasing BMI and increasing %WL. Different shades of blue in the figures indicate significant differences (P < .05) in median survival between deciles. (*) WS is ± 2.4%.

Published in: Lisa Martin; Pierre Senesse; Ioannis Gioulbasanis; Sami Antoun; Federico Bozzetti; Chris Deans; Florian Strasser; Lene Thoresen; R. Thomas Jagoe; Martin Chasen; Kent Lundholm; Ingvar Bosaeus; Kenneth H. Fearon; JCO 2015, 33, 90-99.
Weight loss in Cancer, present-day

- Obesity increasing worldwide
- Classification of Weight loss should be based on contemporary data
- European and Canadian study of 8160 patients
- Prognostic significance of Weight loss in patients who initially have a low, intermediate, or high BMI

Published in: Lisa Martin; Pierre Senesse; Ioannis Gioulbasanis; Sami Antoun; Federico Bozzetti; Chris Deans; Florian Strasser; Lene Thoresen; R. Thomas Jagoe; Martin Chasen; Kent Lundholm; Ingvar Bosaeus; Kenneth H. Fearon; Vickie E. Baracos; JCO 2015, 33, 90-99.
Additional domains

- Body composition\(^1\)
- Patient reported outcomes
  - Appetite\(^2\)
  - Nutrition Impact symptoms\(^3,4\)
- Fatigue and function\(^5\)
- Dietary intake\(^6\)
- Physical Function\(^7\)
- Chronic inflammation\(^8\)
- Other- chemo & endocrine dysfunction\(^9\)