Nutritional requirements in advanced cancer patients

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Cancer cachexia

“multifactorial syndrome with loss of skeletal muscle mass (with or without loss of fat mass), not fully reversed by conventional nutritional support. Leads to progressive functional impairment. Pathophysiology characterized by negative protein & energy balance driven by a variable combination of reduced food intake and abnormal metabolism”

weight loss, energy intake, advanced stage

p < 0.002

advanced disease & cancer histological aggressiveness

$\leftrightarrow$ ↑REE, wasting, marked intake deficits

Cachexia and QoL: cancer stage & location, weight loss and/or ↓ intake are independent determinants of QoL.

Ravasco et al. Support Care Cancer 2011
advanced disease & cancer histological aggressiveness

$\iff$ ↑ TNF-α, IL1ra, IL-6, IFN-γ, VEGF $\iff$ ↑ REE, wasting, intake deficits

Ravasco et al. Cancer 2012 (in press)
<table>
<thead>
<tr>
<th>Variable</th>
<th>Starvation</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake</td>
<td>↓</td>
<td>↓(*↑)</td>
</tr>
<tr>
<td>Energy expenditure (resting)</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Body fat</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>→</td>
<td>↓</td>
</tr>
<tr>
<td>Liver</td>
<td>↓†</td>
<td>↑†</td>
</tr>
</tbody>
</table>
Clinical Heterogeneity

- e.g. Small cell lung cancer patient with severe B-type symptoms (pyrexia, sweating etc) and cachexia mainly due to hypermetabolism

- e.g. Pharyngeal cancer patient with cachexia mainly due to reduced food intake secondary to dysphagia

- Variable proportion of metabolic change that can be reversed by treating catabolic factors

- Variable proportion of reduced food intake that can be reversed by treating ‘secondary anorexia’
I. Depletion of Reserves
- Underweight
- Weight loss
- Lean tissue wasting
- Sarcopenia (severe muscle wasting)

II. Limitation of food intake
- Nutrition impact symptoms:
  - Anorexia
  - Dysphagia
  - Nausea
  - Social / psychological

III. Catabolic Drivers
- Inflammation
- Tumor burden
- Insulin resistance
- Hypogonadism
- Corticosteroids
- Comorbidities

IV. Impact and outcomes
- Physical function
- Quality of life
- Distress
- Survival
- Treatment outcomes
- Costs
Early intervention: pre or early cachexia
<table>
<thead>
<tr>
<th><strong>Incurable patients: screening and assessment</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STRONG</strong></td>
</tr>
</tbody>
</table>

| **Questions for research** | Effects of malnutrition screening programs combined with multidisciplinary interventions on quality of life in incurable cancer patients |

ESPEN Guidelines Cancer, 2016
<table>
<thead>
<tr>
<th></th>
<th>Energy requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRONG</td>
<td><strong>Total energy expenditure of cancer patients, if not measured individually, be assumed to range between 25 and 30 kcal/kg/day.</strong></td>
</tr>
<tr>
<td>Questions for research</td>
<td>improve prediction of energy requirements in individual patient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Protein intake</th>
</tr>
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<tbody>
<tr>
<td>STRONG</td>
<td><strong>Above 1 g/kg/day and if indicated go up to 1.5 g/kg/day</strong></td>
</tr>
<tr>
<td>Questions for research</td>
<td>effect on outcome of increased supply and composition of protein/amino acids</td>
</tr>
</tbody>
</table>
### Choice of energy substrates

<table>
<thead>
<tr>
<th>STRONG</th>
<th>In most patients general recommendations are applicable. In weight-losing patients with advanced cancer, in addition to an adequate protein intake, we recommend a fat intake of 35-50% of total energy requirement.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Questions for research</td>
<td>effect of high fat on outcome in specific patient groups</td>
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</table>
### N-3 fatty acids to improve appetite and body weight

**WEAK**

*In incurable cancer patients undergoing chemotherapy and at risk of weight loss, we suggest to use the supplementation with long-chain n-3 fatty acids or fish oil to stabilize or improve appetite, food intake, lean body mass and body weight.*

<table>
<thead>
<tr>
<th>Questions for research</th>
<th>Effect of long-chain N-3 fatty acids on body composition and clinical outcome in cancer patients undergoing antineoplastic treatment</th>
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</table>
Nutrition

• Main goal is to promote energy balance and optimise protein intake
• Usual deficits are approx. 300-400 kcal/d and 0.5g Protein/kg/d
• Best approach is with normal food
• Can use conventional oral supplements but recent meta-analysis did not show benefit after correction for heterogeneity*
• EPA enriched supplements result in increased energy and protein intake, increased LBM (1.6kg) and improved appetite and fatigue**

** Sanchez-Lara K et al Clin Nutr 2014;e-pub
ORIGINAL ARTICLE
Oral nutritional supplements containing n-3 polyunsaturated fatty acids affects quality of life and functional status in lung cancer patients during multimodality treatment: an RCT
BS van der Meij¹, JAE Langius², MD Spreeuwenberg², SM Slootmaker³, MA Paul⁴, EF Smit⁵ and PAM van Leeuwen⁴

Figure 1. Physical activity (daily PAM score) over time for the I and C groups. Values are mean ± s.d., baseline: n = 12 (I), n = 16 (C); week 3: n = 13 (I) and n = 17 (C); week 5: n = 8 (I), n = 13 (C). *P < 0.05, difference between the I and C group (analysed by generalised estimating equations, with baseline value and sex as covariate).
Spontaneous PA (time spent sitting / lying, time standing, time walking and number of steps/day) of cancer patients at different stages of disease (n = 75) and healthy volunteers (n = 20).

Ferrioli et al et al 2012
Exercise alongside nutrition

- Improved lower and upper limb strength (~20%)
- Increased lean body mass (~1kg)
- Improved HRQoL including physical functioning, role functioning, social functioning and fatigue

Mishra SI et al Cochrane 2012
Stene GB et al Crit Rev Oncol Haematol 2013
At home

A Home-Based Exercise Program to Improve Function, Fatigue, and Sleep Quality in Patients With Stage IV Lung and Colorectal Cancer: A Randomized Controlled Trial

- 66 patients (half on active treatment)
- resistance training + pedometer
- 90min, four times weekly, 8 weeks
- improved mobility, fatigue, sleep quality

Cheville et al. JPSM 2013;45:811-21
Interdisciplinary rehabilitation (10-12w) in advanced cancer (n=188)

- 30% did not complete all sessions
- Physician, nurse, dietician and regular visits and calls
- Improved QoL; activity and physical fatigue (E.S. 0.8-1.1)
- Six min walk increased by 41m (10%)
- Gait speed increased by 0.15m/s (10%)

Gagnon B et al Curr Oncol 2013;20:310-8
Evolution of Cachexia and Therapy

- Single agents/elements
- Definition of best supportive multimodal care
- Phase III trials incorporating best supportive care
- Supportive Oncology (nutritional response, QoL, treatment tolerance, survival)
- Palliative therapy (symptoms, nutritional response)

Time (years/decades)
CONCLUSIONS...

• No simple solution
• Cachexia therapy should be integrated in overall oncology management
• Early intervention
• Professionals and nurses need adequate knowledge on nutrition and exercise
• Assessment should be linked to treatment
• Goals should be realistic
• Multimodal care pathways are self-evident but still to be evidence-based