PRECEPTORSHIP ON SUPPORTIVE AND PALLIATIVE CARE

Cancer cachexia: Practical assessment, prevention and treatment, including when is invasive nutrition neeeded

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DISCLOSURE OF INTEREST

Honoraria for scientific presentations from:
Baxter, B.Braun, Chugai, Danone/Nutricia, Fresenius Kabi, Seca
SESSION 6: MULTIMODAL AND MULTIPROFESSIONAL MANAGEMENT I

Cancer cachexia: Practical assessment, prevention and treatment, including when is invasive nutrition needed
In advanced cancer, weight loss is frequent and associated with impaired prognosis.

Weight loss at cancer diagnosis

- Loss >10%
- Loss 5-10%
- Loss <5%
- Stable

N=3047 cancer patients with advanced disease

Severe weight loss until time of diagnosis

- Breast
- Sarcoma
- Prostate
- Colon
- Lung
- Lymphoma
- Pancreas
- Stomach

Fraction with weight loss >10% during 6 months (%)

Weight loss at time of diagnosis in patients with advanced cancer
Point prevalence of malnutrition: Multi-center, Australia, 2012 and 2014, outpatient chemotherapy, radiotherapy, in-patients
Of all cancer patients 45% are losing body weight. 25% will die from cachexia.

“Nutrition” as a topic in oncology is found...

- Medline 3.4% of all “cancer” abstracts
- ASCO 2.4% of all abstracts
- ESMO 2.3% of all abstracts
- NCI 0.2% of all grant proposals aim at “cachexia”

Survival in advanced cancer
Association with BMI, weight loss and muscularity

<table>
<thead>
<tr>
<th>Weight Loss (%)</th>
<th>13.1</th>
<th>10.2</th>
<th>8.1</th>
<th>6.1</th>
<th>4.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>21.5</td>
<td>19.9</td>
<td>15.7</td>
<td>13.5</td>
<td>8.4</td>
</tr>
<tr>
<td>25</td>
<td>14.2</td>
<td>11.9</td>
<td>10.5</td>
<td>10.6</td>
<td>7.8</td>
</tr>
<tr>
<td>22</td>
<td>10.7</td>
<td>9.2</td>
<td>6.8</td>
<td>6.7</td>
<td>4.7</td>
</tr>
<tr>
<td>20</td>
<td>8.1</td>
<td>8.1</td>
<td>6.2</td>
<td>5.4</td>
<td>4.4</td>
</tr>
<tr>
<td>Overall</td>
<td>7.1</td>
<td>4.8</td>
<td>4.7</td>
<td>3.7</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Diagnostic criteria for classification of cancer-associated weight loss
Martin L et al. J Clin Oncol 2014

MUSCULARITY

Threshold for increased risk of death

SARCOPENIA

Cancer cachexia
Fearon et al. Nat Rev Clin Oncol 2013
Sarcopenia = muscle mass < 5 percentile of reference population
Use CT scan at L3

BMI 30 kg/m², BSA 2.0 m²
Sarcopenia = low muscle mass, in adults with solid tumors: Systematic review and metaanalysis

N=38 trials, N=7843 patients

Muscle mass index via CT at L3

Low muscle mass associated with

→ **poor overall survival** \( (p<0.001) \)

→ **poor cancer-specific survival** \( (p<0.001) \)

→ **poor disease-free survival** \( (p=0.014) \)

*Shachar SS et al. Eur J Cancer 2016*
Sarcopenic obesity in patients with solid tumors

N=250 obese patients with Advanced GI or lung cancer

→ MS 11 vs 21 m

Prevalence and clinical implications of sarcopenic obesity
Prado CM et al. Lancet Oncol 2008
Systemic inflammation and survival

Survival in patients with colorectal cancer

Survival in patients with colorectal cancer

Liu Y et al. Scientific Reports 2017

Systemic inflammation and survival

25 articles, 5660 participants

Survival rates (%)

Years after ope

272 patients

HR of death

Study ID

Read (2006)
Ishizuka (2007)
Toivama (2011)
Kshioi (2013)
Son (2013)
Xiao (2013)
Nosee (2014)
Kobayashi (2014)
Lin (2015)
Adachi (2015)
Shibutani (2015)
Ghanim (2015)
Song (2015)
Eren (2016)
Park (2016)
Ishizuka (2016)

Overall (χ² = 74.3%, p = 0.000)

NOTE: Weights are from random effects analysis

HR (95% CI)  % Weight

2.27 (1.09, 4.73) 7.26
6.05 (1.37, 27.03) 3.80
2.80 (1.43, 5.49) 7.66
3.71 (1.89, 7.36) 7.51
2.22 (0.72, 6.80) 5.03
1.64 (0.76, 3.53) 7.03
7.41 (3.66, 15.20) 7.40
2.84 (1.28, 6.29) 6.87
3.21 (1.15, 8.93) 5.57
8.09 (1.51, 43.25) 3.07
7.24 (1.18, 44.41) 2.73
3.59 (1.24, 10.42) 5.35
1.79 (0.65, 4.94) 5.62
4.10 (1.42, 11.86) 5.66
1.28 (1.13, 1.45) 10.59
1.81 (1.18, 2.77) 9.24
2.93 (2.00, 4.00) 100.00
Cancer cachexia – Consensus Group definition

- **Precachexia**
  - Weight loss ≤5%
  - Anorexia and metabolic change

- **Cachexia**
  - Weight loss >5% or BMI <20 and weight loss >2%
  - Or sarcopenia and weight loss >2%
  - Often reduced food intake/systemic inflammation

- **Refractory cachexia**
  - Variable degree of cachexia
  - Cancer disease both procatabolic and not responsive to anticancer treatment
  - Low performance score
  - <3 months expected survival

**Definition and classification of cancer cachexia – an international consensus**

Fearon K et al. Lancet Oncology 2011
War of the words

What is „malnutrition“
„undernutrition"
„cachexia“
„sarcopenia“
„protein energy malnutrition“
„marasmus“
„kwashiorkor“
Cachexie = malnutrition in cancer?
weight loss >10%?
Consensus definition?
malnutrition complicated by
metabolic derangements?
### Cachexia: Consensus Group Definition 2011

<table>
<thead>
<tr>
<th>Weight loss</th>
<th>BMI&lt;20</th>
<th>Sarcopenia</th>
<th>Metabolic change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2%</td>
<td></td>
<td></td>
<td>precachexia</td>
</tr>
<tr>
<td>2-5%</td>
<td>cachexia</td>
<td>cachexia</td>
<td>precachexia</td>
</tr>
<tr>
<td>5-10%</td>
<td>cachexia</td>
<td>cachexia</td>
<td>cachexia</td>
</tr>
<tr>
<td>&gt;10%</td>
<td>cachexia</td>
<td>cachexia</td>
<td>cachexia</td>
</tr>
</tbody>
</table>

Fearon K et al. Lancet Oncol 2011
## Cachexia: Pathophysiology-based approach

<table>
<thead>
<tr>
<th>Weight loss</th>
<th>No metabolic change</th>
<th>Metabolic change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2%</td>
<td></td>
<td>pre-cachexia</td>
</tr>
<tr>
<td>2-5%</td>
<td>malnutrition</td>
<td>pre-cachexia</td>
</tr>
<tr>
<td>5-10%</td>
<td>malnutrition</td>
<td>cachexia</td>
</tr>
<tr>
<td>&gt;10%</td>
<td>malnutrition</td>
<td>cachexia</td>
</tr>
</tbody>
</table>

**Treatment:**
- energy, nutrients
- multimodal therapy

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e.g. Cederholm T et al. Clin Nutr 2018
Cachexia

Nutrition in cancer patients

Arends J. Dtsch Aerztebl 2016

- Anorexia
- Dysphagia
- Nausea
- Abdominal pain
- Malabsorption
- Fatigue
- Uncontrolled pain
- Depression
- SIRS, tumor-associated infections
- Infections
- Wounds, surgery

Energy intake

Muscle activity

System. inflammation

BODY

MUSCLE MASS
Nutrition in cancer patients

Cancer cachexia in adult patients
Bozzetti F et al. Ann Oncol in review
Nutrition concept in oncology

What are the limits?

Do not underfeed → screen all patients

Do not overfeed → individualize at the end of life
## Screening

### Nutritional status

<table>
<thead>
<tr>
<th>Points</th>
<th>Food intake</th>
<th>Weight loss</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50-75%</td>
<td>&gt; 5%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>25-50%</td>
<td>&gt; 7.5%</td>
<td>18.5-20.5</td>
</tr>
<tr>
<td>3</td>
<td>0-25%</td>
<td>&gt; 15%</td>
<td>&lt; 18.5</td>
</tr>
</tbody>
</table>

### Age

- ≥ 70 years

### Severity of disease (≈ metabolic stress)

- Chronic disease (oncology, diabetes, ..)
- Severely acute ill (pneumonia, stroke, hematologic malignancy, ..)
- Intensive care (sepsis, bone marrow transplant, ..)

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1 2 3 4 5 6 7

Nutritional support

BMI, body mass index

Nutrition Risk Screening. Kondrup et al., Clin Nutr 2013
Patients with dementia:

Comfort feeding Only (CFO)

What is the goal?

Avoid ineffective tube feeding in dementia by careful hand feeding as long as no distress

Comfort feeding only
Deciding on artificial nutrition in patients with advanced disease: balancing benefits and risks

<table>
<thead>
<tr>
<th>Some examples of arguments ...</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>... favouring interventions</strong></td>
</tr>
<tr>
<td>ongoing anti-cancer treatment</td>
</tr>
<tr>
<td>no or only minimal inflammation or inflammation responsive to treatment</td>
</tr>
<tr>
<td>no or only slow and mild weight loss</td>
</tr>
<tr>
<td>stable or only slowly progressing cancer</td>
</tr>
<tr>
<td>good chance of intervention to improve the patients well being</td>
</tr>
<tr>
<td>strong wish of the patient to accomplish or reach an individual goal</td>
</tr>
<tr>
<td>patient is able and motivated to be physically active</td>
</tr>
<tr>
<td>Severely impaired food tolerance</td>
</tr>
</tbody>
</table>
### Energy and Nutrient Requirements

**Requirements should be fulfilled**

<table>
<thead>
<tr>
<th><strong>Energy</strong></th>
<th>25-30 kcal/kg (STRONG)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protein/Amino acids</strong></td>
<td>1,0-1,5 g/kg or possibly more (WEAK)</td>
</tr>
<tr>
<td><strong>Fat/Carbohydrate</strong></td>
<td>up to 50:50 energy % (STRONG)</td>
</tr>
<tr>
<td><strong>Vitamins and trace elements</strong></td>
<td>RDA (STRONG)</td>
</tr>
</tbody>
</table>

**Nutrition in cancer patients**

Exercise, physical activity

Maintain or increase

level of physical activity (STRONG)

employ trained experts

Nutrition in cancer patients
## Pharmacologic Agents and Pharmaconutrition

*Use only in palliative settings*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>Corticosteroids or Progestins</td>
<td>watch for: side effects <em>(WEAK)</em></td>
</tr>
<tr>
<td>Taste alterations</td>
<td>Cannabinoids</td>
<td>(--)*</td>
</tr>
<tr>
<td>Muscle Mass</td>
<td>Androgens</td>
<td>(--)*</td>
</tr>
<tr>
<td>Fat Free Mass</td>
<td>Amino acids/Metabolites</td>
<td>(--)*</td>
</tr>
<tr>
<td>Weight loss</td>
<td>NSAID</td>
<td>(--)*</td>
</tr>
<tr>
<td>Weight loss: EPA (N-3 fatty acids)</td>
<td>1.5 g/d or more</td>
<td><em>(WEAK)</em></td>
</tr>
<tr>
<td>Early satiety</td>
<td>Metoclopramide, Domperidone</td>
<td><em>(WEAK)</em></td>
</tr>
</tbody>
</table>

### Nutrition in cancer patients

## ESPEN guidelines on nutrition in cancer patients

### Systemic anticancer treatments and Radiooncology (RO)

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensure adequate nutritional intake and maintain physical activity</td>
<td>STRONG</td>
</tr>
<tr>
<td>If oral intake is inadequate, use: enteral nutrition</td>
<td></td>
</tr>
<tr>
<td>if enteral is inadequate use parenteral nutrition</td>
<td>STRONG</td>
</tr>
<tr>
<td>RO: Use tube feeding in severe mucositis or with obstruction</td>
<td>STRONG</td>
</tr>
<tr>
<td>RO: With tube feeding: maintain swallowing function</td>
<td>STRONG</td>
</tr>
<tr>
<td>In dying patients care should be based on comfort</td>
<td>STRONG</td>
</tr>
<tr>
<td>In acute confusional states a short hydration may be used to rule out dehydration as a cause</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions

Acknowledge the prevalence and impact of malnutrition
→ screen all cancer patients
If ‘at-risk’: Assess for
→ nutritional resources
  → metabolic status
  → treatable deficiencies
Optimize
→ energy intake
→ protein intake
→ physical activity
→ systemic inflammation
Conclusions

What will be required?

COMMITMENT
RESPONSIBILITIES
STANDARD OPERATING PROCEDURES
QUALITY CONTROL PROCESS