OPTIMIZING THE NUTRITIONAL SUPPORT IN THE ELDERLY CANCER PATIENT

Federico Bozzetti

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TOPICS

- Detecting malnutrition
- Choosing the way for feeding
- Optimising the nutrients composition
TOPICS

• Detecting malnutrition

• Choosing the way for feeding

• Optimising the nutrients composition
**STRENGTH:** Classes correlate with the type of tumours, cancer stage, symptoms/patient, ECOG and nutritional risk score in 1307 patients

- 10% weight loss “clinically significant” by NIH, ASPEN, ASCN (*JPEN 1997*), ASPEN MALNUTRITION TF (*JPEN 2012*)
- It is a guide to therapy

**LIMITATIONS:** Not consensus-based
Main Malnutrition Risk Screening Tools

<table>
<thead>
<tr>
<th>Malnutrition Risk Screening Tools</th>
<th>Description</th>
<th>Parameters Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malnutrition Screening Tool (MST)(^9)</td>
<td>MST is a simple, quick-to-administer, 2-question tool.</td>
<td>Unintentional weight loss(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Appetite(^a)</td>
</tr>
<tr>
<td>Nutritional Risk Screening–2002 (NRS-2002)(^10)</td>
<td>Developed by ESPEN, this is a preferred tool to screen for malnutrition in European hospital settings.</td>
<td>Unintentional weight loss(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMI(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disease severity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impaired general condition</td>
</tr>
<tr>
<td>Malnutrition Universal Screening Tool (MUST)(^11)</td>
<td>Developed for screening in the community, MUST is widely used in the United Kingdom and Europe.</td>
<td>Unintentional weight loss(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMI(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disease severity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Food intake(^a)</td>
</tr>
<tr>
<td>Short Nutritional Assessment Questionnaire (SNAQ)(^12)</td>
<td>A simple, easy-to-administer, 3-question screening tool developed in the Netherlands for hospital screening.</td>
<td>Unintentional weight loss(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Appetite(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use of oral supplement or tube feeding</td>
</tr>
</tbody>
</table>

BMI, body mass index; ESPEN, European Society for Clinical Nutrition and Metabolism.
\(^a\)Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition diagnostic characteristic.
### Table 1  Initial screening

<table>
<thead>
<tr>
<th></th>
<th>Is BMI &lt;20.5?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Has the patient lost weight within the last 3 months?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Has the patient had a reduced dietary intake in the last week?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Is the patient severely ill? (e.g. in intensive therapy)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Yes:** If the answer is 'Yes' to any question, the screening in Table 2 is performed.  
**No:** If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.

### Table 2  Final screening

<table>
<thead>
<tr>
<th>Absent Score 0</th>
<th>Impaired nutritional status</th>
<th>Severity of disease (≈ increase in requirements)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal nutritional status</td>
<td>Absent Score 0</td>
</tr>
<tr>
<td>Mild Score 1</td>
<td>Wt loss &gt; 5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week</td>
<td>Mild Score 1</td>
</tr>
<tr>
<td>Moderate Score 2</td>
<td>Wt loss &gt; 5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week</td>
<td>Moderate Score 2</td>
</tr>
<tr>
<td>Severe Score 3</td>
<td>Wt loss &gt; 5% in 1 mth (&gt;15% in 3 mths) or BMI &lt;18.5 + impaired general condition or Food intake 0–25% of normal requirement in preceding week in preceding week</td>
<td>Severe Score 3</td>
</tr>
</tbody>
</table>

Score: +  
Score: = Total score
TOPICS

• Detecting malnutrition

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The clinical approach to cancer patients «at nutritional risk»

1. Patients with all GI tract working

2. Patients with upper GI tract not accessible

3. Patients with all GI tract not accessible/working
The clinical approach to cancer patients «at nutritional risk»

1. Patients with all GI tract working
   - use oral feedings and supplements

2. Patients with upper GI tract not accessible

3. Patients with all GI tract not accessible/working
Effects of oral supplementation


13 RCT: 7 non-malnourished, 1 malnourished, 2 mixed, 3 undetermined

1. Dietary counseling alone does not ameliorate the QoL
2. Dietary counseling given with or without ONS is effective at increasing nutritional intake and weight
3. Dietary counseling plus nutritional supplements improves weight more than dietary counseling alone or than the simple usual care
5. Oral nutritional intervention has no effect on mortality
Muscle protein synthesis in cancer patients can be stimulated with a specially formulated medical food

(Deutz NE et al. Clin Nutr. 2011)

OBJECTIVE: to determine if a specially formulated medical food, high in leucine and protein, stimulates muscle protein synthesis acutely in individuals with cancer to a greater extent than a conventional medical food.

DESIGN: The experimental group (n = 13) received a medical food containing 40 g protein, based on casein and whey protein and enriched with 10% free leucine and other specific components, while the control group (n = 12) was given a conventionally used medical food based on casein protein alone (24 g).

RESULTS: medical food increased significantly muscle protein FSR. In contrast, ingestion of the control medical food did not increase muscle FSR.

**AIMS:** to test whether AA can acutely stimulate muscle protein synthesis in cancer patients (CA) undergoing intense chemotherapy.

**METHODS:** ingestion of 40 g of AA given in 30 mL boluses every 10 min for 3h.

Mixed muscle fractional synthetic rate (FSR) in the basal state (white bars) and in response to amino acids (black bars). **Significantly different than basal, P≤0.001.**
ω-3FA enriched supplements

3 systematic reviews, 2 meta-analyses

• recent non-RCT
  ➢ ω-3FA ↑ lean body mass in pts with H&N cancer (*Weed et al, 2011*)
  ➢ ω-3FA ↑ muscle mass and body weight and response to chemotherapy in lung cancer pts (*Murphy et al, 2011*)

• recent RCT
  ➢ ω-3FA improved QoL in lung cancer patients on multimodality therapy (*Van der Meij et al, 2012*)
  ➢ ω-3FA reduced leukopenia in patients on neoadjuvant chemotherapy for esophageal cancer (*Miyata et al, 2012*)
  ➢ ω-3FA decreased the weight loss and was associated with a higher remission rate at months in leukemic pediatric pts (*Bayram et al, 2009*)
How to optimize the use of ONS
(modified from Hubbard et al, 2012)

1. Greater compliance with higher energy density (91% with 2 kcal/ml)
2. Compliance probably better with liquid ONS
3. ONS energy should be additive to food: clinical benefits occurred when the intake was in the range of 250-600 kcal/day for ≥5 weeks, hence:
   - administer ONS between meals
   - increase variety of the products
   - offer small amounts x multiple times (if bolus administration is not possible)
   - identify best times
4. Give AA as a bolus (whenever possible)
5. Use ω-3FA and EAA and/or BCAA and/or leucine-enriched ONS
The clinical approach to nonsurgical cancer patients «at nutritional risk»

1. Patients with all GI tract working:
   - try first with oral nutritional intervention (supplements, better if ω-3 and/or leucine-enriched) +/- counseling and megestrol (?)
   - consider supplemental PN

2. Patients with upper GI tract not accessible:
   - consider tube feeding (NG/J vs PEG)

3. Patients with all GI tract not accessible/working
Effects of tube feeding

- Large experience in H&N cancer pts during RT +/-CT

- Many non-RCT show better weight maintenance, QoL, compliance with RT/CT and fewer readmissions to the hospital in comparison with oral feeding

- RCT of PEG vs NG: better weight maintenance and longer duration of EN (Corry et al. 2008, Silander et al. 2012) and similar (Corry et al. 2008) or better QoL (Silander et al. 2012)
The clinical approach to nonsurgical cancer patients «at nutritional risk»

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   - try first with oral nutritional intervention (supplements, better if ω-3 and/or leucine-enriched) +/- counseling and megestrol (?)
   - consider supplemental PN

2. Patients with upper GI tract not accessible:
   - consider tube feeding (NG/J vs PEG)

3. Patients with all GI tract not accessible/working:
   - consider PN
Effects of parenteral nutrition

Little scientific experience and very few RCT

but

• The approach is very practical in hospitalized patients
• Well accepted by the patients (Scolapio et al. JPEN 2002) who often already harbour a CVC
• Patients may not differentiate between therapy and nutritional support
• Small volume high density emulsions can cover a large part of the energy requirement
SUPPLEMENTAL PN

... is a partial PN and is not used in aphagic-(sub)obstructed-incurable cancer patients, but in an earlier phase of the disease when oral food intake starts declining and patients who may or may not be receiving some kind of oncologic therapy, continuously lose their body weight. Its rationale relies on the awareness that progressive starvation and weight loss adversely affect quality of life and length of survival of the patients...
Improved Clinical Outcomes in Patients With Advanced Esophageal Cancers Utilizing Supplemental Parenteral Nutrition

Patients receiving PN support were able to tolerate higher doses of chemoradiation therapy without increased toxicity.


To better understand the impact of undernutrition, nutritional risk, and nutritional treatment on the clinical outcomes of hospitalized cancer patients in China, the authors conducted a multicenter, cross-sectional study with 2248 cancer patients from 20 hospitals from January to June 2010. The authors defined 19.7% and 26.8% patients as undernourished at baseline and reassessment, respectively. Patients with gastrointestinal malignancies had a higher rate of undernutrition than other patients. The nutritional risk rate was 24.6% and 40.2% at baseline and reassessment, respectively. For patients with nutritional risk, the relative risk (RR) of adverse events (AEs) significantly increased with and without nutritional treatment. In comparison with the nonnutritional treatment subgroup, patients who received enteral nutrition (EN) or total parenteral nutrition (TPN) significantly reduced the RR of AE development. The RR of AEs for EN and TPN were 0.08 (95% CI: 0.01-0.62) and 0.56 (95% CI: 0.33-0.96), respectively. Separated nutrient infusion increased the risk of AEs. The authors concluded that undernutrition and nutritional risk are general problems that impact the outcomes of hospitalized cancer patients in China. Higher NRS2002 scores are related to AE risk but not weight loss. In nutritional treatment, EN and TPN can significantly reduce the risk of AEs.
SUPPLEMENTAL HPN

309 patients with progressive cachexia and receiving indomethacin, EPO and iron (when necessary) were randomized to HPN or no HPN when oral intake dropped to 21-24 Kcal/Kg/d
Total AA intake g/Kg/d: \( \sim 0.8 \) (ent)+ 0.6-0.9 (iv)

At intention-to-treat basis: ↑ energy balance

As-treated analysis: ↑ energy balance
↑ survival
↑ maximum exercise capacity

*Pelzer* (2010): ↑ phase angle
Survival of 414 incurable cachectic (sub)obstructed cancer patients on HPN

(Bozzetti et al. *Annals of Oncology* 2014)

3-month: 57%  6-month: 28%
SPECIFIC NUTRITIONAL REGIMEN for ADVANCED CANCER PATIENTS

- Water ≤ 30 mL/kg
- npEnergy ~30 kcal/kg
- Glucose ≤ 50% (≈3.7g/kg)
- Fat (L/MCT+N-3) ≥ 50% (≈1.6g/kg)*
- Amino acid 1.5-2 g/kg
- Sodium ≤1mEq/kg

* may be administered in 15 hrs (limiting dose for LCT 2.6 g/Kg/d)
Take-home messages

• **Oral supplements**
  - potential use in a large number of patients,
  - efficacy depending on the quantity, quality and timing and duration of administration

• **Tube feeding**
  - the «best» option in pts with non-working UGI

• **Parenteral nutrition**
  - the obligatory option when GI is not working but also a very practical way to integrate an inadequate oral nutrition

In all conditions privilege low-volume high density formulas, with a high FAT to CHO ratio and enriched in EEA, BCAA and leucine
...knowledge is the enemy of disease...
## Effects of PN on protein metabolism

*(from Bozzetti & Bozzetti Clin Nutr in press)*

<table>
<thead>
<tr>
<th>Author</th>
<th>N°pts</th>
<th>Type of tumour</th>
<th>WL*</th>
<th>npKcal/Kg/d</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bozzetti et al. 2000</td>
<td>3</td>
<td>Gastroenteric</td>
<td>22%</td>
<td>36</td>
<td>L-[²H₅] phenylalanine and L-[²H⁴]tyrosine</td>
</tr>
<tr>
<td>Burt et al. 1984</td>
<td>11</td>
<td>Oesophagus</td>
<td>16.1%</td>
<td>36</td>
<td>¹⁵N glycine</td>
</tr>
<tr>
<td>Hyltander et al. 1991</td>
<td>12</td>
<td>Miscellaneous</td>
<td>13.6%</td>
<td>26→44</td>
<td>L-[U-¹⁴C] tyrosine</td>
</tr>
<tr>
<td>Jeevanandam et al. 1988</td>
<td>5</td>
<td>Gastroenteric</td>
<td>18%</td>
<td>29</td>
<td>¹⁵N glycine</td>
</tr>
<tr>
<td>Shaw et al. 1991</td>
<td>43</td>
<td>Miscellaneous</td>
<td>8.4%</td>
<td>24</td>
<td>¹⁴C-leucine</td>
</tr>
</tbody>
</table>

PURPOSE:
This study aimed to test whether a very early nutrition intervention delivered over the telephone was feasible and could improve outcomes amongst patients with upper gastrointestinal cancer.

METHODS:
Participants with a histologically proven new diagnosis of primary oesophageal or stomach cancer and who were to undergo surgery and/or chemotherapy were randomised to receive either standard nutrition care (SC) or early and intensive nutrition intervention (NI) over the telephone/face-to-face. Participants were followed for 6 months. The primary outcome was quality of life (QoL), assessed using the European Organization for Research and Treatment of Cancer Global Quality of Life questionnaire C30 (EORTC QLQ-C30) and the European Quality of Life Instrument (EQ-5D) tool; secondary outcomes were nutritional status and survival.

RESULTS:
Twenty-one participants were recruited (11 SC and 10 NI). At baseline, the prevalence of malnutrition was 90 %. Compared with SC, the NI group had a significantly higher EORTC global QoL score at the first mid-study follow-up (coefficient (95 % CI) 21.0 (12.1, 29.9) adjusted for baseline, p < 0.001) and at 26 weeks (28.4 (21.3, 35.4) adjusted for baseline, p < 0.001). Nutritional risk score was lower (p < 0.001), and loss of body weight attenuated (p < 0.001) in the NI group compared with SC. Six deaths occurred during the study, five in the SC group and one in the NI group (p = 0.06). The mean time spent with a dietitian per contact was significantly less for the NI group compared with SC (16(3) vs 40(6) min per dietetic contact, p < 0.001).

CONCLUSIONS:
This pilot study has shown the potential of a novel telephone-based early and intensive dietetic model of care for newly diagnosed upper gastrointestinal cancer patients.

Silvers et al. Support Care Cancer 2014 (11):3035-44
**Effects of AA (g/Kg/day) on whole body (WBP) and muscular protein (MP) kinetics**
*(from Bozzetti & Bozzetti Clin Nutr in press)*

<table>
<thead>
<tr>
<th></th>
<th>W B P</th>
<th>AA, g</th>
<th>EAA, g</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SYNTHESIS</strong></td>
<td>↑</td>
<td>2.0</td>
<td>nr-0.5</td>
<td>- Shaw et al. 1991</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Hyltander et al. 1991</td>
</tr>
<tr>
<td></td>
<td>↓/=</td>
<td>1.25-1.7</td>
<td>0.34-0.8</td>
<td>- Hyltander et al. 1991</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>- Bozzetti et al. 2000</td>
</tr>
<tr>
<td><strong>CATABOLISM</strong></td>
<td>↓/=</td>
<td>1.25-1.7</td>
<td>nr-0.5-0.8-1.2</td>
<td>- Shaw et al. 1991</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Hyltander et al. 1991</td>
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<td></td>
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<td></td>
<td>- Jeevanandam et al. 1988</td>
</tr>
<tr>
<td><strong>MUSCLE</strong></td>
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<td></td>
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<td></td>
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<tr>
<td><strong>SYNTHESIS</strong></td>
<td>↑</td>
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<td>nr-0.8</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
<td>- Bozzetti et al. 2000</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Jeevanandam et al. 1988</td>
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<tr>
<td></td>
<td>=</td>
<td>1.25-2.0</td>
<td>0.3-0.5</td>
<td>- Hyltander et al. 1991</td>
</tr>
<tr>
<td><strong>CATABOLISM</strong></td>
<td>=</td>
<td>1.4-1.7</td>
<td>0.7-0.8</td>
<td>- Bozzetti et al. 2000</td>
</tr>
</tbody>
</table>
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Take home messages (I)

According to the last ASPEN and ESPEN GL

• the routine use of enteral or parenteral supplementation during CT is not recommended (Grade B)

• If patients are malnourished or facing more than a week of starvation, use ONS and/or enteral nutritional support. If this is not feasible, PN is recommended (Grade B)
Take home messages (II)

- If patients develop GI toxicity from CT or RT, short-term PN may be better tolerated (and efficient) than EN to restore the intestinal function, to prevent a nutritional deterioration and to allow a full compliance to the schedule of therapy (General consensus)

- In selected incurable cancer patients with malignant obstruction, HPN may prolong survival