Nutritional Issues in Palliative Cancer Care: targeted interventions and increasing role of classification (EPCRC et al)
Nutritional Issues
caring for advanced cancer patients

Identify and treat patients with pre-cachexia

Find reversible Secondary – Nutrition Impact Symptoms

Counsel the patients to eat more who will gain strength

Use mechanism-tailored drugs for responsive patients

Perform goal-directed, reachable, educational interventions

Alleviate distress from symptoms and losses

Include family members in care plan
Palliative Care: Key issues are nutrition-relevant

Assessment in daily practice
multidimensional – interdisciplinary – multilevel - modular

Management of symptoms and syndromes
Pain
Anorexia - Cachexia - Fatigue
Anxiety - Depression – Delirium - Distress
Nausea – Vomiting – Constipation
Shortness of breath – Cough

Communication
„Bad news“ – „double way“

Families – Network
Double role family members, complex networks

End-of-Life preparation and care
Decision making procedures – Patients‘ will – „finish business“
Terminal syndromes and management

Tailored service models

Adapted from Foley K et al. IOM report
From End-of-Life-Care to Palliative Cancer Care

Traditional View

Curative: Disease Management
Life

Palliative: Suffering Management
Death

Revised

Anticancer treatment
Supportive Care

Symptom Control
Advanced directives, goal
Family support – Services

Palliative Cancer Care

< 1998

>= 2008

Initial slide courtesy of Michael Fisch, adapted by Florian Strasser
ESMO Policy on Supportive and Palliative Care: Definitions

**Supportive care**: care that aims to optimize, the comfort, function and social support of the patient and their family at **all** stages of the illness.

**Palliative care**: care that aims to optimize, the comfort, function and social support of the patient and their family **when** cure is not possible.

**End of life care**: palliative care when death is imminent
ESMO-Designated Centers for Integrated Oncology and Palliative Care

1. The center provides closely integrated oncology and palliative care clinical services.

2. The center is committed to a philosophy of continuity of care and non-abandonment.

3. The center provides high-level home care with expert back-up and coordination of home care supports and has an infrastructure that responds with appropriate interventions in a timely manner.

4. The center incorporates programmatic support of family members including children.

5. The center provides routine patient assessment of physical and psychological symptoms and social supports and has an infrastructure that responds with appropriate interventions in a timely manner.

6. The center incorporates expert medical and nursing care in the evaluation and relief of pain and other physical symptoms.

7. The center incorporates expert care in the evaluation and relief of psychological and existential distress.

8. The center provides emergency care of inadequately relieved physical and psychological symptoms.

9. The center provides facilities and expert care for in-patient symptom stabilization.

10. The center provides respite care for ambulatory patients for patients unable to cope at home or in cases of family fatigue.

11. The center provides facilities and expert care for in-patient end-of-life care and is committed to providing adequate relief of suffering for dying patients.

12. The center participates in basic or clinical research related to the quality-of-life of cancer patients.

13. The center is involved in clinician education to improve the integration of oncology and palliative care.

www.esmo.org
ASCO: Palliative Cancer Care

Frank D. Ferris, Eduardo Bruera, Nathan Cherny, Charmaine Cummings, David Currow, Deborah Dudgeon, Nora JanJan, Florian Strasser, Charles F. von Gunten, and Jamie H. Von Roenn. Palliative Cancer Care a Decade Later: Accomplishments, the Need, Next Steps – from the American Society of Clinical Oncology. J Clin Oncol In press

Figure 1. Model of Palliative Cancer Care.
Conclusion 1:

To deal with nutritional issues of advanced cancer patients

→ Requires key components of Palliative Cancer Care
Interventions for „nutritional“ issues in palliative cancer care

Screen for symptom, check impact, prioritize

Cause-directed treatments if reversible, and treatment appropriate
Alleviate suffering from multi-dimensional consequences
Empower patient and family to understand cachexia

Diagnosis and multidimensional assessment of cachexia and its impact: far more than weight loss
How to guide interventions:
Cancer Cachexia Phases

Spectrum ranging from early to late cachexia. Not all patients will progress down the spectrum.

Pre-cachexia
- Subtle loss metabolic/endocrine change

Cachexia syndrome
- Weight loss
- Reduced food intake
- Systemic inflammation

Advanced cachexia
- Severe muscle wasting
- Fat loss
- Immunocompromised

Survival
- < 3 months?
- 3 – 9 months?
- > 6-9 months?

Fearon K. Eur J Cancer 2008; 2008;44,1124-32
# How to guide interventions²:

## Secondary Nutrition-Impact Symptoms

<table>
<thead>
<tr>
<th>Nausea</th>
<th>Stomatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>Dysgeusia</td>
</tr>
<tr>
<td>Constipation</td>
<td>Dental problems</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Difficulty chewing</td>
</tr>
<tr>
<td>Defecation after meal</td>
<td>Dysosmia</td>
</tr>
<tr>
<td>Pain</td>
<td>Xerostomia</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>Thick saliva</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Dysphagia</td>
</tr>
<tr>
<td>Anxiety/depression</td>
<td>Epigastric pain</td>
</tr>
<tr>
<td>Sense of hopelessness</td>
<td>Abdominal pain</td>
</tr>
</tbody>
</table>

Many frequent symptoms and complications in Palliative Cancer Care can contribute to **Cachexia**
Ihr Appetit kann negativ beeinflusst werden durch verschiedene Probleme. Bitte beantworten Sie die folgenden Fragen, indem Sie die Zahl ankreuzen, die am besten auf Sie zutrifft.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Antwortoptionen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weil ich an einer Entzündung im Mund leide (Stomatitis):</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil mein Geschmackssinn gestört ist (Dysgeusie):</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich an einer Schluckstörung leide (Dysphagie):</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich Schmerzen im Magen habe:</td>
<td></td>
</tr>
<tr>
<td>Weil ich Schmerzen im Bauch habe:</td>
<td></td>
</tr>
<tr>
<td>Weil ich an einer Entzündung im Mund leide (Stomatitis):</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich verstopft bin (Appetit ist besser nach Stuhlgang):</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich Durchfall habe:</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich direkt nach dem Essen (zu) viel Stuhlgang habe:</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich starke Schmerzen habe und nicht Essen kann:</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich starke Atemnot habe und nicht Essen kann:</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Weil ich starke Müdigkeit habe und nicht Essen kann:</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>

Daily practice: Checklist of S-NIS

Direct (semi-) quantitative questions

Post-pilot version, part of routine care
Generic Definition of Wasting / Cachexia

How to guide interventions³: Cancer Cachexia

- No desire to eat
- Feel no hunger
- Autonomic Dysfunction
- Taste, Smell alterations
- Dysmotility, Early satiety
- Constipation
- Muscle-Protein synthesis ↑
- Muscle-Protein synthesis ↓
- Liver
- Eat

Ghrelin

Catabolism ...
- Tumoractivity
- Inflammation (CRP)
- Resting-Energie-Expenditure

Muscle

„Appetite“

Genetic markers in Development
Generic Definition of Wasting / Cachexia

CACHEXIA DIAGNOSIS

- Weight loss of at least 5% in 12 months or less
  (or BMI <20 kg/m²)

- 3 of 5

- Decreased muscle strength
- Fatigue
- Anorexia
- Low fat-free mass index
- Abnormal biochemistry:
  - Increased inflammatory markers (CRP, IL-6)
  - Anemia (Hb <12 g/dL)
  - Low serum albumin (<3.2 g/dL)

In cancer patients:

→ Fatigue is an omnipresent symptom
→ Always tumor: inflammation (CRP>5mg/dl) omnipresent?

Generic Definition of Wasting / Cachexia

Table 1    Diagnostic criteria for wasting disease (cachexia) in adults

<table>
<thead>
<tr>
<th>Weight loss of at least 5%* in 12 months or less in the presence of underlying illness***, PLUS THREE of the following criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased muscle strength (lowest tertile\textsuperscript{38,39})</td>
</tr>
<tr>
<td>Fatigue\textsuperscript{***}</td>
</tr>
<tr>
<td>Anorexia\textsuperscript{27,****}</td>
</tr>
<tr>
<td>Low fat-free mass index\textsuperscript{40,41,#}</td>
</tr>
<tr>
<td>Abnormal biochemistry</td>
</tr>
<tr>
<td>a) increased inflammatory markers CRP (&gt;5.0 mg/l), IL-6 &gt;4.0 pg/ml\textsuperscript{42}</td>
</tr>
<tr>
<td>b) Anemia (&lt;12 g/dl)</td>
</tr>
<tr>
<td>c) Low serum albumin (&lt;3.2 g/dl)</td>
</tr>
</tbody>
</table>

The literature on cachexia is growing but still somewhat limited. This is particularly true of specific diagnostic criteria. The criteria, below, represents the clinical experiences of the clinicians on the consensus panel and the limited data on patients with cachexia. The following needs to be excluded: starvation, malabsorption, primary depression, hyperthyroidism and age-related loss of muscle mass. *Edema-free.

\*In cases where weight loss cannot be documented a BMI <20.0 kg/m\textsuperscript{2} is sufficient.

\***Fatigue is defined as physical and/or mental weariness resulting from exertion; an inability to continue exercise at the same intensity with a resultant deterioration in performance. \textsuperscript{18}

\****Limited food intake (i.e. total caloric intake less than 20 kcal/kg body weight/d; <70% of usual food intake) or poor appetite.

\#Lean tissue depletion (i.e. mid upper arm muscle circumference <10th percentile for age and gender; appendicle skeletal muscle index by DEXA (kg/m\textsuperscript{2}) by DXA <5.45 in females and <7.25 in males.

\rightarrow To guide clinical practice interventions and clinical trials in Palliative Cancer Care: Cancer-specific classification building on generic definition is needed
Classification & Assessment of Cancer Cachexia
European Palliative Care Research Collaborative

Determine the content of the cachexia assessment tool based upon (a \textit{variable}^2 combination of)

\begin{itemize}
  \item[a)] the literature (Systematic Literature Review)
  \item[b)] the content of widely used forms
  \item[c)] the clinical expert experience
  \item[d)] advice from an expert panel (Delphi – procedure)
\end{itemize}

Reflection and prospective validation in clinical realities of Palliative Cancer Care until death

2: SLR in Pall Care, BMC Palliative 2008
EPCRC: Classification of cancer cachexia

Definition of Cancer Cachexia

Cancer cachexia is a multifactorial syndrome defined by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism.

A key defining feature is ongoing loss of skeletal muscle mass which cannot be fully reversed by conventional nutritional support, leading to progressive functional impairment.
In the absence of simple starvation, cancer cachexia (excluding pre-cachexia) is diagnosed by involuntary weight loss >5% over the last 6 months. Weight loss should be ongoing in the last 1 – 2 months.

In patients with significant fluid retention, large tumor mass or obesity (BMI >30kg/m²) significant muscle wasting may occur in the absence of weight loss. In such patients a direct measure of muscularity is recommended.

→ Clinical Cachexia Expert consensus, ongoing Delphi procedure
The following key components are of high value for clinical assessment of cancer cachexia:

- **Anorexia/ ▼ food intake** (central, chemosensory, gut)
- **Catabolic drive** (Tumor, Inflammation, Hypogonadism)
- **Decreased muscle mass and strength**
- **Impact of cachexia** (Distress, Physical function)
- **Other factors** (e.g. anemia, loss of fat mass)

→ Clinical Cachexia Expert consensus, ongoing Delphi procedure
Patients with late (irreversible) cancer cachexia have advanced muscle wasting (with or without loss of fat). Patients have a low performance status and short life expectancy (<3 months).

It is evident that the burden of artificial nutritional support would outweigh any potential benefit. Therapeutic interventions focus typically on alleviating the consequences/complications of cachexia, e.g. symptom control (appetite stimulation, nausea), eating-related distress of patients and families.

→ Clinical Cachexia Expert consensus, ongoing Delphi procedure
### How to guide interventions: Cancer Cachexia

#### Variables needed for clinical decision-making:

<table>
<thead>
<tr>
<th></th>
<th>Past</th>
<th>Present</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Storage</strong></td>
<td>Individual usual weight (in absence of obesity equal to ideal weight)</td>
<td>Gap of usual to current (depleted) muscle mass and nutrients</td>
<td>Muscle mass required for patients’ meaningful physical function</td>
</tr>
<tr>
<td><strong>Intake</strong></td>
<td>Usual eating habits and dietary preferences</td>
<td>Current amount, quality and route of nutritional intake</td>
<td>Achievable (target) nutritional intake, percentage of needed nutritional intake</td>
</tr>
<tr>
<td><strong>Performance</strong></td>
<td>Pre – cancer usual performance status</td>
<td>Current cancer - and cachexia – related performance status</td>
<td>Patients’ priorities and life goals, achievable activity</td>
</tr>
<tr>
<td><strong>Potential</strong></td>
<td>Tumor-type and anticancer treatment history</td>
<td>Current degree of catabolism (by tumor, inflammation, lack of anabolic stimuli)</td>
<td>Expected life span (prognosis estimation) and control of catabolism</td>
</tr>
</tbody>
</table>
How to guide interventions

Targeted pharmacological Interventions

- Appetitestimulation
  - Melanocortin-Antagonists
  - Olanzapine
  - Ghrelin and Analoga

- Stimulation gastro-intestinal Motility
  - Anti-Myostatin
  - Beta-2-Mimetics
  - SARM’s, Oxandrolone
  - Proteasome-inhibitors
  - Insulin
  - Creatine, Amino-Acids
  - Angiotensin-II-inhibitors
  - ATP-Adenosine

- Anabolic Metabolism
  - Muscleproteins
  - Anti – Inflammation
  - Tumorprogression
  - Anti-TNF, anti-IL-6
  - Melatonin
  - Thalidomide, Lenalominide
How to guide interventions\textsuperscript{5-7}

Counsel, educate, alleviate, include family

Cognitive control of eating\textsuperscript{1}

Understand catabolic process (fabric talk) and gastrointestinal dysmotility (small stomach talk)

Find other means to express love and caring\textsuperscript{2}

Transient use of progestins for appetite, of corticosteroids for fatigue

Work with families to prepare for the worst and hope for the best, express emotions\textsuperscript{2}

\textsuperscript{1} Shragge JE, Wismer WV, Olson KL, Baracos VE. Shifting to conscious control: psychosocial and dietary management of anorexia by patients with advanced cancer. \textit{Palliat Med} 2007;21: 227-33

How to guide interventions\textsuperscript{5-7}

Help patients to understand experiences

Symptoms in cachexia assessment:
„A family of distinct characters“

A Symptoms mirroring the \textit{pathogenesis} of cachexia
   Early satiety, appetite loss, no desire to eat, weakness

B Symptoms & syndromes causing \textit{simple starvation}
   Pain, vomiting, dyspnea,

C Symptoms reflecting the \textit{impact} of cachexia
   Fatigue, eating-related distress
In Conclusion:

Nutritional issues include a spectrum from pre-cachexia to late irreversible cachexia

A cancer-specific cachexia classification (definition, diagnosis, key components) builds on the generic wasting/cachexia definition

Practice-guiding multidimensional assessments may harmonize collaborative clinical standards and build a backbone of quality clinical research

Tailored interventions (cause-specific, alleviating, family) include nutrition, pharmaceutical agents, education, and counseling
Thank you!

Thanks to many collaborating colleagues and societies

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