MALNUTRITION RISK AND SARCOPENIA
HEAD AND NECK CANCER

Mary E. Platek PhD, RD
Adjunct Assistant Professor of Oncology
Roswell Park Cancer Institute

Associate Professor
Department of Dietetics
D’Youville College
Lecture Outline

• **Cancer-Related Malnutrition States**
  • Nutrition implications of cancer and cancer related treatment
  • Malnutrition vs. Sarcopenia vs. Cachexia

• **Roswell Park Pilot Projects**
  • Prevalence of Malnutrition Risk in HN patients
  • Feasibility of using CT scans to assess sarcopenia in HN patients
CANCER RELATED MALNUTRITION STATES

Malnutrition vs. Sarcopenia vs. Cachexia
Inadequate Nutritional Status

- **Nutrition Imbalances due to**
  - Tumor
  - Host response to the tumor
- **Treatment**
  - Other factors
    - Anxiety
    - Depression
    - Lifestyle factors
Intensity of Consequences Vary

• Stage - Advanced

• Site – GI, Lung, Head and Neck

• Treatment: Multi-Modal
Total Effect on Clinical Outcomes

- ↓ Treatment response
- ↓ QOL
- ↑ Treatment complications
- ↑ Treatment toxicity
- ↑ Hospital admissions or re-admissions (infections)
- ↑ LOS
- Early Mortality
Cancer-Related Malnutrition

• Chronic disease-related malnutrition
  • Chronic inflammation of mild-moderate degree

• Acute disease or injury-related malnutrition
  • Inflammation is acute and of severe degree

White et al
JPEN, 2012
Diagnostic Criteria

• Inadequate energy Intake
• Unintentional weight loss
• Pre-BMI
• Changes in
  • Body fat
  • Muscle mass
  • Fluid accumulation
  • Grip strength
## Unintentional Weight Loss: Clinical Definitions

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Significant Loss</th>
<th>Severe Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 Days</td>
<td>1-2%</td>
<td>&gt;2%</td>
</tr>
<tr>
<td>30 Days</td>
<td>5%</td>
<td>&gt;5%</td>
</tr>
<tr>
<td>90 Days</td>
<td>7.5%</td>
<td>&gt;7.5%</td>
</tr>
<tr>
<td>180 Days (6 months)</td>
<td>10%</td>
<td>&gt;10%</td>
</tr>
</tbody>
</table>
Demographics of Body Weight

• ↑ Prevalence of overweight and obesity
  • Unclear definition of clinically significant weight loss in patients with cancer
  • Levels of BMI associated with ↓er survival are highly variable
Demographics of Body Weight

• Body weight and weight loss vary in their composition
  • Muscle mass/fat composition
  • Sarcopenia (severe muscle depletion)
    • Independently prognostic of ↓ survival in obese patients with cancer
Increasing Age of Cancer Patients

- ↓ muscle mass of 1-2% annually after 50
- ↓ muscle strength by 1.5% annually between 50-60
- ↓ muscle strength by 3% annually > 60
Sarcopenia

- Cancer Related Sarcopenia
  - Muscle mass loss
  - Loss in muscle strength
  - Decline in performance
- ICD-10 Coding (M62.84)
- October 2016
Survival of obese patients with and without sarcopenia
Colour online) Illustration of three male patients of different BMI presenting with similar amount of muscle cross-sectional area (skeletal muscle index = about 42·4 cm²/m²).
Cancer Cachexia

Multifactorial syndrome
  • Ongoing loss of skeletal muscle mass (with or without loss of fat)
    • Negative protein and energy balance
      • Driven by decreased food intake and abnormal metabolism

Fearon et al. Lancet Oncol 2011

• 50-80% of cancer patients
• Leads to death in 20% of cancer patients

MALNUTRITION RISK

Methods and Results
Methods

Inclusion criteria

• ≥ 18 years of age undergoing radiation therapy for head and neck cancer at Roswell Park Comprehensive Cancer Center

• And agree to take a survey during the first and last week of radiation treatment

Exclusion Criteria

• Do not speak and understand English
Methods: HN Patients

• Radiotherapists identify new patients during their first week and last week of treatment

• Provide patient with the SF PG-SGA (pencil/paper)
<table>
<thead>
<tr>
<th>PG-SGA Score</th>
<th>Triage Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>No intervention required at this time. Re-assessment on routine and regular basis during treatment</td>
</tr>
<tr>
<td>2-3</td>
<td>Patient &amp; family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey and laboratory values as appropriate</td>
</tr>
<tr>
<td>4-8</td>
<td>Requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms</td>
</tr>
<tr>
<td>≥ 9</td>
<td>Indicates a critical need for improved symptom management and/or nutrient intervention options</td>
</tr>
</tbody>
</table>

Ottery et al. Nutrition 1996
Outcomes

• Initiated in June 2017
• Up through July 2018
  • 100 patients with beginning and end surveys
    • 85% Male
    • 92% White/95% Non-Hispanic
    • 55% Definitive CCRT
    • 46% Oropharynx/18% Larynx
## Definitive CCRT Patients Only (n=55)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (%)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HN Cancer Site</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>39 (71%)</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>6 (11%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10 (18%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at First Treatment</strong></td>
<td>61.1 (9.0)</td>
<td></td>
</tr>
</tbody>
</table>
## Definitive CCRT Patients Only (n=55)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (%)</th>
<th>Mean (SD)/Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI Categories</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>6 (11%)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>8 (15%)</td>
<td></td>
</tr>
<tr>
<td>Overweight/Obese</td>
<td>18 (33%)/23 (41%)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>28.8 (7.5)</td>
<td>14.6-56.1</td>
</tr>
</tbody>
</table>
# Mean SF PG-SGA Scores

<table>
<thead>
<tr>
<th>Survey Time</th>
<th>Weight (SD)</th>
<th>Food (SD)</th>
<th>Symptoms (SD)</th>
<th>Function (SD)</th>
<th>Total (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning Treatment</td>
<td>1.0 (1.4)</td>
<td>0.7 (0.8)</td>
<td>2.2 (2.9)</td>
<td>0.6 (1.0)</td>
<td>4.6 (5.1)</td>
</tr>
<tr>
<td>End Treatment</td>
<td>3.2 (1.5)</td>
<td>2.3 (1.1)</td>
<td>8 (4.3)</td>
<td>1.8 (1.0)</td>
<td>15.2 (5.9)</td>
</tr>
<tr>
<td>Maximum Score</td>
<td>5</td>
<td>4</td>
<td>27</td>
<td>3</td>
<td>39</td>
</tr>
</tbody>
</table>

Paired T test for all categories p<0.001

Average Total Score $\Delta: \downarrow 10.6$ points (SD=7.8)
<table>
<thead>
<tr>
<th>PG-SGA Score</th>
<th>Triage Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>No intervention required at this time. Re-assessment on routine and regular basis during treatment</td>
</tr>
<tr>
<td>2-3</td>
<td>Patient &amp; family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey and laboratory values as appropriate</td>
</tr>
<tr>
<td>4-8</td>
<td>Requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms survey</td>
</tr>
<tr>
<td>≥ 9</td>
<td>Indicates a critical need for improved symptom management and/or nutrient intervention options</td>
</tr>
</tbody>
</table>

Ottery et al. Nutrition 1996
Clinical Interpretation of Scores

<table>
<thead>
<tr>
<th>Score Category</th>
<th>Beginning Treatment Frequency (%)</th>
<th>End Treatment Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Intervention</td>
<td>18 (33%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Education /Pharma</td>
<td>12 (22%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Intervention</td>
<td>13 (23%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Critical</td>
<td>12 (22%)</td>
<td>50 (90%)</td>
</tr>
</tbody>
</table>
Unplanned Hospitalizations

• 10 (18 %) patients
  • 1 patient was hospitalized twice
• Total unplanned hospitalizations=11
# Unplanned Hospitalizations

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Score Change</th>
<th>LOS (days)</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>↑ 1</td>
<td>2</td>
<td>Dehydration, Hypercalcemia, Hypokalemia</td>
</tr>
<tr>
<td>6</td>
<td>↑ 17</td>
<td>12</td>
<td>Lingual Artery/Tonsillar Fossa Bleed</td>
</tr>
<tr>
<td>16</td>
<td>↑ 13</td>
<td>2</td>
<td>Fever</td>
</tr>
<tr>
<td>24</td>
<td>↑ 12</td>
<td>5</td>
<td>Fever</td>
</tr>
<tr>
<td>35</td>
<td>↑ 19</td>
<td>3</td>
<td>ARF</td>
</tr>
</tbody>
</table>
## Unplanned Hospitalizations

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Score Change</th>
<th>LOS (days)</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>↑ 21</td>
<td>#1: 3 #2: 3</td>
<td>Fever Neutropenia</td>
</tr>
<tr>
<td>78</td>
<td>↑ 15</td>
<td>3</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>87</td>
<td>↑ 16</td>
<td>11</td>
<td>ARF, Electrolyte Imbalance</td>
</tr>
<tr>
<td>96</td>
<td>↑ 3</td>
<td>3</td>
<td>Acute Kidney Injury</td>
</tr>
<tr>
<td>99</td>
<td>↑ 17</td>
<td>4</td>
<td>↑ Creatinine, Hypotension</td>
</tr>
</tbody>
</table>
SARCOPENIA

Methods and Results
Methods

• Inclusion
  • 14 head and neck cancer, CCRT, Roswell
• Full body PET CT Scans
  • Within 30 days before treatment
  • Within 90 days post treatment
• Anonymized and sent to University of Alberta
University of Alberta Methods

• Quantified muscle mass and adipose tissues cross-sectional areas using a specific software

• Selected a single CT scan at the third lumbar vertebra (L3)
  • ↑ correlation with tissue volumes at whole body level
CT Imaging Analysis

As you can see from this analyzed image, based on each tissue's unique Hounsfield unit range, muscle is tagged as red, IMAT in green, VAT in yellow and SAT in blue.

Definitions

• **Skeletal Muscle Index (SMI)**
  - Cross-sectional skeletal muscle area (SMA, cm$^2$) measured at L3 (correlated with total body skeletal muscle mass)
  - Adjustment of SMA for height$^2$ results in skeletal muscle index (SMI, cm$^2$/m$^2$)
    - Measure for relative muscle mass
Definitions

• Muscle Radiation Attenuation (MRA)
  • MRA, Hounsfield Units (HU)
• Measure of muscle quality
  • Inversely related to muscle fat content
Predefined Cut-offs

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>SMI (cm²/m²)</th>
<th>Skeletal MA HU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt;20)</td>
<td>Men:&lt; 43</td>
<td>Men: &lt;41</td>
</tr>
<tr>
<td></td>
<td>Women: &lt;41</td>
<td>Women: &lt;41</td>
</tr>
<tr>
<td></td>
<td>Women: &lt;41</td>
<td>Women: &lt;41</td>
</tr>
<tr>
<td>Overweight (25.0-29.0)</td>
<td>Men:&lt; 43</td>
<td>Men:&lt;33</td>
</tr>
<tr>
<td></td>
<td>Women: &lt;41</td>
<td>Women: &lt;33</td>
</tr>
<tr>
<td>Obesity (≥30)</td>
<td>Men: &lt;53</td>
<td>Men: &lt;33</td>
</tr>
<tr>
<td></td>
<td>Women: &lt;41</td>
<td>Women: &lt;33</td>
</tr>
</tbody>
</table>

Martin, J Clin Oncol 31:1539-1547
## Results: Cohort Description

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (%)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (64%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5 (36%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at Diagnosis (years)</strong></td>
<td>55 (6.71)</td>
<td></td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>8 (57%)</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>4 (29%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (14%)</td>
<td></td>
</tr>
</tbody>
</table>
## Results: Cohort Description

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (%)</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretreatment BMI</td>
<td></td>
<td>30.28 (5.37)</td>
<td>21.61-38.71</td>
</tr>
<tr>
<td><strong>BMI Category</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td>3 (22%)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td></td>
<td>2 (14%)</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td></td>
<td>9 (64%)</td>
<td></td>
</tr>
<tr>
<td>Treatment Weight Loss</td>
<td></td>
<td>11.26% (5.37)</td>
<td>5.75%-19.92%</td>
</tr>
</tbody>
</table>
Men (n=9) BMI (32.7, 89% Obese)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-Treatment Mean (SD)</th>
<th>Pre-Treatment Frequency (%)</th>
<th>Post Treatment Mean (SD)</th>
<th>Post Treatment Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMI (cm²/m²)</td>
<td>63.1 (5.5)</td>
<td>8 (89%)</td>
<td>53.3 (7.9)</td>
<td>6 (67%)</td>
</tr>
<tr>
<td>Muscle Attenuation (HU)</td>
<td>45.2 (5.3)</td>
<td>1 (11%)</td>
<td>41.0 (8.0)</td>
<td>3 (33%)</td>
</tr>
<tr>
<td><strong>Sarcopenia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Muscle Attenuation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

42
## Women (n=5) BMI (25.8, 20% Obese)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-Treatment</th>
<th>Post Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>SMI (cm²/m²)</td>
<td>41.2 (6.7)</td>
<td>35.3 (4.9)</td>
</tr>
<tr>
<td>Muscle Attenuation (HU)</td>
<td>35.2 (5.4)</td>
<td>32.2 (4.3)</td>
</tr>
<tr>
<td><strong>Sarcopenia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (80%)</td>
<td>4 (80%)</td>
</tr>
<tr>
<td><strong>Muscle Attenuation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3 (60%)</td>
<td>3 (60%)</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (40%)</td>
<td>2 (40%)</td>
</tr>
</tbody>
</table>
# Progression (n=3)

<table>
<thead>
<tr>
<th>ID</th>
<th>Sex</th>
<th>Age</th>
<th>Progression</th>
<th>Profile</th>
</tr>
</thead>
</table>
| 2  | M   | 56  | Distant Mets     | BMI 30.5  
20% weight loss  
No sarcopenia or low muscle quality |
| 6  | M   | 61  | Distant Mets     | BMI 34.4  
10.4% weight loss  
Post sarcopenia  
No low muscle quality |
| 8  | M   | 62  | Local Recurrence | BMI 39.0  
12% weight loss  
Post sarcopenia and low muscle quality |
NEXT STEPS

Expansion of Pilot Studies
Nutritional Milieu

Hormonal Milieu

Exercise

Optimal body composition and physiologic function
Thank You - Roswell

• Dr. Singh/ Singh Lab: Alexis Platek, Austin Iovoli, Luke DeGraff
• Radiotherapists: Tracy Hails, Larry Alford and Julie Hanes
• Dr. Matthew Podgorsak
• Karen Hulme (Cancer Prevention/Control)
• Bill Duncan (Biomedical Data Science Shared Resource)
• Katherine Jastrzab
Thank You - University of Alberta

• Dr. Carla Prado, PhD/RD
  Associate Professor / CAIP Chair in Nutrition, Food and Health

• Sherin Fernandes, Research Assistant

• Jingjie Xiao, PhD, Postdoctoral Fellow

• Department of Agricultural, Food and Nutritional Science - Division of Human Nutrition
EXTRA SLIDES
Clinical Setting

• Until recently, no universally agreed upon operational definition for inadequate nutrition states in the setting of cancer
  • Cancer-related malnutrition
  • Cancer Cachexia

• Non-standardized screening, assessment and intervention

• Inadequate availability of nutrition services in the outpatient setting
Availability of Outpatient Nutrition Services

• Telephone Survey of NCI-designated CCCs
  • April-October 2012
  • 32 out of 40 centers surveyed (80%)

• Overall Conclusions
  • Referral or consult-based clinical nutrition service (98%)
    • Not consistently part of multidisciplinary service
      • No assurance that a patient is referred
      • No assurance that a referred patient receives service

Platek et al. JOP 2014
Take Away Message

• It is established that there is a role for
  • Individualized Dietary Counseling
  • Nutrition Support
    • Accompanied by *education and counseling*
    • *Immune enhanced nutrition support in specified surgical patients*
      • Perioperative
Take Away Message

• Intervention is needed especially when treatment is multimodal

• Early intervention is best

• Intervention should vary based on the nutritional status of the patient
Summary for the Current Decade

• Early and validated nutrition screening/assessment and intervention
• Repetitive and intensive individualized nutrition counseling with nutrition support
• Malnourished surgical patient
  • Perioperative nutrition support
  • In very specific cases, evidence is emerging to support consideration of immune enhanced formulas (arginine with O-3FA)
General Limitations of Nutrition Research-

• Observational studies
  • Lack of a true comparison group
  • Inconsistent measurement of nutritional status

• Poorly measured outcomes
  • Inconsistent use of standardized measurement tools

• Vague description of intervention

• Trials - not powered for primary objective
## Unintentional Weight Loss: Clinical Definitions

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Significant Loss</th>
<th>Severe Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 Days</td>
<td>1-2%</td>
<td>&gt;2%</td>
</tr>
<tr>
<td>30 Days</td>
<td>5%</td>
<td>&gt;5%</td>
</tr>
<tr>
<td>90 Days</td>
<td>7.5%</td>
<td>&gt;7.5%</td>
</tr>
<tr>
<td>180 Days (6 months)</td>
<td>10%</td>
<td>&gt;10%</td>
</tr>
</tbody>
</table>
Three Clinically Relevant Stages

- **Stage 1: Precachexia**
  - Weight loss $\leq 5\%$

- Early clinical and metabolic signs
  - Anorexia
  - Impaired glucose tolerance
  - Often occur before substantial involuntary weight loss

- Risk of progression varies depending on
  - Cancer type and stage
  - Systemic inflammation
  - Low food intake
  - Lack of response to anticancer therapy
Three Clinically Relevant Stages

• **Stage 3: Refractory Cachexia**
  - Active catabolism
    - Management of weight loss is no longer possible

• Characterized by
  - Low performance status
  - Life expectancy less than 3 months

Fearon  *Lancet Oncol*  2011
Severity of Cachexia

• Classification of severity
  • Rate of ongoing weight loss
  • Degree of depletion of energy stores
  • Degree of depletion of body protein mass

• A loss of 5 kg/m² for BMI of 20 vs. 35 shows more severe complications

• At BMI of 30 risk increases if weight loss is associated with loss of LBM

Fearon  Lancet Oncol  2011
CANCER CACHEXIA

Pathophysiology

Treatment Targets
Cachexia

Anorexia
- Food Intake
- Intestinal Absorption
- Gastric Emptying
- Dysphagia
- Hypogeusia
- Hyposmia

Metabolic Disturbances
- Energy Expenditure
- Inflammation
- Glucose Intolerance
- Fat Mobilization
- Protein Breakdown

Bodyweight
- Lean Body Mass
  - Physical Performance
    - QOL
- Fat Mass
  - Survival

Couch  Head & Neck  2015
Skeletal Muscle

- **MPS**: muscle protein synthesis
- **MPB**: muscle protein breakdown

- Skeletal muscle homeostasis relies on a balance between the two
- **Cancer cachexia** involves increased MPB and decreased MPS
  - Various drivers

Couch *Head & Neck* 2015
Potential Biomarkers

• Cytokines
  • CRP
  • IL 6
  • TNF-α

• Hormones
  • Ghrelin
  • Adiponectin
  • Leptin
Treatment of Cancer Cachexia

• Currently only 2 drugs are widely prescribed in practice (Europe)
  • Progestational agents (megestrol acetate)
  • Corticosteroids

• No FDA approved cancer cachexia drugs in US
Clinical Trials of Interventions

- Inflammation
  - NSAIDS, Thalidomide, Beta-blockers, anti-TNFs, anti-IL6
- Nutrition Supplements
  - Omega-3 fatty acids
- Muscle homeostasis-anabolic steroid replacements
  - Enobosarm
  - New SARMS in ongoing trials: LY2454473, GSK2849466
    - Small molecule SARM: VK5211
- Appetite enhancement-ghrelin stomach peptide
Weakness of Previous Cachexia Related Trials –

- Included patients in terminal stage alongside earlier stage

- Allowed for varied degree of weight loss
  - Patients grouped together with extremely wide ranges of weight loss

- Used life expectancy of > 6 months/unreliable
  - Substantial proportion of patients died within just a few weeks of randomization

- Most trials investigated single agents in unselected patients presenting with weight loss of any etiology
Screening and Assessment Tools

• **Scored Patient-Generated Subjective Global Assessment (PG-SGA)**
  
  • In the 1990s the SGA tool was revised to include common nutrition impact symptoms related to cancer and the history section of the assessment became patient generated.
  
  • Additionally, a scoring and triage component was added and the tool was validated for use in oncology patients as well as specifically in head and neck cancer ambulatory patients receiving radiotherapy.
  
  • Furthermore, the PG-SGA has been shown to correlate with quality of life and can predict the magnitude of change in quality of life of patients undergoing ambulatory radiation therapy.

Ottery et al. Nutrition 1996
## Treatment Effects

<table>
<thead>
<tr>
<th>Radiation Therapy</th>
<th>Chemotherapy</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucositis</td>
<td>Nausea/Vomiting</td>
<td>Delayed Gastric Emptying</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>Diarrhea</td>
<td>Early Satiety</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Taste Changes and Acquired Food Aversions</td>
<td>Nausea/Vomiting Diarrhea/Bloating</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Anorexia</td>
<td>Anorexia</td>
</tr>
</tbody>
</table>

- Nutrition problems **BEFORE** diagnosis may intensify
- Treatment Toxicity is reported more often in patients who are poorly nourished
**Cancer Cachexia Continuum**

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

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

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

---

Fearon *Lancet Oncol* 2011
SF PG-SGA associated with features of cachexia

• 207 advanced lung and GI cancer patients

• Higher aPG-SGA scores (≥9 (n=97) vs. 0 to 1 (n=43))
  • Higher WBC
  • Lower Hgb
  • Increased CRP
  • Decreased BMI, fat mass, handgrip strength/leg strength
  • Increased LOS, dose reduction in chemo, increased mortality

Vigano J Acad Nut Diet 2014
Log–rank test, $P < 0.001$

Blue (0-1)
Green (2-8)
Yellow ($\geqq 9$)
### PG-SGA Short Form vs. Full version

Chemotherapy outpatients

<table>
<thead>
<tr>
<th>Method</th>
<th>Area under curve (95% CI)</th>
<th>Risk cut-off score</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>PG-SGA SF (boxes 1–4) score</td>
<td>0.85 (0.80–0.89)</td>
<td>≥3</td>
<td>80.4</td>
<td>72.3</td>
</tr>
<tr>
<td>Boxes 1–3 of PG-SGA score</td>
<td>0.85 (0.81–0.89)</td>
<td>≥2</td>
<td>90.2</td>
<td>67.5</td>
</tr>
<tr>
<td>Symptoms (box 3 only) score</td>
<td>0.78 (0.73–0.83)</td>
<td>≥1</td>
<td>82.4</td>
<td>69.9</td>
</tr>
<tr>
<td>Box 1 + 3 PG-SGA score</td>
<td>0.85 (0.80–0.89)</td>
<td>≥2</td>
<td>86.3</td>
<td>71.1</td>
</tr>
<tr>
<td>Box 2 + 3 PG-SGA score</td>
<td>0.78 (0.73–0.83)</td>
<td>≥1</td>
<td>82.4</td>
<td>63.1</td>
</tr>
</tbody>
</table>

*PG-SGA Patient-Generated Subjective Global Assessment, PG-SGA SF Patient-Generated Subjective Global Assessment Short Form, CI confidence interval*

N = 300

*PG-SGA form was completed by professional instead of patient*
**PG-SGA Short Form scores predict clinical outcome**

Table 2. Association of abridged Patient-Generated Subjective Global Assessment scores with clinical, biological, and administrative characteristics of advanced cancer patients: Multivariable regression models

<table>
<thead>
<tr>
<th>Dependent variables</th>
<th>aPG-SGA&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 to 8</td>
</tr>
<tr>
<td></td>
<td>B&lt;sup&gt;c&lt;/sup&gt;  95% CI</td>
</tr>
<tr>
<td>Laboratory parameters</td>
<td></td>
</tr>
<tr>
<td>White blood cell count (×10&lt;sup&gt;9&lt;/sup&gt;/L)</td>
<td>0.5</td>
</tr>
<tr>
<td>Lymphocytes (×10&lt;sup&gt;9&lt;/sup&gt;/L)</td>
<td>−0.2</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>−3.4</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3.4</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>−2.3</td>
</tr>
<tr>
<td>Apolipoprotein A (g/L)</td>
<td>−0.01</td>
</tr>
<tr>
<td>Apolipoprotein B (g/L)</td>
<td>−0.03</td>
</tr>
<tr>
<td>Hospitalization, no. of days admitted/follow-up days (%)</td>
<td>2.2</td>
</tr>
<tr>
<td>Chemotherapy toxicity</td>
<td></td>
</tr>
<tr>
<td>Any cycle dose reduction (yes/no)</td>
<td>2.2</td>
</tr>
<tr>
<td>Line completed (yes/no)</td>
<td>0.9</td>
</tr>
<tr>
<td>Survival</td>
<td>1.7*</td>
</tr>
<tr>
<td></td>
<td>1.0 to 2.8</td>
</tr>
</tbody>
</table>

© PG-SGA/Pt-Global Platform 2016

Vigano et al., JAND 2014
Body Composition and Survival  (Grossberg, 2016)

• HNSCC curative RT
  • Whole Body PET-CT scans
    • 35.3% skeletal muscle loss before treatment
    • Additional 30.5% after treatment
    • Decrease OS and DSS for patients with muscle loss before treatment compared to those with normal skeletal muscle
      • No difference in locoregional control
    • Decrease OS, DSS (p=0.09), and LRR for patients who developed depletion after treatment
    • Decreased OS, DSS with lower pre-treatment BMI
      • No difference in locoregional control
  • Weight loss without skeletal muscle depletion did not affect outcomes
Head and Neck CT Imaging (Swartz, 2016)

- Can skeletal muscle mass be assessed by routine CT scan for head and neck?
  - 51 non HNC (trauma) patients – whole body PET CT scan
  - 52 HNC patients – whole body routine PET CT scan
    - Radiotherapy planning

- Volumetool Research Software package
  - C3 was the reference point
    - Paravertebral muscles (PVM) at C3 and sternocleidomastoid muscles (SCM) at C3
    - Correlation between C3 and L3 (L3 correlates with DEXA)
  - C3 strongly predicted L3 cross sectional muscle area
  - HNC patients had significantly lower cross sectional muscle than trauma patients - but no information on weight loss
Increasing Age of Cancer Patients

• After 50 years old
  • ↓ muscle mass of 1-2% annually
  • ↓ muscle strength by 1.5% annually between 50-60
  • ↓ muscle strength by 3% annually > 60

• Prevalence
  • 60-70 years old: 5-13%
  • ≥ 80 year old: 11-50%
PG-SGA Short Form and full PG-SGA as compared to SGA categories

Chemotherapy Outpatients

- PG-SGA: AUC = 0.967
- PG-SGA SF: AUC = 0.956
- MST: AUC = 0.823

Strong correlation between PG-SGA SF and full PG-SGA: r=0.984; P<0.001

Reference line of ROC = 0.5

© PG-SGA/Pt-Global Platform 2016
# Mean SF PG-SGA Scores

<table>
<thead>
<tr>
<th>Survey Time</th>
<th>Weight (SD)</th>
<th>Food (SD)</th>
<th>Symptoms (SD)</th>
<th>Function (SD)</th>
<th>Total (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning Treatment</td>
<td>1.0 (1.4)</td>
<td>0.7 (0.8)</td>
<td>2.2 (2.9)</td>
<td>0.6 (1.0)</td>
<td>4.6 (5.1)</td>
</tr>
<tr>
<td>Range</td>
<td>0-4</td>
<td>0-3</td>
<td>0-9</td>
<td>0-3</td>
<td>0-17</td>
</tr>
<tr>
<td>End Treatment</td>
<td>3.2 (1.5)</td>
<td>2.3 (1.1)</td>
<td>8 (4.3)</td>
<td>1.8 (1.0)</td>
<td>15.2 (5.9)</td>
</tr>
<tr>
<td>Range</td>
<td>0-5</td>
<td>0-4</td>
<td>0-21</td>
<td>0-3</td>
<td>0-32</td>
</tr>
<tr>
<td>Maximum Score</td>
<td>5</td>
<td>4</td>
<td>27</td>
<td>3</td>
<td>39</td>
</tr>
</tbody>
</table>

Paired T test for all categories p<0.001
## Results: Cohort Description

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>Range</td>
</tr>
<tr>
<td>Never Smoker</td>
<td>3 (21%)</td>
</tr>
<tr>
<td>Ever Smoker</td>
<td>11 (79%)</td>
</tr>
<tr>
<td>PPY</td>
<td>38.18 (18.75)</td>
</tr>
<tr>
<td></td>
<td>5-80</td>
</tr>
<tr>
<td>Progression</td>
<td>11 (79%)</td>
</tr>
<tr>
<td>No</td>
<td>3 (21%)</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>
Outcomes

• **Average Age:** 63.5 years (SD=10.41)
• **Average BMI:** 28.15 (SD=6.9)

- Underweight: 10%
- Normal: 21%
- Overweight: 35%
- Obese: 34%
Anabolic Competence:
Core to Clinical Success Regardless of How Defined

Anabolic Competence:
That state which optimally supports protein synthesis and lean body mass, as well as global aspects of muscle & organ function, immune competence, and quality of life.