Beyond BMI: Nutritional Strategies to Manage Loss of Muscle Mass and Function in Hospital and Community
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Disclosures

No Conflict of interest

Abbott Nutrition
Learning objectives

✓ Raise awareness of the need to identify loss of muscle mass and function in high risk populations

✓ Implement appropriate nutritional strategies for the prevention and treatment of muscle loss across the healthcare continuum

✓ Address recent evidence on nutritional interventions in hospital and community-dwelling subjects
Ageing and muscle
Loss of muscle mass and strength, a natural part of ageing

Original Study

Age-Related Variations of Muscle Mass, Strength, and Physical Performance in Community-Dwellers: Results From the Milan EXPO Survey

Francesco Landi MD, PhD *, Riccardo Calvani PhD, Matteo Tosato MD, PhD, Anna Maria Martone MD, Domenico Fusco MD, PhD, MD, Alex Sisto BA, Elena Ortolani MD, Giulia Savera BS, Sara Salini MD, Emanuele Marzetti MD, PhD

Department of Geriatrics, Neurosciences, and Orthopedics, Catholic University of the Sacred Heart, Rome, Italy
Ageing and muscle
Beyond BMI

Kg/m² (Mean ± SD)
Ageing and muscle

Loss of muscle mass and strength, a natural part of ageing

![Graph showing age-related loss of muscle mass and strength](image-url)
Ageing and muscle

Loss of muscle mass and strength, a natural part of ageing
Ageing and muscle

Loss of muscle mass and strength, a natural part of ageing
Ageing and muscle

Body composition

% Body composition (by weight)$^1$

- **Fat Mass**: 25%
- **Lean Body Mass (LBM)**: 75%

Muscle is a major component of LBM and plays a vital role in maintaining health$^1$

- Strength
- Energy
- Mobility
- Skeletal support and balance
- Wound healing
- Immune function
- Digestive function
- Skin health

Ageing and muscle
Optimal LBM over a lifetime

For optimal maintenance with ageing, it is important to build muscle when young, maintain it in mid-life, and minimize loss in older adulthood.

Build
Maintain
Minimize Loss

LOW MUSCLE LOSS
Range of muscle mass and strength between individuals
HIGH MUSCLE LOSS

Sarcopenia and frailty: From theoretical approach into clinical practice

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Malnutrition as a driver of muscle insufficiency/failure

- Physical inactivity and decreased dietary intake
- Decreased protein synthesis and increased protein breakdown
- Infiltration of fat into muscle
Risk factors for sarcopenia

Association of anorexia with sarcopenia in a community-dwelling elderly population: results from the i/SIRENTE study

Francesco Landi · Rosa Liperoti · Andrea Russo · Silvia Giovannini · Matteo Tosato · Christiana Barillaro · Ettore Capoluongo · Roberto Bernabei · Graziano Onder

Study sample
N=354
Women=236
Men=118

Gait Speed
- Normal >0.8 m/s
  - N=284
- Slow ≤0.8 m/s
  - N=70

Grip Strength
- Normal ≥30 Kg for male
  - ≥20 Kg for female
  - N=206
- Low <30 Kg for male
  - <20 Kg for female
  - N=45

Muscle Mass
- Normal 1st tertile of MAMC
- Normal 2nd and 3rd tertile of MAMC

Sarcopenia
N=103

No Sarcopenia
N=45

Anorexia of ageing → Sarcopenia

Anorexia, physical function, and incident disability among the frail elderly population: Results from the iLISIRENTE Study

Higher risk of quantitative malnutrition due to low-calorie intake

Poor alimentary variety of choice – Liquid and/or semi-solid foods

Pleasure of eating only few foods in the elderly (taste/smell – chewing – swallowing)

Higher risk of qualitative low intake of single nutrients (protein, vitamin D, zinc)

Anorexia of Aging: Risk Factors, Consequences, and Potential Treatments

Francesco Landi *, Riccardo Calvani, Matteo Tosato, Anna Maria Martone, Elena Ortolani, Giulia Savera, Alex Sisto and Emanuele Marzetti

Nutrients 2016 Jan 27;8(2).
Tools traditionally used to assess malnutrition (or at risk of) rely on measurements of recent weight loss and BMI for diagnosis.

BMI is an imperfect measure – low muscle mass occurs at any BMI.

Low lean mass can be a hidden condition under overweight and obesity conditions, as individuals with equal body weight may present different LBM.

Muscle loss is at the core of malnutrition.

Clinicians need to measure not only weight, but also muscle mass, to tailor interventions appropriately.
Can sarcopenia be prevented and/or treated?
Can sarcopenia be prevented and/or treated?

Preventing loss of muscle mass and function is easier than recovering it.
Potential therapeutic strategies

- Testosterone
- Growth Hormone
- Ace-inhibitors
- Estrogen
- Statin
- DHEA
- Cytokines inhibitors
- Leptin
- Essential fatty acids (Ω-3)
- Myostatin inhibitors
- Anti oxidants (Zn, Se)
- Creatine
- Physical exercise
- Nutritional supplements
- Protein,
- HMB, Vitamin D
Nutrition-muscle connection

• Usual diet, ONS and Tube Feeding can be used alone or in combination to cover the whole spectrum of patient care to modify the life trajectory of muscle loss

• Optimal dietary intake, including individual ingredients, is associated with improved metabolic and muscle-related outcomes

• Therapeutic ONS enriched with specific ingredients such as vitamin D, protein, CaHMB, Omega-3, BCAA, and other micronutrients could have a positive impact on older adults under catabolic conditions - especially when hospitalized
**Nutrition-muscle connection**

**Dietary protein**

- **Protein**: The principal component of all muscles
- **Dietary intake** required for muscle maintenance
- **High quality protein** to help support adults’ protein needs; most aging adults do not consume enough protein
- **Inadequate levels** reduce muscle reserves and immune function; increase skin fragility

*Nutrients 2016 May 14;8(5).*
DIETARY PROTEIN REQUIREMENTS:
HOW MUCH PROTEIN IS ENOUGH FOR OLDER ADULTS?

Lower quintiles of protein intake are associated with higher risk of frailty

<table>
<thead>
<tr>
<th>Quintile (Q)</th>
<th>Protein Intake (g/day)</th>
<th>Risk of Frailty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q2</td>
<td>70.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Q3</td>
<td>72.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Q4</td>
<td>74.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Q5</td>
<td>78.5</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Increasing dietary protein intake, % of kcal

Risk of frailty by quintile of protein intake (% kcal) (n= 24,417)
DIETARY PROTEIN REQUIREMENTS:
HOW MUCH PROTEIN IS ENOUGH FOR OLDER ADULTS?

PROT-AGE summary

New recommendations call for higher protein intake (g per kg of bodyweight) in those aged >65 years

- Minimum protein intake*: 1.0-1.2 g/kg
- People with acute or chronic diseases*: 1.2-1.5 g/kg
- People with severe illness or injury, or marked malnutrition*: Up to 2.0 g/kg

*Caution needed among those with severe kidney disease (i.e. estimated Glomerular Filtration Rate <30mL/min/1.73m²), calculating their needs differently.
Nutrition-muscle connection
HMB, a metabolite of the amino acid leucine

HMB is an active metabolite of the amino acid leucine

- HMB regulates protein in muscle cells
  - Supports muscle protein synthesis and slows down muscle protein breakdown $^{1,2}$
  - Helps rebuild muscle mass lost naturally over time $^{1,3,4}$
  - Helps rebuild LBM to support muscle strength and functionality $^{4,5}$

Effects of HMB in non-exercising older adults

- **Objective:**
  Evaluate the effect of HMB on LBM and strength in older adults (with and without resistance training (RT) exercise)

- **Study Design:**
  - Prospective, randomized, placebo-controlled trial
  - Older adults (age ≥ 65 y), n=27/group - 4 groups
  - **HMB at 3g/day** vs. placebo (with or without progressive RT)
  - 24-wks supplementation; Outcomes: lean mass and leg strength

Results: HMB increased lean mass and strength in non-exercising older adults


* p<0.05, Change from baseline by paired t-test

Effect of HMB on bed rest-associated loss of total lean mass

Lean body mass is maintained by β-hydroxy-β-methylbutyrate (HMB) during 10 days of bed rest in elderly women

J Nutrition 2013
Effect of HMB on Hospitalized patients

The NOURISH Study

Randomized control trials

Readmission and mortality in malnourished, older, hospitalized adults treated with a specialized oral nutritional supplement: A randomized clinical trial

- Malnourished older adults hospitalized for congestive heart failure, acute myocardial infarction, pneumonia, or chronic obstructive pulmonary disease

- Interventions: standard-of-care plus high-protein ONS containing HMB (HP-HMB) or a placebo supplement (2 servings/day)
Effect of HMB on Hospitalized patients

The NOURISH Study

D. Kaplan-Meier Survival Curve: Mortality

Proportion

Days postdischarge

Placebo, n 309 290 280 272 264 257 253 248 246 190
HP-HMB, n 313 302 292 283 280 273 268 262 259 211

Percent of patients (95% CI)

90-day mortality

Placebo: 9.7% (p = 0.018)
HP-HMB: 4.8%
Evaluation of an Oral Nutritional Supplement Containing HMB

Original Study

Impacts of High-Protein Oral Nutritional Supplements Among Malnourished Men and Women with Sarcopenia: A Multicenter, Randomized, Double-Blinded, Controlled Trial

Joel T. Cramer PhD, Alfonso J. Cruz-Jentoft MD, PhD, Francesco Landi MD, PhD, Mary Hickson PhD, RD, Mauro Zamboni MD, Suzette L. Pereira PhD, Deborah S. Husted PhD, Vikkie A. Mustad PhD

Cramer et al. JAMDA 2016
Evaluation of an Oral Nutritional Supplement Containing HMB

- Prospective, randomized, double–blind, controlled, 24-week intervention trial
- 330 men and women ≥65 years with malnutrition (SGA) and sarcopenia (EWGSOP)
- Stratified by gender and age
- 2 servings per day HP ONS+HMB vs. HP ONS

Cramer et al. JAMDA 2016
Evaluation of an Oral Nutritional Supplement Containing HMB

Results - Leg Strength (Nm), Change from Baseline at 12 weeks

Cramer et al. JAMDA 2016
Evaluation of an Oral Nutritional Supplement Containing HMB

Results - Leg Strength (Nm), Change from Baseline at 24 weeks

Cramer et al. JAMDA 2016
Evaluation of an Oral Nutritional Supplement Containing HMB

Dietary intakes of energy, protein, and serum vitamin D at baseline and 12 and 24 weeks

Cramer et al. JAMDA 2016
35 elderly, malnourished adults with recent weight loss (>5% in previous 3 months)

3 month prospective, open label, intervention study.

ONS twice daily (each: 330 kcal, 18 g protein, 1.5 g CaHMB, 12 μg vitamin D)

Group 1: Lower ONS consumption & weight improvement < 3.4%

Group 2: High ONS consumption & weight improvement > 3.4%

de Luis et al. Nutr Hosp 2015
ONS with HMB improved anthropometric measures, nutritional indices, handgrip strength and QOL

<table>
<thead>
<tr>
<th>Median weight improvement</th>
<th>Mean ONS consumption (servings /d)</th>
<th>Mean vitamin D intake (μg/d)</th>
<th>Parameters with significant improvement from baseline to 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.4%</td>
<td>1.25±0.78</td>
<td>13.2±4.3</td>
<td>Pre-albumin, vitamin D status</td>
</tr>
<tr>
<td>&gt;3.4%</td>
<td>1.86±0.82</td>
<td>35.8±4.3</td>
<td>BMI, weight, FFM, FM, pre-albumin, vitamin D status, handgrip strength, QOL (SF36: role physical and general health domains)</td>
</tr>
</tbody>
</table>

de Luis et al. *Nutr Hosp* 2015
ORAL SUPPLEMENT ENRICHED IN HMB COMBINED WITH PULMONARY REHABILITATION IMPROVES BODY COMPOSITION AND HEALTH RELATED QOL IN PATIENTS WITH BRONCHIECTASIS

Randomised n=30

Pulmonary Rehabilitation n=15

Completed Program 12 weeks n=15

Completed 24 weeks follow-up n=14
- Unwell (non-respiratory) n=1

Pulmonary Rehabilitation + Supplementation* n=15

Completed Program 12 weeks n=15

Completed 24 weeks follow-up n=14
- Unwell (non-respiratory) n=1

Improved Bone Mineral Density

↑ Maximal Handgrip Strength

Improved Quality of Life Physical Functioning

* 1 serving/d: 330kcal, 1.5g CaHMB, 20g protein, 400 IU vit D)

EFFECT OF CALCIUM β-HYDROXY-β-METHYLBUTYRATE, VITAMIN D AND PROTEIN SUPPLEMENTATION ON POST-OPERATIVE IMMOBILIZATION IN MALNOURISHED OLDER ADULT PATIENTS WITH HIP FRACTURE: A RANDOMIZED CONTROLLED STUDY

Elderly female patients with hip fracture

Intervention Group
Standard Post-Op Nutrition + Specialised ONS* (n=32)

Control Group
Standard Post-Op Nutrition Alone (n=30)

Measurements at Post-Operative Days 15 & 30
• Anthropometric
• Wound-healing
• Immobilisation period
• Muscle strength


* 2 x 220 ml servings / day Ensure Plus Advance
Specialised ONS improved wound healing and mobility in patients undergoing surgery for hip fracture

Increase in number of **mobile patients** (15 & 30 days)

Increase in **muscle strength** (30 days)

Improved **wound healing** (30 days)

EFFECTIVENESS OF NUTRITIONAL SUPPLEMENTATION ON SARCOPENIA AND RECOVERY IN HIP FRACTURE PATIENTS: A MULTI-CENTRE RANDOMISED TRIAL

Elderly patients with hip fracture admitted to rehabilitation therapy

**Intervention Group**
- Standard Diet + 2/day Specialised ONS (n=49)

**Control Group**
- Standard Diet (n=43)

**Malafarina V et al. Maturitas. 2017**

**Improved Muscle Mass & Reduced Onset of Sarcopenia in Hip Fracture Patients on Specialised ONS**

**Weight**

**MM**

**aLM**

**FM**

**Graphs**

- Weight: Comparison between admission and discharge weights with a significant decrease in the intervention group (p<.001).
- MM: Decrease in muscle mass with a significant p-value (p=.031).
- aLM: Significant decrease in arm muscle mass (p=.020).
- FM: Significant decrease in fat mass (p=.155).
Nutrition-muscle connection
The “Pachinko Model”

CURRENT NUTRITIONAL RECOMMENDATIONS AND NOVEL DIETARY STRATEGIES TO MANAGE SARCOPENIA
Take home messages

- Muscle loss is a key feature of malnutrition in community dwelling and hospitalized older adults

- Early identification and management of malnutrition and muscle loss in high risk populations may help to prevent hospitalization rates and reduce healthcare costs

- Current malnutrition screening and assessment tools based on weight measures may not reflect muscle loss

- Malnutrition needs to be addressed as a muscle-related disorder across the continuum of patient care

- Multimodal interventions need to be implemented to counteract malnutrition-related muscle loss

- Nutrition is a promising approach to restore muscle anabolism and combat malnutrition
Round Table Discussion, ICFSR April 2017

Muscle Mass Loss: The New Malnutrition Challenge

• Dr. Francesco Landi, Italy
• Dr. Alfonso Cruz, Spain
• Dr. Vincenzo Malafarina, Spain
• Dr. Tommy Cederholm, Sweden
• Dr. Ailsa Welch, UK
• Dannielle Bear RD, UK

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