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The Underappreciated Role of Low Muscle Mass in the Management of Malnutrition

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A B S T R A C T

Preserving muscle is not only crucial for maintaining proper physical movement, but also for its many metabolic and homeostatic roles. Low muscle mass has been shown to adversely affect health outcomes in a variety of disease states (eg, chronic obstructive pulmonary disease, cancer, cardiovascular disease) and leads to an increased risk for readmission and mortality in hospitalized patients. Low muscle mass is now included in the most recent diagnostic criteria for malnutrition. Current management strategies for malnutrition may not prioritize the maintenance and restoration of muscle mass. This likely reflects the challenge of identifying and measuring this body composition compartment in clinical practice and the lack of awareness by health care professionals of the importance that muscle plays in patient health outcomes. As such, we provide a review of current approaches and make recommendations for managing low muscle mass and preventing muscle loss in clinical practice. Recommendations to assist the clinician in the optimal management of patients at risk of low muscle mass include the following: (1) place muscle mass at the core of nutritional assessment and management strategies; (2) identify and assess low muscle mass; (3) develop a management pathway for patients at risk of low muscle mass; (4) optimize nutrition to focus on muscle mass gain versus weight gain alone; and (5) promote exercise and/or rehabilitation therapy to help maintain and build muscle mass. The need to raise awareness of the importance of screening and managing 'at risk' patients so it becomes routine is imperative for change to occur. Health systems need to drive clinicians to treat patients with this focused approach, and the economic benefits

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need to be communicated to payers. Lastly, further focused research in the area of managing patients with low muscle mass is warranted.

Starvation, disease, and advanced aging, alone or in combination, can all result in malnutrition.[1] The risk of developing malnutrition increases by at least 2-fold in older adults and those with chronic diseases, and 3-fold in individuals living in residential long-term care.[2] Between 20% and 60%[3–5] of patients are malnourished on hospital admission; many others develop malnutrition during hospitalization. Malnutrition and its consequences place an economic burden on the health care system. Health economic studies have estimated the direct medical costs at more than €31 billion in Europe,[3] $9.5 billion in the United States,[6] and £19.6 billion in the United Kingdom.[7]

Malnutrition is frequently identified and associated with low body weight and, therefore, management strategies focus on generalized weight gain or maintenance through a higher energy intake. However, more accurately, malnutrition leads to an altered body composition with reduced fat and fat-free body cell mass, leading to diminished physical and mental function and impaired clinical outcome from disease.[1] Specifically, low muscle mass is associated with several negative outcomes across health care settings[8] such as poor respiratory function in chronic obstructive pulmonary disease[9] and poor wound healing after surgery.[10] Furthermore, low muscle mass results in an increased risk of readmission, falls and fractures, longer hospital stays, disability, reduced functional capacity, loss of independence, and higher risk of mortality in hospitalized patients.[8,11] This suggests that loss of muscle mass is one of the most critical consequences of malnutrition. Additionally, certain measures of muscle function have been correlated with muscle mass and can be used to identify patients at nutritional risk and to monitor progress (Table 1). In addition to being a consequence of malnutrition, a natural reduction in muscle mass and function occurs with age resulting in diminished quality of life, greater susceptibility to infection, and an increased risk of mortality.[14] Therefore, ideally, identifying and treating malnutrition should have a focus on maintaining or minimizing the loss of muscle mass and function rather than simply focusing on body weight itself.

Managing loss of muscle mass and function is a significant challenge for clinicians, and current treatment approaches warrant revision. In this article, we look at the role that low muscle mass has on health outcomes and discuss some of the available tools and techniques to assess this. Additionally, we provide a series of recommendations that aim to provide useful guidance for clinicians to optimally manage patients at risk of declining muscle mass or those who already present with low muscle mass.

Table 1
Overview of Available Tools and Techniques to Measure Muscle Mass, Strength, and Function[1,12,13]

Technique	Advantages	Disadvantages
Anthropometry (eg, skinfold thickness measurements, mid–upper arm circumference, calf circumference)	• Quick • Accessible	• Lacks precision • Room for human error
Dual-energy x-ray absorptiometry (DXA)	• Quick • 3 body composition compartments • Appendicular muscle • Low radiation • Available in many hospitals • High precision with low errors	• Accessibility in certain clinical or care settings eg, nursing homes, GP practices • Weight limitation of DXA table • Individual hydration levels can impact soft tissue readings • Not portable
Bioelectrical impedance analysis (BIA)	• Accessible • Low cost • Portable • Enables phase angle measurement • Safe and noninvasive • Does not require highly trained personnel	• Fasting recommended • Assumes constant hydration factor for most equations to calculate body compartments • Not accurate for extreme BMIs (<16 or >34) • Lacks precision • Prediction error for estimated muscle mass • Multiple devices available with different body composition outputs
Ultrasonography	• Portable • Low/moderate cost • Quick • No radiation • Separate visceral and subcutaneous adipose tissues	• Several anatomical sites needed for the analysis • Sensitive to hydration levels • Specific user protocols in place requiring trained personnel • Lack of cut-off values to diagnose low muscularity
Computerized tomography (CT)	• Precise • Muscle mass quantification • Frequently available in cancer and other conditions: critical illness, COPD, HIV, cardiovascular disease, kidney disease, and cirrhosis	• Radiation exposure • Opportunistic only at this time • Healthy cohort reference values are scarce
Magnetic resonance imaging (MRI)	• Safe • Reliable • No radiation risk • High resolution of skeletal mass	• High cost • Requires technical expertise and training for analysis of outputs • Multiple images are required to assess the composition of the total body
Techniques to measure muscle strength and function		
Muscle strength	• Handgrip strength • Knee flexion/extension • Peak expiratory flow	
Muscle function	• Gait speed • Short Physical Performance Battery • Timed up and go test	

BMI, body mass index; COPD, chronic obstructive pulmonary disease; GP, general practitioner; HIV, human immunodeficiency virus.

The Importance of Muscle as a Metabolic Organ

Besides its role in the structural maintenance of the body, muscle has been recognized as an important metabolically active and homeostatic organ. Muscle mass is vital in helping to maintain an individual's health, quality of life, and longevity.[15,16] It also plays an important role in influencing energy and protein metabolism throughout the body.[16] When the body is not being supplied with enough fuel, amino acids stored as protein in muscle are broken down to provide the body with energy by way of gluconeogenesis.[17] This occurs when energy demands are high (as seen in certain disease states), when supplies are low (malnutrition), or during disease-related loss of appetite.[16]

Loss of muscle can also cause increases in local and/or systemic chronic inflammation, causing the production of proinflammatory cytokines, which in turn aggravates muscle atrophy.[16] Inflammation can also contribute to the loss of muscle in critical illness.[18] The release of these cytokines can result in further disruption to metabolism and neuroendocrine control of appetite.[19,20]

Maintenance and restoration of muscle mass with optimal nutritional strategies and, if possible, exercise approaches are crucially important. Both dietary intake (particularly amino acids) and resistance exercise are required to stimulate muscle protein synthesis.[21] However, these aspects of patient care can often be overlooked, with clinicians' focus of treatment being the primary disease or condition. Raising awareness of the impact muscle has on health outcomes is an important first step in changing the treatment focus.

Current Malnutrition Screening and Diagnosis Tools Lack a Focus on Muscle Mass

Malnutrition is often unrecognized and undertreated. In a Europe-wide survey of 325 hospitals in 25 countries of more than 21,000 patients, only half reported routine use of nutrition screening tools.[22] Furthermore, although basic diagnostic criteria have been defined for malnutrition, there has been a fundamental lack of consensus on these.[23]

Previous diagnostic criteria for malnutrition have not included muscle loss within their definitions and have had a strong focus on body mass index (BMI) and weight loss.[23,24] This has several issues, including the failure to recognize that patients with obesity may also be at risk of malnutrition and have low muscle mass. This leads to a focus on increased energy provision for overall weight gain rather than targeting muscle.

To reach global standardization on the identification and endorsement of criteria for the diagnosis of malnutrition, the Global Leadership Initiative on Malnutrition convened to develop a consensus scheme for diagnosing this condition in adults in various clinical settings.[23] This definition has been endorsed by all major nutrition societies (American Society for Parenteral and Enteral Nutrition, European Society for Parenteral and Enteral Nutrition, Federación Latino Americana de Terapia Nutricional, Nutrición Clínica y Metabolismo, and Parenteral and Enteral Nutrition Society of Asia). The scheme consists of 2 criteria: phenotypic (weight loss, reduced BMI, and reduced muscle mass) and etiologic (reduced food intake/assimilation and disease burden/inflammation). For the diagnosis of malnutrition, the Global Leadership Initiative on Malnutrition recommends using the combination of at least 1 phenotypic criterion and 1 etiologic criterion. The authors of these guidelines indicated that reduced muscle is a strong phenotypic criterion with solid evidence to support its inclusion in the diagnostic process for malnutrition. Thus, the importance of measuring muscle mass during nutrition assessment is acknowledged, and this new criterion will be central to enabling clinicians to center muscle mass within their diagnosis and treatment pathways.

A number of screening tools for identifying patients at risk of malnutrition also exist. However, only one of these include a measure of muscle mass or low mobility—the Mini-Nutritional Assessment (Table 2).

Assessment of Muscle Mass in Clinical Practice

Measurement of muscle mass and function can be used to risk-stratify patients and to monitor response to targeted nutrition interventions. Given the shortcomings of using BMI and weight loss to accurately assess body composition, there are a number of alternative, complementary tools and techniques available that can be used. Each technique varies both in precision and availability (Table 1).

Dual x-ray absorptiometry is frequently regarded as the gold standard for measuring body composition, providing a measure of appendicular lean mass, which is regarded a valid indicator of muscle mass. However, significant barriers including cost, access, and applicability in certain care settings (eg, intensive care unit) limit its use outside of the research and specific clinical settings. Other available techniques for assessing muscle mass, strength, and function are described in Table 1.

Currently, bioelectrical impedance analysis (BIA) is the most widely available and applicable tool to routinely use in clinical practice and can provide a useful guide for estimating muscle mass. One disadvantage of this tool is that the equations used in the estimation of body composition are often not specific to patient cohorts, with the results needing cautious interpretation. Also, a variety of population- or age-specific equations are lacking. Despite this, the use of BIA does seem to be a reasonable choice of technique for tracking longitudinal changes in body composition during treatments and, therefore, could be the method of choice for clinical practice.[25–27] Other available techniques for assessing muscle mass and function are described in Table 1.

Despite the availability of a variety of methods to directly or indirectly assess muscle mass (Table 1), it is not routinely measured in clinical practice. As described previously, the reasons for this includes incomplete knowledge and awareness of the condition, how and when to measure, a poor availability of assessment tools, and importantly, a lack of time.[28] This is further compounded by variations in cost and access to equipment (eg, dual x-ray absorptiometry) and a paucity of regional/population-specific cut-offs to define low muscle mass (eg, in different ethnicities and age groups). Despite these challenges, even in the most resource-limited settings, simple muscle function tests (as described in Table 1) can provide a good surrogate marker, and these tools should be incorporated into clinical practice.[29]

Patients who are experiencing weight loss are at high risk of losing muscle. This includes those who are malnourished or at risk of becoming malnourished, including frail adults; patients with age-associated weight loss; those who are bed-bound or immobile; or patients with diseases or conditions with inflammatory components such as cancer and chronic kidney disease; and those who are critically ill.[16] Screening patients such as these is crucial for predicting risk and allowing timely interventions to be put in place to stop any further muscle loss. A multidisciplinary approach is ideal but not always feasible in resource-constrained settings, or where there is poor continuity of care as patients are transferred from one clinical setting to another.

A Way Forward—Establishing How Muscle Mass Can Be Maintained and Improved by Nutritional Interventions

Despite the challenges faced, we make the following recommendations to manage and reduce the loss of muscle mass to improve clinical outcomes:

1. Place muscle mass at the core of nutritional management strategies

Screening and assessment of patients at risk of low muscle mass (eg, older age, inflammation, bed-bound, immobile, in the intensive care unit or those in chronic disease states) is recommended. Furthermore, it would be beneficial for current guidelines to recommend that clinicians include an evaluation of muscle mass and/or function, in addition to other diagnostic criteria, within their nutritional assessment. This will enable optimal management strategies to be put in place, which are focused on maintaining muscle mass.

2. Improve the management pathway for patients at risk of low muscle mass

Following a specific management pathway to ensure that muscle mass is at the core of the entire nutrition care process, that is, a cycle of screening, assessment, intervention, and monitoring (Figure 1).

3. Identify and assess low muscle mass for those at risk of malnutrition

Current BMI and weight measurements need to be complemented with practical and precise tools and techniques that will directly assess muscle mass. Estimating muscle mass with BIA may be the most universally practical approach because of its wide availability. However, its limitations still need to be taken into consideration. Using BIA together with muscle function assessment would provide clinicians with readily available ways to better clinically quantify muscle loss. The sensitivity and specificity of these measurements to assess longitudinal changes in different patient cohorts needs to be explored. Where available, dual x-ray absorptiometry scanning is recommended as the gold standard to estimate muscle mass. The use of ultrasound or computed tomography scans may be more applicable and readily available in some clinical settings, especially within oncology and critical care.

4. Optimize nutrition to focus on muscle gain versus weight gain alone

As a first step, nutritional interventions must provide the patient with adequate energy to hinder muscle catabolism (as protein is used as an energy source).[16,30] Protein requirements should then be addressed, as the maintenance or restoration of muscle is dependent on the equilibrium between protein synthesis and degradation. Although protein requirements will vary from person to person, the recommendations are higher for older adults (at least 1.0-1.5 g/kg body weight/d),[30] patients with polymorbidities (>1 g/kg body weight/d),[31] and those who are critically ill (1.3-1.5 g/kg body weight/d).[1,32,33] Trying to achieve protein targets from diet alone can be challenging in some situations (eg, cancer or critical illness). Supplementing with higher protein feeds can act as an aid to help reach these higher targets. Using high protein oral nutritional supplements (ONS) in the clinical setting has been shown to significantly

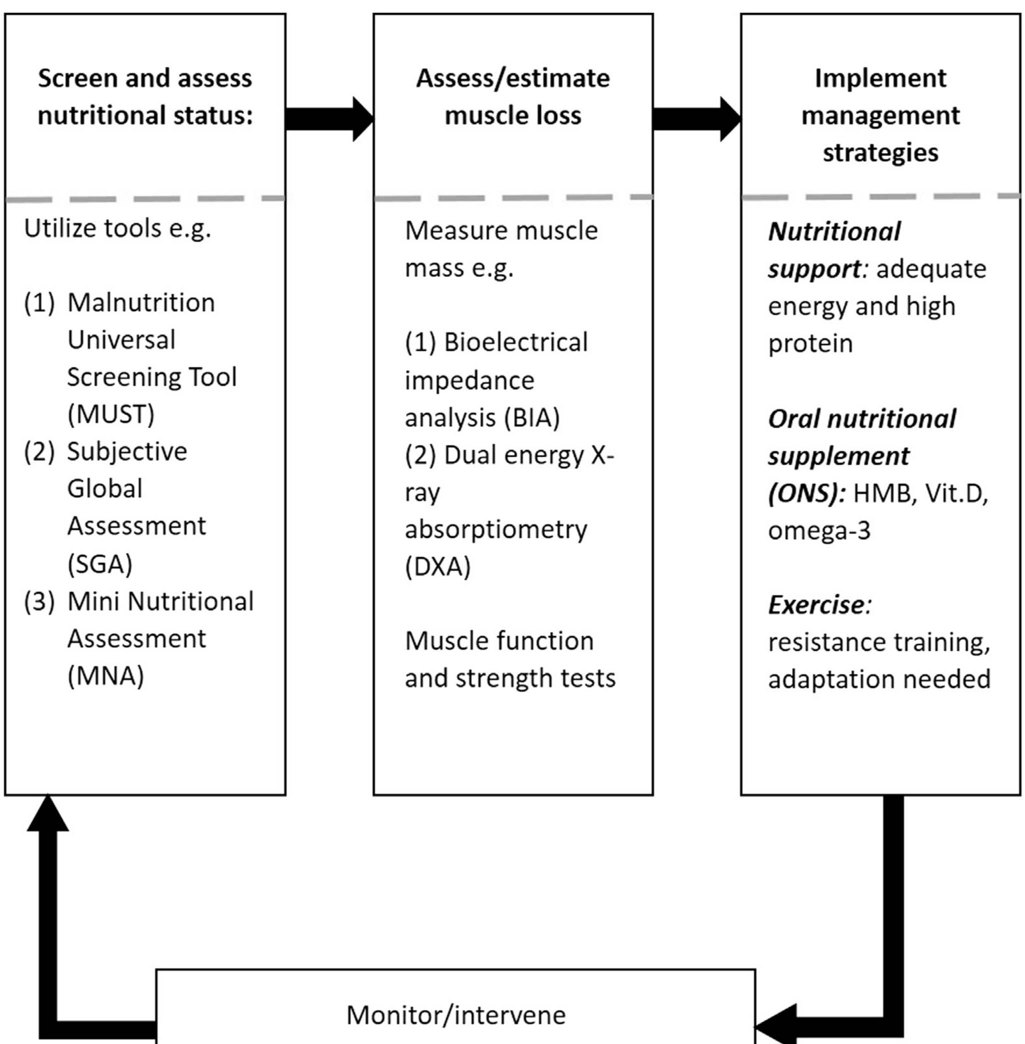

Fig. 1. Algorithm depicting the management pathway for identifying, assessing, and managing low muscle mass.

Table 2
An Overview of Parameters Measured by Nutritional Screening or Assessment Tools for Identifying Patients at Risk of Malnutrition

Parameter Assessed	MNA	NRS 2002	SNAQ	MUST	SGA
Low BMI	<19	<20.5		<20	
Weight loss	>1 kg	>5%	>3 kg	>5%	>5%
Loss of appetite/ reduced food intake	Y/N	<75% normal	Y/N and supplements or tube feeding	Not fed for >5 d	Suboptimal diet
Low mobility	Bed or chair bound				≥ Reduced capacity
Disease effect	Psychological issues	Mild, moderate, or severe		≥ Acute	Gastrointestinal symptoms upon intake

MNA, Mini-Nutritional Assessment; MUST, Malnutrition Universal Screening Tool; NRS 2002, Nutritional Risk Screening 2002; SGA, Subjective Global Assessment; SNAQ, Short Nutritional Assessment Questionnaire.

reduce complications, lower readmissions to hospital and improve handgrip strength and body weight.[34] Therefore, the use of high-protein ONS may be beneficial in ensuring nutritional demands are met.[35] Likewise, ESPEN guidelines for polymorbid inpatients or those at a high risk of malnutrition recommend considering ONS, high in energy and protein, to improve nutritional status and quality of life.[31]

Essential amino acids also play a central role in the protein status of a patient. Although many play a role in protein synthesis, branched-chain amino acids and their derivatives are of particular importance for building and maintaining muscle mass.[36,37] Of particular note is leucine, the most important regulator of muscle growth, and its metabolite derivative β-hydroxy-β-methylbutyrate (HMB). HMB has been shown to act as a potent stimulator of protein synthesis as well as an inhibitor of protein breakdown.[38] A growing body of evidence suggests that HMB or oral nutrition supplements containing HMB may help to slow or even reverse muscle loss in aging, illness, or starvation[39,40] and improve other important outcomes such as wound healing,[41] physical function,[42] and mortality.[43] Therefore, using a high-protein ONS or enteral tube feeding that contains HMB may help in the management of malnutrition and muscle mass loss.

Several other dietary interventions could also help mitigate muscle loss. Vitamin D and omega 3 have been shown to be useful in maintaining and restoring muscle mass and function. Vitamin D supplementation has been shown to improve muscle strength, particularly in those most deficient and within an older age group.[44] Likewise, supplementing with omega 3 in the diet has been shown to help reduce inflammation in a number of clinical settings[45,46] and maintain muscle mass and function in older adults.[47]

5. Promote exercise to help maintain and build muscle mass

Although the correct level and type of nutrition is important and contributes significantly to the improvement of muscle mass, anabolic potential can be maximized with an exercise intervention.[30,48] Regular exercise helps maintain skeletal muscle strength and function in older adults.[49] A combination of resistance training and adequate dietary protein is recommended for healthy muscle aging.[49] International groups make the following recommendations:

- ESPEN guidelines for older patients:
  - Regular exercise to include resistance training[30]
- American College of Sports Medicine guidelines for older patients[50]:
  - Endurance training several times per week plus resistance training twice a week
  - Flexibility (eg, stretching) and neuromotor (eg, Tai-chi) is also recommended

Aerobic exercise is encouraged, but it is resistance training that has been shown repeatedly to improve rates of protein synthesis and reverse muscle loss.[51] However, individuals who are suffering muscle loss through malnutrition, illness, or aging may have difficulty engaging in physical activities. Adaptations to exercise regimens will need to be made for this population.

Implications for Practice, Policy, And/Or Research

In order for muscle mass to be routinely screened, assessed, and actively managed, there will need to be widespread changes in clinical practice and more focus within the research setting:

- Raising awareness—the importance of maintaining/improving muscle mass for patient outcomes needs to be reinforced with both patients and health care professionals
- Improved education—more education describing how to assess and manage muscle loss in different health and care settings is needed
- New treatment pathways—identifying those at risk of muscle mass loss or with low muscle mass requires different approaches, for example through the involvement of a multidisciplinary team (including medical doctors, registered dietitians, nurses and exercise physiologists), where professionals meet frequently, set up common goals for the patient, and monitor progress together
- Better assessment—to identify patients with the correct tools and techniques meant for the right clinical setting
- Optimal management—ensure that treatment approaches are optimized to maintain or improve muscle mass
- Additional research—determination whether specific nutrition interventions can prevent and/or reverse muscle loss and whether maintenance/gain of muscle is associated with better outcomes in the general patient population as well as in specific conditions
- Empowering health professionals to advise on physical activity

Conclusions/Relevance

The management of patients with malnutrition requires a change to focus on optimizing body composition, specifically muscle mass. A change in our approach starts with the need to raise awareness of the importance of maintaining and building muscle mass to improve health outcomes in our at-risk patients. Screening patients (and thus subsequent treatment) for low muscle needs to become routine, and a variety of assessment tools are already available to help clinicians no matter which clinical setting they practice in. Health systems need to reflect the need to screen at-risk patients and drive clinicians to treat according to this new focus. The economic benefits of this treatment approach need to be more clearly articulated to payers and those in charge of funding decisions. Most importantly for clinicians, placing the maintenance of muscle mass as a focus of our management strategies (including both nutritional support and exercise) will be an effective way to improve the clinical outcomes and quality of life for our patients.

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