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Special Article

Skeletal Muscle Function Deficit: A New Terminology to Embrace the Evolving Concepts of Sarcopenia and Age-Related Muscle Dysfunction

Rosaly Correa-de-Araujo and Evan Hadley

U.S. Department of Health and Human Services, Division of Geriatrics and Clinical Gerontology, National Institute on Aging, National Institutes of Health, Bethesda, Maryland.

Address correspondence to Rosaly Correa-de-Araujo, MD, MSc, PhD, U.S. Department of Health and Human Services, Division of Geriatrics and Clinical Gerontology, National Institute on Aging, National Institutes of Health, 7201 Wisconsin Avenue, Bethesda, MD 20892-9205. Email: Rosaly.correa-de-araujo@nih.gov

Background. Concerns remain as to the best terminology to embrace sarcopenia's evolving conceptualization. Many of these concerns stem from the fact that age-related decrements in muscle performance associated with physical impairment are only partially explained by decreases in muscle mass and that other pathophysiologic factors contribute to age-related impairments in muscle performance.

Methods. Review of literature on the evolving conceptualization of sarcopenia since its early definition in 1989 and concerns with terminology.

Results. Early definitions of sarcopenia were based solely on muscle mass in relationship to the range of muscle within a reference population. Subsequent definitions added performance criteria to muscle mass alone. The Foundation for the National Institutes of Health Sarcopenia Project identified criteria for clinically relevant low muscle strength (weakness) and low lean mass. Progress on the sarcopenia's evolving definitions has not been accompanied by recommendations on specific terminologies that address the lack of sufficient specificity from the use of an anatomic term to define a functional condition with numerous now known nonanatomic contributory factors. Skeletal Muscle Function Deficit is a broader construct that accommodates a set of diagnoses that includes both sarcopenia and other age-related muscle dysfunctions.

Conclusions. Skeletal Muscle Function Deficit is proposed as a new terminology to embrace the evolving conceptualization of sarcopenia and other age-related muscle dysfunctions. It comprises a variety of contributory etiologies and has the potential to provide a framework for developing diagnostic categories that are useful for both clinical practice and research.

Key Words: Sarcopenia—Skeletal muscle—Muscle weakness—Muscle strength—Muscle function—Skeletal muscle function deficit—Deficit.

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SINCE 1989, when sarcopenia was first defined by Rosenberg as an age-related reduction in muscle mass (1), scientific and technological advances have helped us better understand the mechanisms underlying age-related alterations in muscle mass, muscle strength, and muscle quality, and the relationships of these muscle changes to mobility impairment, disability, fatigue, risk of metabolic disorders, falls, and mortality in older adults (2,3). Various definitions of sarcopenia have evolved throughout the past years in an attempt to better characterize sarcopenia, identify biomarkers, establish criteria for its definition and diagnosis, and identify outcomes of relevance in clinical and research practices. These efforts have been stimulated by the potential value of one or more well-accepted clinical definitions that could identify patients who might benefit from currently available therapeutic or preventive interventions and could serve as criteria for evaluating new interventions.

Sarcopenia's Operational Definitions

Early definitions of sarcopenia were based exclusively on muscle mass in relationship to the range of muscle mass within a reference population. Baumgartner and colleagues (4) defined sarcopenia as the relative muscle mass 2 *SD*s below the mean of a large sex-specific reference population 18–40 years old. This definition was based on a measure of relative muscle mass obtained by dividing absolute muscle mass estimated by dual energy x-ray absorptiometry by height squared. Janssen and colleagues (5) classified sarcopenia according to its severity, with class I sarcopenia

referring to skeletal muscle index between 1 and 2 *SD*s below the young adult values and class II sarcopenia as skeletal muscle index more than 2 *SD*s below the young adult reference. Skeletal muscle index was calculated by dividing total muscle mass by total body mass, with muscle mass evaluated by bioelectrical impedance.

Subsequent definitions have made considerable progress by adding performance criteria to muscle mass alone. The European Working Group on Sarcopenia in Older People consensus conference proposed a diagnosis for sarcopenia that requires low muscle mass (estimated by the ratio of appendicular lean mass over height squared, ≤7.23 kg/ht^2 for men and ≤5.67 kg/ht^2 for women) accompanied by either low muscle strength (measured by grip strength <30 kg for men and <20 kg for women) or low physical performance (measured by gait speed <0.8 m/s). The group defined three stages for the condition: presarcopenia (loss of muscle mass), sarcopenia (loss of muscle mass accompanied by either loss of strength or physical performance), and severe sarcopenia (all three aspects are present) (6). Reports of three consensus conferences, convened by the International Working Group on Sarcopenia (7), the European Society for Clinical Nutrition and Metabolism Special Interest Groups on cachexia-anorexia in chronic wasting diseases and nutrition in geriatrics (8), and the Society of Sarcopenia, Cachexia, and Wasting Disorders (9), have included both lean mass and gait speed as diagnostic criteria for sarcopenia.

The Foundation for the National Institutes of Health Sarcopenia Project, whose reports are presented in this issue, has extended the methodologic approach to diagnostic characterization of sarcopenia in a notable way. It applied Classification and Regression Tree analysis to epidemiologic and clinical trial data in a two-step approach to identify criteria for clinically relevant low muscle strength (weakness) and low lean mass. First, by addressing the relationship between mobility impairment (defined as gait speed ≤0.8 m/s) and muscle strength (measured by grip strength), strength cutpoints (<26 kg for men and <16 kg for women) were determined below which low strength is especially likely to contribute to slow gait. Second, by relating these strength cutpoints to muscle mass (estimated by appendicular lean mass adjusted to body mass index [BMI]), cutpoints were determined (<0.789 for men, <0.512 for women), below which low lean mass is especially likely to contribute to low muscle strength. The cutpoints resulting from these analyses were also found to have a predictive value on incident mobility impairment over 3 years of follow-up (10).

Table 1 summarizes the final recommended evidence-based, data-driven cutpoints for weakness and low lean mass in men and women.

By providing a more direct basis for determining the value of specific cutpoints for diagnostic characterization of mobility impairment than do approaches like multivariate analyses, the Classification and Regression Tree–based approach can provide useful guidance both to practitioners in determining candidates for treatment and to researchers evaluating new interventions. In addition, the two-step analyses that links a clinical condition (mobility impairment) to a functional test result (low strength), which is in turn linked to a potential therapeutic target (muscle atrophy) is useful for establishing participant selection criteria and outcome measures for trials of pharmaceutical or other interventions. The latter consideration is particularly important because, as noted in a recent review of issues regarding evaluation of new drugs directed at sarcopenia, "a more specific definition of sarcopenia may not only be necessary to align it with new scientific advances, but it is highly desirable on practical grounds because specific criteria are critical for identifying candidate patients for clinical trials that test therapies aimed at reversing or alleviating the complications of sarcopenia and its associated manifestations (11)."

Table 1. Recommendations for Cutpoints for Weakness and Low lean Mass

Cutpoints	Men	Women
Weakness		
Recommended:		
Grip strength (GSMax)	< 26 kg	< 16 kg
Alternate:		
GS adjusted to body mass index [BMI] ($GSMax_{BMI}$)	< 1.0	< 0.56
Appendicular Lean Body Mass		
Recommended:		
Appendicular lean mass (ALM) adjusted to BMI (ALM_{BMI})	< 0.789	< 0.512
Alternate:		
ALM	< 19.75 kg	< 15.02 kg

As noted by authors of the Foundation for the National Institutes of Health Sarcopenia Project papers, additional work is needed to validate and refine their proposed diagnostic criteria. This includes evaluation of the value of alternative measures of physical impairment and muscle performance in different populations, including ones with substantial physical impairment, as well as more data on the sensitivity of measures of physical impairment to changes in muscle performance, and on the sensitivity of changes in muscle performance to changes in muscle mass (10).

Terminology and Nosology Issues: Sarcopenia in the Context of Skeletal Muscle Function Deficit

Concerns remain as to the best terminology to embrace sarcopenia's evolving conceptualization. Many of these concerns stem from the fact that age-related decrements in muscle performance associated with physical impairment are only partially explained by decreases in muscle mass and that other pathophysiologic factors contribute to age-related impairments in muscle performance.

Based on this rationale, decrements in muscle performance and in muscle mass should be evaluated independently. The term *dynapenia* has been used to describe age-related loss of muscle strength (12) or power (9), which can be caused by a variety of factors independent of loss of muscle mass (13), and the importance of evaluating muscle quality, for example, strength per unit of appendicular skeletal muscle mass, has been noted (3). However, although the consensus groups noted above have incorporated the criterion of impaired physical and/or muscle performance into recommended definitions of sarcopenia, they have not recommended specific diagnostic terminologies for age-related impairments in muscle function due to other factors than decreased mass. Concerns remain about potential confusion or lack of sufficient specificity resulting from the use of an anatomic term to define a functional condition with which it is imperfectly correlated, and for which nonanatomic contributory factors have been identified (14). Other concerns stem from the fact that diminished muscle mass per se is a feature of several other conditions that occur in both older and younger persons, thus raising the question of whether these phenomena should collectively be termed "sarcopenia," or whether the term should be an exclusionary diagnosis reserved for older persons and if so, what the excluded conditions should be.

There would be value in a nosology that accommodates the concept of sarcopenia in its literal meaning of diminished muscle mass while applying other diagnostic terms for other age-related muscular conditions that contribute to impaired physical performance. We suggest that it may be useful to apply the broader concept of "Skeletal Muscle Function Deficit" (SMFD) to describe the variety of muscular conditions, some already well defined and some not, that contribute to clinically meaningful mobility impairments. The diagnostic criteria for "SMFD" could be those measures of muscle performance (eg, strength, power, fatigability) that are shown by Classification and Regression Tree analysis or other techniques to provide effective cutpoints for distinguishing individuals whose mobility disability is related to impairments in these muscle performance measures. Using these criteria for "SMFD," a variety of known and putative muscular pathologies could be evaluated in regard to their contribution to it. Newly identified contributory pathologies could be given an appropriate nomenclature, and diagnostic tests and cutpoints for them could be developed analogously to the approach taken by the Foundation for the National Institutes of Health Sarcopenia Project, or by other methods. Thus, "SMFD" attributable to diminished muscle mass could be termed "sarcopenic SMFD," whereas impairments in muscle strength or power that contribute to "SMFD" independent of muscle mass (and even in the presence of normal muscle mass) could be termed "dynapenic SMFD." Mixed categories could of course also be defined.

This approach would have the virtue of specifying already recognized conditions that cause "SMFD" (eg, diabetic polyneuropathy or secondary malnutrition), which could be distinguished from age-related conditions contributing to "SMFD" but whose etiology is not yet well defined. Further, it provides a framework for diagnostic specificity to the extent provided by current understanding of pathologic mechanisms responsible for age-related impairments in muscle function while accommodating future increases in diagnostic specificity based on increased understanding of these mechanisms. Discoveries regarding the contributions of specific neurogenic factors, intrinsic muscle factors, or systemic factors may lead to the characterization of specific subtypes of age-related sarcopenia and dynapenia, to methods for diagnosing them, and to identification of new therapeutic targets. The substantial level of research activity focused on such factors suggests that such diagnostic refinements could become possible in the not-too-distant future (2,12,15). The concept of "SMFD" that comprises a variety of contributory etiologies could provide a framework for developing diagnostic categories that are useful for both clinical practice and research.

For other conditions that are clinically manifested as impaired physiologic functions (eg, congestive heart failure, chronic obstructive pulmonary disease) and have multiple contributory factors, this type of diagnostic evolution has accommodated both therapeutic progress at the stage when mechanistic information has been limited, and further progress as mechanistic understanding has increased. It is likely that the same could apply to progress in diagnosis and evaluation of new treatments for pathologies contributing to "SMFD."

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