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Authors

Bauer, Juergen
Morley, John E
Schols, Annemie MWJ
et al.

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Sarcopenia: A Time for Action. An SCWD Position Paper

Juergen Bauer¹, John E. Morley^{2*}, Annemie M.W.J. Schols³, Luigi Ferrucci⁴, Alfonso J. Cruz-Jentoft⁵, Elsa Dent^{6,7}, Vickie E. Baracos⁸, Jeffrey A. Crawford⁹, Wolfram Doehner^{10,11,12}, Steven B. Heymsfield¹³, Aminah Jatoi¹⁴, Kamyar Kalantar-Zadeh¹⁵, Mitja Lainscak¹⁶, Francesco Landi^{17,18}, Alessandro Laviano¹⁹, Michelangelo Mancuso²⁰, Maurizio Muscaritoli¹⁹, Carla M. Prado²¹, Florian Strasser²², Stephan von Haehling^{23,24}, Andrew J.S. Coats²⁵ & Stefan D. Anker^{10,11,12}

¹Center for Geriatric Medicine, Heidelberg University, Heidelberg, Germany, ²Division of Geriatric Medicine, Saint Louis University School of Medicine, St. Louis, USA, ³Department of Respiratory Medicine, Research School NUTRIM, Maastricht University Medical Center, Maastricht, The Netherlands, ⁴Longitudinal Studies Section, Translational Gerontology Branch, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA, ⁵Servicio de Geriatria, Hospital Universitario Ramón y Cajal (IRYCIS), Madrid, Spain, ⁶Torrens University Australia, Adelaide, Australia, ⁷Baker Heart and Diabetes Institute, Melbourne, Australia, ⁸Division of Palliative Care Medicine, Department of Oncology, University of Alberta, Edmonton, AB, Canada, ⁹Duke Cancer Institute, Duke University, Durham, NC, USA, ¹⁰BIH Center for Regenerative Therapies (BCRT), Charité Universitätsmedizin Berlin, Berlin, Germany, ¹¹Department of Cardiology (Campus Virchow-Klinikum), Charité-Universitätsmedizin Berlin, Berlin, Germany, ¹²German Center for Cardiovascular Research (DZHK), partner site Berlin, Germany, ¹³Pennington Biomedical Research Center, LSU System, Baton Rouge, LA, USA, ¹⁴Department of Oncology, Mayo Clinic, Rochester, MN, USA, ¹⁵Division of Nephrology and Hypertension, University of California Irvine Medical Center, Orange, CA, USA, ¹⁶Division of Cardiology, General Hospital Murska Sobota, Murska Sobota, Slovenia, ¹⁷Institute of Internal Medicine and Geriatrics, Università Cattolica del Sacro Cuore, Rome, Italy, ¹⁸Fondazione Policlinico Universitario 'Agostino Gemelli' IRCCS, Rome, Italy, ¹⁹Department of Translational and Precision Medicine, Sapienza University, Rome, Italy, ²⁰Department of Clinical and Experimental Medicine, Neurological Institute, University of Pisa, Pisa, Italy, ²¹Human Nutrition Research Unit, Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, AB, Canada, ²²Department of Medical Oncology and Hematology, Cantonal Hospital, St. Gallen, Switzerland, ²³Department of Cardiology and Pneumology, University Medicine Goettingen (UMG), Goettingen, Germany, ²⁴German Center for Cardiovascular Research (DZHK), partner site Göttingen, Germany, ²⁵Department of Cardiology, IRCCS San Raffaele Pisana, Rome, Italy

Abstract

The term sarcopenia was introduced in 1988. The original definition was a “muscle loss” of the appendicular muscle mass in the older people as measured by dual energy x-ray absorptiometry (DXA). In 2010, the definition was altered to be low muscle mass together with low muscle function and this was agreed upon as reported in a number of consensus papers. The Society of Sarcopenia, Cachexia and Wasting Disorders supports the recommendations of more recent consensus conferences, i.e. that rapid screening, such as with the SARC-F questionnaire, should be utilized with a formal diagnosis being made by measuring grip strength or chair stand together with DXA estimation of appendicular muscle mass (indexed for height²). Assessments of the utility of ultrasound and creatine dilution techniques are ongoing. Use of ultrasound may not be easily reproducible. Primary sarcopenia is aging associated (mediated) loss of muscle mass. Secondary sarcopenia (or disease-related sarcopenia) has predominantly focused on loss of muscle mass without the emphasis on muscle function. Diseases that can cause muscle wasting (i.e. secondary sarcopenia) include malignant cancer, COPD, heart failure, and renal failure and others. Management of sarcopenia should consist of resistance exercise in combination with a protein intake of 1 to 1.5 g/kg/day. There is insufficient evidence that vitamin D and anabolic steroids are beneficial. These recommendations apply to both primary (age-related) sarcopenia and secondary (disease related) sarcopenia. Secondary sarcopenia also needs appropriate treatment of the underlying disease. It is important that primary care health professionals become aware of and make the diagnosis of age-related and disease-related sarcopenia. It is important to address the risk factors for sarcopenia, particularly low physical activity and sedentary behavior in the general population, using a life-long approach. There is a need for more clinical research into the appropriate measurement for muscle mass and the management of sarcopenia. Accordingly, this position statement provides recommendations on the management of sarcopenia and how to progress the knowledge and recognition of sarcopenia.

Keywords Sarcopenia; Cachexia; Geriatric assessment; Muscle; Skeletal; Muscle strength

*Correspondence to: John E. Morley, Division of Geriatric Medicine, Saint Louis University School of Medicine, 1402 S. Grand Blvd., M238. St. Louis, MO 63104, USA. Email: john.morley@health.slu.edu

The term, sarcopenia, was coined in 1988 by Irwin Rosenberg at a meeting in Albuquerque, New Mexico, to refer to muscle wasting of the older people¹. Its etymological origins are two

Greek words: *sarx* for flesh and *penia* for reduced or deficiency. Baumgartner *et al.*² proposed an operational definition of sarcopenia in 1998. Utilizing dual energy X-ray

absorptiometry (DXA) to measure lean soft tissue, the authors defined sarcopenia as being <2 SDs of appendicular muscle mass (ASM, kg) per height squared (m^2) below the mean of a young reference group. Using this criterion, Baumgartner *et al.* showed that the prevalence and the severity of sarcopenia significantly increased with age and that it was associated with physical disability. In 2002, Janssen *et al.*,³ using bioelectrical impedance analysis (BIA), showed that in the Third National Health and Nutrition Examination Survey (NHANES III), functional impairment was three times as likely in persons with an estimated lean mass below 2 SDs of the mean. Baumgartner *et al.*⁴ found that in older persons with obesity, those who had lost muscle mass had worse outcomes than those who had maintained their muscle mass. They coined the term ‘sarcopenic obesity’ for this condition. By the early 2000s, it was recognized that there are numerous causes of age-related sarcopenia, including loss of motor units innervating muscle, systemic inflammation, oxidative stress, decline in anabolic hormones, and the ‘anorexia of aging’ coupled with a decrease in physical activity^{5,6} (Figure 1). At this stage, it was recognized that there were both primary sarcopenia (age related) and secondary sarcopenia (disease related, as with diabetes mellitus, cancer, chronic obstructive pulmonary disease, or heart failure).

Evolving definition of sarcopenia

Primary sarcopenia (sarcopenia of aging)

In 2010, the European Working Group on Sarcopenia for Older Persons⁷ recommended a new operational definition of sarcopenia of aging, i.e. the presence of low muscle mass together with low muscle function (strength or performance). Over the last decade, numerous other consensus groups have agreed to this revision to the meaning of sarcopenia of aging.^{8–12} However, these groups all used different cut-offs to

define sarcopenia of aging, highlighting the fact that different cut-offs are necessary for different ethnic groups.¹²

Towards the end of last year, two consensus articles on sarcopenia of aging were published. One was an update by the European Working Group on Sarcopenia (EWGSOP2),¹³ and the other was on the management of sarcopenia of aging by the International Clinical Practice Guidelines for Sarcopenia (ICFSR).¹⁴ The EWGSOP2 requires low muscle strength as a key characteristic of low muscle quality and the presence of low muscle quantity to confirm the diagnosis. If a person also has functional impairment, confirmed with a physical performance measure,¹⁵ this is characterized as severe sarcopenia. The authors recommended measuring muscle strength with either grip strength or the chair stand test. Muscle mass can be measured by DXA, magnetic resonance imaging, or computed tomography. Either gait speed, the short physical performance battery (SPPB), the Timed Up and Go test, or the 400-m-walk can be used for the assessment of physical performance.

Recognizing the limited time available during a typical visit to a health care professional, the EWGSOP2 also suggested that case finding should be used to identify older persons at risk for sarcopenia. They recommended the use of clinical symptoms usually associated with sarcopenia or the SARC-F (Figure 2), a questionnaire with five questions, which has high specificity, albeit low sensitivity, to identify persons with sarcopenia.^{16–20} The SARC-F has been translated into multiple languages. The SARC-F is also recommended by the ICFSR for screening.¹⁴ The specificity of the SARC-F can be improved by measuring calf circumference as well.²¹ The Ishii screening test (age, grip strength, and calf circumference) is recommended as an alternative screening test.^{22,23} However, this already includes grip strength, which is a core measure of sarcopenia.

While BIA was not strongly supported by the EWGSOP2, to measure muscle mass, they recognize that its portability, affordability, and availability make BIA a feasible tool to estimate muscle mass in many care settings. Ultrasound of

Figure 1 The factors involved in the pathogenesis of primary (age related) sarcopenia.

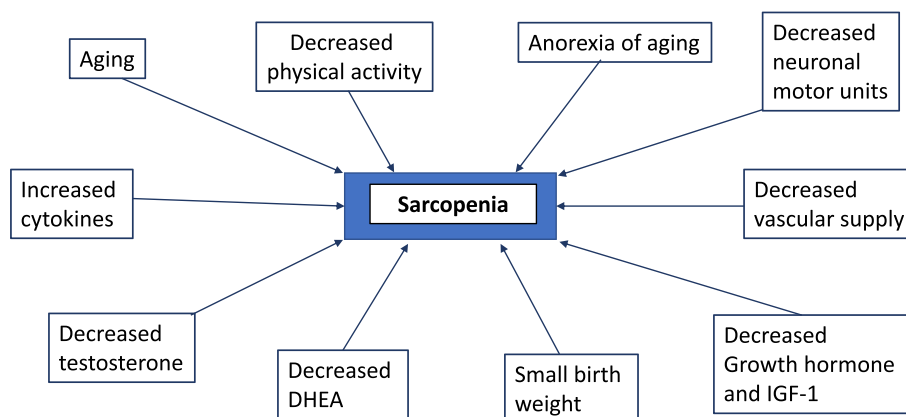


Figure 2 SARC-F questionnaire (includes scoring).

| Component | Question | Scoring |
|-----------------------|--|--|
| Strength | How much difficulty do you have in lifting and carrying 10 pounds? | None = 0 Some = 1 A lot or unable = 2 |
| Assistance in walking | How much difficulty do you have walking across a room? | None = 0 Some = 1 A lot, use aids, or unable = 2 |
| Rise from a chair | How much difficulty do you have transferring from a chair or bed? | None = 0 Some = 1 A lot or unable without help = 2 |
| Climb stairs | How much difficulty do you have climbing a flight of 10 stairs? | None = 0 Some = 1 A lot or unable = 2 |
| Falls | How many times have you fallen in the past year? | None = 0 1 – 3 falls = 1 ≥ 4 falls = 2 |

muscle such as the quadriceps is emerging as a potential tool to measure muscle quantity and, because it excludes intermuscular adipose tissue from the measurement, also muscle quality^{24,25}; a protocol for using ultrasounds in sarcopenia has recently been proposed by the European Geriatric Medicine Society.²⁶

There is increasing evidence that creatine dilution, implemented by ingesting a dose of the deuterium labelled isotope, may also offer an accurate approach for measuring muscle mass.^{27,28} Studies so far suggest creatine dilution estimates of muscle mass may have good correlations with functional outcomes.^{27,28} Nonetheless, its relevance and practicality in clinical settings remain to be determined.

The ICFSR consensus made similar conditional recommendations utilizing the SARC-F for screening and applying either the original EWGSOP or Foundation for NIH (FNIH) diagnostic criteria.¹⁴

Secondary sarcopenia

Malignant disease has been the most studied secondary sarcopenia, and international consensus definitions specific to cancer sarcopenia²⁹ are predicated on disease specific outcomes: mortality, complications of cancer surgery, and chemotherapy toxicity. Whether this secondary sarcopenia should be considered early cachexia or sarcopenia remains controversial,³⁰ but it is becoming clearer that sarcopenia is only one of the different features of muscle changes during cancer cachexia. Owing to the prevalent use of computed tomography imaging in cancer diagnosis and follow-up, secondary analysis of oncologic imaging for skeletal muscle cross-sectional areas or volumes is the current standard for the quantification of muscle mass in this domain.

There are several points of relevance regarding age-related and disease-related loss of muscle mass. Loss of muscle mass with age occurs in a continuous fashion after reaching peak

muscle mass in young adulthood (at about 30 years of age). A variety of longitudinal observational studies provide information on the rate of muscle loss per decade. The percentage loss of ASM per 10 years is of the order of ~5% in men and is usually reported to be somewhat lower in women. Chronic illness-related muscle loss is also progressive; however, these are non-linear and of a considerably greater magnitude than the values seen in aging. For example, cancers of advanced stage induce muscle loss over time that take an exponential course^{31,32} with increasing intensity according to the disease progression, varying from 2% per 100 days to 15% per 100 days. Total cumulative loss in 12 months in colon cancer patients was 15.6%, equivalent to circa 30 years of aging³¹; this is partially disease-related but also in part a consequence of cancer surgery or systemic antineoplastic therapies which induce punctate short-term losses. Acute illness requiring hospitalization is associated with even higher intensity of muscle loss than in cancer. In elective hip replacement surgery during an average of 5.6 ± 0.3 days of hospitalization, associated with significant decline in quadriceps ($-3.4 \pm 1.0\%$) and thigh muscle cross-sectional area (CSA) ($-4.2 \pm 1.1\%$) in the non-operated leg ($P < 0.05$) aging.^{33,34} This could be in part due to bed rest as 5 days of one-legged knee immobilization using a full leg cast resulted in decline of quadriceps muscle CSA from baseline of $3.5 \pm 0.5\%$ ($P < 0.0001$). Acute sarcopenia secondary to hospitalization or chronic disease exacerbations may be partially recoverable or may lead to heightened risk of developing sarcopenia at a young age.³⁵

Management of sarcopenia

For the management of sarcopenia, there is a strong recommendation that individuals with sarcopenia should be enrolled in a resistance exercise programme. There is a reasonable

amount of evidence that resistance exercise will increase both muscle mass and strength.^{36–38} The use of a protein rich diet (1 to 1.5 g/day) or protein supplementation received a conditional recommendation based on a small amount of evidence and a previous consensus conference.^{39–41} Higher doses of protein (up to 2 g/day) may be appropriate in persons with severe illness or injury or when there is evidence of a pro-inflammatory/catabolic state.^{39,40} β -hydroxy β -methylbutyrate (HMB) has been shown to improve muscle mass and to preserve muscle strength and function in older people with sarcopenia or frailty.⁴² Vitamin D supplementation specifically for sarcopenia was found to have insufficient evidence, though there is evidence that persons with low vitamin D levels may improve their strength with vitamin D supplementation.⁴³ Similarly, while testosterone can increase muscle mass and strength in older individuals and a meta-analysis has confirmed its safety,^{44–47} the lack of evidence in persons with sarcopenia did not lead to its integration into these recommendations. Preliminary data with anamorelin, a growth hormone secretagogue receptor type 1 (ghrelin receptor) agonist that increases muscle mass but not strength,^{48,49} and anti-myostatin antibodies^{49–53} were considered insufficient to make recommendations in favour of their use.

Recommendations

Recently, an ICD-10-CM code for sarcopenia as a disease has become available allowing physicians to formally include sarcopenia in the list of diagnosis that can be used and funded.^{54–56} Based on the available evidence and the two recent consensus recommendations, the task force of the Society for Sarcopenia, Cachexia and Wasting Disorders recommends for clinical application the following:

- 1 Health care professionals are encouraged to screen for sarcopenia using simple screening tools such as the SARC-F.
- 2 Where available and feasible, physicians should make a formal diagnosis of sarcopenia utilizing grip strength or chair stand and—if available—a measurement of fat-free mass. At present, we recommend ASM per height squared estimated by DXA, but recognize CT, BIA, ultrasound, or creatine dilution techniques may be as good or more accurate approaches for estimating muscle mass in the future.
- 3 Resistance exercise should be prescribed for any older person suspected of having sarcopenia both for secondary prevention and/or treatment.
- 4 A protein intake of 1 to 1.5 g/kg/day in conjunction with physical exercise seems reasonable for a person with sarcopenia.
- 5 At present, there is insufficient evidence that vitamin D, anabolic steroids, or newer pharmacological agents should be used to treat sarcopenia.

- 6 These recommendations apply to both primary (age related) sarcopenia and secondary (disease related) sarcopenia. In the second, treating the disease(s) related to sarcopenia is also essential.

Consensus documents on sarcopenia in older persons (EWGSOP and ICSFR) as well as those for sarcopenia in chronic disease²⁹ have something in common: they intend to put sarcopenia in the clinical frontline. It is time that health professionals are educated in the diagnosis and management of sarcopenia and are encouraged to screen for sarcopenia and educate their patients on primary and secondary prevention of sarcopenia.

To progress the knowledge and recognition of sarcopenia, the task force recommends the following actions:

- 1 promotion of sarcopenia measurement in epidemiological studies of older adults, including in studies of chronic disease, and also in other disease or organ oriented specialties;
- 2 collaboration with health care policy makers and health care providers regarding medical claims using the ICD diagnosis code for sarcopenia;
- 3 development and assessment of new treatments for sarcopenia in individuals with either primary or secondary sarcopenia;
- 4 advocating common standards in the quality of clinical trials for sarcopenia, including consistent outcome measurements and recognition of such measures by regulatory agencies;
- 5 address the risk factors for sarcopenia, particularly low physical activity and sedentary behaviour in the general population, using a life-long approach;
- 6 explore the impact of targeted nutritional approaches to countermeasure muscle loss alone and in a multimodal approach to maximize anabolic potential (e.g. exercise and anabolic therapy); and
- 7 identify the pathophysiological pathways leading to sarcopenia.

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Conflict of interest

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