Sarcopenia

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KEYWORDS

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• Cachexia • Exercise • Vitamin D • Amino acids

Sarcopenia is operationally defined as an appendicular skeletal muscle mass divided by height in meters of more than 2 standard deviations less than the normal mean in younger persons. The term is derived from the Greek "sarx" or "flesh" and "penia" or "loss." The ability to easily measure body composition by dual emission x-ray spectrometry or bioelectrical impedence analysis has led to intensive research on skeletal muscle mass in aging.[1,2]

Using this operational definition, Baumgartner and colleagues[3] found that 14% of men younger than 70 years, 20% of men aged 70 to 74 years, 27% of men aged 75 to 80 years, and 53% of men older than 80 years had sarcopenia by dual energy x-ray absorptiometry (DEXA). In women, 25%, 33%, 36%, and 43% in the same age groups had sarcopenia. Cultural effects confound this observation, showing that Hispanic men and women have higher rates of sarcopenia.

A second method of defining sarcopenia was developed by Janssen and colleagues.[4] Skeletal muscle mass assessed by bioelectrical impedance was expressed as a percentage of total body weight to adjust for height and nonskeletal muscle tissues (fat, organ, bone). Using an approach similar to osteoporosis algorithms, class I sarcopenia was defined as between 1 and 2 standard deviations less than the sex-specific mean of a young reference group and class II sarcopenia was defined as 2 standard deviations less than this mean. The frequency of class II sarcopenia was 7% in men and 10% in women. The difference in frequency may reflect the differences in methodology.

That muscle mass decreases with age has been known for some time. Earlier work demonstrated that the excretion of urinary creatinine, a measure of tissue creatine content and total muscle mass, decreases by nearly 50% between the ages of 20 and 50 years.[5] This age-related loss of muscle mass occurs in sedentary and active aging adults. By contrast, in healthy young adults, no net change occurs in skeletal muscle mass under equilibrium conditions because of the balance in skeletal muscle protein synthesis and degradation.

Maximal oxygen consumption declines with age at a rate of 3.8% per decade beginning at the age of 30 years.[6] After correction for muscle mass, there is no important

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decline in $V_{O_{2max}}$ with aging, indicating that the change in muscle mass is the significant factor.[7,8] Dynamic, static, and isokinetic muscle strength decreases with age.[9]

The association of age-related loss of muscle mass and functional decline drives the current interest in sarcopenia. The loss of muscle mass with aging is clinically important because it has been postulated to lead to diminished strength and exercise capacity. In the Italian InCHIANTI population, calf muscle cross-sectional area in men and women had an almost linear relationship with knee extension, handgrip strength, and lower extremity muscle power in participants with sarcopenia defined by age and gender T scores.[10]

In the New Mexico study population, an approximately fourfold increase in the risk of disability in at least 3 of the instrumental activities of daily living, a two- to threefold increase in the risk of having a balance disorder, and a twofold greater likelihood of having to use a cane or walker was observed in men with sarcopenia. An approximately fourfold increase in the risk of disability in at least 3 of the instrumental activities of daily living was seen in women.[11]

Janssen found a significant association for the presence of any disability in the study subjects in the lowest tertile of skeletal muscle mass divided by the square of height, an effect that persisted after adjustment for age, race, health behaviors, comorbidity, and fat mass.[12] The likelihood of physical disability was highest when the skeletal muscle mass divided by height squared was less than 8.50 kg/m^2 in men (odds ratio [OR], 4.71; 95% confidence interval [CI], 2.28, 9.74) and lower when the skeletal muscle divided by height squared was between 8.51 and 10.75 kg/m^2 (OR, 3.65, 95% CI,1.92, 6.94). In women, the OR for physical disability was 3.31 (95% CI, 1.91, 5.73) when the skeletal muscle mass divided by height squared was less than 5.75 kg/m^2. No difference was seen in women with skeletal muscle mass divided by height squared between 5.76 and 6.75 kg/m^2 or higher.[12] Janssen suggested that these cutoff points be used to define normal muscle mass, moderate sarcopenia, or severe sarcopenia.

The relationship between sarcopenia and functional impairment/disability is confounded by other variables. After adjustment for age, race, body mass index, health, and comorbidity, the strength of the association with severe sarcopenia was attenuated. Among 12 functional measures in men, class II sarcopenia was related only to tandem standing performance and self-reported limitation in stooping or kneeling. In women, class II sarcopenia was associated with difficulty climbing 10 stairs, lifting/carrying 10 pounds, stooping/crouching/kneeling, standing from a chair, and performing household chores.[12]

This has led to questioning the relationship between low muscle mass (sarcopenia) and low muscle strength. In subjects older than 70 years, poor lower extremity performance was predicted by leg muscle strength but not leg muscle mass.[13] Low muscle strength, but not low lean body mass, is a strong predictor of mortality in older adults.[14] Hand grip strength is a predictor of all-cause mortality not explained by muscle size or other body composition measures.[15] Exercise produces an increase in muscular strength and improvement in balance, independent of any change in body composition.[16] Whether sarcopenia is linked to muscle strength and whether sarcopenia is reversible represent important clinical questions.

The definition of sarcopenia continues to evolve. The prediction of disability and impaired functional status in sarcopenic subjects has focused on the inclusion of function in the definition.

Sarcopenia is at present defined as the loss of muscle protein mass, muscle function, and muscle quality, which accompanies advancing age.[17] Only severe sarcopenia is associated with future disability, whereas moderate sarcopenia conveys no apparent