Sarcopaenia: Where do we stand after two decades of research?

Mollentze WF
Professor/Chief Spcialist: Internal Medicine, University of the Free State, Bloemfontein

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Age-related loss of muscle mass has received increased attention over the past two decades from both clinician and basic science researchers.[1] Evans and Campbell labeled the age-related loss of muscle mass as sarcopaenia (Greek *sarx*=flesh and *paenia*=loss).[2] The estimated relative annual rate of loss of muscle mass is 1% in men and 0.84% in women.[1] The average age of onset of decline in muscle mass is approximately 40 years and progress in a linear fashion to reach approximately 50% by the 8th decade.[3,4]

Sarcopaenia is characterised by a decrease in muscle mass and cross-sectional area, the infiltration of muscle by fat and connective tissue, a decrease of type 2 muscle fiber size and number, and also a decrease of the number of type 1 fibers.[5] In addition to muscle atrophy, a decline in muscle quality and function also plays a part in muscle dysfunction of aging.[6] Changes in muscle quality in aged subjects include a decreased concentration of myosin, the most important motor protein; fewer cross-bridges per muscle fiber area; post-translational chemical modifications of the myosin molecule such as protein methylation, glycosylation, and/or oxidation; and finally, a decrease in muscle elasticity.[6] The decline in physical activity frequently accompanying aging may also exert synergistic effects on these changes. Furthermore, the regulation of skeletal muscle mass and regeneration is intricately linked to skeletal muscle metabolism and the recruitment of skeletal muscle stem cells - also referred to as satellite cells.[7]

The mechanisms underlying sarcopaenia of aging are numerous and include endocrine conditions, age-related changes in sexual hormones, apoptosis, mitochondrial dysfunction, neuro-degenerative conditions, inflammation, disuse, malnutrition, and cachexia associated with serious underlying disease states.[5] The end result, however, is an imbalance between muscle protein synthesis and breakdown with a disproportionately higher rate of breakdown over a prolonged period.[1] The mammalian target of rapamycin complex 1 (mTORC1) signaling pathway in muscle plays a key role in regulating exercise-induced protein synthesis.[8] Fry et al demonstrated that aging impairs contraction-induced human skeletal muscle mTORC1 signaling and protein synthesis.[9] This observation may partially explain the blunted hypertrophic response observed after resistance exercise training in older adults and highlights the mTORC1 pathway as a potential therapeutic target for pharmacological intervention in sarcopaenia.[9]

The European Working Group on Sarcopaenia in Older People (EWGSOP) recognises sarcopaenia as a geriatric syndrome characterised by progressive and generalised loss of muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.10 EWGSOP suggests the following diagnostic criteria for sarcopaenia:[10] the presence of low muscle mass and low muscle function defined by either loss of muscle strength or performance. Dual energy X-ray absorptiometry (DXA) has become the gold standard in measuring muscle mass in clinical practice as part of body composition assessment.[10,11] Bio-impedance analysis (BIA) may be an affordable and portable alternative to DXA.[10] Muscle strength can be measured in various ways of which measuring handgrip strength with a handheld dynamometer is the most popular.[11] Physical performance can be measured in a variety of ways of which either the Short Physical Performance Battery (SPPB), with gait speed over 4 meters; or the "timed-get-up-and-go test" (TGUGT) is most popular in the clinical setting.[10,11] Cut-points for these frequently-used criteria are readily available.[11]

The prevalence of sarcopaenia in the elderly differs widely according to methodology used and population studied. Morley estimated the prevalence

of sarcopaenia to be 5-13% in 60-70 year-old persons and 11-50% in those 80 years and above.[12] The clinical consequences of sarcopaenia are future disability,[13] mobility limitation,[14] and impaired quality of life.[11] Obese older people with reduced handgrip strength are particularly at risk of walking limitation.[11] Lower grip strength is also positively associated with future fracture risk, cognitive decline, coronary heart disease, hospitalisation, risk of falling, and death.[11]

Cruz-Jentoft et al recently reviewed published interventions to prevent or improve sarcopaenia.[15] Exercise intervention may have a role in increasing muscle strength and improving physical performance although the impact of exercise training is inconsistent in improving muscle mass in frail elderly individuals. The effect of nutrition intervention in terms of protein and Vitamin D supplementation is uncertain due to methodological problems in the design of most studies. Some studies report encouraging findings in terms of essential amino acid supplementation in the form of leucine and HMB (β-hydroxy β-methylbutyric acid), the active metabolite of leucine, alone or in addition to exercise training.

The International Sarcopaenia Initiative (ISI) concluded in a recent review that sarcopaenia is present in at least 1 in 20 community dwelling individuals and in as many as 1 in 3 frail older people living in nursing homes.[15] The ISI urge clinicians to screen for the presence of sarcopaenia both in community as well as geriatric settings and to consider supervised resistance exercise training for periods of at least 3 months. The ISI also supports the recommendation of the PROT-AGE study group to increase protein intake of elderly people (65-years and older) to 1.0-1.2 g/kg per day to help them regain and maintain lean body mass.[16]

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