Aging

Skeletal Muscle Function Deficits in the Elderly: Current Perspectives on Resistance Training

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A variety of changes in skeletal muscle occur with aging. Sarcopenia is the age-associated loss of muscle mass and is one of the main contributors to musculoskeletal impairments in the elderly. Traditional definitions of sarcopenia focused on the size of human skeletal muscle. However, increasing evidence in older adults suggests that low muscle mass is associated with weakness, and weakness is strongly associated with function and disability. In recent years a global trend has shifted toward more encompassing definitions for the loss of muscle mass which include decreases in physical function. This review focuses on skeletal muscle function deficits in the elderly and how these age-associated deficits can be ameliorated by resistance training. We set forth evidence that skeletal muscle deficits arise from changes within the muscle, including reduced fiber size, decreased satellite cell and fiber numbers, and decreased expression of myosin heavy chain (MHC) isoform IIa. Finally, we provide recommendations for clinical geriatric practice regarding how resistance training can attenuate the increase in age-associated skeletal muscle function deficits. Practitioners should consider encouraging patients who are reluctant to exercise to move along a continuum of activity between "no activity" on one end and "recommended daily amounts" on the other.

Resistance training | Sarcopenia | Aging | Postural balance

Introduction

Over the next two decades, 77 million baby boomers in the United States will reach retirement age, and by 2030, one in five Americans will be 65 or older (1). As these individuals age, there is a concomitant decline in voluntary physical activity which is associated with decreases in maximal aerobic capacity and muscle strength (2). Muscle strength is a critical component in preserving functional activity in older adults. Consequently, numerous studies have investigated the factors that contribute to the loss of strength in elderly persons.

Sarcopenia, the age-related reduction in muscle mass, is one of the leading factors in the etiology of strength decline with aging (3, 4) . This age-related reduction in muscle mass was first described in 1966 by Irwin H. Rosenberg, at a symposium titled "Sarcopenia: Diagnosis and Mechanisms" (5). The term sarcopenia is derived from the Greek roots *sarx*, meaning flesh, and *penia*, signifying loss. Sarcopenia however, did not gain substantive recognition until 1989 when Rosenberg published what many consider to be his seminal manuscript on the topic of age-related muscle loss (6).

Early operational definitions of sarcopenia were based exclusively on the amount of muscle mass within a reference population. However, increasing evidence in community dwelling older adults suggests that low muscle mass is associated with weakness (7) and weakness is strongly associated with function and disability (8, 9). Indeed, functional tasks such as rising from a chair and performing home and personal care are directly associated with sarcopenia (10). Consequently, traditional definitions of sarcopenia have been left behind in favor of more encompassing definitions. New terms such as Skeletal Muscle Function Deficit have been recommended because they incorporate strength and physical function together with muscle mass (11).

The purpose of this review is to provide current perspectives on the evolution of sarcopenia in modern literature and to inform clinical providers of the effect that skeletal muscle dysfunction has on physical function. We present evidence that a large source of the physical function deficits that emerge with aging arise from changes within the muscle, including decreased satellite cell and fiber numbers, reduced fiber size, and decreased expression of myosin heavy chain (MHC) isoform IIa. We finish by providing clinicians with recommendations for exercise, specifically resistance training interventions, which may attenuate aging-related changes in muscle function.

Sarcopenia and physical function

Citing the need to improve diagnostic criteria and treatment guidelines, the European Working Group on Sarcopenia in Older People developed a consensus statement in 2010 for the diagnosis of sarcopenia. The large European group met and eventually endorsed a definition that requires the use of low muscle mass, accompanied by either low muscle strength or low physical performance (12). Additional working groups have also recently adopted statements requiring both lean mass and gait speed as diagnostic requirements for sarcopenia (13-15). As a further sign of an evolving conceptualization of sarcopenia, the Foundation for National Institutes of Health Sarcopenia Project applied a Classification and Regression Tree analysis to large clinical trial and epidemiologic data to identify clinically relevant cutpoints for low muscle mass and weakness that would lead to functional decline in men and women (16). The addition of these functional measures and specific cutpoints highlights the recognition from the clinical and research communities that loss of muscle mass does not occur without concomitant impairments in function and decreases in physical function. These cutpoints also promise to allow practitioners to readily assess the diagnostic classification of patients at risk for functional decline. Additional work is needed however to validate the proposed diagnostic criteria.

Biology of aging skeletal muscle

The motor unit is the basic functional unit of the neuromuscular system and translates all synaptic input into force production and movement (17). The motor unit is comprised of the alpha motor neuron and the muscle fibers it innervates. Advanced age is accompanied by decreasing motor unit properties resulting from

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changes with morphology and size, and leading to skeletal muscle function deficits (18-20). Moreover, muscle fibers play an important role in the function of the motor unit. Important structural changes within muscle fibers accompany aging as follows: 1) decreased satellite cell and fiber numbers; 2) reduced fiber size; 3) declines in expression of MHC IIa. 1) Decreased satellite cell and fiber numbers. Older adults have a higher rate of fiber denervation relative to reinnervation (motor unit remodeling), and experience greater amounts of oxidative stress and apoptosis, which can decrease satellite cell regeneration of muscle fibers and result in fiber loss (21, 22). 2) Reduced fiber size. Muscle fibers are generally smaller in older adults compared to young persons, especially in the lower limbs (23-25). This is problematic for functional activities requiring strength for balance and postural control (26). Muscle atrophy occurs to a greater extent in type II fibres in older adults compared with young adults, although all fiber sizes can be reduced with aging (24, 25, 27). Reasons for the reductions in fiber size with aging include fewer satellite cells in type II fibers and lower protein synthesis, which reduces the speed of skeletal muscle growth and repair (28-30). 3) Decreased expression of MHC IIa. In general, MHC IIa isoforms play a key role in muscle's strength and power, and have smaller proportional area expressed in muscles of older adults compared with young persons (31, 32). The smaller proportion of type IIa isoforms occurs in conjunction with reports of a shift to proportional increases in MHC IIx isoform expressions in older adults (23, 33). These age-related changes result in slowed myosin actin cross-bridge kinetics and reduced power for functional task performance (34).

Resistance training for older adults

Muscle mass decreases by 1-2% in an annual rate after the age of 50 (35). In addition, muscle strength can decrease by 12-15% every 10 years after an individual reaches the mid-century mark (36). However, attenuation of the loss of muscle strength and muscle mass in older adults can be accomplished with resistance training (strength training exercise with progressive overload where muscles exert a force against an external load). It is recommended that older adults participate in resistance training 2-3 days per week, (37) but no clear definitive regimen has been identified due to heterogeneity of research studies (38). A large meta-analysis of various types of resistance training programs concluded that 12 - 24 weeks of training has the ability to increase muscle strength by at least 25% in men and women over the age of 50, with greater improvements being associated with higher intensity training (39).

Resistance training offers numerous benefits beyond improvements in muscle strength alone for older individuals. Several reports have demonstrated improvements in balance, functional mobility and fall prevention. Pijnappels et al., found that reactive balance strategies (recovery after tripping over obstacles) were improved after 16 weeks of resistance training (40). Day et al., reported that overall balance was improved and the number of falls in individuals over the age of 70 was reduced after 15 weeks of resistance training (41). Gait speed and stair climbing power are also improved with resistance training (42, 43). In support of previous reports, a Cochrane systematic review noted that resistance training results in modest improvements in functional limitations for older adults with physical disabilities (44). The positive implications of these results reinforce the notion that resistance training can play a vital role for the older individual in improving functional mobility during activities of daily living. The effect of this intervention on more substantive outcomes such as health related quality of life however, remains unclear (44).

Recommendations for clinical practice

Because skeletal muscle function deficits are amenable to improvement, resistance training has been widely accepted as an appropriate modality of treatment. However, the literature investigating resistance training and functional task performance is characterized by heterogeneity of populations, training regimen (mode, dose, and progression) and task outcomes. Consequently, the ability to make clinical recommendations based on the panoply of evidence has been difficult. Despite the inevitable challenges with heterogeneity in resistance training studies, most authors are certain of one conclusion: doing something is better than doing nothing (44-48). For example, Smith and colleagues conducted a longitudinal study on the effects of resistance training over a 5 year period in 3 different groups of older adults (mean age 72.5 yrs) (49). One group participated in resistance training continuously over the 5 years (Trained), while another group trained for 2 years and then stopped (Detrained). During the training period both groups trained hard, at 80% of their own 1-repetition maximum (RM) for up to 3 sets. The third group acted as a control, without any resistance training over the 5 years, but participated in all the testing procedures at baseline, 2 years and 5 years. Both the Trained and the Detrained groups significantly improved muscle strength at the end of 2 years. At the end of 5 years, the Trained group had increased muscle strength by ~44% over baseline. Meanwhile, the control group declined in strength over the 5 year period. Interestingly, the Detrained group lost strength at the 5 year follow-up, but their overall muscle strength was still 15.6% higher compared to baseline. Thus, doing something is clearly better than doing nothing, and older adults who stay physically active might expect to attenuate the age-associated loss in skeletal muscle mass.

Summary

The most obvious consequence of sarcopenia is a loss of muscle strength; however there is a constellation of consequences greater than that of muscle size alone. Additional structural changes within muscle fibers accompany aging such as decreased satellite cell and fiber numbers, reduced fiber size, and declines in expression of MHC IIa. These changes are not benign in terms of functional ability, as they can lead to decreased mobility, loss of functional independence, and greater risk of falls. Resistance training however can attenuate the effects of skeletal muscle function deficits in older adults. Documented structural changes in the muscle have been demonstrated, but improvements extend beyond structural impairments. Significant benefits in activities of daily living have been reported such as improved walking endurance, gait speed, and stair-climbing ability. Despite the well-known advantages of resistance training, many older adults have difficulty achieving recommended dosages of daily physical activity. Consequently, practitioners should focus on what older adults *can do* instead of what they *cannot do*. The adage "doing something is better than doing nothing" is paramount. Practitioners might consider exercise as a spectrum, with "no activity" on one end and "recommended daily amounts" on the other end. In-between those points exists a continuum. Getting individuals who are reluctant to perform resistance training to move along that continuum is an important goal.

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