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Review Article

Therapeutic potential of eccentric exercises for age-related muscle atrophy

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ABSTRACT

Recent studies have focused on evidence-based interventions to prevent mobility decline and enhance physical performance in older adults. Several modalities, in addition to traditional strengthening programs, have been designed to manage age-related functional decline more effectively. In this study, we reviewed the current relevant literatures to assess the therapeutic potential of eccentric exercises for age-related muscle atrophy (sarcopenia). Age-related changes in human skeletal muscle, and their relationship with physical performance, are discussed with reference to *in vitro* physiologic and human biomechanics studies. An overview of issues relevant to sarcopenia is provided in the context of the recent consensus on the diagnosis and management of the condition. A decline in mobility among the aging population is closely linked with changes in the muscle force–velocity relationship. Interventions based specifically on increasing velocity and eccentric strength can improve function more effectively compared with traditional strengthening programs. Eccentric strengthening programs are introduced as a specific method for improving both muscle force and velocity. To be more effective, exercise interventions for older adults should focus on enhancing the muscle force–velocity relationship. Exercises that can be performed easily, and that utilize eccentric strength (which is relatively spared during the aging process), are needed to improve both muscle force and velocity.

1. Introduction

By the age of 80 years, humans generally lose ~30–40% of their skeletal muscle fibers, particularly Type II fibers.[1] The decline in muscle mass and strength with age is well documented.[2,3] In general, the muscle mass of 60–70-year-olds decreases to 70–80% of that of younger people (<60 years old).[4,5] The main features associated with aging skeletal muscles are muscle weakness, decreased flexibility, vulnerability to certain types of injury, and impaired functional restoration, which result in the deterioration of physical performance and function.[6] Lower extremity strength decreases linearly with

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age in both men and women, as shown by numerous cohort studies.[7–9] Physical performance, with respect to balance and gait speed, for example, is closely linked with muscle mass and strength.[10] Therefore, age-related changes in muscle mass and strength should be carefully monitored for signs of decline. Although functional decline with increased age is typical, the mechanisms underlying this decline, and the features that characterize it, are complex and variable. Therefore, it is important to develop specific interventions that will prevent or delay functional decline based on understanding age-related changes in the muscular systems of older adults.

Concerning exercise interventions that have therapeutic potential specifically for age-related muscle atrophy, recent studies have focused on evidence-based interventions aimed at preventing mobility decline or enhancing physical performance in older adults.[11–13] Several different treatment modalities, other than traditional strengthening programs, have been designed to manage age-related functional decline more effectively.[12,14] In this study, we reviewed the literature to delineate the role of physical function in disability and falls in older adults, and to assess the therapeutic potential of eccentric exercises for age-related muscle atrophy.

2. Sarcopenia: Definition and diagnosis

Sarcopenia is defined as the loss of skeletal muscle mass and strength with increased age.[15–17] This results in weakness, limited mobility, and increased susceptibility to injury. Several operational definitions have been used to diagnose sarcopenia, of which the most prevalent is an appendicular skeletal muscle mass (ASM) value ≥ 2 standard deviations below the ASM of young adults, divided by height squared (kg/m^2) or weight. As a rule, the relationship between mass and strength is linear, as is that between muscle strength and performance. However, there is no linear correlation between muscle mass and function. We found that muscle mass was not associated with physical performance in weak older adults, suggesting that measures of muscle strength may be of greater clinical importance in this population than muscle mass per se. The correlation between muscle mass and functional performance was significant in the higher strength group, but not in the weaker group.[18] This is because fatty or connective tissue infiltration into muscle tissues are included in muscle mass in those patients such that we cannot distinguish abnormal intramuscular changes by evaluating muscle mass alone, particularly in patients with mobility impairments. Therefore, the functional status of intramuscular tissues should be included in any assessment of sarcopenia.[8,18]

Mobility decline among the aging population is closely linked with changes in the muscle force–velocity relationship.[19] Such changes have functional implications, e.g., slower walking speeds. In recent studies, gait speed, or walking velocity, was highlighted as a major indicator of mobility decline or sarcopenia in geriatric populations.[20–22] Predicted years of remaining life, for both sexes, increases commensurate with gait speed regardless of age, according to a pooled analysis of nine cohort studies on walking speed and survival.[23] Gait speeds of 1.0 m/s or higher were consistently associated with longer survival than would be expected based on age and sex alone. According to the consensus in European group for determining sarcopenia, gait speed should be measured initially, and mass profiles should be evaluated when gait speed is abnormal. Sarcopenia should be diagnosed when gait speed is normal only if strength is abnormal.[22]

3. Changes in skeletal muscle structure and function with advancing age

The mechanical properties of muscles can be assessed according to their active, contractile characteristics, and passive tension or stiffness. Intrinsic contractile characteristics related to the cross-bridge mechanics of single fibers change with aging.[24] Some studies have reported that both a decrease in contractile materials and a reduced force-generating capacity per cross-bridge affect the contractile properties of aging muscles. A selective loss of Type II (fast twitch) muscle fibers is associated with the age-related decline in strength.[25] Cross-sectional dissections of whole thigh muscles of older cadavers have also shown an 18% decline in total muscle area and a 25% decrease in the total number of muscle fibers, with a particular decrease in the number of Type II muscle fibers.[26] These results are also supported by other cross-sectional studies that have shown that the area of Type I mean fibers is preserved with aging, whereas Type II fibers show atrophy.[27] In addition to changes in muscle fiber size and number with advancing age, specific changes in the intrinsic ability of aged muscles to generate force have also been observed. In humans, decreased specific force (i.e., force normalized by cross-sectional area [CSA]) and unloaded shortening velocity in the Type I and IIa fibers of older sedentary males have been reported relative to young sedentary controls.[28,29] These changes are also consistent with those observed in rat skeletal muscle throughout life. Thompson et al [30] reported decreases in the specific force and unloaded shortening velocity of the soleus muscles of aging rats. They further noted a dissociation between loss of muscle CSA and a decline in maximal force. These human and rat data provide evidence that intrinsic changes in muscle quality may also be important for understanding age-related changes in the function of skeletal muscle. Future studies should evaluate the relationship between the intrinsic force and shortening velocity of aging skeletal muscle, and the relationship between these factors and age-related declines in whole muscle strength and peak power.

Changes in both the fiber elasticity and contractility of Type I and Type IIa fibers have been assessed in terms of instantaneous stiffness, that is, according to the ratio between force changes and corresponding length changes.[24] As an active component of elasticity, instantaneous stiffness reflects the elastic characteristics of muscle fibers but has some limitations with respect to indexing passive components. Passive elastic properties are instead assessed in terms of passive stiffness, or tension, which is thought to be related to sarcolemma, connective tissues, and titin filaments.[31] Passive stiffness is measured by the tensile force associated with displacement during stretching of the skeletal muscles.[32] Increased stiffness, or decreased extensibility, of the muscle or muscle-tendon unit has been reported in aging skeletal muscles.[33]