Contractile Properties of Aging Skeletal Muscle

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According to the World Health Organization, life expectancy at birth has been increasing steadily in many countries around the world (12). As a consequence, by the year 2025, the number of people above age 60 in the world is projected to exceed 1 billion. However, as Banks and Fossel state (2), age per se does not determine aging. The main problem associated with advanced adult age is the loss of functional capacity and independence. Since maximal physiological capacities are greatly diminished with aging, the ability to perform physical tasks at the same level of energy expenditure or muscular force becomes limited. In other words, an activity that represents a submaximal effort in young adults could become a maximal or supramaximal endeavor in the elderly.

One important contributor to the functional loss leading to disability is the loss of skeletal muscle strength and mass associated with advancing age. Muscle strength correlates with walking speed, balance, time to rise from a chair, ability to climb stairs, incidence of falls, and survival rates (see 11). Thus, understanding the mechanism underlying contractile muscle dysfunction could help us design better rehabilitative interventions to enhance functional independence.

This brief review summarizes some of the research on the contractile properties of aging skeletal muscle and is not intended to be a critical analysis of the literature. We emphasize the results of our own cross-sectional and longitudinal work and, when appropriate, also make reference to studies published in the literature.

Changes in Muscle Strength With Aging

A cross-sectional study of muscle strength and mass in 45- to 78-year-old men and women showed that isokinetic strength of the elbow and knee extensors and flexors was lower (range, 15.5–26.7%) in the 65- to 78- than in the 45- to 54-year-old men and women (3). Others have reported similar differences in strength among age groups. More recently, approximately 10 years after the first evaluation, we tested again 64% of the volunteers (54 men and 78 women) who participated in that cross-sectional study (7). Significant strength losses were observed in the isokinetic strength of the knee and elbow extensors and flexors of both men and women (Figure 1). Men, however, lost absolute strength at a faster rate than women.
This recent study gave us the opportunity to compare strength losses using cross-sectional and longitudinal designs in the same cohort of subjects. Figure 2 illustrates the cross-sectional and longitudinal changes seen in men and women in muscles of the lower extremities over 10 years. No sex-related differences were seen in the cross-sectional design, so the data were combined. However, in men, longitudinal losses of strength in the knee extensors and flexors were significantly higher than cross-sectional losses. This may be due to the selection of healthier (i.e., those who have survived) older groups in cross-sectional studies. For the elbow
extensors and flexors (analysis not shown), cross-sectional and longitudinal analysis revealed similar rates of changes, except for elbow flexors in women.

Finally, it is of interest to note that, depending on the muscle group and sex, between 7 and 32% of the subjects showed gains in muscle strength. The factors preventing muscle weakness with advancing age merit serious study.

**Changes in Muscle Size and Composition**

A reduction in muscle size explains, at least partially, the muscle weakness commonly seen in the elderly. The relative contribution of muscle atrophy, however, is not clear. In a subset of subjects \(n = 9\) participating in our longitudinal study, strength at the time of the first evaluation and the change in muscle cross-sectional area over 12 years accounted for 90% of the variability in strength in the second evaluation \(4\). In that group, a 25% decline in the strength of the knee extensors was accompanied by a 16% reduction in muscle cross-sectional area by computerized tomography (CT). It is of interest to note that macroscopic changes in thigh cross-sectional area may reflect, not only muscle atrophy, but also an increase in the non-contractile tissues (i.e., fat and connective tissue). Kent-Braun et al. \(8\) have recently reported differences in the relative composition of the thigh between young and older subjects as determined by magnetic resonance imaging. In that study, the percent of the muscle cross-sectional area representing contractile tissue was reduced from 94 to 86% and from 94 to 84% in older men and women, respectively.

In addition to muscle wasting, a change in muscle quality could also contribute to muscle weakness in the elderly. Indeed, a report from the Baltimore Longitudinal Study show a reduction in the in vivo strength to whole muscle size ratio \(10\). It is of interest to determine if specific age-related cellular alterations in skeletal muscle contribute to contractile dysfunction independent of the absolute reduction in contractile proteins.

**Studies of Single Human Muscle Fibers**

The question of change in specific force (strength corrected for size) due to alterations in the intrinsic ability of muscle fibers to generate force can be studied using the chemically skinned single muscle fiber technique. With this method, the contractile properties of single fibers obtained using the biopsy needle can be studied in isolation from the influences of the nervous system. Also, since the process of chemical skinning disrupts the sarcolemma and sarcoplasmic reticulum, weakness in single fibers can be interpreted as representing structural and/or functional alterations in the regulatory and/or contractile proteins.

Recently, we have reported an age-related reduction in the specific force (Figure 3) of single muscle fibers expressing type I and IIa myosin heavy chain isoforms in older men \(5\). In both age groups, fibers expressing type IIa myosin heavy chain had higher specific forces than type I fibers. Also, our results demonstrated significant sex-related differences in single-fiber maximal force that were dependent on fiber type and not explained by differences in fiber size.
Myosin Alterations

One possible site for the alteration resulting in contractile dysfunction is the myosin protein. An age-related decline of the myosin heavy chain synthesis rate has been observed in humans (1). At least three molecular mechanisms may contribute to a quantitative or qualitative alteration in myosin: (a) reduction in gene transcription, (b) slow protein turnover rate resulting in accumulation of dysfunctional myosin molecules, and (c) post-translational modifications such as glycosylation or oxidation. Alone or in combination, these changes could alter the basic properties of the molecule, resulting in a reduction in force generated per cross-bridge. In fact, recent data from Lowe et al. (9) support this hypothesis. The possibility that alterations in the myosin molecule could also result in changes in other contractile properties such as the shortening velocity is supported by the work of Höök et al., (6) using an in vitro motility assay to study rat muscle.

References


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