Journal of Gerontology: MEDICAL SCIENCES
2008, Vol. 63A, No. 8, 829–834

Special Article ''Green Banana''*

Sarcopenia ≠ Dynapenia

Brian C. Clark[1] and Todd M. Manini[2]

[1]Interdisciplinary Institute for Neuromusculoskeletal Research, Department of Biomedical Sciences, Ohio University College of Osteopathic Medicine, Athens.
[2]Department of Aging and Geriatric Research, Institute on Aging, University of Florida College of Medicine, Gainesville.

Maximal voluntary force (strength) production declines with age and contributes to physical dependence and mortality. Consequently, a great deal of research has focused on identifying strategies to maintain muscle mass during the aging process and elucidating key molecular pathways of atrophy, with the rationale that the loss of strength is primarily a direct result of the age-associated declines in mass (sarcopenia). However, recent evidence questions this relationship and in this *Green Banana* article we argue the role of sarcopenia in mediating the age-associated loss of strength (which we will coin as dynapenia) does not deserve the attention it has attracted in both the scientific literature and popular press. Rather, we propose that alternative mechanisms underlie dynapenia (i.e., alterations in contractile properties or neurologic function), and urge that greater attention be paid to these variables in determining their role in dynapenia.

Key Words: Aging—Strength—Atrophy—Sarcopenia—Dynapenia.

THE loss of muscle mass with age has long been anecdotally recognized as Shakespeare (1) eloquently pointed out nearly a half millennium ago in his monologue *The Seven Ages of Man* when he wrote:

> ''. . .The sixth age shifts into the lean and slipper'd pantaloon,
> With spectacles on nose and pouch on side;
> His youthful hose, well sav'd, a world too wide,
> For his shrunk shank. . .''

In 1989 this observation was brought to the forefront of science when Dr. Irwin Rosenberg wrote: ''No decline with age is more dramatic or potentially more functionally significant than the decline in lean body mass. . . Why have we not given it more attention? Perhaps it needs a name derived from the Greek. I'll suggest a couple: sarcomalacia or sarcopenia'' (2). These thoughts ignited a frenzy of research to determine what caused this age-related loss of lean mass and its functional consequences. The proposed term *sarcopenia* (translated as ''poverty of flesh'') stuck, and was originally defined as the age-related loss in muscle mass (3). However, over the past decade *sarcopenia* has become a catch-all term that is now regularly defined as the age-related loss of skeletal muscle mass and strength (4,5), with even the National Institute on Aging public health service documents now referring to sarcopenia in this manner (6).

The linking of changes in muscle mass AND strength (defined here as the maximal force or power produced *voluntarily*) via the same word (sarcopenia) implies that these are causally linked and that changes in skeletal muscle mass are directly and fully responsible for changes in strength. In this *Green Banana* article we argue that there is abundant evidence indicating other factors that function to regulate strength simply beyond muscle mass. Thus, linking these two outcomes has resulted in a disproportionately larger research emphasis on the mechanisms of muscle mass change rather than the mechanisms regulating strength. The recent observation that strength greatly reduces the association between muscle mass and functional decline (7) and early death (8) to a statistically nonsignificant level suggests that the contribution of muscle mass on certain outcomes may be primarily due to its association with strength. Thus, it is imperative that a greater understanding of the mechanisms of age-associated losses in strength be developed. Therefore, to encourage research endeavors focusing on understanding the mechanisms of strength, we propose changes in the nomenclature that distinctly separates the age-associated changes in muscle mass and strength.

We suggest that sarcopenia be limited to its original definition of an age-related loss in skeletal muscle mass, and that the term ''dynapenia'' be applied to describe the age-related loss of strength. We feel that this Greek term is appropriate as it translates to ''poverty of strength,'' which is consistent with other words used in a similar descriptive manner to define age-related losses (i.e., osteopenia, sarcopenia). In the following sections we will discuss the current evidence indicating a disassociation between changes in muscle mass and strength, followed by an overview of other physiological factors that regulate changes in strength that may serve to modulate the weakness observed with aging.

Associations of Skeletal Muscle Mass With Strength

The initial investigations evaluating the association between muscle mass and strength were cross-sectional studies with relationships between the two explaining approximately 35% of the variability in young individuals (9), and in older individuals adjusting for muscle mass eliminated age-related differences in strength for most muscle groups (10). Recently, however, several longitudinal studies

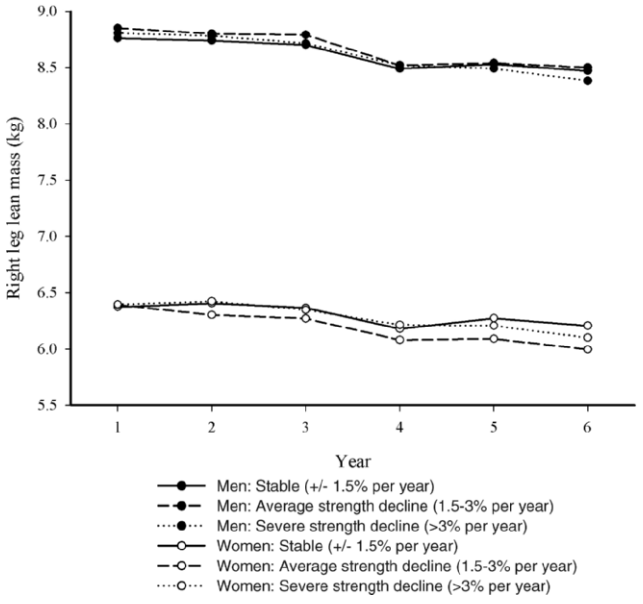

Figure 1. Changes in skeletal muscle mass and knee extensor strength in older (70–79 years) individuals followed longitudinally for 6 years. Leg lean mass data were stratified by gender and three categories of strength change: stable (±1.5%/year, $n = 218$), moderate decrease (1.5–3%/year, $n = 473$), and severe decrease (>3%/year, $n = 464$). Note that the respective groups lost similar amounts of lean mass over time despite having different levels of strength loss. These longitudinal changes illustrate the disassociation between the loss of skeletal muscle and strength. Standard errors are not visible on the figure because the symbols overlap the error bars.

have begun to shed new light on this relationship. One of these reported that the decline of strength was ~ 60% greater than estimates from cross-sectional comparisons, and that the age-associated changes in muscle mass explained <5% of the variance in the change in strength (11). These results have recently been replicated with a 3-year longitudinal study, where although leg muscle mass was significantly correlated with leg strength, the changes did not track each other and maintaining or actually gaining lean mass did not prevent the age-associated loss in strength (12). An updated illustration of this disassociation, presented at the 2007 Scientific Meeting of The Gerontological Society of America, is demonstrated in Figure 1 (13). Here, changes in leg strength followed over 6 years showed little, if any, resemblance to changes in leg muscle mass, as exemplified by individuals maintaining their strength having changes in muscle mass similar to those of individuals who had excessive strength declines (≥3% per year) (Figure 1). This recent longitudinal data indicating the disassociation between muscle mass and strength support the notion that other adaptations in physiologic function (i.e., cellular, neural, metabolic contributors) are mediators of the age-associated loss of strength.

An even greater understanding of the disassociation between muscle mass and strength can be garnered from the examination of the changes in strength associated with increased (i.e., resistance exercise training) and decreased physical activity levels. The principle argument here is that increased strength observed during the early phases of resistance training occurs before the exercise stimulus is actually capable of eliciting gross morphological changes in muscle. The principle argument here is that increased strength observed during the early phases of resistance training occurs before the exercise stimulus is actually capable of eliciting gross morphological changes in muscle, as evidence by increases in maximal voluntary force occurring before changes are observed in electrically stimulated maximal force (14,15). This suggests that short-term gains in strength are not related to factors associated with the intrinsic capacity of the muscle itself. These factors constitute a complex interaction between changes in activation and discharge properties of motor units as well as the adaptation in the central command for learning. [For reviews, see (16,17)]. A similar phenomenon of an excessive loss of strength compared with muscle mass is observed with prolonged unweighting (disuse atrophy). We recently reported that 4 weeks of leg muscle unloading results in a greater loss in strength (~ 15%) than mass (~ 9%), and that adaptations in ''neurological factors'' explained nearly 50% of the loss of strength whereas 'muscular factors' explained around 40% (18). Whereas muscle mass (atrophy) was significantly associated with the loss of strength, its individual contribution was less than the contribution from alterations in central command deficits and indices of excitation–contraction (E-C) uncoupling.

Another example of the dissociation of strength from muscle mass is demonstrated in exogenous supplementation of androgens or growth factors to ameliorate sarcopenia/dynapenia and improve physical function. While these experiments largely rescue the age-related declines in both testosterone and insulin-like growth factor 1 yielding increased muscle mass, the effect on muscle performance is marginally altered (19,20). For example, Snyder and colleagues (20) showed that 3 years of testosterone replacement in hypogonadal men resulted in a 3.1 kg average increase in lean body mass without a significant change in either maximal knee extension or flexion strength. Additionally, Papadakis and colleagues (19) found that 6 months of growth hormone supplementation increased lean body mass 4.4% without significant changes in knee extension or hand grip strength. However, these observations are not universal, as recently Bhasin and colleagues (21) observed that supraphysiologic doses of testosterone supplementation remarkably increased muscle mass and improved leg press strength between 11% and 19% in older men receiving 125 mg, 300 mg, or 600 mg doses.

In summary, based on a synthesis of the literature we believe the commonly assumed equivalence between muscle mass and strength is not the case because (i) longitudinal aging studies indicate a disassociation between the loss of muscle mass and strength, and (ii) the changes in muscle mass and the changes in strength resulting from alterations in physical activity levels (i.e., exercise training or disuse) do not follow the same time course. Thus, adaptations in other properties in the human neuromuscular system must be involved in the regulation of strength, suggesting that muscle mass should not be used as an intermediate endpoint in interventions designed to improve functional or physical capacity. Unfortunately, these other modulating mechanisms have received far less attention than those associated with muscle growth. Below we will briefly review some of the

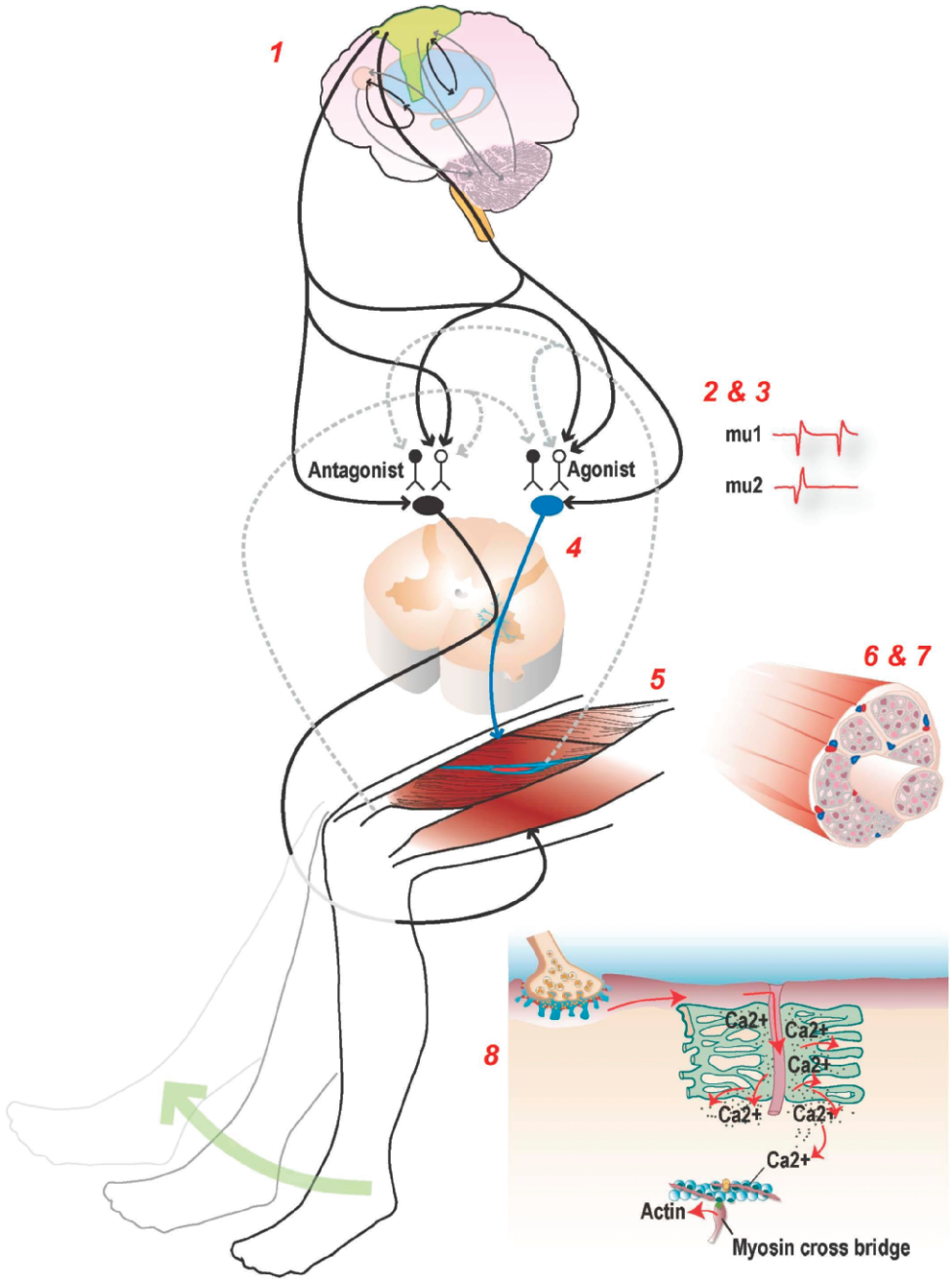

Figure 2. Potential sites and physiological mechanisms that regulate strength. The neuromuscular system contains several potential sites that can affect voluntary force or power production, such as excitatory drive from supraspinal centers, α-motoneuron excitability, antagonistic muscle activity, motor unit recruitment and rate coding, neuromuscular transmission, muscle mass, excitation-contraction (E-C) coupling processes, and muscle morphology and architecture. There is evidence of aging-induced alterations at nearly every denoted site within the system such as, but not limited to, the following: (1) decreased cortical excitability (36); (2) decreased spinal excitability (29); (3) decreased maximal motor unit discharge rate (28); (4) slowed nerve conduction (37); (5) alterations in muscle architecture (reduced fascicle length and pennation angle, and tendon stiffness) (33); (6) decreased muscle mass (sarcopenia) (12); (7) increased myocellular lipid content (38); (8) E-C uncoupling (i.e., decreased number of dihydropyridine receptors) (35). Please see Figure 3 for a more detailed processes related to dynapenia.

physiological sites and properties that alter neuromuscular strength with special reference to age-associated losses.

Control Mechanisms of Neuromuscular Strength

The mechanisms accounting for an increase or decrease in strength can arise from two broad categories: (i) neurological and (ii) skeletal muscle factors, as it is well known that the output from these sources controls force production (Figure 2). As such, ''muscle strength'' is probably a misnomer and ''neuromuscular strength'' a more apt alternative. The neuromuscular system contains several potential sites that can affect maximal voluntary force output, such as

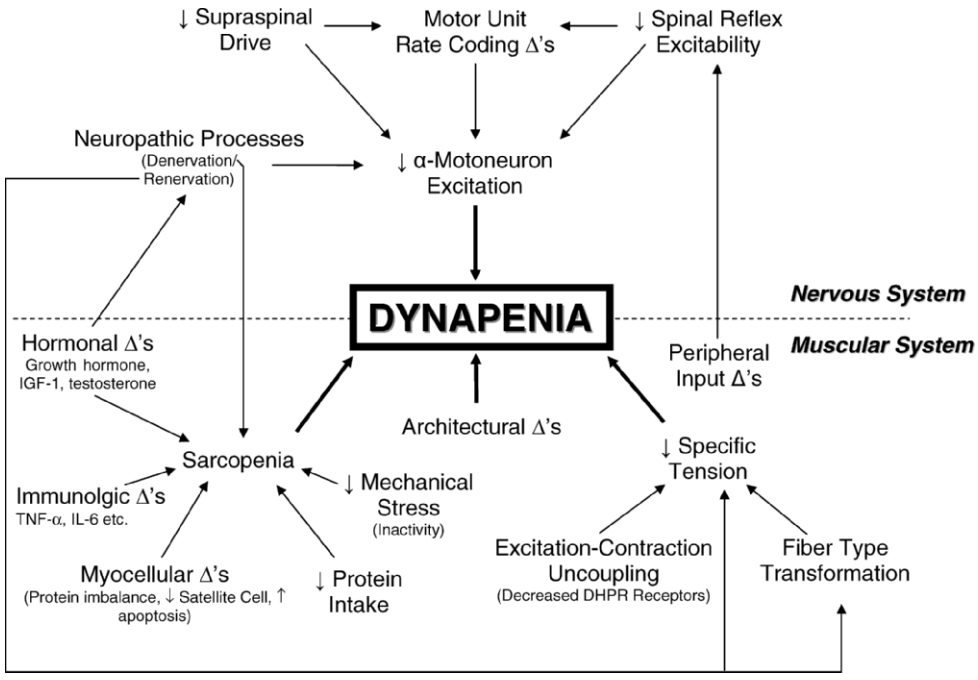

Figure 3. Etiology of the age-associated loss of strength (dynapenia). Figure summarizes the influence of multiple factors that may lead to dynapenia. IGF-1 = insulin-like growth factor 1; DHPR = dihydropyridine receptors; TNF-α = tumor necrosis factor-α; IL-6 = interleukin 6.

excitatory drive from supraspinal centers, α-motoneuron excitability, antagonistic muscle activity, motor unit recruitment and rate coding, neuromuscular transmission, muscle mass, E-C coupling processes, and muscle morphology and architecture. Both the neurological and muscular factors potentially leading to dynapenia are described below and illustrated in Figure 3.

Neurological Factors

The nervous system can regulate strength through a variety of different mechanisms that ultimately result in behavioral modulation of the motor unit pool (i.e., recruitment, discharge rate, synchronization). Much of our understanding of the neural influences on strength is through indirect observations following strength increases due to resistance exercise training. For instance, the observation of strength increasing ~10% in the contralateral limb following 6 weeks of resistance training (cross-education) supports the notion that a portion of the increased voluntary force output is due in part to adaptations in neurophysiologic performance (22). Although there are numerous observations supporting the assertion that neural factors mediate strength, it has proven difficult to identify the specific mechanisms associated with aging, but these adaptations may involve changes in supraspinal drive generated from the cortex, coactivation of the antagonist muscle, as well as maximal spinal cord output and muscle coordination (synergism).

The primary way to control exerted muscle force is via recruitment of additional motor units within a given α-motoneuron pool and/or increased motor unit discharge rate. When these two physiologic properties are optimized, maximal muscle activation results. The most common way to globally investigate whether neural deficits are responsible for a reduction in strength is to deliver a supramaximal electrical stimulus to a nerve or muscle during a maximal voluntary contraction to evaluate the 'added force.' Although there is discrepancy in the literature on the effect of aging on central neural activation, a recent study with the largest sample size to date ($n = 46$ young adults and 46 older adults) indicates that indeed older adults do present with a reduced ability to voluntarily activate their quadriceps with voluntary activation of older (64–84 years) participants being reduced in comparison to young (18–32 years) participants (87% vs 98%) (23). Furthermore, frail elderly persons show an even greater deficit in voluntary activation (24). Although these findings do not provide an indication of the specific neural mechanism causing a deficit in exerted forces, they do suggest that compromised nervous system function may be an important contributor to age-associated losses in strength. Furthermore, these findings suggest that the commonly used calculation of 'muscle quality' that is frequently expressed as strength divided by muscle mass is not necessarily representative of the intrinsic force producing properties of the muscle but that it also comprises the aspect of neural deficits in activation.

The mechanism(s) of age-associated deficits in activation are unclear, but there is evidence that aging reduces the number of motor units as well as alters their functional properties. For example, age-related remodeling of motor units appears to involve denervation of type II (fast) skeletal muscle fibers with collateral reinnervation allowing for the type I (slow) motor units to gain control of the denervated muscle fibers (25). Data indicate that motor units are

preserved until approximately 60 years of age, at which time there is a dramatic loss (25); thus, it has been suggested that, as denervation outpaces re-innervation, populations of muscle fibers atrophy and are not functionally relevant resulting in a decline in muscle-specific force (26). In addition, the behavioral properties of motor units are also altered with aging. For example, cross-sectional studies have indicated that there is a reduced incidence of motor unit doublets (27) and that maximal motor unit discharge rates are lower in older adults (25–60 pulses/s in young vs 18–45 pulses/s in old) (28). In addition to these behavioral modifications of motor units, aging has been shown to result in both motor cortex and spinal reflex hypoexcitability (29,30), as well as a slowing in nerve conduction velocity (31). Theoretically, alterations in these neural factors could explain to some extent the progression in weakness exhibited with aging.

Muscular Factors

We fully acknowledge that skeletal muscle mass, or more specifically the total amount of contractile proteins present in a muscle, is partially responsible for the amount of voluntary force output. However, it is readily apparent that this is not the sole variable. Above we stated that a number of neural factors may be implicated in the age-associated loss of neuromuscular strength, but there are also a number of potentially influential adaptive sites within the muscular system (beyond the simple loss of muscle mass), such as changes in muscle architecture, fiber type transformations, and the processes involved in E-C coupling.

Architectural differences between muscles is one of the best predictors of force generation (32), and as such it seems reasonable that it may explain a change in strength with aging as older adults have been observed to have a reduced fascicle length, pennation angle, and tendon stiffness (33), as well as decreased muscle density (31). At the cellular and molecular levels, skeletal muscles can be further subdivided and classified based on a number of characteristics such as myosin isoform expression. At a functional level, aging slows the twitch contraction speed of whole muscle; this slowing may be caused by several factors, such as the fast-to-slow muscle fiber type transition observed with aging (34) and/or maladaptations in E-C coupling. Regarding the latter, aging mammals exhibit a reduction in the number of dihydropyridine receptors at the t-tubule and sarcoplasmic reticulum membrane, resulting in uncoupling of Ca^{2+} release channels or ryanodine receptors and failure in the transduction of action potentials into a mechanical response (35). Thus, aging-induced negative alterations in any of these aforementioned muscular properties would theoretically result in a reduction in skeletal muscle-specific force (force per fiber cross-sectional area), which would thus directly reduce strength.

Perspectives

Delineating the relative contributions of neural and muscular factors in modulating the age-related loss of strength will be important for targeting future interventions aimed at strength preservation in the elderly population. One of the technical challenges of research endeavors to this end is the difficulty in tracking changes in both muscular and neurologic physiological parameters over a long period of time, as the equipment to make detailed measurements is expensive and at times invasive (i.e., biopsy), and requires a high degree of expertise. However, a simple difference in one of these variables between young and old humans or animals does not prove a cause–effect relationship. Ergo, it is imperative that future investigations focus on identifying the role of these various physiological properties in regulating the loss of strength over time via longitudinal studies. Thus, to facilitate study in this area there is a significant need for advancements in technological innovations to allow for reliable and non-invasive assessments of the human neuromuscular system. Overall, work in this area will more fully elucidate the integrative effects of physiological changes during aging and their effects on physical function.

Therefore, in an effort to spearhead an increased awareness of and interest in the mechanisms regulating neuromuscular strength losses associated with aging, we propose distinctly different terminology for reduced muscle mass and strength. Again, we suggest that sarcopenia be limited to its original definition of an age-related loss in skeletal muscle mass, and that the term dynapenia be applied to describe the age-related loss of strength. Because research endeavors and funding mechanisms are frequently driven by such semantics, it is imperative that we foster this terminology. In doing so, we simply ask, ''What's in a name?''

*Note

From Ferrucci L, Simonsick E. Of green bananas and chili peppers [Editorial]. J Gerontol A Biol Sci Med Sci. *2006;61:259*

Main attributes of a Green Banana are a provocative title and brief abstract (less than 150 words) that presents the idea in essence with crisp journalistic wording. Diagrams, models, and figures are preferred over tables and text to illustrate concepts and convey ideas, with no more than 30 references that support the plausibility of the hypotheses presented. We acknowledge that many Green Bananas may fail to ripen and may quickly rot, but if only one grows sweet, we believe the cost worth the effort.

Acknowledgment

Drs. Clark and Manini contributed equally to this work.

Correspondence

Address correspondence to Brian Clark, PhD, Department of Biomedical Sciences, Ohio University, 211 Irvine Hall, Athens, OH 45701. E-mail: clarkb2@ohio.edu or Todd Manini, PhD, Department of Aging & Geriatric Research, University of Florida, P.O. Box 112610, Gainesville, FL 32611. E-mail: tmanini@aging.ufl.edu

References

1. Shakespeare W. The seven ages of man (Act 2, Scene 7). *As You Like It.* In: *Comedies, Histories and Tragedies*. London: First Folio; 1623.
2. Rosenberg IH. Summary comments. *Am J Clin Nutr*. 1989;50:1231–1233.

3. Evans WJ. What is sarcopenia? *J Gerontol A Biol Sci Med Sci.* 1995; 50 Spec No:5–8.
4. Adamo ML, Farrar RP. Resistance training and IGF involvement in the maintenance of muscle mass during the aging process. *Ageing Res Rev.* 2006;5:310–331.
5. Roubenoff R, Hughes VA. Sarcopenia: current concepts. *J Gerontol Med Sci.* 2000;55A:M716–M724.
6. National Institutes of Health. *Exercise: A Guide from the National Institute on Aging.* U.S. Department of Health and Human Services. 2004:34.
7. Visser M, Goodpaster BH, Kritchevsky SB, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. *J Gerontol A Biol Sci Med Sci.* 2005;60:324–333.
8. Newman AB, Kupelian V, Visser M, et al. Strength, but not muscle mass, is associated with mortality in the Health, Aging and Body Composition Study cohort. *J Gerontol A Biol Sci Med Sci.* 2006;61: 72–77.
9. Maughan RJ, Watson JS, Weir J. Strength and cross-sectional area of human skeletal muscle. *J Physiol.* 1983;338:37–49.
10. Frontera WR, Hughes VA, Lutz KJ, Evans WJ. A cross-sectional study of muscle strength and mass in 45 to 78-year-old men and women. *J Appl Physiol.* 1991;71:644–650.
11. Hughes VA, Frontera WR, Wood M, et al. Longitudinal muscle strength changes in older adults: influence of muscle mass, physical activity, and health. *J Gerontol Biol Sci.* 2001;56A:B209–B217.
12. Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the Health, Aging and Body Composition Study. *J Gerontol A Biol Sci Med Sci.* 2006;61: 1059–1064.
13. Manini TM, Chen H, Angleman S, et al. The role of disease in initial differences and longitudinal trajectories of muscle strength and quality among older adults. *Gerontologist.* 2006;46:153.
14. McDonagh MJ, Hayward CM, Davies CT. Isometric training in human elbow flexor muscles. The effects on voluntary and electrically evoked forces. *J Bone Joint Surg Br.* 1983;65:355–358.
15. Young K, McDonagh MJ, Davies CT. The effects of two forms of isometric training on the mechanical properties of the triceps surae in man. *Pflugers Arch.* 1985;405:384–388.
16. Semmler JG, Steege JW, Kornatz KW, Enoka RM. Motor-unit synchronization is not responsible for larger motor-unit forces in old adults. *J Neurophysiol.* 2000;84:358–366.
17. Gabriel DA, Kamen G, Frost G. Neural adaptations to resistive exercise: mechanisms and recommendations for training practices. *Sports Med.* 2006;36:133–149.
18. Clark BC, Manini TM, Bolanowski SJ, Ploutz-Snyder LL. Adaptations in human neuromuscular function following prolonged unweighting: II. Neurological properties and motor imagery efficacy. *J Appl Physiol.* 2006;101:264–272.
19. Papadakis MA, Grady D, Black D, et al. Growth hormone replacement in healthy older men improves body composition but not functional ability. *Ann Intern Med.* 1996;124:708–716.
20. Snyder PJ, Peachey H, Berlin JA, et al. Effects of testosterone replacement in hypogonadal men. *J Clin Endocrinol Metab.* 2000; 85:2670–2677.
21. Bhasin S, Woodhouse L, Casaburi R, et al. Older men are as responsive as young men to the anabolic effects of graded doses of testosterone on the skeletal muscle. *J Clin Endocrinol Metab.* 2005;90:678–688.
22. Munn J, Herbert RD, Hancock MJ, Gandevia SC. Training with unilateral resistance exercise increases contralateral strength. *J Appl Physiol.* 2005;99:1880–1884.
23. Stevens JE, Stackhouse SK, Binder-Macleod SA, Snyder-Mackler L. Are voluntary muscle activation deficits in older adults meaningful? *Muscle Nerve.* 2003;27:99–101.
24. Harridge SD, Kryger A, Stensgaard A. Knee extensor strength, activation, and size in very elderly people following strength training. *Muscle Nerve.* 1999;22:831–839.
25. Lexell J. Evidence for nervous system degeneration with advancing age. *J Nutr.* 1997;127:1011S–1013S.
26. Delbono O. Neural control of aging skeletal muscle. *Aging Cell.* 2003;2:21–29.
27. Christie A, Kamen G. Doublet discharges in motoneurons of young and older adults. *J Neurophysiol.* 2006;95:2787–2795.
28. Kamen G. Aging, resistance training, and motor unit discharge behavior. *Can J Appl Physiol.* 2005;30:341–351.
29. Kido A, Tanaka N, Stein RB. Spinal excitation and inhibition decrease as humans age. *Can J Physiol Pharmacol.* 2004;82:238–248.
30. Oliviero A, Profice P, Tonali PA, et al. Effects of aging on motor cortex excitability. *Neurosci Res.* 2006;55:74–77.
31. Lauretani F, Bandinelli S, Bartali B, et al. Axonal degeneration affects muscle density in older men and women. *Neurobiol Aging.* 2006;27: 1145–1154.
32. Lieber RL, Fridén J. Clinical significance of skeletal muscle architecture. *Clin Orthop Relat Res.* 2001;(383):140–151.
33. Narici MV, Maganaris CN. Adaptability of elderly human muscles and tendons to increased loading. *J Anat.* 2006;208:433–443.
34. Pette D, Staron RS. Myosin isoforms, muscle fiber types, and transitions. *Microsc Res Tech.* 2000;50:500–509.
35. Delbono O. Regulation of excitation contraction coupling by insulin-like growth factor-1 in aging skeletal muscle. *J Nutr Health Aging.* 2000;4:162–164.
36. Sale MV, Semmler JG. Age-related differences in corticospinal control during functional isometric contractions in left and right hands. *J Appl Physiol.* 2005;99:1483–1493.
37. Scaglioni G, Ferri A, Minetti AE, et al. Plantar flexor activation capacity and H reflex in older adults: adaptations to strength training. *J Appl Physiol.* 2002;92:2292–2302.
38. Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. *J Appl Physiol.* 2001;90:2157–2165.

Received May 7, 2007
Accepted November 11, 2007
Decision Editor: Luigi Ferrucci, MD, PhD