

Age- and Stroke-Related Skeletal Muscle Changes: A Review for the Geriatric Clinician

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ABSTRACT

Independently, aging and stroke each have a significant negative impact on skeletal muscle, but the potential cumulative effects of aging and stroke have not been explored. Optimal interventions for individuals post-stroke may include those that specifically target skeletal muscle. Addressing changes in muscles may minimize activity limitations and enhance participation post stroke. This article reviews the impact of aging and stroke on muscle morphology and composition, including fiber atrophy, reductions in muscle cross-sectional area, changes in muscle fiber distributions, and increases in intramuscular fat. Relationships between changes in muscle structure, muscle function, and physical mobility are reviewed. Clinical recommendations that preserve and enhance skeletal muscle in the aging adult and individuals post-stroke are discussed. Future research directions that include systematic comparison of the differences in skeletal muscle between younger and older adults who have sustained a stroke are suggested.

Key Words: aging, intramuscular fat, sarcopenia, stroke

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INTRODUCTION

Stroke is the leading cause of serious long-term neurological disability in the United States.¹ According to the 2007 statistics from the Centers for Disease Control and Prevention, approximately 700 000 strokes occur yearly in the United States, with three-fourths of these occurring in those 65 years and older.² A myriad of impairments occur as a result of a stroke, including, but not limited to poor muscle acti-

vation,³ decreased sensation,^{4,5} and incoordination.^{6,7} Among older adults, muscle deterioration due to aging, decreased physical activity, and suboptimal dietary intake,⁸ underlie and may compound the deleterious effects of a stroke. The purpose of this article is to discuss the potential cumulative impact of aging and stroke on skeletal muscle. This article reviews healthy, skeletal muscle structure and function, and the effects of aging and a stroke on muscle size, composition, and performance. It presents relationships between muscle impairments and activity limitations and discusses current physical therapy treatments for age-related and post-stroke skeletal muscle changes. Suggestions are made for future research that compares younger and older individuals post-stroke to enhance our understanding of the impact of stroke in the presence of age-related changes.

SKELETAL MUSCLE: AN OVERVIEW

The motor unit is the smallest functional element within the skeletal muscle that the central nervous system can control⁹ and consists of an alpha-motor neuron and the multiple muscle fibers the axon innervates. Each individual presynaptic nerve fiber innervates a single muscle fiber, which is classified as a type I or type II fiber. Type I fibers contain slow forms of myosin ATPase, resulting in slow twitch contractions.^{10,11} High mitochondrial levels¹² in conjunction with large capillary networks allow increased blood flow, enabling slow-twitch muscle fibers to produce sustained, low-load tension required by the postural muscles. Type II fibers have fewer mitochondria, smaller capillary networks, and rely on anaerobic forms of energy production.¹⁰⁻¹² Anaerobic energy production allows faster contraction times and greater muscle tension, rendering type II fibers beneficial during activities that require quick bursts of movement.^{11,13-15}

A single action potential results in a single muscle twitch; as the firing rate of the motor unit increases, multiple action potentials result in twitch summation, which leads to a synchronized, tetanic contraction of all muscle fibers innervated by a given motoneuron.^{16,17} Motor units typically consist of a single muscle fiber type, with motor unit size dependent on fiber type and the number of innervated fibers. Motor units that innervate type I fibers are smaller than those that innervate type II fibers. During voluntary contractions, motor

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units innervating type I fibers are preferentially recruited.⁹ Progressive force demands increase the firing rate of smaller motor units, termed rate coding, followed by recruitment of larger motor units.⁹

MUSCULAR CHANGES

Muscle Atrophy

Aging

Fiber-level changes within skeletal muscle are prevalent in the aging adult population. Skeletal muscle biopsy studies performed on the vastus lateralis show a reduction in type II fibers after 50 years of age.^{13,14,18,19} Decrease in type II fibers with progressive aging is further supported by evidence in both weight-bearing and nonweight bearing muscles including the gastrocnemius, tibialis anterior, and biceps brachii.^{13,14} Reduction in fiber number and size leads to a decline in overall muscle cross-sectional area. Cross-sectional area may be used to quantify the force production capabilities of a muscle²⁰ and assess the loss of skeletal muscle due to sarcopenia, which is the age-related decline of skeletal muscle mass. In aging adults, loss of skeletal muscle cross-sectional area ranges from 21% to 40%, when compared with healthy, younger adults.^{21,22} Cross-sectional area reductions are progressive, with increasing loss with advanced age.²³ Furthermore, reduced cross-sectional area has been associated with poorer physical performance in healthy, older adults.²⁴ Consequently, fitness regimens for older adults should include resistance training exercises for both the upper and lower extremities, particularly in the later years of life, to combat type II fiber changes, cross-sectional area reductions, and activity limitations.

In addition to fiber number loss, disuse may affect the cross-sectional area of individual fibers to a greater degree in older adults when compared with younger adults.²⁵ Simulating disuse in a healthy population, Hvid et al²⁵ found that 2 weeks of quadriceps immobilization resulted in greater deleterious effects on muscle fibers in older men when compared with younger men, with older individuals requiring increased recovery time post immobilization. This study provides preliminary evidence for early rehabilitation in older adults post immobilization and suggests longer episodes of care may be necessary to reestablish premorbid skeletal muscle status. Future studies should consider stratification of younger versus older individuals to allow comparisons of skeletal muscle response rates to immobilization and subsequent interventions.

Links between muscle size, physical activity, and disability in older adults are emerging.^{26,27} Park et al²⁶ found adults, aged 65 to 84 years, are less likely to have sarcopenia if they walk at least 7000 to 8000 steps per day and/or spend 15 to 20 minutes per day performing moderate physical activity (ie, >3 metabolic equivalents). Moderate physical activity may include “brisk walking” at 3 to 4 miles per hour, cycling, house repair, and yardwork.²⁸ Furthermore, sarcopenia is associated with physical disability.²⁷ For example, Chien et al²⁷ found an odds ratio for physical disability of 3.03 (95% confidence interval: 1.21-7.61) for

elderly men with sarcopenia when compared with healthy, older men with normal skeletal muscle mass indices. These emerging relationships require longitudinal, prospective investigations to determine whether sarcopenia precedes activity level decline and disability.

Decreased muscle cross-sectional area ultimately impacts the ability of the muscle to produce force. There is a direct relationship between increasing age and decreased force production.^{21,23} The force per cross-sectional area of the vastus lateralis is reduced by approximately 1.5% per year and a total of 21% over 15 years.²¹ Frontera et al²³ reported similar results, with an annual decline in isokinetic muscle strength from 1.4% to 2.5% for the knee and elbow flexors and extensors over 12 years. Between the ages of 65 and 80 years, Jubrias et al²¹ demonstrated a 39% drop in force capabilities during isokinetic knee extension. Given the overwhelming evidence for progressive loss, resistance training may preserve muscle function in the older adult enabling generation of forces required for everyday activities such as lifting, pulling, pushing, and stair negotiation.^{29,30}

Post-stroke

Regardless of the age of the individual, muscles post-stroke demonstrate many similarities to aging muscle. After a stroke the number of type II fibers progressively decrease, resulting in a loss of skeletal muscle cross-sectional area.^{11,31,32} Similar to age-related muscle atrophy, after stroke there is a progressive decrease in muscle fiber size bilaterally, with greater decreases on the more involved side.³² Stroke-induced muscle fiber reductions lead to a decrease in muscle cross-sectional area. In individuals post-stroke, diminished force production and contraction speed secondary to muscle atrophy may be observed as difficulty with sit-to-stand transfers,^{33,34} limitations in stair negotiation,³⁵ and impaired balance on compliant surfaces.³⁶

When a stroke occurs in an older adult, the paretic muscles have an accelerated rate of the normal, detrimental skeletal muscle changes typically associated with aging alone.^{31,37,38} This decline is most often demonstrated by comparing the paretic and nonparetic sides of older adults post-stroke.^{31,37-39} Hachisuka et al³¹ reported an average difference in type I fiber diameter of 8.5 micrometer when comparing muscles in the paretic and nonparetic limbs. At the whole muscle level, others have reported approximately a 20% reduction in the mid-thigh muscle area and muscle volume of the paretic limb compared with the nonparetic limb in older adults.^{37,38} In the upper extremity, Ploutz-Snyder et al³⁹ reported the triceps brachii of the more affected side was 25% smaller than the less affected triceps brachii, with a corresponding strength deficit of 61% in individuals an average of 65 months post-stroke.

Furthermore, post-stroke skeletal muscle changes may occur in both limbs,⁴⁰⁻⁴³ therefore studies that evaluate interlimb differences in the older adult may be underestimating the impact of a stroke on skeletal muscle. For example, Noskin et al⁴² reported that even at 1 year, ipsilateral impairments in grip strength and hand coordination, as measured

by the 9-Hole Peg Test, persisted in individuals who sustained a first-time hemiparetic stroke. Thus, age-matched comparisons to healthy adults as opposed to inter-limb comparisons within patients post-stroke may be preferable. *Age-matched* comparisons may be essential due to the potential cumulative impact of stroke and aging. Enhanced understanding regarding the influence of stroke and aging on muscle fiber atrophy, decreased cross-sectional area, and decreased strength may be achieved through comparison studies of older versus younger individuals post-stroke.

Disuse post-stroke appears to be an important indicator of skeletal muscle loss and may influence strength⁴⁴ and lean muscle mass.⁴⁵ Andrews and Bohannon have shown that strength of 8 paretic muscles were only 29% to 45% of the age-matched subjects' strength as tested with handheld dynamometry, in individuals aged 44 to 85 years.⁴⁴ Jorgensen et al⁴⁵ found that individuals who learned to walk within 2 months of their stroke had preservation of lean muscle mass. For those unable to walk at 2 months, lean muscle mass was lost in both lower limbs and regained only in the nonparetic limb at 7 months.⁴⁵ The gradual loss of muscle strength due to aging, coupled with the loss of strength due to paresis may cause a significant and progressive strength deficit in older individuals after stroke. Whether the loss of muscle strength is accelerated in the presence of advanced age has yet to be experimentally tested. Longitudinal, clinical trials evaluating younger versus older individuals post-stroke may assist with answering this question. Controlling for physical activity level may be critical given an association between muscle cross-sectional area and activity level in healthy, older adults.²⁶ Paired comparisons are recommended that consider not only daily activity but physical capacity.

Muscle Composition Changes

In older adults, an even more important factor than decreased cross-sectional area in age-related strength loss may be muscle composition changes. Decreased muscle strength may be 2 to 5 times greater than the age-related loss of muscle size in healthy elders, implicating poorer muscle composition as a major factor in age-related strength decline.⁴⁶ Motor neuron death and denervation-reinnervation influences overall muscle composition. With increased age, due to the death of motor neurons, the ratio of muscle fibers to alpha-motor axon increases.⁴⁷ Newly denervated muscle fibers will significantly atrophy unless reinnervated.⁴⁷ Denervated fibers may be reinnervated by the remaining healthy motor neurons, which preserves fiber cross-sectional area and results in larger motor units.^{9,47,48} In healthy, older adults, the natural remodeling processes of nerve resprouting and reinnervation occurs at a slower rate than in younger individuals.^{9,47,49} Reinnervation favors type I fiber clusters.^{14,18,50} The morphological result of this denervation and reinnervation is a change in distribution of type I and type II fibers within older muscle.^{18,50}

When investigating the effects of stroke on motor neurons, we find strikingly similar end results to aging (See Figure 1), despite different mechanisms in aging and stroke.⁵¹ post-

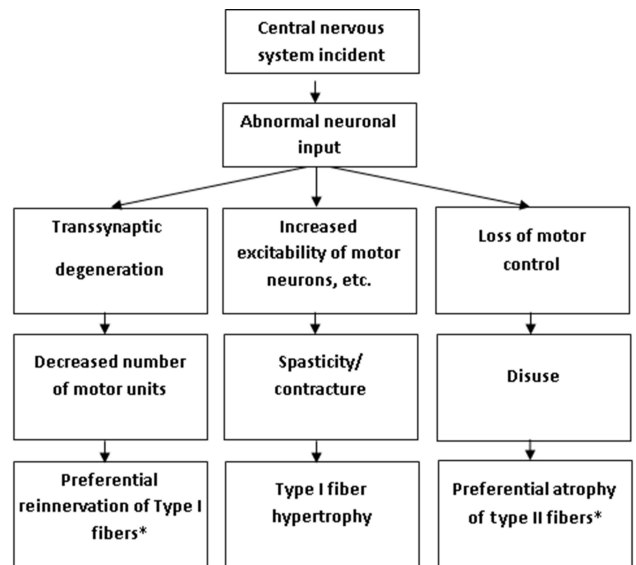


Figure 1. Changes in skeletal muscle secondary to abnormal neuronal activity after stroke. *indicates end-results that parallel skeletal muscle changes that occur with aging.

stroke, transsynaptic degeneration may result from a lack of synaptic input and decreased lower motor neuron activation.¹² An inability to activate higher threshold motor units post-stroke may partially explain the increased proportion of type I fibers.¹¹ post-stroke, motor neuron function may be maintained for the first 2 months, but thereafter the number of functioning motor neurons is greatly reduced.¹² In fact, researchers suggest that the number of motor units is significantly decreased as early as 9 days after a stroke.⁵² Furthermore, motor unit action potentials may be altered post-stroke. Lukacs et al⁵³ propose that abnormal increases in action potential duration and amplitude signify dense, reinnervated motor units, which have expanded to replace lost motor units. Thus, the hypertrophy of type I fibers post-stroke may be the result of increased alpha motor neuron excitability.³¹ Increased fiber density occurs in the first 10 months post-stroke and then remains stable.⁵³

Under the pathological conditions created by a stroke, in an older adult, the denervated fibers may or may not be reinnervated⁴⁷ and the rate of reinnervation is slowed secondary to biological aging. This compounding effect may hinder recovery of the functional motor unit and ultimately impact force production. To date, no studies have evaluated post-stroke muscle fiber reinnervation in older versus younger skeletal muscle. Studies assessing reinnervation, while controlling for age, may help explain why an older individual, who experiences a stroke of the same magnitude and distribution as a younger individual, may require an extended episode of rehabilitative care.

Concurrent with age-related motor neuron changes, intramuscular fat, which is an increase in intramyocellular lipids within the muscle, is augmented in older adults.^{51,54-59} Intramuscular fat, is highest in oxidative, type I fibers and serves as a dynamic and immediate source of energy during submaximal physical activities.⁶⁰⁻⁶² However, excessive

intramuscular fat compromises muscle quality, affects muscle function, and is associated with reduced physical functioning.^{38,63,64} Taaffe et al⁶³ reported that in the limbs of healthy, older adults, cessation of resistance training resulted in increased quadriceps intramuscular fat and decreased quadriceps strength (as evaluated using a 1-repetition maximum), without a significant reduction in muscle size. Visser et al⁶⁵ reported that intramuscular fat independently predicted self-expressed mobility difficulties, including walking one quarter of a mile and climbing 10 steps without resting. In the trunk of older adults, Hicks et al⁶⁴ reported greater intramuscular fat was associated with lower functional capacity and physical performance, including increased time with sit-to-stand transfers, decreased gait speed, and poorer balance. Future investigations may attempt to determine effective treatments to reduce intramuscular fat in older adults and whether or not reductions result in improvements in activities and participation.

In the older adult, an increasingly sedentary lifestyle coupled with inappropriate dietary intake may result in excessive intramuscular fat within skeletal muscle. With aging, there is a significant reduction in physical activity and a drop in resting metabolic rate, resulting in an overall reduction in caloric expenditure.^{66,67} There is preferential oxidation of carbohydrates over fats,⁶⁷ which may result in increased intramuscular fat stores in skeletal muscle, as free fatty acids reform into triglycerides as opposed to entering the mitochondria for energy metabolism.^{68,69} Diets high in fat can further increase intramyocellular lipids.^{61,70} Furthermore, protein synthesis, which is necessary for building skeletal muscle mass, declines by 3.5% per decade⁷¹ and may be attenuated in the presence of inactivity.⁷² Thus, although older adults may consume less protein than younger individuals, they require more protein than their younger counterparts for maintenance of lean muscle mass.⁷³ The net effect of the imbalance between energy expenditure and intake results in sarcopenic obesity, defined as decreased skeletal muscle mass and increased fat mass.⁷⁴ Increased fat mass may appear in part as increased intramuscular fat affecting skeletal muscle function, as lower intramuscular fat is associated with greater muscle torque and force production.⁷⁵

After a stroke, intramuscular fat proportion is further increased beyond age-related progression.³⁷ Ryan et al³⁷ assessed patients with residual hemiparetic deficits at least 6 months post cerebral infarction and found intramuscular fat of the involved thigh was significantly greater than the uninvolved side. More recently, using a rat model, de Castro Rodrigues et al⁷⁶ reported that the intramuscular fat increase after denervation is greater than the age-related increase observed in healthy muscle, with greater fat invasion in slow-twitch muscles. The functional implications of increased intramuscular fat in individuals post-stroke remain unexplored.

INTERVENTION

Concurrent negative changes occurring in skeletal muscle as a result of aging and stroke (See Figure 2), including atrophy

and remodeling in the presence of pathology result in a weaker muscle. Understanding the potential for an additive effect of aging and stroke may help explain the differences in disability between a younger adult and an older adult, who present with a stroke of the same distribution and magnitude. To date, no studies have stratified persons with a stroke by age; therefore, clinical recommendations for addressing muscle structure and function deficits must be extrapolated by synthesizing 2 bodies of literature: (1) interventions for the aging adult and (2) interventions for individuals post-stroke.

In the Aging Adult

Resistance training results in improved skeletal muscle size, composition, and performance in the aging adult, as well as improvements in physical function.^{29,63,77-79} In 2006, Martel et al⁷⁸ reported that 9 weeks of heavy-resistance training of the quadriceps resulted in an increase in type II fiber cross-sectional area in healthy, older adults. In 2008, Suetta et al²⁹ reported that 12 weeks of resistance training of 60- to 86-year-old individuals post unilateral hip arthroplasty resulted in type I and type II fiber area increases, increases of 29% to 30% in dynamic muscle strength, and improved stair climbing power. These increases were found to be related to greater type II fiber area.²⁹ A similar study of older individuals post hip arthroplasty, found 12 weeks of resistance training increased cross-sectional area of the quadriceps by 12% and isokinetic muscle strength by 22% to 28%.⁷⁷ Recently, Kukulijan et al⁸⁰ reported improvements in thigh muscle cross-sectional area, lower extremity strength as assessed by a 1-repetition maximum on the leg press, and gait speed after 18 months of weight-bearing resistance training of the lower extremities. Hanson et al⁸¹ also reported improvements in lower extremity strength as assessed by a 1-repetition maximum on the leg press and gait speed, as well as chair rise and

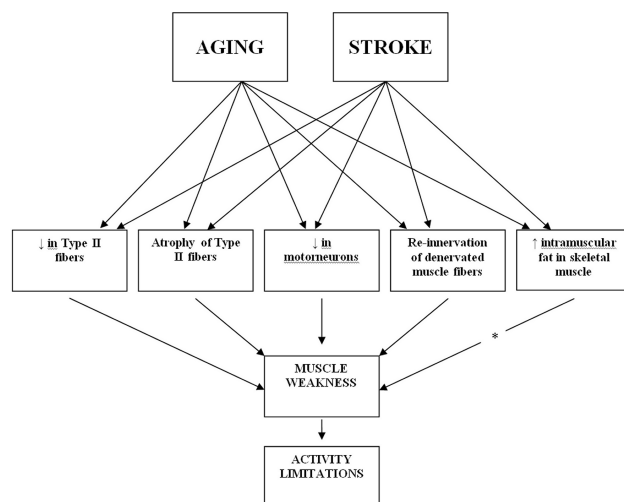


Figure 2. The potential cumulative impact of aging and stroke on skeletal muscle structure and function. *indicates impact of increased intramuscular fat on muscle function post-stroke remains unknown.

stair climbing, following 22 weeks of upper and lower extremity resistance training in a group of sedentary older adults. In older adults, given age-related muscle changes and the potential benefits of resistance training, clinicians should encourage all older clients to consider gym memberships to continue resistance training post physical therapy and work with community-centers to develop senior programs that incorporate resistance training.

Resistance training may also reduce intramuscular fat.^{63,79} In 2008, Nakai et al⁷⁹ demonstrated that a 1-month walking program with training equipment that applied additional resistance to the lower extremities resulted in decreased intramuscular fat by 4% compared with walking without an external load. More recently, Taaffe et al⁶³ showed that cessation of upper and lower extremity resistance training in older adults resulted in increased intramuscular fat while resumption at twice weekly resulted in decreased fat. The ability to improve muscle composition is noteworthy as increased intramuscular fat in older adult muscle has been associated with a greater risk of reduced mobility-related function over time.⁶⁴

Although assessing skeletal muscle size and composition is difficult, physical therapists can use dynamometers and 1-repetition maximum tests to evaluate extremity strength in addition to “geriatric” clinical tests such as gait speed, timed repeated chair stands, and timed stair climbing. Strength and functional tests may allude to underlying skeletal muscle deficits that may be addressed through interventions targeting muscle morphology and composition. Rehabilitative ultrasound imaging is emerging as a reliable⁸² and valid⁸³ noninvasive, clinical assessment tool to evaluate muscle and related soft tissue morphology and function.⁸⁴ Unfortunately, most research to date has focused on younger populations. Future studies including adults over the age of 60 years may allow rehabilitative ultrasound imaging to be used for objective documentation of skeletal muscle size and function pre- and posttreatments in our geriatric patients.

Post-stroke

Among older adults (aged 50 to 76 years) at least 6 months post-stroke, Ryan et al⁸⁵ recently published the first article on the beneficial effects of resistance training on skeletal muscle. Participants of the 12-week resistance training program demonstrated increases in mid-thigh muscle cross-sectional area (13% paretic; 9% nonparetic); increases in 1-repetition maximum strength for leg press (33% paretic side; 32% nonparetic) and knee extension (56% paretic; 31% nonparetic); and muscle attenuation indicative of a significant reduction in mid-thigh intramuscular fat for both limbs.⁸⁵ This study supports bilateral resistance training of the lower extremities after a hemiparetic stroke to address both contralateral and ipsilateral changes in muscle size, function, and composition. Future investigations post-stroke may help determine the optimal time frame for initiation of resistance training and whether similar results are possible in upper extremity muscles, which differ from lower extremity muscles in their weight-bearing requirements.

post-stroke, evidence regarding the impact of traditional resistance training on disability is inconclusive.⁸⁶⁻⁸⁹ For example, Weiss et al⁸⁷ reported improvements in chair rise with 12 weeks of high-intensity resistance training at 70% of a 1 repetition-maximum in individuals post-stroke. In contrast, Ouellette et al⁸⁸ reported a lack of significant improvements in chair rise with a similar program, although participants reported improvements in activity and participation domains. Furthermore, isokinetic resistance training of the affected side post-stroke has not resulted in substantial improvements in stair negotiation.⁸⁹

Future investigations are necessary to understand the relationship between skeletal muscle changes and disability in older individuals post-stroke. Older individuals may need more vigorous strengthening than provided in these studies to address changes in body structure and function and to improve activity and participation domains due to the potential cumulative impact of aging and stroke. Unilateral strengthening may not address the baseline impairments in bilateral lower extremity strength as a result of biological aging and the stroke. Others argue that we should employ the principle of specificity, selecting exercises such as sit-to-stands, step-ups, and squats that mimic everyday activities to improve muscle structure and function and/or enhance activity and participation levels.^{86,90} For example, Rose et al⁹¹ found that early post-stroke, a circuit training rehabilitation program addressing patient-specific, everyday activity limitations had superior results for improving gait speed when compared with a standard inpatient stroke rehabilitation program, consisting of gait retraining, transfer training, bed mobility, balance activities, range-of-motion exercises, and strengthening.

Prolonged disuse post-stroke may result in skeletal muscle weakness beyond that expected due to biological aging, further impairing function.⁴⁵ Therapists should intervene as soon as the patient is medically stable to counter disuse.⁹² This may be particularly important, due to the overwhelming evidence for large scale loss of type II fibers.¹ Functionally relevant activities, such as sit-to-stand transfers and stair climbing, require large force production and therefore, may assist in ameliorating the reduction of type II fibers. Use of neuromuscular electrical stimulation, which may recruit type II fibers alongside type I fibers, may assist with increasing motor unit recruitment when voluntary muscle activation is impaired.⁹²⁻⁹⁵ Functional electrical stimulation, a specific type of neuromuscular electrical stimulation, may be used as an adjunct to treadmill training to improve muscle performance in the lower extremities and assist with gait retraining in individuals with acute and chronic stroke-related deficits.⁹²

post-stroke, treadmill use is reserved for individuals without cardiac risk for treadmill training.⁹² Aerobic treadmill training has demonstrated superior results in 6-minute walk distance and self-reported walking mobility when compared with a low-intensity walking and stretching program in individuals post-stroke.⁹⁶ Treadmill training, with use of partial body-weight support of up to 40% of the patient's weight,⁹⁷ is recommended to address lower

extremity muscle impairments,^{92,98} decreased gait speed,^{98,99} and poor cardiovascular fitness.^{96,99,100} The mechanisms that have been suggested for body-weight support treadmill training's success have focused mainly on neuroplasticity,¹⁰¹⁻¹⁰³ but muscle size and composition changes may also be contributing to the beneficial effects of body-weight support treadmill training. Future investigations of early ambulation interventions may consider skeletal muscle measurements in addition to measures of physical performance. This is in line with current post-stroke clinical practice guidelines that recommend evaluations include assessments at the impairment level, that is, muscle size and strength, as well as the activity level, that is, performance in real-life or simulating daily activities.⁹²

CONCLUSION

In summary, clinicians must be cognizant that post-stroke there may be an acceleration of negative skeletal muscle changes typically associated with aging,^{31,37,38,76} resulting in a greater disadvantage for optimal muscle performance when compared to younger individuals post-stroke. Furthermore, post-stroke skeletal muscle changes may occur in both limbs,^{40,41,43} warranting caution when comparing the paretic limb to the nonparetic limb. Comparisons with age-matched normative data may reveal bilateral skeletal muscle impairments and provide impetus for interventions targeting both the paretic and nonparetic limbs. Future investigations evaluating relationships between post-stroke skeletal muscle impairments and physical performance may support interventions that target skeletal muscle. Such interventions may improve the activity and participation levels in older adults post-stroke.

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