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Effects of Resistance Training on Older Adults

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Abstract

Using an integrative approach, this review highlights the benefits of resistance training toward improvements in functional status, health and quality of life among older adults. Sarcopenia (i.e. muscle atrophy) and loss of strength are known to occur with age. While its aetiology is poorly understood, the multifactorial sequelae of sarcopenia are well documented and present a major public health concern to our aging population, as both the quality of life and the likelihood of age-associated declines in health status are influenced. These age-related declines in health include decreased energy expenditure at rest and during exercise, and increased body fat and its accompanying increased dyslipidaemia and reduced insulin sensitivity. Quality of life is affected by reduced strength and endurance and increased difficulty in being physically active. Strength and muscle mass are increased following resistance training in older adults through a poorly understood series of events that appears to involve the recruitment of satellite cells to support hypertrophy of mature myofibres. Muscle quality (strength relative to muscle mass) also increases with resistance training in older adults possibly for a number of reasons, including increased ability to neurally activate motor units and increased high-energy phosphate availability.

Resistance training in older adults also increases power, reduces the difficulty of performing daily tasks, enhances energy expenditure and body composition, and promotes participation in spontaneous physical activity. Impairment in strength development may result when aerobic training is added to resistance training but can be avoided with training limited to 3 days/week.

By the year 2030 approximately 30% of the US population will be elderly and will potentially experience some health problems as well as loss of function.[1] According to the US National Center for Health Statistics[2] an average person spends about 15% of their lifespan in an unhealthy state due to disability, injury or disease occurring in old age. Sarcopenia (i.e. muscle atrophy) and loss of strength are known to occur with age.[3-7] While its aetiology is poorly understood, the multifactorial sequelae of sarcopenia are well documented and present a major public health concern to our aging population, as both the quality of life and the likelihood of age-associated declines in health status are influenced. For example, reduced lean mass with aging is associated with decreases in resting energy expenditure and whole body fat oxidation[8] as well as reductions in physical activity and energy expenditure.[9-17] These metabolic changes are likely to be associated with increased adiposity and visceral fat distribution in older persons, increasing the risk of developing dyslipidaemia, insulin resistance and cardiovascular disease.[18] Further, bone mineral density is related to muscle mass and strength in older adults, implicating sarcopenia in the development of osteopenia and its progression to osteoporosis.[19,20]

In addition to its role in disease progression, the strength loss and general neuromuscular deconditioning accompanying sarcopenia decrease the capacity to perform daily living tasks (figure 1)[18,21,22] and increase exercise difficulty.[23-27] For example, large numbers of individuals over the age of 55 years have difficulty walking 0.4km or carrying 11kg.[1] By the age of 80 years up to 57% of men and 70% of women are unable to do heavy housework.[1] Since the incidence of obesity and physical inactivity is increasing across all age groups in the industrialised world, these estimates of dysfunction are probably understated.

Many of these changes in function are related to a loss of muscular strength.[28-30] Reductions in contractile strength accelerate in the fifth or sixth decade.[31-33] Cross-sectional data indicate that strength peaks in the third decade, remains unchanged or decreases slightly into the fifth decade, and then declines more rapidly at a rate of 12–15% per decade after that.[34] These reductions in strength with age are most notable in weight-bearing lower limb muscle groups.[23,35] Muscle power output and the ability to develop force quickly decline with age[36-38] and appear to decline more rapidly than strength with aging,[36,38] and may be more important than strength in the prevention of falls[39] and performance of weight-bearing tasks such as rapidly standing from a chair and walking.[33] Overall, indices of sarcopenia appear to accelerate beyond age 50 and advanced sarcopenia leads to functional decline and to the frailty phenotype which confers high risk for dependence, disability, hospitalisation and mortality.[40]

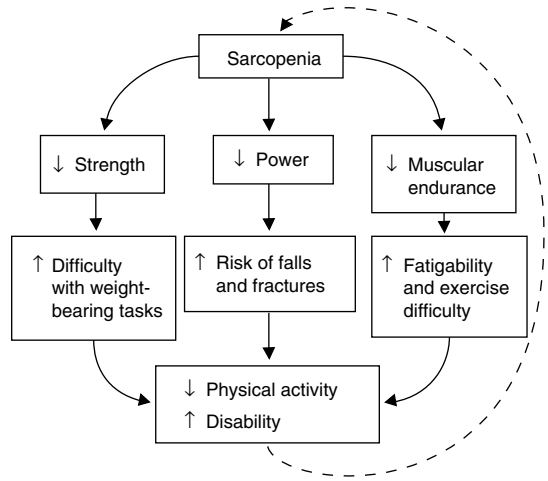

Fig. 1. A model of the functional consequences of age-related sarcopenia and the positive feedback loop by which the end result of reduced physical activity further exacerbates progression of the disorder. ↓ indicates decrease; ↑ indicates increase.

The sarcopenia of aging is apparently not exclusively the result of aging *per se*, as a high degree of

individual variation is inherent in what is generally characterised as a progressive loss of muscle mass and strength with aging. Tests of means in cross-sectional studies comparing muscle mass and/or strength among two or three adult age groups typically report significant age group differences, but variance estimates are often large, such that the mean minus 2 standard deviations (SD) for the younger group and the mean plus 2 SD for the older group display considerable overlap.[31,41] Age accounts for only 30% of the variance in strength in adults ranging 20–93 years of age.[32] These data indicate there are multiple factors independent of age that influence sarcopenia. Declining physical activity is certainly one of these factors, and we suggest a substantial portion of the reductions in strength and muscle function that occur with age are mediated by decreases in physical activity. The result is a positive feedback loop as reduced activity further decreases strength, ease of physical activity and participation in physical activity (figure 1). Interrupting this feedback loop is a vital step toward maintaining the quality of life and health of an aging population. A growing body of evidence supports resistance training (i.e. weight lifting) as an effective means of disrupting this deleterious loop. Therefore, the primary purpose of this review is to summarise the research concerning the effects of resistance training as a countermeasure against reductions in strength, power, muscle mass, ease of physical activity, and free living physical activity that are associated with the sarcopenia of aging. In addition, we review how adding endurance training to resistance training in the elderly may alter the adaptations seen with resistance training alone.

1. Muscle Size

1.1 The Aging Muscle

A primary focus of resistance exercise training prescription among the elderly is the induction of muscle growth (i.e. hypertrophy) in an effort to counteract sarcopenia. In this regard, a brief review of age-related atrophy follows.

1.1.1 Common Phenotypical Traits

Age-associated skeletal muscle sarcopenia is generally characterised by reduced muscle mass and strength and is manifested by preferential type II myofibre atrophy,[41-43] myofibre necrosis and myofibre type grouping,[44] and increased intramuscular content of non-muscle (i.e. adipose and connective) tissues.[44,45] Preferential type II myofibre atrophy at least partially accounts for an accelerated loss of power with age. The maximum velocity of shortening and power production are higher in type II myofibres than in type I myofibres;[46] thus, a preferential reduction in total type II myofibre area decreases overall muscle contractile velocity. The decreased strength/power production also appears to result from impaired excitation-contraction coupling, as calcium release[47] and dihydropyridine receptor expression[48] both decline with age. Myofibre type grouping is thought to be neurogenic in origin, resulting from denervation and reinnervation of myofibres as motor units are lost. Because myofibres will change fibre type (I, IIa, IIx) following reinnervation by a different axon type, the heterogeneous fibre type distribution pattern normally found in younger muscle is significantly altered in older muscle. Based on studies of whole vastus lateralis muscle cross-sections, reductions in myofibre size and myofibre number with age appear to accelerate beyond age 50 years.[44] Adults appear to lose only 5–10% of muscle mass from ages 20 to 50 years, but subsequently may lose an additional 30–40% from ages 50 to 80 years.

1.1.2 Potential Mechanisms

Correlative data point toward declines in serum anabolic hormones (e.g. insulin-like growth factor-I [IGF-I], testosterone) as potential contributors,[49,50] and anabolic/androgenic hormone (i.e. testosterone, dehydroepiandrosterone) 'replacement' therapy has been shown to induce modest improvements in strength in older adults.[51,52] There is evidence that basal muscle protein synthesis rates slow with age;[53,54] however, more recent findings indicate that basal muscle protein turnover is similar in young and older men.[55] Reduced myofibre number may result from the inability to repair damaged myofibres (i.e. necrosis) and/or apoptosis. These two processes may occur simultaneously in aging muscle. A growing body of evidence indicates that skeletal muscle precursor cells, termed satellite cells, are integral to the repair, regeneration and growth processes in skeletal muscle (we discuss

Table I. A summary of a select few factors that modulate muscle mass. The effects of age and resistance loading found in both human and animal models to date are highlighted

	Effect of increasing age	Effect of resistance exercise training or loading	
		young adults	older adults
Select factors that promote muscular growth and development			
Muscle IGF-I	↓ mRNA	↑ Protein ↑ mRNA	↑ Protein
MGF	↓ mRNA	↑ Protein ↑ mRNA	↑ Protein
Myogenic regulatory factors (MyoD, myf-5, myf-6, myogenin)	↑[a]	↑ Protein ↑ mRNA	↑ Protein ↑ mRNA
Satellite cell activation	↓	↑	↑
Mixed muscle protein synthesis rates	Equivocal	↑	↑
Select factors that inhibit muscular growth and development			
Myostatin (GDF-8)	↑ Protein ↔ mRNA	?	?
TNFα	↑ Protein ↑ mRNA	↔ Protein	↓ Protein ↓ mRNA

a Increased myogenic regulatory factor expression with advanced age is similar to that seen in neurodegeneration.

GDF-8 = growth and differentiation factor-8; **IGF-I** = insulin-like growth factor-I; **MGF** = muscle-specific isoform of IGF-I termed mechanogrowth factor; **TNF**α = tumour necrosis factor-α; ↓ indicates decrease; ↑ indicates increase; ↔ indicates no change; **?** = unknown.

satellite cells in more detail in section 1.2).[56,57] Whether the satellite cell pool declines in older muscles is as yet unclear;[58-60] however, it is possible that a reduced capacity for satellite cell activation with age[61] could increase susceptibility to irreparable myofibre damage and consequent necrosis. Additionally, there is evidence that myonuclear apoptosis occurs with neurodegeneration similar to that described in aging muscles.[62]

Although a multitude of circulating and local factors are most likely involved in the inhibition of satellite cell activity and/or muscle growth/regeneration in aging muscle, two candidate factors that have recently received significant attention are myostatin (i.e. growth and differentiation factor-8) and tumour necrosis factor-α (TNFα) [table I]. Myostatin may be a key player in sarcopenia by limiting satellite cell activity with age. As a member of the transforming growth factor-β family, myostatin impairs muscle growth by inhibiting myoblast proliferation (myoblasts are differentiated satellite cells)[63] and, by down-regulating MyoD expression, also inhibits differentiation[64] (MyoD is one of a family of myogenic regulatory factors discussed in section 1.2). The inhibitory function of myostatin appears to be quite powerful, as myostatin knockout mice develop more than twice the muscle mass of their wild-type counterparts.[65] In cattle, the double-muscle Belgian Blue phenotype results from heritable mutations in the myostatin coding sequence.[66] Further, overexpression of the myostatin inhibitor follistatin results in extreme muscle growth in mice.[67] These growth patterns result from both excessive myofibre hypertrophy and hyperplasia.

In humans, myostatin polymorphic variants have recently been shown to partially account for strength differences in older adults.[68,69] Further, the predominant myostatin allele is associated with a blunted hypertrophy response to resistance training in older women (i.e. women with the less common allele showed 68% greater muscle hypertrophy).[70] Disuse has been shown to increase myostatin protein levels[71,72] and the magnitude of disuse myofibre atrophy correlates with the magnitude of increased myostatin mRNA.[73] Moreover, myostatin expression is elevated in HIV-infected men with muscle wasting.[74] Although no differences in myostatin mRNA were reported recently in a comparison of 62- to 77- and 21- to 31-year-old men,[75] myostatin protein is elevated in the serum of elderly men and women and is inversely related to lean mass.[76,77] Additionally, myostatin levels decline during muscle loading in rodents.[78] Although further research is needed, these initial findings suggest myo-

statin may play an inhibitory role in the myogenic response to resistance training.

The catabolic cytokine TNFα induces muscle atrophy by suppressing protein synthesis and increasing protein breakdown. As such, it has been implicated in a variety of diseases causing muscle wasting (cachexia).[79,80] TNFα also induces apoptosis in muscle cells.[81,82] Through its activation of nuclear factor-kappa B (NF-κB), TNFα suppresses MyoD, thereby blocking myogenesis.[58,83,84] It is interesting to note that MyoD is preferentially expressed in type II myofibres, and type II myofibre atrophy is characteristic of sarcopenia while type I myofibre size is unchanged. TNFα mRNA and protein expression both are elevated in muscle samples from frail elderly patients when compared with young adults.[85] Interestingly, TNFα mRNA and protein expression both declined after 3 months of resistance training in the elderly patients.[85]

1.2 Cellular/Molecular Mechanisms of Hypertrophy

Skeletal muscle is a highly plastic tissue influenced by changes in loading patterns. Myofibre atrophy is a rapid response to unloading (e.g. bed rest, cast immobilisation),[86,87] while hypertrophy occurs in normal muscle following increased loading (e.g. stretch, resistance training).[87-89] While these represent extreme deviations from the typical daily loading pattern, muscle tissue also undergoes turnover daily in response to the nominal loading and stress associated with weight bearing. Even though changes in muscle size are not measurable day-to-day, the repair/regenerative responses to daily muscle loading must remain intact to prevent a cumulative loss of muscle mass over an extended period.

Myofibres are permanently differentiated, multinucleated cells. In the multinucleated myofibre, the myonuclear domain (volume of cytoplasm per myonucleus) is tightly controlled, which theoretically maintains the genetic machinery for myofibre homeostasis.[90,91] Myofibre growth or repair thus requires the addition of myonuclei. Satellite cells, which lie beneath the basal lamina of differentiated myofibres, are the primary source for the needed nuclei. These normally quiescent cells can be stimulated to enter the mitotic cycle, differentiate, and fuse to myofibres during growth or regeneration.[92] The requisite role of satellite cells during hypertrophy has been demonstrated, as irradiation of these cells abolishes the hypertrophic response to increased loading.[56,57] Whether the satellite cell pool declines in older muscles is as yet unclear;[58-60] however, there is evidence that surviving satellite cells themselves 'age' with reduced basal proliferative capacity.[61] Using myofibre cultures from rats in which the satellite cells are maintained in their position beneath the basement membrane, delayed proliferation and blunted differentiation are noted with aging.[93] While an impaired satellite cell population would probably limit the growth and repair/regeneration capabilities of older muscle, given appropriate stimuli, the abilities to proliferate and to fuse into myotubes are not affected by age.[58] Providing a sufficient stimulus for satellite cell activation may be the key to counteracting sarcopenia. For example, virally mediated overexpression of muscle IGF-I in aging mice increases muscle mass and strength, probably as a consequence of IGF-I-mediated satellite cell activation.[90] Fibroblast growth factor-2 also doubles proliferation of satellite cells in myofibre cultures from aging rats.[93] In response to resistance training, older men maintain myonuclear domain in the face of marked myofibre hypertrophy, suggesting the load-induced satellite cell recruitment mechanism remains intact.[94]

The family of myogenic regulatory factors (MRFs) including MyoD, myf-5, myf-6 and myogenin are muscle-specific transcription factors that control muscle cell differentiation and gene expression and are therefore important during myofibre development and during satellite cell-mediated growth, repair and regeneration in developed muscle. These proteins have basic helix-loop-helix sequences that bind to DNA in the regulatory region of muscle-specific genes. Myogenin is preferentially expressed in type I myofibres while MyoD is mainly expressed in type II myofibres.[95,96] To date, the bulk of our knowledge regarding the function of MRFs and any age-associated alterations has been derived from cell culture systems and animal models. MRF expression increases in muscles undergoing regeneration following tissue damage[97] and in humans[89] and rodents[98] undergoing resistance training-induced hypertrophy. There is some evi-

dence that MRF responses to resistance exercise[99] and stretch overload (a hypertrophy model)[100] are attenuated in the muscles of aged animals, including the recent report in humans of a nearly 2-fold (non-significant) increase in MyoD mRNA expression in young but not old men following a bout of resistance exercise.[101]

Results from *in vitro* and *in vivo* studies of tissue growth factors indicate IGF-I is a potent modulator of skeletal muscle growth and repair, suggesting IGF-I expression and/or availability may play a role in the progression of sarcopenia and training-induced hypertrophy. The myogenic and mitogenic effects of IGF-I *in vitro* are well recognised. IGF-I stimulates proliferation and differentiation of satellite cells and is associated with increased expression of muscle-specific proteins.[92,102] Induced expression of muscle IGF-I may restore satellite cell proliferative capacity, attenuating age-related atrophy.[103] A load-sensitive isoform of IGF-I (termed mechanogrowth factor [MGF]) expressed in skeletal muscle has been characterised,[104] and increased MGF expression after resistance exercise has been noted.[98] Data from cell culture[105] and rodent[98,106] experiments suggest IGF-I (or MGF) may activate the MRFs and the myogenic programme. Recent evidence in humans indicates basal IGF-I mRNA expression in muscle declines with advancing age.[75] In young adults, IGF-I mRNA expression increases after resistance exercise.[107] MGF expression also increases acutely after resistance exercise in young but not old men.[101] As with numerous peptide growth factors, binding of IGF-I to its cell surface receptor (IGF receptor 1) induces an intracellular phosphorylation cascade that includes activation of the mitogen-activated protein kinase pathway. Recent findings indicate divergent effects of acute resistance exercise on these intracellular signals in older and younger men,[108] demonstrating potentially important age-related differences in the capacity for load-mediated muscle adaptation.

1.3 Resistance Training-Induced Hypertrophy in the Aging Muscle

Despite what could be interpreted as a blunted 'physiologic reserve' in aged skeletal muscle, numerous studies provide encouraging evidence that older muscles adapt vigorously to resistance training with marked myofibre hypertrophy (table II). Myofibre hypertrophy following a typical 2–3 days per week training programme can be substantial, ranging from 10% to 62% after 9–52 weeks of training.[30,42,46,109-122] These findings fuel the ongoing debate over the degree to which sarcopenia is attributable to biological aging versus chronic low levels of physical activity. Certainly both play a role, but the older myofibre has proven to be adaptable to loading time and time again. In fact, similar gains in myofibre size have been noted in younger and older men following the same resistance training programme.[115]

The total amount of muscle mass gained in response to resistance training is determined not only by the degree to which each myofibre grows but also by the number of myofibres present in a muscle. Therefore, at the whole muscle level, hypertrophy in an older muscle is presumably limited (in comparison to a younger muscle) as a result of age-related motor unit loss. Measurements of training-induced muscle hypertrophy using magnetic resonance imaging and computed tomography tend to be modest compared with muscle cell cross-sectional measurements.[70,112,124] This finding is not unique to older adults[105,128] and probably reflects differences in measurement techniques and the inclusion of non-contractile tissue in the whole muscle measurements. In one mixed sex report, however, improvements in whole muscle volume were lower in older compared with younger adults.[129]

1.3.1 Sex Differences

While evidence of resistance training-induced myofibre hypertrophy is overwhelming, recent findings indicate important sex differences in the efficacy of these training programmes among older adults.[42,46,130,131] Given the same relative training stimulus, the hypertrophic response appears blunted in older women (table II). We recently reported relative myofibre hypertrophy was 5-fold higher in older men (36%) than in older women (7%) following identical 6-month resistance training programmes.[42] The physiological basis for this apparent sex difference is not known, but early findings from our current studies suggest sex differences in MRF expression (24 hours after a bout of resistance exercise) may play a role (unpublished observations).

Table II. Summary of resistance training studies in older men and women in which changes in myofibre size and strength were assessed[a]

Study	Subjects (F/M)	Age (y)	Knee extensor resistance training programme[b]				Site of muscle biopsy	Δ size (%) by myofibre type	Δ strength (%)
			duration (wk)	frequency (days/wk)	volume (set × rep)	intensity (% 1RM)			
Sexes combined									
Pyka et al.[119]	4F/4M	61–78	30	3	6 × 8	65–75	VL	I = 48, II = 62	61
Singh et al.[120]c	2F/5M	84 ± 1	10	3	3 × 8	80	VL	I = NS, II = 10	257
Women									
Bamman et al.[42]	5F	61–74	26	3	4 × 8–10	65–80	VL	I = NS, II = NS	58
Charette et al.[110]	13F	70 ± 1	12	3	6–12 × 6	65–75	VL	I = NS, II = 20	93
Ferketich et al.[123]d	7F	67 ± 2	12	3	4 × 12–15	80 (of 10RM)	VL	I = 20, II = NS	112
Hakkinen et al.[124]	10F	64 ± 3	21	2	2–6 × 5–20	40–80[e]	VL	I = 18, II = 32	29
Hakkinen et al.[114]	10F	67 ± 3	26	2	6–12 × 3–15	50–80[e]	VL	I~35, II~40	31
Taaffe et al.[122]	HI = 7F	65–79	52	3	1 × 14, 2 × 7	40, 80	VL	I = 28, II = NS	~85
	LO = 7F				3 × 14	40		I = 10, II = NS	~60
Trappe et al.[46]	7F	74 ± 2	12	3	3 × 10	80	VL	I = 24, II = NS	56
Men									
Bamman et al.[42]	9M	62–77	26	3	4 × 8–10	65–80	VL	I = 29, II = 42	82
Brown et al.[109]	14M	60–70	12	3	2–4 × 10	50–90	BB	I = 15, II = 30	48
Frontera et al.[112]	12M	60–72	12	3	3 × 8	80	VL	I = 34, II = 28	107
Grimby et al.[125]	8M	78–84	9	2–3	21 × 2–8[f]	100 (IK)	VL	NS	10–19[f]
Hakkinen et al.[115]	10M	61 ± 4	10	3	6–12 × 3–10	60–90[e]	VL	I = 23, II = 38	17[g]
Hakkinen et al.[114]	11M	72 ± 3	26	2	6–12 × 3–15	50–80[e]	VL	I = NS, II = NS	21
Hepple et al.[116]	9M	65–73	9	3	12 × 6–12	~65–85	VL	MFA = 23	58
Hikida et al.[94]	9M	64 ± 5	16	2	9 × 6–8	85–90	VL	I = 46, II = 41	50
Larsson[126]	6M	56–65	15	2	5 × 20–30	Low	VL	I = 38, II = 52	NS
Taaffe & Marcus[127]h	11M	65–77	24	3	6 × 8	75	VL	I = 17, II = 26	57
Trappe et al.[46]	7M	74 ± 2	12	3	3 × 10	80	VL	I = 20, II = 13	50

a Unless otherwise noted, strength results represent the relative change in 1RM for the movement most specific to the biopsied muscle.

b Resistance training programme: duration = weeks; frequency = days/week per muscle group; volume = sets × repetitions; intensity = % of 1RM. For volume, sets = total number of sets performed for the biopsied muscle and may represent more than one exercise.

c Combined intervention of resistance training and nutritional supplementation.

d Combined endurance and resistance training.

e Periodised programme.

f Combination of isometric and/or concentric and eccentric isokinetic contractions.

g Strength determined isometrically (i.e. maximum voluntary isometric knee extension).

h Six of 11 subjects received human growth hormone treatment with no apparent additive effect.

BB = biceps brachii; **F** = female; **HI** = high intensity; **IK** = isokinetic contractions at multiple velocities; **LO** = low intensity; **M** = male; **MFA** = mean fibre area; **NS** = nonsignificant; **RM** = repetition maximum; **VL** = vastus lateralis.

Sex differences in myostatin expression may also play a role, as recent findings in rodents indicate myostatin expression is 40–60% lower in older males than older females.[132]

It is interesting to note (table II) the most effective training programme in women (for the induction of hypertrophy) was conducted at a frequency of just 2 days per week.[124] In fact, recent work by Hakkinen et al.[114] indicates that at this reduced twice per week training frequency, older women actually show greater hypertrophy than men. In addition, we have shown that older women adapt well to nontraditional resistance training programmes designed with either reduced intensity[133] or less frequent high-intensity loading.[134] These data suggest older women may require longer periods of recuperation between high-intensity loading bouts to reap benefits obtained by men on a more frequent loading schedule.

1.4 Power Production

Perhaps the most important functional deficit associated with sarcopenia is a decline in muscle power output. The blunted capacity to contract muscle forcefully and quickly has implications for increased risk of falls as well as increased difficulty during weight-bearing tasks. Fortunately, a number of studies have demonstrated rather robust improvements in power production in older adults as a consequence of resistance training.[114,118,135-141] These improvements in power are also seen at the single myofibre level.[46,117] Gains in power development are specific to the mode of training, indicating that a training programme incorporating high-velocity contractions induces greater gains.[114,118,135,137] Because of its importance to daily function, we suggest incorporating low-resistance, high-velocity contractions into a resistance training prescription for older adults (e.g. on at least 1 of 3 weekly training days).

1.5 Muscle Quality

A number of studies suggest that strength decreases with age are independent of decreases in muscle mass. Hakkinen and colleagues[142] propose that age-related strength losses are multifactorial and are in part caused by changes in neural drive or qualitative changes in muscle. Brooks and Faulkner[143] found a 20% deficit in electrically stimulated strength in aging rodents even after adjusting for muscle cross-sectional area and suggested that the deficit probably resulted from a decrease in cross-bridges per area or force per cross-bridge. Consistent with this premise, a number of studies have demonstrated lower muscle quality (strength adjusted for muscle size, sometimes defined as specific strength) in older adults when compared with younger adults.[23,144-150] However, not all studies have found consistent age-related declines in muscle quality. Martin et al.[37] reported that muscular power adjusted for muscle volume and optimal pedalling rate (a surrogate measure of fibre type) of trained cyclists were stable to age 50 years and decreased modestly thereafter, suggesting that intense training may slow the age-related change in muscle quality. In addition, other studies have evaluated muscle using urinary creatinine excretion and examined muscle quality longitudinally.[6,146] Another factor that may affect comparison of results in various human studies is the difficulty in measuring cross-sectional area because of architectural complexity, which makes estimates of muscle quality problematic in humans.[143] The longitudinal studies also may have been limited by a relatively short period of follow-up and the lack of precision in the estimation of muscle using urinary creatinine excretion.

Strength training studies, especially in older adults, typically show increases in strength beyond what would be expected by the increases in muscle mass[42,130,131,151,152] (table II). This increase in muscle quality is typically felt to be due to increased motor unit activation.[153-155] However, not all resistance training studies show increased motor unit activation as measured by integrated electromyography during maximal isometric contractions.[156-160] In addition, Phillips et al.[161] showed that decreased isometric maximal force was not accompanied by a decrease in eccentric strength, suggesting maximum isometric muscle quality is not due to just a decrease in myosin cross-bridges in cross-section or an inability to activate motor units. Consistent with the above-cited work on rodents[143] in which large age-related differences in electrically stimulated strength exist even after adjusting for muscle cross-sectional area, work with humans sug-

gests that factors other than motor unit activation also contribute to muscle quality. Factors such as differences in muscle architecture,[162] fibre type area[41,44] and increased encroachment of lipid and connective tissue into muscle[163] all potentially could contribute to differences in muscle quality with age as well as strength training-induced increases in muscle quality.

A factor normally not considered that may affect muscle quality is availability of adenosine triphosphate (ATP) in the vicinity of the myosin cross-bridge heads. Since myosin cross-bridge heads are known to cycle at very rapid rates (300–600Hz), it seems reasonable to propose that local ATP availability may limit cross-bridge binding potential, even in maximal muscle contractions lasting a second or less. Several factors suggest that this may influence both the age-related differences and training-related changes in muscle quality. We have shown that phosphorous magnetic resonance spectroscopy (^{31}P MRS)-measured skeletal muscle creatine kinase activity during maximum isometric contractions is related to muscular strength independent of muscle cross-sectional area.[164] In addition, myokinase activity (adenosine diphospate [ADP] + ADP $\leftrightarrow$ ATP + adenosine monophosphate [AMP]) is related to maximum strength and declines with age,[165] supporting the concept that high-energy phosphate availability may influence muscle quality. We have found that maximum creatine kinase activity is negatively related to age.[166] The significant age and muscular strength relationship disappears when adjusted for maximal creatine kinase and anaerobic glycolytic rates (unpublished observations), suggesting the age-related decline in muscular strength is mediated at least in part by declines in the ability to generate ATP rapidly from anaerobic sources.

Finally, although results have not been universal, several studies have shown increases in strength after only 10–20 days following creatine supplementation.[167-171] This is too short a time to induce muscle hypertrophy. The increases in strength could be explained by increases in high-energy phosphate availability in the form of creatine phosphate (CrP). Taken together these results are consistent with the hypothesis that the decrease in maximal force production in aging muscle could be caused in part by decreased ability of the myofibre to maintain ATP levels through myokinase and creatine kinase activity (figure 2). Little is known concerning the effects of exercise training on myokinase and creatine kinase activity, although ATP and CrP concentrations have been reported to be higher in trained men.[172] It is thus possible if not probable that strength is affected by numerous factors as we age but can be modified at least in part by high-intensity resistance training (figure 3).

1.6 Function in Physical Activity

The ability to perform tasks of daily living reaches a peak in the early thirties and thereafter declines with age.[24-26] Although physical activity can modify the decrement, it occurs regardless of activity levels.[24-27] For example, progressive declines in performance of highly trained athletes occur with age.[27,173] Decreased ability to perform tasks with age probably results from a variety of factors, including muscle weakness and increased fat mass.[30,44] Indeed, we have previously reported decreased difficulty in such tasks as standing from a chair, carrying a simulated box of groceries, climbing stairs, bicycling and walking following weight loss even though no changes in physical activity occurred.[174] A number of studies have shown a positive relationship between strength and functional abilities,[175-180] with strength effects on function most evident for the more frail and weakest adults.[181]

Paralleling the decrease in muscle function, age is independently related to decreases in muscle metabolic capacity.[166,182-186] Most of these studies did not measure regular physical activity, so it is difficult to know what role age-related reductions in physical activity plays in the decrease in muscle metabolic capacity. Kent-Braun and Ng,[184] using

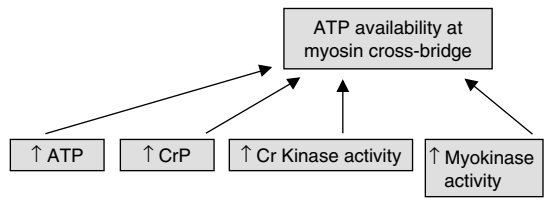

Fig. 2. Hypothetical model for training-induced increases in ability to sustain high ATP at the myosin cross-bridge head during maximal force production. **ATP** = adenosine triphosphate; **Cr** = creatine; **CrP** = creatine phosphate; ↑ indicates increase.

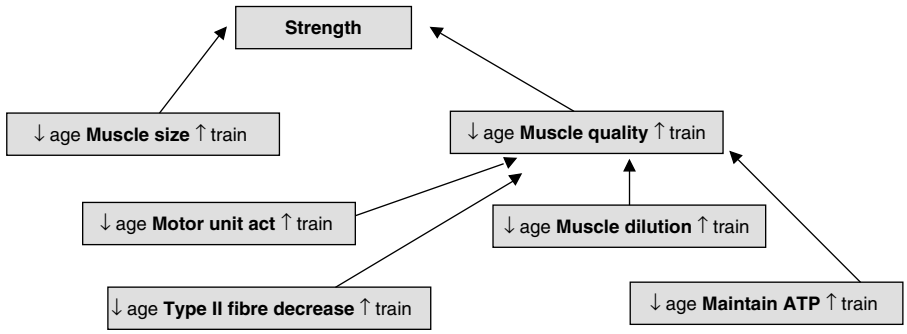

Fig. 3. Hypothetical model for interaction of age and resistance training on strength. ↓ indicates decrease; ↑ indicates increase.

^{31}P MRS, have recently reported data suggesting that the lower values found in older adults are mediated by reduced physical activity and disappear when older adults have activity patterns similar to younger adults. The consistent finding that locomotor muscles are more susceptible to age-related declines in muscle function than non-locomotor muscles[23,183,187,188] is also supportive of the hypothesis that declining muscle metabolic capacity with age is primarily mediated by decreases in physical activity.

However, we have recently shown that age is significantly related to decreased treadmill endurance, plantar flexion strength, maximum oxygen uptake ($\dot{V}O_{2max}$), muscle ^{31}P MRS ADP recovery rate (a measure of ability of skeletal muscle to generate ATP from oxidative processes), and muscle anaerobic glycolytic capacity even after adjusting for free living activity-related energy expenditure as measured with doubly labelled water.[166] Muscle biopsy data in this study also show an independent relationship between age and citrate synthase, glyceraldehyde-3-phosphate dehydrogenase, phosphofructokinase and phosphorylase activities, suggesting the age-related decreases in muscle oxidative and anaerobic capacities are mediated by both decreases in physical activity and an independent aging effect.

Based on these studies, it is obvious that the ability to do activities of daily living may be improved with physical training. However, since strength, aerobic capacity and anaerobic capacity all decrease with age parallel to reductions in the ability to do activities of daily living, it is not apparent what form of training might be best for improvement. We suggest that resistance training might be a better choice than endurance training if only one form of exercise is chosen to improve the ability to do daily tasks. First, most functional tasks used in normal day-to-day activities are of relatively short duration and therefore are not strongly related to aerobic or even anaerobic capacity but are related to muscular strength and/or power.[189-191] Second, available data relating fitness to free living activity-related energy expenditure show that strength is more strongly related to free living activity-related energy expenditure than aerobic fitness (unpublished observations). For example, women who are successful at maintaining weight have not only increased physical activity levels but increased muscular strength.[192] Third, numerous studies have shown that in older adults, performance in activities of daily living are improved following strength training.[30,141,193-197]

Strength is independently related to endurance capacity, further furnishing indirect evidence that strength and resistance training are important in maintenance of function as we age. We have recently shown that quadriceps isometric strength and ^{31}P MRS muscle oxidative capacity (post-exercise ADP recovery rate × volume of muscle/bodyweight) are independently related to treadmill endurance time.[164] When whole body $\dot{V}O_{2max}$ was substituted for muscle oxidative capacity, similar results were found. Previous studies have shown that increases in strength following resistance training are related to increased time to exhaustion in endurance activities even though little or no increase in aerobic capacity was found.[195,198-200] One possible explanation for a relationship between physical strength and endurance performance is that less muscle activation would be needed to perform a task when a muscle is

stronger,[198] hence delaying fatigue. Since previous work has shown that resistance training can decrease the energy needed to do a task,[201] as well as decrease activation of muscle for a standard task such as standing from a chair or carrying a simulated box of groceries,[21] it is probable that at least some of this improvement in resistance training-mediated endurance performance is the result of myofibre hypertrophy. Essentially, if myofibres of all types are larger and therefore capable of greater tension development on activation, more work can be accomplished by low-threshold, efficient fatigue-resistant (type I) motor units, decreasing the need to activate less efficient, fatigable type II motor units.[202]

1.7 Energy Expenditure and Weight Maintenance

Both resting[10,12-16,174,203] and activity-related[1,204] energy expenditure decline with age. The decrease is more pronounced in activity-related rather than resting energy expenditure. Westerterp[204] has recently reported in a review on physical activity and aging that daily activity-related energy expenditure as measured by doubly labelled water decreases from 35% of the total energy expenditure at age 20 years to 25% at age 90 years. Decreased energy expenditure and especially decreased activity-related energy expenditure can have a major adverse effect on weight maintenance. Several studies have shown that high levels of physical activity and energy expenditure are associated with weight maintenance, while low levels of physical activity and energy expenditure are associated with weight gain.[192,205-209] In fact, in a doubly labelled water study in which we measured total, resting and activity-related energy expenditure and then evaluated subsequent 1-year weight gain, we demonstrated that differences in activity-related energy expenditure between gainers and maintainers account for 77% of the 1-year weight gain of the gainers.[192] Presumably, the rest of the weight gain in the gainers was caused by increased energy intake.

Although many studies have shown that resistance training is associated with decreases in fat mass, most studies have shown a concomitant increase in fat-free mass[42,121,151,152,210-212] and thus little or no change in total bodyweight. Because of this, it has normally been assumed that the main effect of resistance training on body composition is a shift from fat to muscle mass with the individuals remaining in caloric balance. This is not the case for aerobic training, since the typical response to aerobic training has been little or no increase in fat-free mass but a loss of body fat and bodyweight.[121] The assumption that weight training has little effect on caloric balance may be in error, however. Determination of caloric balance or imbalance over any time period must include changes in fat and fat-free mass. However, there is a large difference between the energy cost of forming new lean tissue and the energy stored in fat mass. The energy cost of forming new lean mass plus its stored energy value is 1.8 kcal/g,[213-215] whereas the energy stored in a gram of fat is 9 kcal, 7.2 kcal more than the energy cost of forming new lean tissue. This discrepancy can lead to quite large differences in calculation of energy balance at least during the first months of training, when increases in muscle are rapid.

For example, we have recently reported the results of a 26-week resistance training programme in older men and women (61–77 years) in which the average increase in fat-free mass was 2kg and the average loss of fat mass was 2.7kg.[152] Although bone mineral content increased as a consequence of the resistance training, the increase was only 37g. Therefore, the lean soft tissue increase was 1963g, costing 3533 kcal (1.8 kcal/g × 1963g). The energy stored in 2700g of fat is 24 300 kcal (9 kcal/g × 2700g). The difference is 20 767 kcal (kcal no longer stored as fat but not stored as fat-free mass either). Therefore, the men and women in this study must have been in caloric deficit averaging ~114 kcal/day over the 26 weeks, or equivalent to 2.3kg fat loss. Interestingly, these estimates of calorie loss during resistance training are similar to those typically observed during aerobic training.[121] For example, in comparing resistance with aerobic training, we have reported a 1.6kg reduction in fat mass after 10 weeks of aerobic training in young men with no change in fat-free mass, while 10 weeks of resistance training led to a 2.2kg fat-free mass gain and a 1.9kg fat loss.[121] Thus, using the same calculations, the daily caloric deficits were similar for aerobic (206 kcal/day deficit) and resistance (188 kcal/day) training.

Although a number of studies have shown that resistance training will increase resting energy expenditure, at least if the training is intense enough to induce a measurable increase in fat-free mass,[121,152,210,211,216,217] few studies have actually measured total energy expenditure with doubly labelled water in an untrained state and then post-training. Even though resting energy expenditure may increase and additional energy is expended during the training, it is possible total energy expenditure may be unchanged or even decrease if the older adults choose to be less active outside the training sessions. This can occur in older adults who are exposed to a very vigorous aerobic training programme. Goran and Poehlman[218] have shown that older adults compensate during nontraining time by expending less energy in free living non-training physical activity, perhaps because of fatigue from the intense, relatively high-volume training. Although this may occur in the early stages of a resistance training programme with older adults, it does not seem to be present if the training programme is sustained long enough to obtain suitable adaptations. For example, in our previous work, older adults felt that they were chronically tired and tended to lack energy during the first 6–12 weeks of training of a 26-week resistance training programme.[219] However, by the end of the 26-week study the participants felt that they had much more energy and were able to do physical tasks with greater ease. These self-reports corresponded with an increase in total daily energy expenditure, as measured by doubly labelled water, of 231 kcal even though the average daily energy cost of the three times per week training was only 51 kcal and the increase in resting energy expenditure was only 87 kcal.

1.8 Combined Strength and Endurance Training

Owing to specificity of training effects, a combination of both strength and endurance training have been advocated for optimal physical function and health in the elderly.[220-223] Cardiovascular endurance training appears to be the most efficacious training mode in the elderly for maintaining and improving maximal aerobic power, cardiovascular function and submaximal endurance performance.[220,221,223] A number of studies involving young adults have reported impairment in strength development when endurance training is added to strength training in a combined training programme,[224-228] although a number of others report no impairment.[121,229-231] Impairment in strength development may be a particularly important consideration in the elderly, where strength and muscle mass levels may affect both energy expenditure and functional capacity in a number of activities of daily living. It should also be noted that studies investigating the interaction of strength and endurance training provide consistent evidence that adding strength training to endurance training does not interfere with cardiorespiratory endurance development.[121,227,228]

Although some investigations have reported substantial improvements in both strength and endurance with combined training in the elderly,[123,232-234] only one study made direct comparisons between elderly subjects in strength-only and combined training regimens. Wood et al.[230] report similar muscular endurance development (assessed with 5 repetition maximum [RM] tests) with strength-only and combined strength and endurance training regimens over a 12-week period. All groups in this study trained 3 days per week and the study was different from all other combined training investigations involving younger individuals, in that the combined training group performed resistance and endurance training at a reduced volume as compared with individual strength and endurance training regimens. The reduced volume in the combined training equated all groups in terms of training bout duration and frequency of training. This reduced volume as employed by Wood et al.[230] may point to a crucial factor in designing training regimens to optimise performance adaptations with combined training.[121,156,228] All training studies that report impairment in strength development used young adults and compared strength-only training with a much higher volume of concurrent training.[225-228] Combined training groups performed the same strength-only programmes plus a substantial amount of endurance training. Also striking is the contrast in frequency of training (number of days per week) between studies that report impairment in strength development and those that do not. Studies that utilised combined training with some type of exercise (strength, endur-

ance or both) being performed 5[226] or 6 days per week[224,225,227,235] consistently report some type of impairment in strength development compared with groups that performed the strength training only (which performed fewer training sessions per week).

In contrast, when concurrent training is limited to 3 days per week, as in the Wood et al.[230] study, strength and accompanying muscle size are consistently increased to the same magnitude with strength-only and combined training.[121,156,236] Studies utilising young and middle-aged adults in 4 days per week combined training regimens report equivocal results, with one study[228] reporting some impairment in strength gains and two studies[229,231] reporting similar improvements with both strength-only and combined training. Thus, our recommendation (based primarily on results from young adults) for combining both strength and endurance modes of training is an exercise frequency of no more than 3 or 4 days per week for training of the same muscle group. It should be noted that any impairment in strength development with combined training occurs only in muscle groups that are recruited during both strength and endurance training.[121,227]

One caution with higher volume of exercise is a possible decrease in compliance to training.[222] Additionally, there may be a reduction in free-living activity due to overtraining and/or due to the time commitment to exercise training limiting participation in other physical activities. Studies that report impairment in strength development with combined training also reported a potentially undesirable increase in cortisol levels (associated with protein degradation) with the combined training.[225,228,235] Strength-only protocols in the same studies did not have increases in cortisol, which suggests a type of 'overtraining response' with the higher volume of the combined training.[228]

For some areas of functional performance, there is evidence to support a synergistic or an additive enhancement with combining strength and endurance training in the elderly as compared with performing either training mode alone. First, there is evidence to support a synergistic effect in endurance performance when combining strength and endurance training in comparison to endurance-only training. Ferketich et al.[123] report that elderly women who participated in either an endurance-only or a combined strength and endurance training protocol had equal increases in peak aerobic capacity. However, the combined training induced substantially greater increases (more than 2-fold) in a submaximal cycle endurance test (workload equal to 80% of peak oxygen uptake. In a similar study, involving patients in an outpatient cardiac rehabilitation programme, Beniamini et al.[237] compared a group that completed a combined strength and endurance regimen with a group that completed a combined flexibility and endurance training regimen. The combined strength and endurance protocol induced almost a 2-fold greater increase in a progressive treadmill endurance-walking test. Several studies in which strength training was added to training programmes of endurance-trained young adults also report enhanced endurance performance despite no change in $\dot{V}O_{2max}$.[238-241] Osteras et al.[240] indicated that the increase in aerobic endurance performance may be due to an increase in work economy partly explained by enhanced changes in the force-velocity relationship and enhanced mechanical power output. Strength training alone has also been shown to enhance walking endurance in healthy elderly individuals.[195,242]

A second potential synergistic effect of combined training in the elderly was reported by Wood et al.[230] in an agility/dynamic balance test. Compared with strength-only and endurance-only training, combined training induced significantly greater improvements in a timed test involving repeated standing from a chair, walking around cones and returning to the chair. These results and the enhanced endurance performance reports discussed above suggest that combination training in the elderly is more effective than strength or endurance training performed alone in certain aspects of functional performance.

Lastly, a recent study implicates an important functional concern with combining strength and endurance training in the elderly. Hakkinen et al.[229] compared adaptations to strength-only and a combination strength and endurance training regimen in middle-aged adults and reported similar strength development in three different lower-extremity strength tests. The strength training regimen included a portion of the knee extension repetitions performed with light loads (50–60% of maximum) and

executed as 'explosively' as possible. Interestingly, despite similar strength improvements and muscle hypertrophy in the two groups, only the strength-only training produced an increase in rate of force development during isometric knee extensions. The impairment in rate of force development with the combined training was apparently mediated by an accompanying impairment in rapid voluntary neural activation of the trained muscle over the first 500 msec of contraction as assessed by electromyography. These results suggest that in elderly individuals adding endurance training to strength training may limit improvements in important functional tasks that require rapid force generation (i.e. maintaining balance when bumped or when standing on a bus or subway car when it changes speed, or stopping at a crosswalk to avoid a car). It should be noted that among the elderly, any improvement in functional capacity following training, whether or not it is blunted by combined training, is undoubtedly important. Owing to the diverse physiological and performance effects of strength and endurance training, and their important influence on functional abilities and health in the elderly, further research is needed to clarify potential impairments, compatibility, or synergistic adaptations with combined training.

2. Conclusions

Evidence that resistance training is of benefit to older adults is overwhelming. We have taken an integrative approach in this overview, highlighting positive adaptations in a myriad of factors considered important in determining functional status, health and quality of life. Resistance training in older adults markedly increases muscle mass, strength and power, reduces the difficulty of performing daily tasks, enhances energy expenditure and body composition, and promotes participation in spontaneous physical activity apart from regimented exercise training. These beneficial adaptations are dependent upon the training stimulus. However, no consensus exists for the optimal training programme. To further complicate matters, individual variations as to genetic predisposition, fitness level, prior experience, age and sex probably influence the optimal training design. Results from a recent meta-analysis by Rhea et al.[243] offer some basic guidance for designing programmes. Based on this meta-analysis and the research findings found in this article, we offer the following resistance exercise prescription general guidelines. The loading intensity to promote hypertrophy should approach 60–80% (more highly trained individuals 80%) of 1RM with a volume ranging from 2–4 sets of 8–15 repetitions per exercise. Each muscle group should be exercised 2–3 days per week. Rhea and colleagues' meta-analysis[243] and results from our lab[133,194] suggest that older adults, especially older women, should train 2 days per week. We also recommend low intensity (e.g. 40%), high velocity contractions on at least 1 day per week to develop muscle power. Individuals demonstrating signs of advanced sarcopenia and/or elderly women may benefit from a variable-intensity exercise prescription to maximise recuperation between high-intensity bouts. Lastly, to minimise impairment of strength and muscle mass gains, any addition of endurance training to resistance training should be performed no more than 3 days per week.

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