The Aging Athlete: Paradigm of Healthy Aging

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Key words
aging, maximal oxygen consumption, metabolic health, lifelong exercise, single muscle fiber, sarcopenia

accepted 01.02.2022
published online 08.04.2022

Bibliography
Int J Sports Med 2022; 43: 661–678
DOI 10.1055/a-1761-8481
ISSN 0172-4622

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ABSTRACT

The Exercise Boom of the 1970's resulted in the adoption of habitual exercise in a significant portion of the population. Many of these individuals are defying the cultural norms by remaining physically active and competing at a high level in their later years. The juxtaposition between masters athletes and non-exercisers demonstrate the importance of remaining physically active throughout the lifespan on physiological systems related to healthspan (years of healthy living). This includes ~50 % improved maximal aerobic capacity (VO_2max) and enhanced skeletal muscle health (size, function, as well as metabolic and communicative properties) compared to non-exercisers at a similar age. By taking a reductionist approach to VO_2max and skeletal muscle health, we can gain insight into how aging and habitual exercise affects the aging process. Collectively, this review provides a physiological basis for the elite performances seen in masters athletes, as well as the health implications of lifelong exercise with a focus on VO_2max, skeletal muscle metabolic fitness, whole muscle size and function, single muscle fiber physiology, and communicative properties of skeletal muscle. This review has significant public health implications due to the potent health benefits of habitual exercise across the lifespan.

Introduction

Masters athletes are a source of inspiration as they continue to compete past their physiological prime and maintain a highly active lifestyle regardless of cultural expectations [1]. These veteran athletes are increasing in population and performing at an exceedingly high level as indicated by their performances in the World Masters' Athletic Championships [2]. Their remarkable performances suggest that these athletes have exceptional physiology that allows them to be more endurant, faster, and stronger relative to sedentary age-matched individuals.

Recently, masters athletes have been described as silhouettes of human aging as their performance over time mirrors the negative trajectory of physiology during the aging process [3]. Physiological systems which contribute to the loss in performances include aerobic capacity, skeletal metabolic fitness (metabolic enzymes and capillarization), whole muscle size and function, single muscle fiber physiology, muscle-to-organ communication (e. g., inflammation), among others. Along with athletic performance, these systems are also likely related to healthspan (years of healthy living) [4]. As masters athletes continue to perform at a high-level, the years of exercise training appears to result in unique adaptations to prolong healthspan compared to elderly non-exercisers. This review will provide an overview of aging and compare masters athletes to non-exercisers as it pertains to 1) Maximal aerobic capacity, 2) Skeletal muscle size and function, 3) Skeletal muscle metabolic fitness, 4) Single muscle fiber size, function, and distribution, and 5) Communicative properties of skeletal muscle. For the purposes of this review, masters athletes (athletes beyond typical peak competitive years) and lifelong exercisers (individuals who had participated in exercise training throughout their lifespan) are present-

ed. This review has large public health implications for the importance of maintaining active throughout the lifespan.

Maximal Aerobic Capacity

Oxygen consumption (VO_2) is a function of cardiac output [heart rate (HR) x stroke volume (SV)] and the difference in oxygen content between arterial and mixed venous blood (a-vO_2diff) [5]. These two variables have also been defined as central (cardiac output) and peripheral (a-vO_2diff) components. From an athletic perspective, VO_2max (maximal amount of oxygen consumption) is a key variable in endurance performance as the more oxygen an individual can consume for aerobic metabolism at higher workloads, the more endurant one will be [6]. VO_2max is also related to health status as a low VO_2max is closely linked to co-morbidities such as cardiovascular disease and type 2 diabetes, and is a stronger predictor of relative risk of death than more traditional risk factors (e. g. smoking, obesity, hypertension, and dyslipidemia) [7, 8]. A seminal paper by Myers et al. reported a relative VO_2max less than 17.5 ml kg^{-1} min^{-1} [5 metabolic equivalents (METs)] in males increased the relative risk of death 4.5-fold. Therefore, a VO_2max value of 5 METs has been termed the "frailty threshold" [8]. Furthermore, Kodama et al., suggested a 1-MET (3.5 ml kg^{-1} min^{-1}) increase in VO_2max results in a 13–15 % decrease in relative risk of death [9]. To further stress its clinical importance, the American Heart Association published a scientific statement, stating VO_2max should be a vital sign for medical providers to more accurately evaluate patients' health [10]. These data support that a relatively high VO_2max is critical for not only endurance performance, but also for overall health.

Measuring VO_2max in individuals aged 6 y to 75 y, Sid Robinson reported a linear 1 % decrease per year in relative VO_2max after the age of 20 y [11]. To further expand on this data, large-scale database studies in the United States and Norway (> 1800 subjects per study) have been published to establish normative values in males and females [12, 13]. The United States and Norwegian data show an overall ~9 % decrease per decade across the lifespan in relative VO_2max, which was similarly shown by Robinson [11, 12]. However, by reviewing the decade-by-decade data, there appears to be a deflecting point in the 5th decade of life in Americans, after which the rate of decline increases rapidly from 7 to 15 % throughout the remaining lifespan. In contrast to Americans, the Norwegian data presents a decrease in relative VO_2max that remains ~9 % per decade. Along with the slightly lower decline in VO_2max in later years, Norwegians also have a consistently higher aerobic capacity throughout the lifespan compared to Americans. In late life, this equates to Norwegians having a substantial 2-MET benefit (~30 % reduction in relative risk of death) compared to average Americans, which likely translates to an overall greater health status [9, 13]. Although genetics play a role in VO_2max, physical activity differences between these two countries appear to be the cause of the large discrepancies seen in aerobic capacity [14, 15], suggesting an equal or greater potential benefits of long-term exercise regimens as done by masters athletes.

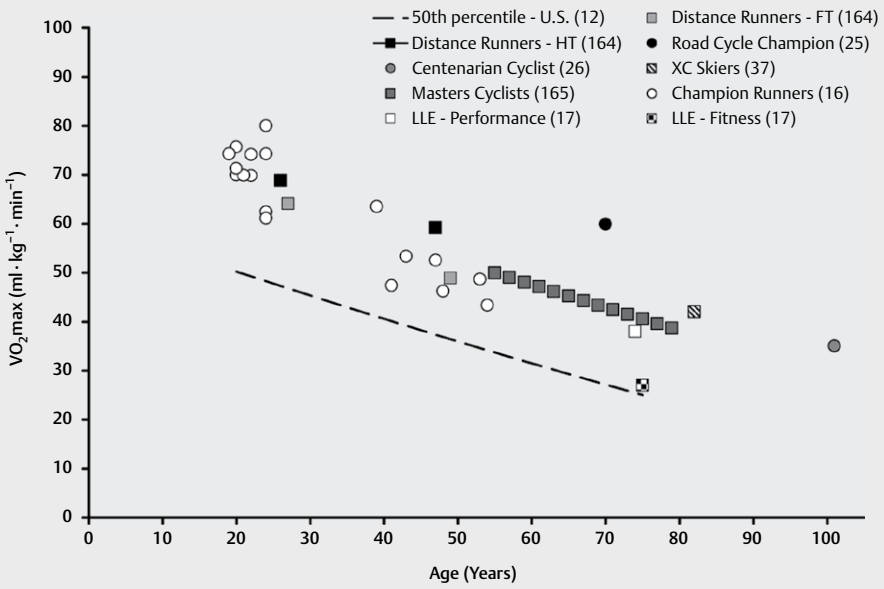
Following up on the effects of aging and VO_2max by Sid Robinson, David Bruce Dill and colleagues of the Harvard Fatigue Lab led an investigation reviewing aerobic capacity in former male champion runners through various follow-ups for ~50 y [16]. These athletes, particularly those who continued exercising at a high-intensity, had VO_2max values 20–45 % above average for their age [12, 16]. Maintaining a high-level of exercise intensity has similarly been shown to confer greater benefits compared to those who trained recreationally (VO_2max = 38, 27, and 22 ml kg^{-1} min^{-1} in ~75 y lifelong performance trained, lifelong fitness trained, and age-matched non-exercisers, respectively) [17].

Overall, masters athletes have a decrease in their VO_2max of 5–12 % per decade [18–21]. This rate of decline has been suggested to be similar or even greater than during sedentary aging [20–22]. However, this equal or greater rate is most likely due to the higher beginning value (often > 65 ml kg^{-1} min^{-1}) and/or decreases in training volume. Several investigations have shown similar rates of decline among male and female masters athletes (males: 0.5–2.4 % y^{-1}; females: 1.0–4.6 % y^{-1}) [21–23]. Even though the rate of decline may be similar, masters athletes will remain above the frailty threshold until later in life as 70 y to 79 y masters athletes maintain a higher VO_2max by ~50 % compared to age-matched sedentary individuals [17]. The enhanced VO_2max in these athletes minimizes their risk of morbidities and mortality and is a key factor in their impressive athletic achievements [6, 8, 9].

Case studies have allowed for analysis of impressive VO_2max values in masters athletes. Of note, Wally Hayward, a 70 y ultra-distance runner, recorded a VO_2max of 56.8 ml kg^{-1} min^{-1} weeks after running 3:06:24 at the 1979 Johannesburg marathon [24]. This VO_2max was then bested (59.9 ml kg^{-1} min^{-1}) by a similarly aged cyclist who completed a 16.1-km time trial in 26:51 just prior to testing [25]. This 70 y cyclist also completed a 3400-mile cycle ride from California to Canada in 34 days one month prior to testing. Another noteworthy case study was on a centenarian cyclist who increased his VO_2max from 31 to 35 ml kg^{-1} min^{-1} from the ages of 101 y to 103 y by increasing his training intensity [26]. This individual also broke the centenarian record for the distance covered in one hour of cycling (26.9 km). These remarkable athletes help demonstrate that although aging results in an inevitable impairment in physiological health, exercising at high-levels and producing impressive performances is still possible with advancing age. These masters athletes, along with other publications on elite masters athletes across various endurance sports, are compared to the 50th percentile of the population in the United States in ▶ **Fig. 1**. These data represent a "gold standard" for VO_2max values across the lifespan as these athletes have ~50 % greater VO_2max values compared to average Americans.

Cardiac Output

A.V. Hill initially suggested and was later supported, that VO_2max was centrally limited by the ability to deliver oxygenated blood to the exercising muscles (cardiac output) [27, 28]. The relationship between VO_2max and cardiac output is linear in that every 1-L increase in absolute VO_2, there is a ~5.5-liter increase in cardiac output [29, 30]. Proctor et al. showed this linear relationship did not change with young and old age groups and further supports the strong relationship of VO_2max and cardiac output [30]. Ogawa et al. reported that maximal cardiac output was ~22 % smaller in old (60–72 y) compared to young (20–31 y) in both males (21.2 to 16.3 L min^{-1}) and females (15.2 to 11.9 L min^{-1}) [31]. In compari-



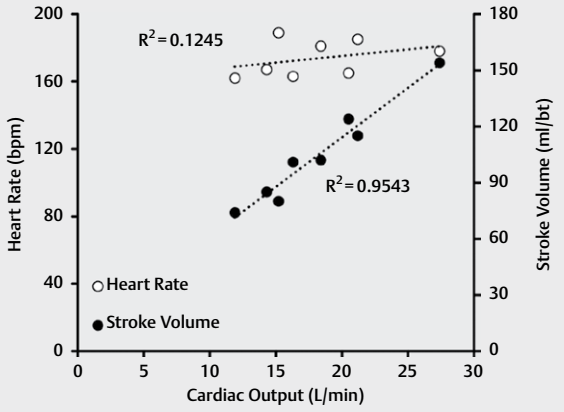
▶ **Fig. 1** Relative VO_2max values of elite-male masters athletes compared to the 50th percentile of males in the United States (U.S.) [12]. Circles represent individual data points where squares represent averages for the respective group [16, 17, 25, 26, 37, 169, 170]. HT, Highly Trained; FT, Fitness Trained; XC, Cross Country; LLE, Lifelong Exercisers (mixed aerobic exercise modes).

son, trained older subjects (59–72 y) had a ~25 % larger cardiac output (20.5 L min^{-1} and 14.3 L min^{-1} in male and females, respectively) compared to age-matched non-exercisers and were similar to untrained individuals ~40 y younger [31]. The relatively high cardiac output translates to greater VO_2max values and likely one of the core contributors of their remarkable performances.

Maximal cardiac output is a function of maximal heart rate (HR_{max}) and SV. HR_{max} appears to decrease at a rate of 0.6–0.8 beats per minute (bpm) y^{-1} regardless of sex as indicated in large-scale investigations [12, 23, 32]. In contrast to the effects of aging, there are conflicting reports of whether lifelong exercise can slow down the age-related decline in HR_{max}. Several studies suggest that the age-related decline in HR_{max} is independent of habitual exercise status and therefore cannot be attenuated with exercise training [22, 31–33]. Contrary to these data, others have shown statistically greater HR_{max} values in masters athletes compared to age-matched sedentary individuals [34–36]. Comparing elite octogenarian athletes, Trappe et al. reported HR_{max} values ranging from 134 to 181 bpm in the athlete group, which included a 91 y former Olympian with a HR_{max} of 169 bpm (~40 bpm greater than expected) [37]. However, the masters athletes were not statistically different from the age-matched sedentary controls, as a large variability was present within the groups. Gries et al. reported ~75 y male lifelong exercisers who trained at high levels for competition had a greater HR_{max} (167 bpm) compared to those who trained for recreational purposes (138 bpm) [17]. Along with an effect of lifelong exercise intensity, Gries et al. also reported potential sex differences as lifelong exercising females may preserve their HR_{max} to a greater extent than lifelong exercising males. Together, the conflicting data suggest a need for more research to determine if lifelong exercise does indeed attenuate the age-related decline in HR_{max} with a specific focus on the influences of sex and exercise training intensity.

Along with the deleterious effects of aging on HR_{max}, SV also appears to be negatively affected as a result of aging. Ogawa et al. reported a 12 % and 8 % lower SV in older males and females compared to sex-matched younger cohort [31]. Using a cross-sectional analysis approach, cardiologist Ben Levine and colleagues comprehensively characterized the effects of aging on ventricular function and demonstrated significant decreases in size and compliance of the left ventricle beginning in mid-life (~50 y) and accelerating in late life (≥ 65 y) [38, 39]. The compromised left ventricular compliance appears to be related to fewer cardiomyocytes and an increase in fibrotic tissue with age [40]. These negative alterations likely result in a diminished end diastolic volume, greater end systolic volume, and consequently a decreased SV. Together with the linear decline in HR_{max}, these data suggest a curvilinear decrease in cardiac output and thus help explain the greater decline in VO_2max with advanced age.

Exercise across the lifespan appears to partially counteract the decline in SV as Ogawa et al. reported the SV of trained elderly athletes were 15–25 % greater than age-matched sedentary subjects [31]. Using a similar cross-sectional approach as previously mentioned, Ben Levine and colleagues sought to determine the effects of lifelong exercise on SV mechanics by comparing elderly sedentary individuals to various groups of elderly males and females who exercised for at least 25 y (casual, committed and masters athletes) [33, 41]. Carrick-Ranson et al. reported elderly who exercised ≥ 4 days per week (committed and masters athletes) had significant benefit in SV compared to the casual (< 4 days per week) and sedentary groups [33]. Masters athletes who trained 6–7 days a week and participated in competitive events (i. e. potentially greater intensity) had an even greater SV compared to the other groups, like-



▶ **Fig. 2** The relationship between maximal heart rate and stroke volume on maximal cardiac output in trained and untrained, male and female, and young (~25 y) and elderly (~63 y) populations [31]. Regression analysis reveals stroke volume has a greater influence on cardiac output than maximal heart rate, regardless of age, training status, or sex.

ly due enhanced total blood volume and left ventricular function. The larger SV in the masters athletes may help explain the greater preservation of VO_2max in these individuals with greater exercise intensity as previously mentioned [16, 17].

Together with the HR_{max} data, ▶ **Fig. 2** shows a strong correlation between SV and cardiac output, while the relationship between HR_{max} and cardiac output is fairly weak, regardless of age, training status, and sex. Given the inconclusive data on the effects of lifelong exercise on HR_{max}, it appears the benefits from lifelong exercise on cardiac output are mostly due to enhanced SV. While sex differences in cardiovascular dynamics as a result of age and lifelong exercise have been suggested [17, 42, 43], future research is needed to understand the mechanism of these potential sex differences across the lifespan.

Arterial and Mixed Venous Oxygen Difference (a-vO_2diff)

Following the ejection of oxygenated blood from the left ventricle to the systemic circulation, oxygen is extracted by metabolically active tissue and then returns to the right atrium through the venous system. The difference between the arterial and venous oxygen content is defined as a-vO_2diff. Investigations report a minor decrease in maximal a-vO_2diff from ~15 to 13 ml O_2/100 ml of blood in young and older males, respectively and ~14 to 12 ml O_2/100 ml of blood in young and older females, respectively [31, 44]. Conversely, other studies suggest no change, potentially due to the small sensitivity and large variability across the lifespan [45, 46]. Regardless, several masters athletes (~70 y) investigations suggest that these athletes were similar to young and had greater a-vO_2diff than sedentary age-matched individuals [31, 33, 44]. These data, collectively with cardiac output, suggest that while there may be a slight decrease of a-vO_2diff, the age-related decrease in VO_2max is most likely due to diminished cardiac output, primarily as a result of decreased SV. Masters athletes, in turn, have remarkable VO_2max values (~50 % greater than age-matched sedentary) mostly due to their adaptations to preserve SV, with mixed evidence on HR_{max} and a-vO_2diff.

Skeletal Muscle Metabolic Fitness

Skeletal muscle metabolic fitness (capillarization and mitochondrial function) is mainly responsible for the diffusion of oxygen and carbon dioxide, transport of cytokines and nutrients, as well as energy production (adenosine triphosphate, ATP). With aging, there appears to be a ~25 % loss in capillary density (capillaries mm^{-2}), capillary/fiber ratio, and capillaries in contact with each muscle fiber (CCEF) between young (~25 y) and old (~64 y) males and females [47, 48], primarily affecting the fast fibers [49, 50]. Skeletal muscle perfusion is vital for the transportation of metabolic substrates and cytokines, which may be useful for performance as well as decreasing their risk of morbidities such as peripheral artery disease [51] and non-insulin dependent diabetes mellitus [52, 53].

Chronic exercise training in masters athletes appears to fully preserve capillarization [17, 50, 54, 55]. By comparing masters runners (63 y) to performance matched young runners (26 y), Coggan et al. found similar capillary density between the groups [54]. Pollock et al. also reported similar capillarization in masters cyclists between 55–70 y [56]. Furthermore, lifelong exercising males and females, regardless of intensity (performance vs. fitness), had similar skeletal muscle capillarization than those ~50 y younger [17]. Together, these studies suggest skeletal muscle capillarization can be preserved with lifelong aerobic exercise, regardless of sex and intensity.

Skeletal muscle metabolic fitness also includes both aerobic and anaerobic metabolic enzyme activity. During the aging process, aerobic enzyme activity declines (e. g. citrate synthase, CS; succinate dehydrogenase, SDH; and 3-hydroxyacyl-CoA dehydrogenase, β-HAD) [47, 50, 57, 58]. The decrease in aerobic enzyme activity appears to be due to the loss of mitochondrial content and function [59, 60]. On the other hand, anaerobic enzyme activity (e. g., glycogen phosphorylase, phosphofructokinase, and lactate dehydrogenase) is more variable across the lifespan [47, 58, 61]. In a fiber type-specific manner, Murgia et al. suggested that aging results in fast fibers having a decrease in both oxidative and glycolytic function, while slow fibers shift from oxidative to glycolytic [58]. The fiber type-specific data supports the variability of anaerobic enzymes compared to the ubiquitous decrease in aerobic enzyme function during the aging process.

Along with skeletal muscle perfusion capabilities, chronic exercise training appears to preserve aerobic enzyme capacity [50, 54, 57, 62]. Trappe and Costill showed that greater training in former elite runners (running 69 km wk^{-1}) resulted in elevated aerobic enzyme capacity (CS and SDH) than the former elite runners who trained at a lower amount (running 39 km wk^{-1}) [55]. This positive relationship with training volume and aerobic enzyme capacity has been similarly found in masters cyclists [56]. Conferring the significant influence of training volume on skeletal muscle aerobic metabolic fitness, lifelong exercising males and females had similar aerobic enzyme function (CS and β-HAD) regardless of training intensity (performance vs. fitness) [17]. Therefore, it appears that skeletal muscle aerobic metabolic fitness can be preserved by main-

taining a relatively high volume of endurance exercise, which likely improves endurance performance and mitigates risk of metabolic morbidities in these veteran athletes.

Whole Muscle Size and Function

Muscle mass is critical for older adults to preserve VO_2max [63–65], metabolic rate [66], muscle strength and power [67, 68], and serves as a protein reservoir for amino acid metabolism [69]. The latter role, serving as a protein reservoir, has been stated as "under-appreciated" in a classic 2006 review by Robert Wolfe [69]. Wolfe states in this review, "… altered muscle metabolism plays a key role in the genesis, and therefore the prevention, of many common pathological conditions and diseases." Older adults who are able to mitigate the age-related loss of muscle mass and function as a result of primary aging (i. e., sarcopenia) have a lower risk of mortality from acute infections [70], more favorable outcomes during hospitalizations [71], and likely better functional measures from diseases including cancer and heart failure [72–74].

Muscle Mass

Skeletal muscle accounts for ~40 % of total body mass, peaking early in adult life (30–40 y) and then decreases throughout the lifespan [75–77]. Females appear to have a lower rate of decline (~0.8 kg decade^{-1}) than males (~1.5 kg decade^{-1}), with both sexes having a more precipitous decrease after the age of 70 y [76, 78, 79]. In relative terms, a comprehensive review by Mitchell et al. suggested that aging results in 0.8–1.3 % and 0.5–0.8 % muscle loss per year in males and females, respectively [80]. Caution must be given while comparing different muscle groups as not all muscle groups age similarly [78, 80, 81]. As the knee extensors (i. e., quadriceps) are a commonly studied muscle group, unless noted, they will be the focus of this review.

Whole muscle atrophy during aging appears to be a function of both fiber loss and fiber atrophy [82–84]. Using male cadavers between the ages of 15 y and 83 y, Lexell et al. suggested that the loss of fiber number begins at ~25 y and accelerates thereafter, resulting in a loss of ~50 % of muscle fibers from the 3rd to 9th decade of life (▶ **Fig. 3**). The loss of muscle fibers appears to be the primary cause of muscle atrophy until ~70 y, in which fiber atrophy, specifically fast fibers, becomes more pronounced [82]. However, given the difficult nature of directly counting muscle fibers *in vivo*, fiber number is often estimated through measurements of whole muscle and single muscle fiber size.

In contrast to sedentary aging individuals, masters athletes that continue moderate to vigorous exercise across various sports require muscle mass and strength to propel them forward (i. e. running, swimming, cycling) or to move as much weight as they can (i. e. weight lifting, powerlifting). To assess muscle mass in these aging athletes, magnetic resonance imaging (MRI) is considered the current gold standard [85]. Prior to MRI development and widespread use, computed tomography (CT) was utilized, and more recently dual energy x-ray absorptiometry (DEXA) has been implemented to assess lean body mass. Using MRI, Chambers et al. reported male lifelong aerobic exercisers in their 70's had ~50 % greater quadriceps size than age-matched non-exercisers, while no benefit was observed with greater intensity (performance vs. fitness) of lifelong exercise or in lifelong exercising females [65]. Wroblewski et al. reported masters athletes aged 40 y to 69 y had similar quadriceps size (MRI), while veteran athletes > 70 y had lower muscle mass than younger masters athletes [86], suggesting aerobic exercise training delayed the loss of muscle mass until 70 y. Similarly, Crane et al. reported higher leg-lean mass (DEXA) in young (31 y) and middle-age (53 y) masters athletes compared to age-matched sedentary, while older (72 y) masters athletes were similar to their respective age-matched sedentary cohort [87]. Tarpenning et al. also reported lean body mass (DEXA) was similar in run-trained groups up to mid-life (40–69 y), however lean body mass began to decline after age 70 y [88].

While lesser is known on the effects of lifelong strength training on muscle mass, several investigations have reported hypertrophy with strength training programs (12-wks to 1 year) in > 60 y males and females [89–93]. Masters strength athletes (68 y) who had been training for the last 12–17 years had 18 and 29 % larger quadriceps femoris and elbow flexors, respectively, compared to age-matched non-exercisers and were similar to untrained young individuals (28 y) [94]. While less is known on the effects of muscle mass in lifelong strength trained athletes, these data suggest strength training is a potent modality to enhance and/or preserve muscle mass during the aging process. Whereas endurance training appears to augment muscle mass particularly in early and mid-life, the data are mixed if endurance focused masters athletes can fully preserve muscle mass through late-life.

Intermuscular Adipose Tissue

Often included in muscle size measurements is intermuscular adipose tissue (IMAT). IMAT is accumulated adipose tissue beneath the fascia of skeletal muscle and in between muscle groups [95]. IMAT infiltration of the skeletal muscle of the thigh appears to increase as a result of aging by 116 % and 162 % in males and females, respectively [65]. This age-related IMAT accumulation was attenuated by ~50 % in lifelong aerobic exercising males and females, with additional benefits as a result of greater intensity (performance vs. fitness) of exercise training [65]. The decreased IMAT content in these veteran athletes is likely due to the enhanced lipid oxidation and regulation that is associated with aerobic exercise [96–99]. Given IMAT is related to several co-morbidities including insulin resistance, cardiovascular disease, and several other skeletal muscle impairments [100, 101], the lower IMAT content with chronic exercise training likely has large metabolic health and functional benefits for these lifelong exercisers.

Muscle Function

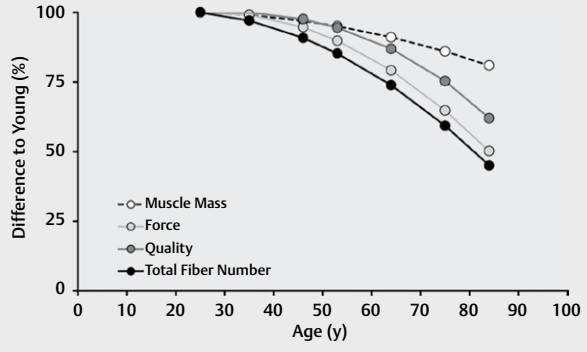
Muscle function is often measured via maximal voluntary contraction (MVC; strength) and/or maximal power. Along with the age-related loss of muscle mass, muscle function decreases beginning at ~40 y at a rate of 2–5 % y^{-1} [80, 102]. The loss of function is 2–5-fold greater than the loss of muscle mass potentially due to the infiltration of connective tissue and the aforementioned IMAT [103–105], neuromuscular recruitment impairments [106, 107], and alterations within the muscle fiber [84, 108–110]. Muscle quality (function per unit size), subsequently, also decreases throughout the lifespan, albeit less than the loss of function [79, 83, 102]. Together, muscle function, size, and quality (function/size), all appear

to decline at different rates (function > quality > mass) during the middle to late life as an effect of primary aging, resulting in diminished functional independence and overall health (▶ **Fig. 3**).

Muscle strength in masters athletes appears to be enhanced by 15–50 % compared to elderly non-exercisers, while muscle power (function of strength and speed) is varied [65, 94, 111]. The discrepancies between strength and power are likely a result of neuromuscular and/or fiber type adaptations which will be discussed in further detail below. Klitgaard et al. and Aagard et al. reported masters runners (~70 y) had ~30 % greater knee extensor strength than age-matched sedentary [94, 111]. Additionally, Tarpenning et al. reported masters runners in age groups from 40 y to 69 y had similar knee extensor strength, which then decreased in masters runners > 70 y [88]. Endurance training was also able to decrease the expected rate of strength loss in athletes up 81 y [86].

Masters strength athletes (68 y) exhibited 72 and 38 % more strength in the knee extensors and elbow flexors, respectively, compared to age-matched control and were similar to untrained subjects ~50 y younger [94]. Likewise, Aagard et al. reported ~70 y strength trained lifelong exercisers were ~25 % stronger than age-matched untrained individuals [111]. While age-matched endurance athletes had similar strength measurements as the strength-trained group, the strength-trained athletes had a greater rate of force development compared to both endurance and untrained group. Together, these studies suggest strength training throughout the lifespan increases muscle strength and rate of force development compared to elderly non-exercisers which may be beneficial for preserving whole muscle power and various aspects of muscle metabolic health (e. g., amino acid reservoir).

It appears that more studies are needed to tease out the influence of aging, sex, and lifelong exercise on skeletal muscle size and function as the data are varied. Muscle size and function adaptations are likely mode-specific, therefore making these comparisons difficult, particularly as lifelong exercisers may switch training modes throughout their life. Strength training across the lifespan appears to be more beneficial for preserving muscle mass and function than endurance exercise, however more research is needed. Further, these investigations had methodological differences in measuring muscle size and function, thus compromising the ability to synthesize the data. While there does appear to be some benefit to muscle mass and function, the decrease in IMAT in lifelong aerobic exercisers may suggest an aerobic phenotype that may contribute to an enhanced endurance performance and overall health. To qualitatively visualize the effects of lifelong exercise on muscle size and adiposity, ▶ **Fig. 4** shows MRI images of a young exerciser (25 y), as well as a lifelong exerciser and an age-matched non-exerciser in their 70's.



▶ **Fig. 3** The relationship of leg muscle mass (kg), peak torque of knee extensors (Nm), and muscle quality (Nm/kg leg muscle mass) in males [102]. Leg muscle mass was measured via Dual X-Ray Absorptiometry (DXA). Peak torque of the knee extensors was measured via isokinetic dynamometer at an angular velocity of 0.52 rad/s. Total fiber number was estimated using the vastus lateralis of human cadavers as previously described [82].

Single Muscle Fiber Size, Distribution, and Function

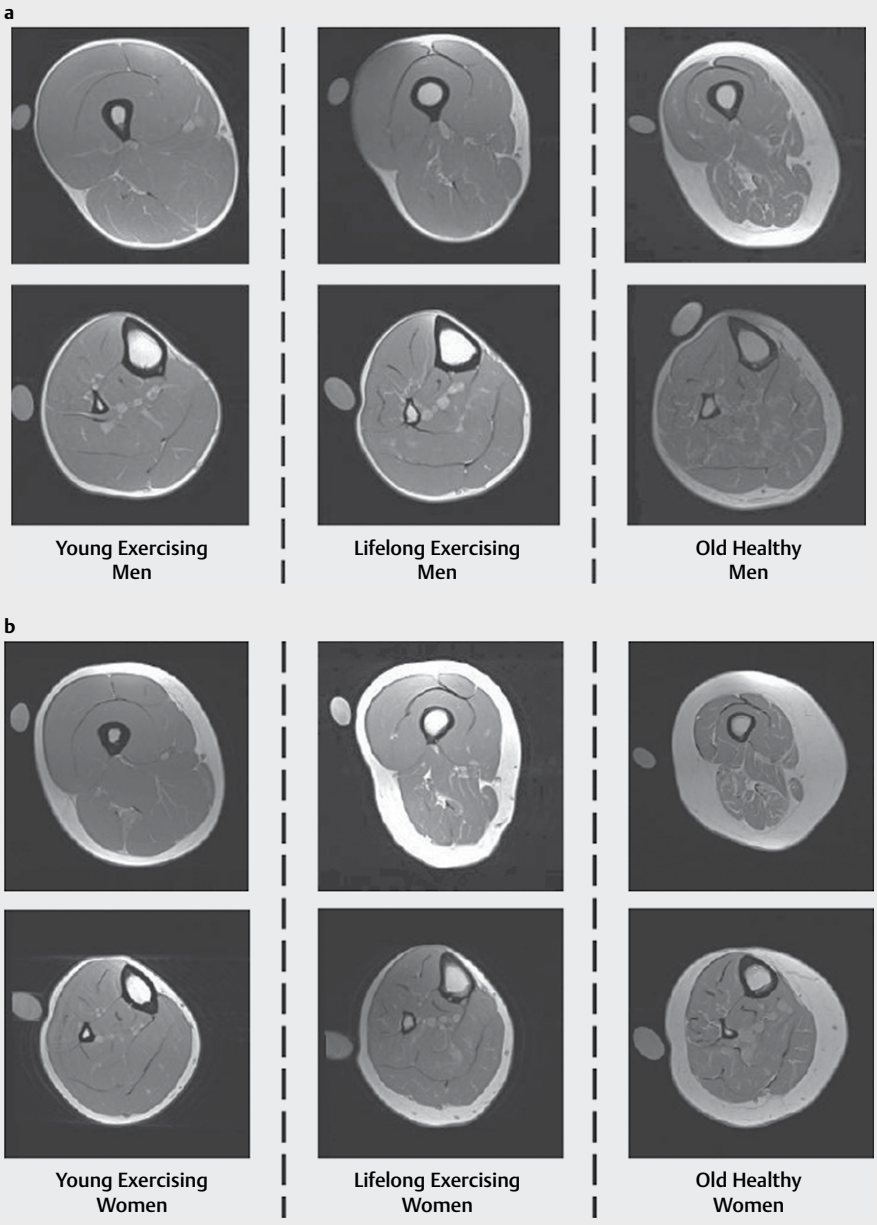
The loss of muscle function is 2–5-fold greater than the loss of muscle mass during aging, resulting in a decreased muscle quality across the lifespan. This relationship between whole muscle size and function suggests an intrinsic effect of aging within the muscle that may be due to, at least partially, the deterioration and dysfunction of contractile units (muscle fibers).

Single Muscle Fiber Size

As previously suggested by Lexell et al., a main contributor to the loss of whole muscle size during aging is muscle fiber atrophy, predominantly the fast fibers [82]. Studies which investigated the effects of aging and fiber size using the mATPase histochemistry approach are shown in ▶ **Table 1** and summated in ▶ **Fig. 5**. Collectively, these studies confer that aging results in atrophy of the fast fibers at ~40 y, while slow fibers remain relatively stable. The rate of fast fiber atrophy appears to increase significantly after the age of 70 y. While these studies are in males, females appear to follow a similar trend [83, 112]. These declines are further supported by measuring fiber size through single muscle fiber isolation techniques [84, 110, 113].

Contrary to these cross-sectional studies, a novel longitudinal study by Aniansson et al. measured the muscle morphology within the same cohort three times over an 11 year span during the critical age range of 69 y to 80 y and reported hypertrophy of the slow fibers from ages 76 y to 80 y [114]. The authors suggested that due to aging, there was a decrease in number of motor units and muscle fibers. As the subjects remained active, they had a greater relative amount of activity per motor unit which contributed to the hypertrophy of the slow muscle fibers. Using the single muscle fiber technique, Frontera et al. also showed hypertrophy of fast fibers in a 9 y longitudinal study in the elderly (71 y to 80 y) [115]. These data further suggest hypertrophic plasticity within these fibers are possible by remaining active.

Studies of male masters athletes measuring fiber size are shown in ▶ **Table 2** (mATPase) and ▶ **Table 3** (single fiber analysis). By comparing masters runners (63 y) to performance-matched young runners (26 y), Coggan et al. reported the masters runners had 25 % and 19 % larger slow and fast fibers, respectively [54]. The benefits of run-training on fiber size was also shown by Tarpenning et al. who suggested running preserved fast fiber size until the age of 70 y [88]. While these studies support the notion that masters runners have enhanced fiber size, others reported no benefit in slow



▶ **Fig. 4** Representative Magnetic Resonance Imaging (MRI) images for men (A) and women (B) of the upper leg (top) and lower leg (bottom) of a young exerciser, lifelong exerciser, and old healthy non-exerciser. Figure adapted with permission from Chambers et al. [65]. [rerif].

fiber size of old (79 y) elite track and field athletes [116], and a ~17 % smaller slow and fast fibers in middle-aged (44 y) elite masters runners compared to age-matched controls [117]. The divergence of fiber size in runners is similarly seen in young runners as novice marathon training decreased slow and fast fiber size [118], while young competitive runners had ~20 % larger slow and fast fibers than recreational runners [119]. Therefore, these discrepancies are likely a result of years of training and competitive focus (i. e., intensity) to optimize muscle size and metabolic efficiency.

Due to orthopedic limitations and changing interests, masters athletes commonly transition to different modes (e. g., run to cycling). By comparing mixed-mode masters athletes to age-matched non-exercisers, large discrepancies are apparent as studies report 12 % smaller [111], no change [120], and 25–40 % larger [50, 94, 121, 122] slow fiber size. Fast fiber size appears to be generally the same size as age-matched non-exercisers [50, 94, 111, 120, 121], while Dubé et al. reports ~40 % larger fast fibers in the endurance trained group [62]. While the discrepancies of these studies are unknown, it is likely at least partly due to the varying exercise training modalities throughout the lifespan. As previously stated, running appears to have a minimal effect on fiber size in late life. Conversely, cycling may have a greater hypertrophic response as 12-weeks of cycle training increased slow fiber by 16 % [123] and has also been positively correlated with cycling volume in masters athletes [56]. Cycling and running also have varying recruitment patterns which often results in cycling investigations including samples from the

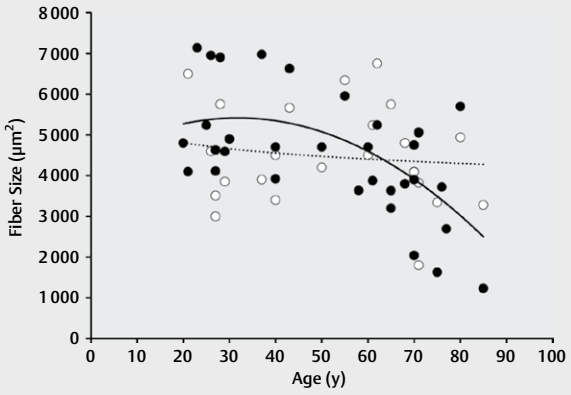
▶ **Table 1** Fiber size during aging using mATPase histochemistry technique in males.

Citation	Muscle Biopsied	Age (y)	Fiber Area (μm²)		Fiber Type (%)	
			Slow	Fast	Slow	Fast *
Larsson et al. 1978 [165]	VL	26	5666	6953	41	59
		37	6344	6975	37	63
		43	6754	6627	48	52
		55	5941	5954	52	48
		62	5591	5243	55	45
Essén-Gustavsson and Borges, 1986 [106]	VL	20	4500	4800	57	43
		30	4200	4900	60	40
		40	4500	4700	49	51
		50	4100	4700	59	41
		60	4600	4700	60	40
		70	3900	3900	62	38
Aniansson et al. 1980, 1986 [108, 169–170]#	VL	70	4940	4750	48	52
		76	4530	3720	52	48
		80	5970	5700	53	47
	BB	77	4500	6060	51	49
		80	6030	8090	51	49
Poggi et al. 1987 [167]	VL	40	3343	3923	35	65
		65	3280	3631	64	36
		75	1800	1629	70	30
		85	1484	1230	75	25
Jakobsson et al. 1988 [171]	TA	29	3950	8070	76	24
		70	4050	5700	84	16
Lexell and Taylor 1991 [166]	VL	27	3855	4113	N/R	N/R
		77	3609	2696	N/R	N/R
Coggan et al. 1992 [46]	Gas	26	4696	5960	59	41
		64	4770	5193	60	40
Proctor et al. 1995 [49]	VL	25	3855	5238	40	60
		58	3510	3638	41	59
Fayet et al. 2001 [172]	Del	55	2902	3440	42	58
		64	2315	3135	49	51
		74	2524	3327	55	45
Klein et al. 2003 [173]	BB	21	4384	5229	48	52
		82	3883	3976	41	59
Ryan et al. 2006 [47]	VL	21	3500	4100	48	52
		65	3400	3200	55	45
Verdijk et al. 2007 [168]	VL	20	5589	6126	43	57
		76	5471	4451	53	47
Nilwik et al. 2013 [174]	VL	23	6500	7136	44	56
		71	5750	5050	44	56

* Fast fiber type included type IIa and IIx where applicable. #Longitudinal investigation. VL, Vastus Lateralis; BB, Biceps Brachii; Gas, Gastrocnemius; Del, Deltoid; N/R, Not Reported.

vastus lateralis, while running studies commonly utilize the gastrocnemius. Nevertheless, the differing mode and muscle specific adaptations demonstrate the vast adaptability of muscle fibers in a sport specific manner [124]. Additionally, slow fibers appear to be more responsive to habitual endurance training than fast fibers, suggesting the potential need for more explosive training (i. e., strength training, high-intensity intervals, plyometrics).

As the aforementioned studies were completed in males, less is known about the effect of lifelong exercise on fiber size in females. Pollock et al. measured fiber size in a cohort of females 55 y to 79 y who continued to cycle on average 551 km month^{-1} [56]. Upon comparing these data to the sedentary subjects in the Essén-Gustavsson et al. investigation, the slow fibers in female masters athletes ranged from similar to ~80 % larger, while fast fibers appeared similar to untrained elderly females [112]. Gries et al. reported similar slow and fast fiber size between mixed-mode aerobic lifelong exercise and age-matched non-exercisers [125], further suggest-



▶ **Fig. 5** Slow and fast fiber size in males across the lifespan. These data include average slow and fast fiber size in the vastus lateralis of male cohorts presented in ▶ **Table 1** [48, 50, 94, 112, 114, 122, 171–174].

ing limited benefit in fast fiber size with habitual endurance exercise in females.

Single Muscle Fiber Distribution

The dramatic changes in size and number of fast fibers have significant whole muscle implications as these fibers are 5–10 times more powerful than slow fibers [84, 110, 121, 125, 126]. mATPase staining suggest a greater slow fiber phenotype as a result of atrophy of the fast fibers (▶ **Table 1**). Using the more sensitive SDS-PAGE fiber typing technique, the muscle appears to undergo an age-related slow-to-fast transition with an increase in hybrids (muscle fibers containing multiple fiber type isoforms) [116, 127]. In order to compensate for losses in whole muscle size, overall fiber distribution shifts from slow-to-fast fiber type may be an attempt to preserve whole muscle performance and related to the apoptotic pathways of the muscle fiber as seen with periods of unloading (i. e. space flight or bedrest), and even further pronounced in those with spinal cord injury [128–132]. Although this slow-to-fast distribution shift may help with muscle power, as described earlier, a high proportion of fast fibers alters the metabolic profile and is correlated with obesity and insulin resistance [53, 133].

As primary aging results in a slow-to-fast fiber type distribution shift, lifelong exercise appears to result in a slight shift towards slow fiber type distribution (▶ **Table 2**). This slow fiber phenotype appears prominently in elite masters runners who had 73 % and 23 % slow and fast fiber distribution, respectively, compared to the sedentary group who had 51 % and 31 % slow and fast fiber distribution, respectively [117]. This difference is similar in age-group world record holder track and field masters athletes, who had a greater slow fiber distribution (53 %) than age-matched sedentary individuals (35 %) [116]. Masters athletes also have less hybrid fibers compared to the age-matched sedentary controls (~8 % vs. ~22 %, respectively) [116, 117, 121, 125], which is in agreement with what is typically seen in young endurance athletes [119]. While aerobically trained masters athletes likely had more slow fibers to begin with [134], these data suggest that habitual endurance exercise may stabilize or increase the slow fiber distribution and minimize the hybrid fiber population.

Single Muscle Fiber Function

The single muscle fiber technique allows for measurements of fiber performance similar to whole muscle measurements (strength, speed, and power). A key advantage of this approach is that it eliminates the central nervous system (i. e., motivation), neuromuscular system, energetics, and calcium mechanics to tease out alterations within the actin and myosin cross-bridge interaction that are not attainable with whole muscle measurements. When combined with single fiber SDS-PAGE, fiber type specific contractile function can be attained providing insight into performance in slow and fast muscle fibers [126, 135].

As aging primarily impacts the size of the fast fibers, several studies have shown a decline (20–50 %) in fast muscle fiber force [84, 110, 121, 125, 136]. Initial aging profiles for contractile velocity reported a decline [137], but when habitual activity was accounted for, it appears that contractile velocity is maintained throughout the lifespan in both slow and fast muscle fibers [84, 110, 121, 125]. Fiber power is an integrative measure of force and velocity that generally declines (25–50 %) in fast fibers and appears primarily driven by the smaller size and force of these fibers [84, 110, 121, 125]. In contrast to the decrements in fast muscle fiber function with age, slow muscle fiber performance (force and power) is generally preserved with aging [84, 110, 121, 125]. The decline in performance of the fast muscle fibers has significant implications for whole muscle function due to their ability to produce 5–10 times more power than slow fibers [84, 110, 121, 125, 126]. Thus, the loss of fast muscle fibers combined with the reduced power of the remaining fast muscle fibers results in a substantial reduction in quicker more explosive movements at the whole muscle level that increase the risk of falls and subsequent injuries.

Additional insight into aging muscle at the myocellular level can be assessed by normalizing power to myofiber volume, which provides an integrated performance index incorporating quantitative and qualitative aspects of contractile function. Normalized power of fast muscle fibers is maintained or improved with advanced age [108, 138]. The enhanced fast fiber muscle quality with age is theorized to be a "survival of the fittest" phenomenon [108], that as muscle fiber number decreases with age, as suggested by Lexell et al. [82], the healthiest fibers may survive. As atrophy of these healthy fibers occurs, they adapt to produce a relatively greater power due to an increased relative number of cross-bridges and/or an increased myocellular lattice stiffness [108, 139]. While quality of fast fibers appears to improve with advanced age, the quality of slow fibers is largely unaffected, likely due to the preservation of fiber size [84, 110, 121, 125].

Although numerous investigations have reported beneficial effects of short-term resistance and aerobic training on single fiber function in the elderly [89, 93, 123, 138, 140, 141], few investigations have assessed single muscle fiber function in masters athletes. Initial work in this area was published 25 years ago from Widrick et al. that compared elite middle-aged male masters athletes (44 y; VO_2max: 58 ml kg^{-1} min^{-1}) to age-matched non-exercisers (42 y; VO_2max: 40 ml kg^{-1} min^{-1}) [117, 142]. These masters athletes consisted of former elite runners, including one sub 4-min miler and

▶ **Table 2** Fiber size of male masters athletes using mATPase histochemistry technique.

Citation	Muscle Biopsied	Training Mode	Age (y)	Fiber Area (μm²)		Fiber Type (%)	
				Slow	Fast	Slow	Fast *
Coggan et al. 1990 [53]	Gas	CYR	28	4658	4658	73	27
		MYR	26	4346	4346	60	40
		Run	63	5815	5336	60	40
Klitgaard et al. 1990 [88]	VL	Swim	68	3900	4500	57	43
		Run	69	4000	4200	70	30
		Strength	70	5200	5800	44	56
		UT	68	3000	3800	57	43
	BB	Swim	68	4800	5900	57	43
		Run	69	5000	6000	56	44
		Strength	70	5100	9200	N/R	33
		UT	68	4600	5700	52	48
Trappe et al. 1995 [54]	Gas	HI - Run	47	6595	6014	77	23
		FIT- Run	50	N/R	N/R	62	38
		UT-Formers Run	49	N/R	N/R	65	35
Proctor et al. 1995 [49]	VL	Endurance	25	4292	5082	61	39
			57	4424	3465	64	36
Tarpenning et al. 2004 [87]	VL	Run - 51 km/wk	46	4857	4578	50	50
		Run - 45 km/wk	54	5905	4467	51	49
		Run - 44 km/wk	62	6363	4869	48	52
		Run - 27 km/wk	75	4857	4359	50	50
Aagard et al. 2007 [105]	VL	Endurance	72	5072	4844	69	31
		Strength	74	6300	6786	59	41
		UT	71	5753	5068	50	50
Sundstrup et al. 2010 [114]	VL	Soccer	70	5389	5013	53	47
		UT	71	5753	5068	50	50
Zampieri et al. 2015 [116]	VL	UT	27	3825	4630	50	50
		Mixed	70	2998	2779	69	31
		UT	70	2357	2042	54	46
Dubé et al. 2016 [61]	VL	Endurance	28	4400	3800	62	38
			65	4500	2700	75	25

*Fast fiber type included type IIa and IIx where applicable. VL, Vastus Lateralis; BB, Biceps Brachii; Del, Deltoid; Gas, Gastrocnemius; CYR, Competitive Young Runner; MYR, Performance Matched Young Runner; MA, Masters Athlete; HI, Highly trained; FIT, Fitness Trained; UT, Untrained; N/R, Not reported.

five subjects who ran a marathon under 2:30:00 (three under 2:15:00). Although training volume declined since these times were achieved, these veteran athletes continued to run an average of 77 km wk^{-1}. The slow and fast muscle fibers from these veteran runners were smaller, weaker, and less powerful compared to age-matched non-exercisers. In contrast, contractile speed was elevated (slow and fast fibers) in the runners, but not enough to compensate for the decline in force to preserve power. A higher contractile velocity in the veteran runners is not totally surprising as it can be altered with various exercise regimens [118, 119, 143] and may aid in contractile and metabolic efficiency [113, 144]. Normalized power for slow and fast fibers was similar in the veteran runners compared to the non-runners, suggesting that the integrated myocellular performance is largely unaffected in middle aged males regardless of training status.

More recently, single muscle fiber experiments from masters athletes and lifelong exercisers in their 70's and 80's have provided additional insight into aging at the myocellular level (▶ **Table 3**). Elite veteran (> 75 y) track and field athletes (race distances ranging from 80 meters to marathon, and one pentathlete) were compared to age-matched sedentary and young (23 y) cohorts [116]. Due to few fast fibers of the old non-athlete group surviving the testing protocols, only slow fibers were fully analyzed. No differences in slow muscle fibers were noted between the older cohorts; however, slow fiber force, velocity and rate of force development were all lower compared to the young individuals. Given the masters athletes were world record holders in various events, the authors speculated that this superior whole-body function compared to the sedentary elderly group might be due to the masters athletes retaining more muscle fibers.

Additional insight into myocellular function was recently gained from lifelong aerobic exercising (LLE) males and females that had consistent moderate to vigorous exercise habits (5 d wk^{-1} for 7 h wk^{-1}) for ~50 years [121, 125]. LLE males (74 y) had slow muscle

▶ **Table 3** Single muscle fiber physiology experiments of masters athletes > 70 years old.

Citation	Age (y)	Exercise History	Comparison	Slow Fibers		Fast Fibers	
				CSA	Function	CSA	Function
Gries et al. 2019 [119]	Young: 25 LLE: 72 Old: 75	Female Lifelong (~50 y) Aerobic Exercise (LLE) Mixed modes	Primary Aging (Young vs. LLE)	↔	**Force:** ↑11 %	↓31 %	**Force:** ↓19 %
					Velocity: ↔		**Velocity:** ↑13 %
					Power: ↑17 %		**Power:** ↔
					Spec Tension: ↑16 %		**Spec Tension**: ↑19 %
					Norm Power: ↑23 %		**Norm Power:** ↑37 %
			Lifelong Exercise (LLE vs. Old)	↔	**Force:** ↑10 %	↔	**Force:** ↔
					Velocity: ↔		**Velocity:** ↑11 %
					Power: ↑13 %		**Power:** ↑15 %
					Spec Tension: ↑7 %		**Spec Tension**: ↑13 %
					Norm Power: ↑13 %		**Norm Power:** ↔
Grosicki et al. 2021 [115]	Young: 25 LLE: 72 Old: 75	Male Lifelong (~50 y) Aerobic Exercise (LLE) Mixed modes	Primary Aging (Young vs. LLE)	↑25 %	**Force:** ↑14 %	↓18 %	**Force:** ↓16 %
					Velocity: ↑5 %		**Velocity:** ↑10 %
					Power: ↑25 %		**Power:** ↓17 %
					Spec Tension: ↓8 %		**Spec Tension**: ↔
					Norm Power: ↔		**Norm Power:** ↑18 %
			Lifelong Exercise (LLE vs. Old)	↑39 %	**Force:** ↑22 %	↔	**Force:** ↔
					Velocity: ↑4 %		**Velocity:** ↔
					Power: ↑25 %		**Power:** ↔
					Spec Tension: ↓12 %		**Spec Tension** : ↓7 %
					Norm Power: ↓8 %		**Norm Power:** ↓13 %
Power et al. 2016 [110]	Young: 23 MA: 79 Old: 78	Male Elite Masters Track and Field Athletes (MA)	Primary Aging (Young vs. MA)	↔	**Force:** ↓52 %	N/A	
					Velocity: ↓58 %		
					Spec Tension: ↓54 %		
			Lifelong Exercise (MA vs. Old)	↔	**Force:** ↔	N/A	
					Velocity: ↔		
					Spec Tension:↔		

LLE, Lifelong Exercisers; MA, Masters Athletes; CSA, Cross-Sectional Area; Spec Tension, Specific Tension; Norm Power, Normalized Power; ↑ increase; ↓ decrease; ↔ no change.

fibers that were 20 % stronger, 10 % faster, and 30 % more powerful than young exercisers (25 y) and age-matched non-exercisers (75 y). Despite the ~50 years of endurance exercise that likely recruited the fast muscle fibers [145] and have a high degree of plasticity with various exercise regimens [93, 146–148], there were little benefits for fast fiber size and contractile function. In contrast, the LLE females (72 y) had benefits for both slow and fast muscle fibers, which was primarily driven by alterations in contractile properties as no benefits in fiber size were noted. Slow fibers from LLE females were more powerful than young (25 y) and old non-exercisers (75 y) that was driven by an 11 % increase in force. Fast fiber power was maintained in LLE females compared to young exercisers that was driven by an 11 % increase in contractile speed. These data provide unique insight into slow and fast myocellular health with lifelong exercise and highlight various benefits and differences between males and females that are profiled in more detail in ▶ **Fig. 6**.

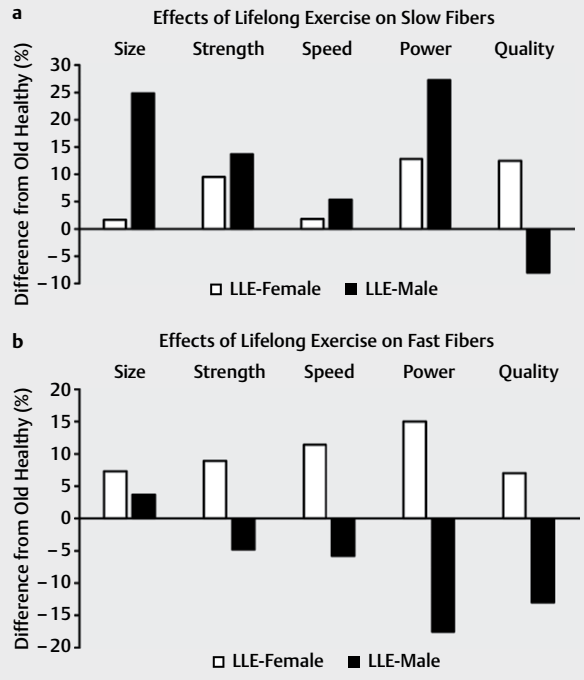
To date, the available single muscle fiber data from masters athletes and lifelong exercisers yield important insights into the intersection of aging and exercise. It is clear from the current data sets that various aspects of slow and fast muscle fiber contractile function are altered with lifelong exercise habits. The underlying mechanisms driving these adaptations are unclear, but likely are the result of years of exercise adaptations to facilitate efficiency and energetics for a given mode of exercise. Future studies should investigate additional modes of exercise (i. e., resistance exercise, concurrent training), additional muscles from the upper and lower body as it is known that distinct contractile alterations occur with chronic adaptations across muscle groups [94, 129, 149, 150], neurological adaptations as motoneuron survival varies with age and exercise [151], molecular probing at the single fiber and single cell level [152–155], and continued comparisons among males and females throughout the lifespan.

Muscle to Organ Communication

In the early 2000's, seminal research from the Copenhagen Muscle Research Centre has demonstrated the potent endocrine-like properties of skeletal muscle. Using a single-leg exercise model, Steensberg et al. reported a 19-fold higher increase in the circulating cytokine interleukin (IL)-6 [156]. Since then, the role of skeletal muscle as an endocrine organ has gained significant attention as several other cytokines were discovered that are produced by skeletal muscle (myokines), including some that are packaged in ex-

tracellular vesicles during/after exercise [157]. Along with metabolic communication to adipose tissue and liver, myokines appear to influence brain, bone, gastrointestinal tract, pancreas, and several other organs that may have significant implications for age-related diseases including Alzheimer's, basal inflammation, diabetes, among many others [158].

Given the role of muscle in movement and the corresponding metabolic demand, skeletal muscle of masters athletes likely have unique communicative properties as lifelong exercising males had lower basal systemic inflammation and enhanced innate immunity compared to non-exercisers [159, 160]. While mechanistic insight is needed, masters athletes have a reduced risk of osteoporosis, Alzheimer's, diabetes mellitus, and various forms of cancer which may be a result of myokine production from the enhanced skeletal muscle health compared to elderly non-exercisers [57, 161, 162]. Along with these health benefits, more robust communicative properties within skeletal muscle may enhance availability of metabolic substrates including fatty acids and glucose [163], which also enhance athletic performance. However, more mechanistic research is needed in the muscle to organ crosstalk capacity in masters athletes, particularly in a sex specific manner [164].

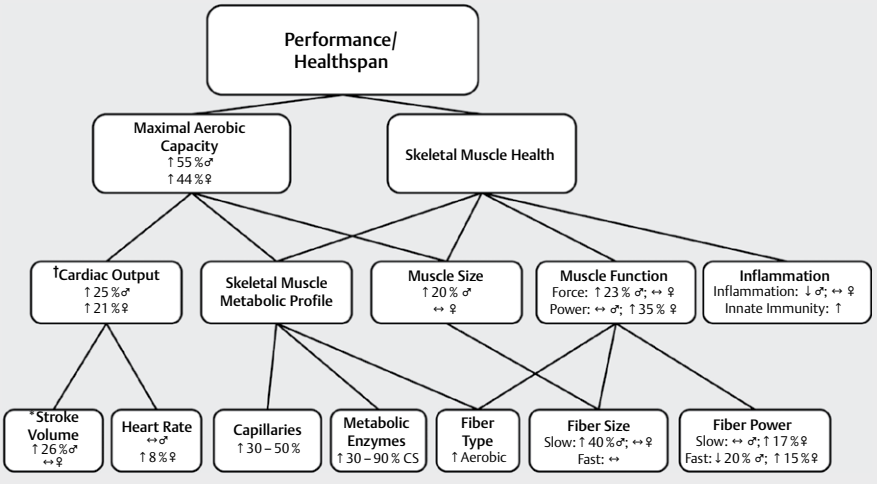


▶ **Fig. 6** Sex specific differences in the effects of lifelong aerobic exercise on slow (A) and fast (B) fiber physiology. Percent differences were calculated by comparing lifelong exercisers (LLE) to age-matched, sedentary controls in a sex specific manner [121, 125].

Conclusion

Aging results in numerous physiological detriments that deteriorate overall health and quality of life. Lifelong exercise, as seen in masters athletes, results in ~50 % greater VO_2max than elderly non-exercisers. This results in lifelong exercisers in their 70's to have VO_2max values similar to the 50th percentile of individuals ~30 y younger and a key factor in these athletes performances and overall healthspan. Their ~50 % higher VO_2max compared to elderly non-exercisers appears to be mostly due to enhanced stroke volume, while the effect of habitual exercise on HR_{max} and a-vO_2diff remains debated.

Lifelong aerobic exercise in masters athletes also benefits skeletal muscle health as they have significant adaptations to optimize endurance performance. These adaptations include a full preservation of capillarization and oxidative enzyme capacity, a slight shift



▶ **Fig. 7** Summary schematic of the aging athlete compared to non-exercisers as it pertains to health and performance. Data presented are from a comprehensive study investigating the effects of lifelong aerobic exercise on cardiovascular and skeletal muscle health and are made relative to age-matched non-exercisers (~75 y) [17, 65, 121, 125, 159, 160, 164]. ↑ increase; ↓ decrease; ↔ no change; ♂, males; ♀, females; * Oxygen pulse was used to estimate stroke volume; †Cardiac output was estimated by absolute VO_2max [30].

to slow fiber type distribution and an attenuated accumulation of IMAT. Mode specific adaptations occur within the skeletal muscle based on cycling and running that affect size and function, which likely results in performance benefits in the respective mode. While lifelong aerobic exercise appears beneficial for metabolic health, there remains ambiguity on its effect on whole muscle size and function, including the fast fibers, suggesting the need for additionally explosive training (i. e., strength training, plyometrics, high intensity interval training).

To illustrate the benefits of lifelong aerobic exercise in cardiovascular and skeletal muscle health, ▶ **Fig. 7** represents a graphical image of a comprehensive investigation recently completed by the Human Performance Laboratory at Ball State University. As these athletes continue to produce impressive performances, the data collectively suggest that lifelong exercise globally preserves numerous physiological systems associated with aging. Although lifelong exercise does not fully maintain indices of the cardiovascular system and skeletal muscle, these athletes appear to extend their healthspan, decrease their risk of morbidities and mortality, and produce high-level of performances in their advanced age.

Future Directions

While this review highlights the wide-ranging benefits of lifelong aerobic exercise training on hallmark traits of aging (i. e., decreased aerobic capacity, sarcopenia, myocellular alterations), there are numerous research opportunities in this expanding cohort of unique individuals. Several of the deleterious effects of aging begin ~30 y in healthy non-exercisers and it is unknown to what extent, if any, that lifelong exercise confers additional health benefits compared to those who begin habitual exercise training in their midlife or late-life years [165]. Mode specific effects of chronic exercise across aerobic, resistance, and concurrent training likely have specific adaptations that contribute uniquely to overall health [166, 167]. Likewise, additional muscle groups (upper and lower body) should be considered in future research designs [94]. Sex differences are apparent from the limited lifelong exercise data sets and should be expanded [17, 65, 125]. Lastly, as we continue to discover the molecular map induced by exercise within and between tissues (i. e., muscle, brain, bone, liver, etc.) [168], more mechanistic research is needed to explore how chronic exercise training minimizes risk of diseases and how exercise can be prescribed as a medication to combat diseases.

Conflict of Interest

The authors declare that they have no conflict of interest.

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