New Records In Aerobic Power Among Octogenarian Lifelong Endurance Athletes

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Running Title: VO\textsubscript{2}\text{max} in Octogenarian Lifelong Athletes

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Abstract

We examined whole body aerobic capacity and myocellular markers of oxidative metabolism in lifelong endurance athletes (n=9, 81±1 y, 68±3 kg, BMI=23±1 kg/m²) and age-matched, healthy, untrained men (n=6; 82±1 y, 77±5 kg, BMI=26±1 kg/m²). The endurance athletes were cross-country skiers, including a former Olympic champion and several national/regional champions, with a history of aerobic exercise and participation in endurance events throughout their lives. Each subject performed a maximal cycle test to assess aerobic capacity (VO₂max). Subjects had a resting vastus lateralis muscle biopsy to assess oxidative enzymes (citrate synthase and βHAD) and molecular (mRNA) targets associated with mitochondrial biogenesis (PGC-1α and Tfam). The octogenarian athletes had a higher (P<0.05) absolute (2.6±0.1 vs. 1.6±0.1 L•min⁻¹) and relative (38±1 vs. 21±1 ml•kg⁻¹•min⁻¹) VO₂max, ventilation (79±3 vs. 64±7 L•min⁻¹), heart rate (160±5 vs. 146±8 b•min⁻¹), and final workload (182±4 vs. 131±14 watts). Skeletal muscle oxidative enzymes were 54% (citrate synthase) and 42% (βHAD) higher (P<0.05) in the octogenarian athletes. Likewise, basal PGC-1α and Tfam mRNA were 135% and 80% greater (P<0.05) in the octogenarian athletes. To our knowledge, the VO₂max of the lifelong endurance athletes is the highest recorded in humans >80 y of age and comparable to non-endurance trained men 40 years younger. The superior cardiovascular and skeletal muscle health profile of the octogenarian athletes provides a large functional reserve above the aerobic frailty threshold and is associated with lower risk for disability and mortality.
Introduction

Maximal oxygen uptake (VO₂max) in humans was initially described in the 1920’s by A.V. Hill (27, 28). Since then, VO₂max has been extensively profiled in numerous populations with the upper limit >90 ml•kg⁻¹•min⁻¹ in a 22 y old highly trained elite cross-country skier (12). In contrast, a VO₂max of ~17.5 ml•kg⁻¹•min⁻¹ (5 metabolic equivalents [METs]) is the prognostic exercise capacity for increased risk of mortality and has recently been shown to be a more powerful predictor of mortality than established risk factors for cardiovascular disease (41). The ~73 ml•kg⁻¹•min⁻¹ (21 METs) difference in VO₂max from the elite endurance athlete and prognostic exercise capacity for mortality represents the largest possible cardiorespiratory reserve in humans. Aerobic capacity is variable (33), can be improved on the magnitude of 15-30% with endurance training (21, 29), and is linked to genetic factors that influence upper limits and trainability (56). While VO₂max gradually declines across the lifespan and is well documented among athletes and non-athletes from age 20 y to ~75 y (26, 43, 59), little information on VO₂max and corresponding cardiorespiratory reserve in relationship to lifelong physical activity patterns is available in individuals >80 y of age. This is an emerging knowledge gap for aerobic capacity given that individuals living beyond age 80 y are the fastest expanding age demographic in our society (63).

We recently had the opportunity to examine aerobic capacity in two cohorts of healthy independently living men >80 y old with differing lifelong physical activity habits. One group consisted of lifelong elite endurance athletes who were still actively engaged in competitive events, while the other group only performed activities of daily living with no history of structured exercise. To complement the VO₂max testing, we obtained
skeletal muscle biopsies from their leg to examine the oxidative profile at the cellular and molecular level. We hypothesized that the lifelong endurance athletes would have a greater aerobic profile compared to the age-matched untrained men. The unique aspect of this investigation is that it offers insight into cardiovascular and skeletal muscle health in two distinct phenotypes of healthy octogenarians and establishes new upper limits for aerobic power in men 80-91 years of age.

Methods

Subjects

Nine lifelong endurance athletes were recruited from a national list of master’s cross-country skiers in Sweden. Criteria for inclusion to the lifelong exercise group included a minimum of 50 years of consistent exercise training with no more than 6 months of no training at any time point in the past 50 years. These endurance athletes included a former two-time Olympic champion and several national/regional champions, with a history of vigorous aerobic exercise (4-6 d/wk) and participation in endurance events (cross-country skiing, track and field, and orienteering) throughout their entire adult lives. On average, these veteran athletes had trained ~8h/wk (range=3-20 hrs.) for the past 50+ years. Six men with no history of consistent exercise (beyond activities of daily living) were recruited from Muncie, IN and served as healthy untrained controls. Subject profiles are shown in Table 1.

All subjects were carefully screened for past exercise history by filling out an extensive exercise and medical questionnaire and personal interview. All participants underwent a physical examination, which included medical history, blood samples for
general health markers, resting electrocardiogram (ECG) and blood pressure.

Participants were excluded if they had any major acute or chronic illness, cardiac, pulmonary, liver, or kidney abnormalities, uncontrolled hypertension, insulin or non-insulin dependent diabetes, abnormal blood chemistries, arthritis, a history of neuromuscular problems, or if they smoked tobacco.

Prior to volunteering for this research, all subjects were briefed on the project objectives and testing procedures by a member of the investigative team. Subjects were informed of the risks and benefits with the research and gave their written consent in accordance with the Human Subjects Institutional Review Boards at Ball State University, Karolinska Institutet and Mid Sweden University. This study was conducted in accordance with the Declaration of Helsinki.

Medications

Four of the nine octogenarian athletes were not taking any prescribed medication, three were taking cholesterol medication, and two were taking blood pressure medication. One of the untrained controls was not taking any prescribed medication. The other five men were taking various cholesterol (n=4), blood pressure (n=2), thyroid (n=2), bladder/prostate (n=3), or acid reflux medications (n=1). All subjects took over-the-counter pain medication on occasion.

Daily Physical Activity

Daily physical activity was indirectly assessed using a pedometer (Lifecorder EX, New LifeStyles Inc., Lees Summit, MO). Subjects were asked to wear the pedometer
for two weeks and to put on the pedometer first thing upon waking and take it off just
prior to going to bed each night. Total steps each day were assessed if the subject
wore the pedometer for a minimum of 12 hours as noted by the first and last movement
recorded on each day. Any periods of time >60 min of no recorded movement was not
included in the determination of the 12 hours.

Body Composition

Following 30 minutes of supine rest, subjects were assessed for body
composition via dual x-ray absorptiometry (Lunar Prodigy full body scanner, Madison,
WI). Data were analyzed using enCore 2008 software by GE Health Care. The
scanner was calibrated each day prior to the first scan.

Maximal Oxygen Consumption (VO₂max)

Subjects performed a continuous incremental cycle ergometer test with 12 lead
ECG to volitional exhaustion. The endurance athletes warmed up at a 50 W load for
two minutes at 60 RPM. Following the warm-up, the watt load on the cycle ergometer
was increased by 15 W per minute in a ramped fashion until the subject reached
volitional fatigue or could not maintain a cadence of 60 RPM. Similarly, the untrained
men warmed up for two minutes at a 20 W load followed by a ramped increase of 10 W
per minute until volitional fatigue or could not maintain a cadence of 60 RPM. Oxygen
uptake was measured breath-by-breath and averaged in 20-second intervals using
indirect calorimetry via an automated open circuit system (Ball State: Parvo Medics,
Sandy, UT; Karolinska: SensorMedics Vmax, Encore, 229; Viasys Respiratory Care,
Inc., Yorba Linda, CA). Both systems were calibrated with standardized gases before each test. In addition, the respective pneumotachs were also calibrated before each test using a standard volume of air (3 L syringe).

Successful test criteria included a plateau in oxygen uptake with increasing workload, achievement of age predicted maximum heart rate, a respiratory exchange ratio (RER) of >1.10 or a rating of perceived exertion >19. A physician monitored all testing to ensure subject safety. The average of the highest three consecutive 20 s time points during the last 120 s of the test were used for the measure of maximal oxygen uptake, maximum ventilation, and respiratory exchange ratio. Maximal heart rate was determined from the 12 lead ECG and peak workload from the highest watt output for a completed 20-second stage.

To compare the Karolinska Institute and Ball State University metabolic carts, a member of the investigative team (S. Trappe) performed a cycle test on each system approximately 10-d apart. Since the highest workload obtained by the subjects was 198 W, a comparison evaluation was performed at 100, 150, and 200 W. The VO₂ (L•min⁻¹) data were nearly identical between systems with values of 1.50, 2.11, 2.78 L•min⁻¹ and 1.50, 2.08, 2.72 L•min⁻¹, respectively on the two different metabolic cart systems. The VO₂ at these workloads was in agreement with the predicted oxygen uptake and power output relationship (23).

**Muscle Biopsy**

The overall approach for the muscle biopsies was identical for the octogenarian athletes and age-matched untrained men. Subjects were asked to refrain from
structured exercise and any physical activity outside of normal activities of daily living for 24 hours prior to the muscle biopsy. Subjects consumed their normal evening meal and were instructed not to ingest any additional food or caloric beverage until after the muscle biopsy. Subjects arrived at the laboratory in the early morning (~7:30am) by car and had a short walk into the laboratory. Once in the laboratory, subjects rested quietly in the supine position for 30-min. Following this rest period, a muscle biopsy was obtained from the vastus lateralis (4). Muscle samples were divided into several pieces, quickly frozen in liquid nitrogen, and stored at -190°C for later analysis of enzyme activity and mRNA levels.

**Skeletal Muscle Enzymes**

Oxidative enzymes were determined from a 10- to 20-mg portion of the muscle specimen. Citrate synthase activity was determined through the reduction of DTNB by the release of CoA-SH in the cleaving of acetyl-CoA (13). β-hydroxyacyl-CoA dehydrogenase (β-HAD) was determined fluorometrically by an indirect measurement of NADH disappearance (13). All samples were analyzed at the same time using the same chemicals to limit any differences due to potential variations in assays.

**Skeletal Muscle mRNA**

*Total RNA extraction and RNA quality check.* Total RNA was extracted in TRI reagent (Molecular Research Center, Cincinnati, OH). The quality and integrity [RNA Integrity Number of 8.32 ± 0.06 (SE)] of extracted RNA [0.11 ± 0.01 (SE)] μg/μl] was
evaluated using an RNA 6000 Nano LabChip kit on an Agilent 2100 Bioanalyzer (Agilent Technologies, Palo Alto, CA).

**Reverse transcription and qPCR.** Oligo (dT) primed first-strand cDNA was synthesized (150 ng total RNA) using SuperScript II RT (Invitrogen, Carlsbad, CA). Quantification of mRNA levels (in duplicate) was performed in a 72-well Rotor-Gene 3000 Centrifugal Real-Time Cycler (Corbett Research, Mortlake, NSW, Australia).

Housekeeping gene (HKG) GAPDH was used as a reference gene, as we have previously described (31, 45). The expression of GAPDH was normalized to a second HKG, RPL01, to compare GAPDH basal level between groups. All primers used in this study were mRNA specific (on different exons and crossing over an intron) and designed for qPCR analysis (Vector NTI Advance 9 software, Invitrogen) using SYBR Green chemistry. Details about primer characteristics and sequences for muscle peroxisome proliferator-activated receptor-gamma coactivator 1-α (PGC-1α) and mitochondrial transcription factor A (Tfam) has been reported previously by our laboratory (14, 24, 64). A melting curve analysis was generated to validate that only one product was present. The details about RT and PCR reaction parameters have been reported previously (14).

The PGC-1α and Tfam gene expression between groups was compared using the $2^{-\Delta C_T}$ (arbitrary units) quantification method (36). A serial dilution curve (cDNA made from 500 ng of total RNA of human skeletal muscle; Ambion, Austin, TX) was generated for each qPCR run to evaluate reaction efficiencies. The amplification calculated by the Rotor-Gene software was specific and highly efficient (efficiency = 1.04 ± 0.01; $R^2 = 0.99 ± 0.00$; slope = 3.22 ± 0.02).
Statistical Analysis

Normality of each variable measured was determined using a qq-plot and the Shapiro-Wilk test. Those data that displayed a normal distribution were analyzed using a parametric independent t-test with the appropriate significance value based on whether equality of variance was assumed or un-assumed as determined by Levene’s equality of variance test. Non-normally distributed data were analyzed with a non-parametric independent t-test. The Pearson correlation test was used for the correlation analyses. All data are presented as means ± SE.
Results

Maximal Aerobic Capacity

The mean (±SE) values for VO$_2$max, ventilation, heart rate, O$_2$ pulse, RER, and final workload achieved during the maximal cycling test are shown in Table 2. Absolute VO$_2$max (L·min$^{-1}$) was 58% higher (P<0.05) in the octogenarian athletes. When expressed relative to body weight, VO$_2$max (ml·kg$^{-1}$·min$^{-1}$) was 80% higher (P<0.05). The octogenarian athletes also had 25% higher ventilation and 41% higher O$_2$ pulse (P<0.05). While the maximal heart rate was, on average, 14 beats·min$^{-1}$ higher in the endurance trained men, this was not significant due to the wide range in observed maximal heart rates. No difference in the maximal RER was observed, with both groups of men achieving levels above 1.10, which was further confirmation of achieving maximal cardiorespiratory values. The maximal workload achieved during the test was 51 Watts (+39%) greater (P<0.05) in octogenarian athletes compared with the untrained octogenarians.

Individual VO$_2$max (ml·kg$^{-1}$·min$^{-1}$) data points for the octogenarian athletes and untrained octogenarians are shown in Figure 1. For comparison, representative VO$_2$max data across the lifespan are shown along with a prognostic value for exercise capacity and mortality (5 METs).

Skeletal Muscle Enzymes

Figure 2 shows oxidative enzyme activity for citrate synthase and β-HAD. Citrate synthase (+54%) and β-HAD (+42%) were higher (P<0.05) in the octogenarian athletes compared with the untrained octogenarians.
Skeletal Muscle Basal Gene Expression

Basal levels of PGC-1α and Tfam mRNA were 135% and 80% greater (P<0.05), respectively, in the octogenarian athletes compared with the untrained octogenarians (Figure 3).

Correlations

A positive correlation between VO$_2$max and final workload was observed (r=0.94; P<0.05). A low correlation was observed between VO$_2$max and maximal heart rate (r=0.27). VO$_2$max was positively correlated to maximal ventilation (r=0.67; P<0.05) and O$_2$ pulse (r=0.89; P<0.05). Additionally, similar positive correlations were observed between VO$_2$max and each of the four skeletal muscle oxidative markers (citrate synthase, β-HAD, PGC-1α, and Tfam) from the vastus lateralis muscle (r=0.55-0.61; P<0.05).
Discussion

The unique aspect of this investigation was the physiological assessment of two cohorts of healthy independent living men >80 y old with different lifelong physical activity habits. The endurance athletes had been engaged in vigorous aerobic exercise their entire adult lives and were still active in various competitive events and exercised 4-6 d/wk. The age-matched untrained men had no history of structured exercise, but must also be considered a unique group of individuals given their age, independent lifestyle, overall health profile, and full engagement in the maximal testing efforts performed in this study. The exercise routine and activities of daily living resulted in the lifelong endurance athletes averaging ~3700 more steps per day compared to the non-exercisers. However, the ~4300 steps per day of the untrained octogenarians is respectable for individuals in this age group and further highlights their overall mobility and health. The primary finding from this investigation was the remarkably high aerobic capacity of the lifelong endurance trained athletes that are the highest ever reported among octogenarians. The high aerobic power profile was complemented by a robust skeletal muscle oxidative profile at the cellular and molecular level. These data provide insight into cardiovascular and skeletal muscle health in two distinct phenotypes of healthy octogenarians and establish new records for aerobic power in men 80-91 years of age.

The VO$_2$max range for the nine lifelong exercisers was fairly homogeneous (34-42 ml$\cdot$kg$^{-1}$$\cdot$min$^{-1}$), with seven men $\geq$36 ml$\cdot$kg$^{-1}$$\cdot$min$^{-1}$ and two men $>$40 ml$\cdot$kg$^{-1}$$\cdot$min$^{-1}$ (Figure 1). The most unique individual in our group was a 91-year old former Olympic champion with an aerobic capacity of 36 ml$\cdot$kg$^{-1}$$\cdot$min$^{-1}$ (2.36 L$\cdot$min$^{-1}$). Likewise, the
untrained healthy octogenarians had a homogeneous VO₂max (17-24 ml•kg⁻¹•min⁻¹),
with four of the six men >20 ml•kg⁻¹•min⁻¹ and the other two near the 5 MET prognostic
equipment capacity for increased risk of dependence and mortality. For comparison, we
identified 21 published studies that measured aerobic capacity in individuals >80 y of
age that are summarized in Table 3. From these studies, a total of 464 individuals were
identified with 42% men and 58% women. We aggregated an average VO₂max from
reported mean data and, in some cases, estimated individual data points presented
graphically in the papers. Overall, the average VO₂max was 21±4 ml•kg⁻¹•min⁻¹ from the
195 men and 18±4 ml•kg⁻¹•min⁻¹ from the 269 women. For the men, this was identical to
the 21±1 ml•kg⁻¹•min⁻¹ of the untrained men in our study. The physical characteristics
and physical activity levels from these 195 men were comparable to the untrained men
in our study and thus it is not surprising that the VO₂max was similar. Only one study
had a subject population that was comparable to the octogenarian athletes in our study.
Harridge and colleagues reported a VO₂max of 27±5 ml•kg⁻¹•min⁻¹ (1.80 L•min⁻¹) in five
men >80 y with a history of lifelong endurance exercise and were described as highly
active at the time of the physiological assessment (25). On average, the octogenarian
athletes in the current study had ~40% greater aerobic capacity in both relative and
absolute terms compared to the lifelong exercisers tested by Harridge et al. (25), and
~80% greater than the age-matched untrained men profiled by us and the other study
populations summarized in Table 3.

Recent studies have shown that all-cause mortality risk with increasing exercise
capacity reaches an asymptote at 10 METs for men (8, 34). The ~11 MET exercise
capacity of the octogenarian athletes places them in the lowest mortality risk category
and further highlights the extraordinary cardiorespiratory fitness level of these men. For every 1-MET level increase in exercise capacity above 5 METs, the mortality risk is 12% lower (34, 41). Based upon exercise capacity, the octogenarian athletes have a ~50% lower all-cause mortality risk compared to the untrained octogenarians. While exercise capacity is typically a modifiable risk factor, the trainability of the cardiorespiratory and skeletal muscle systems appears attenuated among octogenarians (19, 51). Thus, the large cardiorespiratory reserve of the octogenarian athletes (~6 METs), which is nearly equivalent to the exercise capacity of the untrained men, may be even more important to remain above the threshold for aerobic frailty, subsequent disability and mortality (9, 34, 62).

It is also noteworthy that the high aerobic power achieved by the octogenarian athletes is comparable to healthy non-endurance trained men ~20 years younger (75th percentile), ~40 years younger (50th percentile) and ~60 years younger (20th percentile) (Figure 1) (1). While the lifelong vigorous exercise routine of these aging athletes was a key element to their high aerobic capacity measured in our study, their elite athletic achievements as young adults (age 20-30 y) suggest they had aerobic capacities at the upper range for humans. An estimated VO2max of 80 ml•kg⁻¹•min⁻¹ during their prime competitive years would translate to a ~7.5% decline per decade in aerobic capacity. This is comparable to previous longitudinal and cross-sectional studies that have shown the decline in aerobic capacity of highly trained master runners to be ~5-7% per decade (26, 43, 59). However, data from these studies were based upon subjects tested at ages ranging from ~45 to ~70 y old. While data from the aging athletes of the current
study are limited to a single time point, they support the idea that a 5-7% decline in VO$_2$max with age can be extended to lifelong endurance athletes in their 80’s and 90’s. Decreases in maximal heart rate have generally been viewed as the primary cause for a reduction in aerobic capacity with age (22, 26, 55), although this is not universally accepted in aging (>60 y) athletes (47). The average maximal heart rate of 160 beats•min$^{-1}$ in the octogenarian athletes was the highest reported to date for this age group, but should be interpreted with some caution given the high variability we observed among them (range=134-181 beats•min$^{-1}$). However, six of the nine octogenarian athletes (67%) had a maximal heart rate >160 beats•min$^{-1}$, which included the 91 y old Olympian (169 beats•min$^{-1}$). Likewise, the untrained men were also quite variable (range=126-168 beats•min$^{-1}$), but only two individuals (33%) had a maximal heart rate >160 beats•min$^{-1}$. The untrained men’s average maximal heart rate was similar to reports in the literature (Table 3). The variability in heart rate among our subject populations was higher than typically observed across the lifespan (<80 y) (55). The reason for this large variability is unknown, but appears to be related to the age of the subjects as several studies have reported a large range in maximal heart rate in individuals >80 y of age (18, 25, 37, 42, 52). None of our subjects were taking heart medications that would have directly influenced heart rate. The higher heart rate of the octogenarian athletes challenges the idea that the decline in maximal heart rate with age is typically independent of activity level (10, 22, 26, 43, 55, 59). While the high variability in maximal heart rate limits our interpretation, these data provide a preliminary indication that lifelong vigorous endurance exercise may attenuate the decline in maximal heart rate among individuals >80 y of age.
The higher $O_2$ pulse observed in the octogenarian athletes is in agreement with previous studies on master athletes when compared to age-matched non-exercisers (22, 43, 47). Oxygen pulse, an indirect indicator of stroke volume, is typically ~25 ml•min$^{-1}$ in young endurance athletes (59) and declines ~40% (to ~18 ml•min$^{-1}$) in ~70 y old master athletes (43, 59). The 16 ml•min$^{-1}$ $O_2$ pulse of the octogenarian athletes suggest a modest ~12% reduction with the additional 10-20 years of aging and continued endurance training. It has been well established that the cardiac tissue stiffens with age, which decreases compliance and overall performance of the heart (35). However, lifelong endurance exercisers (~65-75 y) have been shown to maintain a large proportion of their cardiac function as they age (2, 10, 48). A higher blood volume is associated with training status and may be higher in older active individuals, which would aid in heart dynamics (15, 32). While we do not have more detailed heart data or blood volume measures, the higher $O_2$ pulse and high correlation to VO$_2$max suggest enhanced cardiac function among the octogenarian athletes compared to the untrained men.

We observed higher maximal ventilation among the octogenarian athletes (range=65-97 L•min$^{-1}$) compared to the untrained men (range=34-78 L•min$^{-1}$). Seven of the nine octogenarian athletes (78%) had maximal ventilation >75 L•min$^{-1}$, while only one of the untrained men (16%) achieved this level. We observed a positive correlation between ventilation and VO$_2$max, which has been previously reported among older individuals with varying habitual activity levels (43). The ventilatory efficiency (minute ventilation/VO$_2$) was ~25% lower among the octogenarian athletes and was comparable to young (25 y) and master level (45-65 y) endurance trained men (22, 47, 59),
suggesting that efficiency at the lungs was relatively unchanged despite the diminished capacity observed in the lifelong endurance athletes.

The muscle biopsy data presented are the first from highly endurance trained octogenarian athletes. We observed a higher oxidative profile of mitochondrial markers in the octogenarian athletes compared to the untrained octogenarians. These data suggest that lifelong endurance training enhances mitochondrial function in individuals >80 y of age. Similarly, middle-aged (45-50 y) and older (70 y) lifelong endurance athletes have a higher oxidative profile compared to untrained counterparts (30, 58). The differences in mitochondrial function between the octogenarian athletes and untrained octogenarians were comparable in magnitude to improvements with endurance training in young individuals (11, 21). It is important to note that mitochondrial function normally declines with age and this decline does not appear to be reversible with endurance training in sedentary adults >80 y old or very old animals (5, 18, 49). Consequently, maintaining a higher oxidative profile as a result of lifelong endurance training likely provides these athletes with greater metabolic flexibility that would be unique for this age category and result in numerous positive health benefits. It must also be considered that in addition to the lifelong endurance exercise of the octogenarian athletes, genetic networks favorable for mitochondrial biogenesis are a potential contributing factor to the enhanced oxidative profile we observed from these men (60).

The higher skeletal muscle oxidative profile among the octogenarian athletes complemented the cardiovascular profile. Both mitochondrial enzyme activity (citrate synthase and β-HAD) and levels of mitochondrial genes (PCG1-α and Tfam) were
positively related to aerobic capacity among our subject pool. In this regard, the integrated performance of the skeletal muscle and cardiovascular systems resulted in a 39% greater dynamic power output on the bicycle ergometer during the maximal test to volitional exhaustion in the octogenarian athletes compared to the untrained octogenarians.

In summary, the cardiovascular and skeletal muscle profile of the octogenarian athletes was approximately double compared to the untrained octogenarians. This is characteristic of a highly trained endurance phenotype and is likely reflective of their lifelong endurance exercise habits as well as their genetic traits. The remarkable aerobic capacity (~11 METs) and corresponding functional reserve among the octogenarian athletes is the highest ever recorded in this age group and places them in the lowest all-cause mortality risk category for men of any age. In contrast, untrained independent-living octogenarians have a low functional capacity (~6 METs) and limited cardiovascular and skeletal muscle plasticity in response to high-intensity exercise programs (18, 19, 46, 51), thereby providing a significant challenge to remain above the aerobic frailty threshold. The current study supports the idea that a lifestyle incorporating lifelong endurance exercise helps maintain the plasticity of numerous physiological systems beyond 80 y of age, which has direct benefits to overall health and reduces the risk of disability and mortality.
Acknowledgements

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Disclosures

The authors have no conflicts to declare.
References


Figure Legends

**Figure 1.** Individual VO\textsubscript{2}max data from the octogenarian lifelong endurance athletes and healthy untrained octogenarians. The dotted line represents the prognostic exercise capacity (5 METs, 17.5 ml/kg/min) generally necessary for an independent lifestyle and associated with an increased risk for mortality as described by Meyers et al. (41). The normative values for healthy men across the lifespan (n=44,549) were originally obtained from the Cooper Institute in Dallas, TX, and have been summarized by the American College of Sports Medicine (1).

**Figure 2.** Citrate synthase and β-hydroxyacyl-CoA dehydrogenase (β-HAD) skeletal muscle enzyme activity from octogenarian lifelong endurance athletes and healthy untrained octogenarian men.

**Figure 3.** Basal PGC-1α and Tfam mRNA levels in skeletal muscle from octogenarian lifelong endurance athletes and healthy untrained octogenarian men.
Normative Values for Healthy Men Across the Lifespan (n=44,549)

Independence

5th Percentile - Very Poor

50th Percentile

95th Percentile - Superior

 Dependence and ↑ Risk of Mortality

$VO_2_{\text{max}}$ (ml•kg$^{-1}$•min$^{-1}$)

Age (y)
Figure 2

- **Citrate Synthase**
- **β-HAD**

**Enzyme Activity (µmol·g⁻¹·min⁻¹)**

- **Octogenarian Athletes**
- **Untrained Octogenarians**

*Denotes significant difference.
Figure 3

- Octogenarian Athletes
- Untrained Octogenarians

Arbitrary Units

PGC-1α

Tfam

* Indicates significant difference.

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Table 1. Subject Profile

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<th>Untrained Octogenarians</th>
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<td>Age (y)</td>
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<td>Height (cm)</td>
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<td>Weight (kg)</td>
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<td>Hb (g/dL)</td>
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<td>43 ± 1</td>
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<td>Daily Steps**</td>
<td>8026 ± 1210*</td>
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*P<0.05; **Does include daily exercise for athletes
Table 2. Maximal Aerobic Power Test Data

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<th>Untrained Octogenarians</th>
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<td>VO₂ (L·min⁻¹)</td>
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<td>1.62 ± 0.14</td>
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<td>VO₂ (ml·kg⁻¹·min⁻¹)</td>
<td>38 ± 1*</td>
<td>21 ± 1</td>
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<tr>
<td>VO₂ (ml·kg LBM⁻¹·min⁻¹)</td>
<td>52 ± 2*</td>
<td>32 ± 2</td>
</tr>
<tr>
<td>Ve (L·min⁻¹)</td>
<td>79 ± 3*</td>
<td>63 ± 6</td>
</tr>
<tr>
<td>Heart Rate (beats·min⁻¹)</td>
<td>160 ± 5</td>
<td>146 ± 8</td>
</tr>
<tr>
<td>O₂ pulse (ml O₂·beat⁻¹)</td>
<td>16.1 ± 0.5*</td>
<td>11.4 ± 1.4</td>
</tr>
<tr>
<td>RER</td>
<td>1.12 ± 0.02</td>
<td>1.19 ± 0.03</td>
</tr>
<tr>
<td>Final Workload (Watts)</td>
<td>182 ± 4*</td>
<td>131 ± 14</td>
</tr>
</tbody>
</table>

*P<0.05
Table 3 - Summary of literature on VO₂max in men and women >80 y

<table>
<thead>
<tr>
<th>Reference</th>
<th>Subject Population</th>
<th>Fitness Profile</th>
<th>Age (y)</th>
<th>Men</th>
<th>Women</th>
<th>Test Mode</th>
<th>Heart Rate (b·min⁻¹)</th>
<th>VO₂max (L·min⁻¹)</th>
<th>VO₂max (ml·kg⁻¹·min⁻¹)</th>
<th>Heart Rate (b·min⁻¹)</th>
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<td><strong>Cross-sectional Studies</strong></td>
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<td>Dill 1964 (17)</td>
<td>Physiologist</td>
<td>Active</td>
<td>90</td>
<td>1</td>
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<td>C</td>
<td>1.31</td>
<td>21.1</td>
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<td>Posner 1987 (44)a</td>
<td>Senior center</td>
<td>Healthy non-active</td>
<td>&gt;80</td>
<td>2</td>
<td>2</td>
<td>C</td>
<td>21.0</td>
<td>18.0</td>
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<td>Fleg 1988 (20)a</td>
<td>Independent living</td>
<td>Healthy non-active</td>
<td>80-87</td>
<td>7</td>
<td>3</td>
<td>T</td>
<td>21.7</td>
<td>19.7</td>
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<td>Babcock 1992 (3)a</td>
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<td>C</td>
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<td>Healthy non-active</td>
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<td>1</td>
<td>2</td>
<td>T</td>
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<td>Malbut 1995 (39)b</td>
<td>&quot;Medically stable&quot;</td>
<td>Not reported</td>
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<td>23.0</td>
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<td>de Wild 1995 (95)a</td>
<td>Independent living</td>
<td>Varied</td>
<td>80-87</td>
<td>18</td>
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<td>C</td>
<td>23.8</td>
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<td>Takeshima 1996 (54)a</td>
<td>Independent living</td>
<td>Active (3d/wk)</td>
<td>≥80</td>
<td>5</td>
<td></td>
<td>C</td>
<td>21.1</td>
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<td>Harridge 1997 (25)b</td>
<td>Lifelong endurance</td>
<td>Vigorous Exercisers</td>
<td>&gt;80</td>
<td>5</td>
<td></td>
<td>C+T</td>
<td>1.80</td>
<td>27.1</td>
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<td>Healthy non-active</td>
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<td>17</td>
<td>19</td>
<td>T</td>
<td>1.30</td>
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<td>144</td>
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<td>Malatesta 2004 (38)b</td>
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<td>Simar 2005 (50)b</td>
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<td>Healthy active</td>
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<td>4</td>
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<td>18.2</td>
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<td>Not clearly stated</td>
<td>80-90+</td>
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<td>1.47</td>
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<td>83±4</td>
<td>23</td>
<td>26</td>
<td>T</td>
<td>1.58</td>
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<td>Trained (36 wk program)</td>
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<td>Vaitkevicius 2002 (61)b</td>
<td>Independent living</td>
<td>Healthy non-active</td>
<td>84±4</td>
<td>11</td>
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<td>1.23</td>
<td>18.3</td>
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<td>15.1</td>
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<td>Evans 2005 (19)b</td>
<td>Independent living</td>
<td>Healthy non-active</td>
<td>77-87</td>
<td>8</td>
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<td>1.61</td>
<td>22.9</td>
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<td>1.81</td>
<td>26.3</td>
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</table>

*Estimated from figure; †Mean data presented in paper; C= Cycling; T=Treadmill; Two papers were not presented in the table since they were data from the same training program (18, 52)*