

Skeletal muscle oxidative capacity in young and older women and men

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Received 22 December 1999; accepted in final form 19 April 2000

Kent-Braun, Jane A., and Alexander V. Ng. Skeletal muscle oxidative capacity in young and older women and men. *J Appl Physiol* 89: 1072–1078, 2000.— It has been suggested that a decline in skeletal muscle oxidative capacity is a general consequence of aging in humans. However, previous studies have not always controlled for the effects of varying levels of physical activity on muscle oxidative capacity. To test the hypothesis that, when matched for comparable habitual physical activity levels, there would be no age-related decline in the oxidative capacity of a locomotor muscle, the postexercise recovery time of phosphocreatine was compared in the tibialis anterior muscle of young [$n = 19$; 33.8 ± 4.8 (SD) yr] and older [$n = 18$; 75.5 ± 4.5 yr] healthy women and men of similar, relatively low, activity levels. The intramuscular metabolic measurements were accomplished by using phosphorus magnetic resonance spectroscopy. The results indicate that there was no age effect on the postexercise recovery time of phosphocreatine recovery, thus supporting the stated hypothesis. These data suggest that there is no requisite decline in skeletal muscle oxidative capacity with aging in humans, at least through the seventh decade.

physical activity; aging; gender; magnetic resonance spectroscopy

A GREAT DEAL OF ATTENTION has been focused on the apparently inevitable decline of skeletal muscle performance that occurs with aging in humans. This attention has included a discussion of whether muscle metabolic capacity is necessarily diminished with age and the extent to which this diminution may be promoted by decreased levels of daily physical activity.

Both invasive (biopsy) and noninvasive [magnetic resonance spectroscopy (MRS)] studies of muscle metabolism in populations varying from subclinical (22) to athletic (6, 28) have suggested a range of adaptations to aging, including a decrease in mitochondrial function (6, 7, 21, 22, 24) with little effect on glycolytic capacity (7). A gradual loss in the capacity to generate adenosine triphosphate oxidatively might be expected to contribute to a loss of muscle performance in the latter part of the life span. An examination of mitochondrial DNA mutations in human skeletal muscle indicated that there is an accumulation of various

mutations with age (23) and that this accumulation may be related to physical activity level (4). The separate influence of reduced physical activity on the decline of muscle oxidative capacity has not been adequately addressed.

The purpose of this study was to examine skeletal muscle oxidative capacity in groups of young and older women and men who were matched for similar levels of habitual physical activity. The hypothesis to be tested was that, in subjects selected for comparable activity levels, there would be no age-related decline in skeletal muscle oxidative capacity. The oxidative capacity of the tibialis anterior muscle, used for locomotion, was measured by using phosphorus MRS.

METHODS

Subjects. Nineteen young (age 27–45 yr; 9 women, 10 men) and 18 older (69–84 yr; 9 women, 9 men) healthy women and men were recruited for this study. The subjects who were recruited were relatively sedentary; they were neither athletes nor participating in a regular exercise regimen. To minimize the possibility of including subjects with latent peripheral vascular disease, all volunteers were required to have an ankle-to-brachial arterial pulse pressure ratio >1.0 on the same leg as studied by MRS. No subject was taking medication that might be expected to affect performance on either the peak oxygen consumption ($\dot{V}O_{2\text{ peak}}$) or MRS tests (e.g., β -blockers, vasodilatory drugs, and so forth). All volunteers were nonsmokers. To further characterize our subjects as healthy, all volunteers were assessed for their general level of symptomatic fatigue by using the 10-point visual analog fatigue scale (VAFS; Ref. 18). All of the older women were a minimum of 13 yr postmenopause. Five of the older women were on estrogen replacement therapy, and four had never been on such replacement therapy.

Informed consent was obtained from all subjects before participation in the study, which was approved by the Committee on Human Research at the University of California, San Francisco and the San Francisco Veterans Affairs Medical Center.

Physical activity measurement. After screening by interview for usual activity habits (e.g., no physical training program), average daily physical activity was measured in all subjects by using a three-dimensional accelerometer (Tritrac R3D, Professional Products, Madison, WI), as performed and

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described previously (15, 26). The accelerometer is a battery-operated unit that measures acceleration along the x -, y -, and z -axes. The net vector magnitude of the three axes was used as a representative measure of motion or activity (26). Subjects were instructed in the use of the accelerometer, which was wrapped in neoprene, placed in a small pack, and worn snugly around the waist during waking hours for 7 days. The monitor was then returned to the laboratory, and the data were downloaded to a computer and visually inspected for compliance. The vector magnitude data were averaged over the 7-day period and reported as average daily activity (arbitrary units/day). For ease of presentation, all daily averages are divided by 1,000. To be representative of usual activity patterns, data were not collected during holiday periods or if the subject was ill (e.g., cold, flu).

A secondary measure of physical activity was also obtained by using a standardized 7-day recall questionnaire (29). This consisted of interviewing each subject regarding how much time was spent in low-, moderate-, and high-intensity activity in the preceding week. The interview was performed on the return of the activity monitor to the laboratory so that both activity instruments reflected the same time period. Data are reported in estimated kilocalories per kilogram per day.

Systemic oxidative capacity measurement. $\dot{V}O_{2\text{ peak}}$. All subjects were tested for $\dot{V}O_{2\text{ peak}}$ on an electronic, motor-driven treadmill (Marquette Electronics, Milwaukee, WI). Breath-by-breath gas analysis was accomplished by using a computerized metabolic cart (Medgraphics, St. Paul, MN) that was calibrated before each study. Each volunteer walked at an individually selected comfortable pace (2.4–4.3 miles/h), and the grade was increased every 2 min for a total increase of 3.5–12.5%. Exercise generally lasted 8–12 min. Ratings of perceived exertion were acquired throughout exercise, by using the Borg 10-point scale (3).

Brachial artery blood pressure and a 12-lead electrocardiogram were monitored by a physician for abnormalities at rest and throughout exercise and recovery. Subjects were eliminated from the study if there was any sign of cardiac abnormality. In eight older adults (3 women, 5 men), the treadmill test was not started because of abnormalities at rest or was stopped because of electrocardiogram signs of abnormalities during exercise. The records for these individuals were later reviewed by a cardiologist, and each volunteer was referred for follow-up. These subjects were eliminated from the study, and additional volunteers were recruited.

The $\dot{V}O_{2\text{ peak}}$ test was terminated on volitional exhaustion or any two of the following: attainment of a plateau in oxygen consumption ($\dot{V}O_2$), a respiratory exchange ratio ≥ 1.1 , and a heart rate $\geq 90\%$ of predicted maximum ($220 - \text{age}$). Each subject was verbally encouraged to achieve a maximal response.

Muscle oxidative capacity measurement: MRS. After muscular contraction, the resynthesis of phosphocreatine (PCr) follows a single exponential time course and is accomplished exclusively via oxidative phosphorylation in the mitochondria (1, 25). Therefore, if it is assumed that oxygen delivery to the mitochondria is not limited, the rate of PCr recovery reflects the oxidative capacity of the muscle. Because under some conditions oxygen delivery may be rate limiting, even in healthy individuals (9), we consider PCr recovery to reflect the functional oxidative capacity of the muscle. That is, it can be used to assess the capacity to deliver, extract, and utilize oxygen. The rate of PCr recovery after a 15-s maximal voluntary contraction (MVC) of the tibialis anterior was measured as an index of locomotor muscle oxidative capacity. This protocol, adapted from that of Walter et al. (33), acti-

vates all fibers in the muscle and results in a significant decrease in PCr with no decrease in intramuscular pH, thus optimizing the conditions for estimating oxidative capacity by using the PCr-recovery measure (1, 11, 25). Recovery was monitored for 10 min. In the study by Walter et al., which used a similar exercise protocol, the coefficient of variation for PCr recovery was 8%.

The metabolic data were acquired with a 30-cm-bore 1.9-T Oxford magnet and Surrey Medical Imaging Systems spectrometer (Surrey, UK), as performed previously (12, 14, 17). All testing took place with the subject seated and legs extended. The right leg was studied unless there was a contraindication to do so (e.g., bunion). The leg was straight and stabilized with a knee brace, and the ankle angle was fixed at 120° plantar flexion. A 3 × 5-cm elliptical copper transmit and receive coil was taped over the belly of the tibialis anterior. The tibialis anterior muscle is a particularly useful model for the examination of the effects of aging because it is used for locomotion and little else. By controlling for physical activity level and therefore selecting groups with comparable amounts of locomotion, we sought to isolate the effects of age alone.

After the subject was secured in the leg exercise apparatus, the leg of interest was loaded into the bore of the magnet and the nonstudy leg was abducted to the side. Care was taken during the setup and loading procedures to maintain the tibialis muscle at rest. After shimming on the water signal, the phosphorus spectra were acquired with a 1.25-s repetition time, nominal 47° pulse, and 2.5-s temporal resolution (2 averages). After the data were averaged to obtain a 1-min rest spectrum and 15-s recovery spectra, the data were processed by using NMR1 software (New Methods Research, White Plains, NY). Eight peaks were fit, corresponding to the broad bone component, phosphomonoesters, P_i , phosphodiesters, PCr, and γ -, α -, and β -ATP. All peaks in the region were fit to avoid inaccurate assignment of peak areas arising from overlapping peaks. Calculations of millimolar concentrations, pH and percent change of PCr were accomplished in a spreadsheet, by using standard equations (1, 32). The metabolic data were corrected for partial saturation, by using experimentally derived correction factors. The recovery of PCr, expressed as percent recovered, was fit to a single exponential in Sigmaplot (SPSS, Chicago IL) by using the following equation

$$f = a[1 - \exp(-t/\tau)]$$

where f is the percent change in PCr above the end-contraction value, a is maximum amplitude of PCr (%recovered), t is time, and $t_{1/2} = 2\ln(\tau)$.

Exercise protocol and force measurement. In response to a verbal command, each subject sustained an MVC for 15 s, during which time force and MRS data were acquired continuously. Muscle force during the 15-s MVC was measured by a transducer mounted under the footplate. The transducer signal was amplified and coupled to a personal computer, as described previously (13). Force data were collected at a sampling frequency of 500 Hz by using Labview software (National Instruments, Austin, TX) and was subsequently transferred to a spreadsheet for analysis. All subjects were verbally encouraged throughout the contraction. Peak force at the onset of the contraction and the percent decline of force (average of last 3 s/initial peak) were recorded as indicators of muscle strength and fatigability, respectively.

Statistical analyses. The data were analyzed by using a two-factor ANOVA, with age and gender as factors. Age or gender main effects and age-by-gender interactions are reported. Exploratory comparisons of the effect of estrogen

replacement therapy were performed by unpaired *t*-test. Linear regression was used to explore the relationship between $\dot{V}O_{2\text{ peak}}$ and PCr $t_{1/2}$. For all analyses, differences were considered significant when $P < 0.05$. Descriptive data are presented as mean \pm SD; all other variables are presented as means \pm SE. To further aid in interpretation of the data (8), the 95% confidence interval and an exact *P* value are provided for the primary outcome variable, PCr $t_{1/2}$.

RESULTS

Subjects. The characteristics of the subject groups are presented in Table 1. There was an ~42-yr difference in mean age between young and older groups. Women were shorter and lighter than men, with no age effect. There was an age-by-gender interaction for height and weight because of the small stature of the older women (Table 1). The amount of symptomatic fatigue reported by using the 10-point scale was small and similar between young (VAFS = 2.9 ± 1.1) and older (3.0 ± 2.0) groups. The ethnic makeup of the young group ($n = 19$) was 13 Caucasian, 4 Asian, and 2 Hispanic; and the older group ($n = 18$) was 15 Caucasian, 1 Asian, 1 Hispanic and 1 Native American.

Physical activity. There were no age or gender effects for either measure of physical activity (Table 1). Thus we were successful in recruiting groups of similar habitual activity level. Within the groups, there was a comparable range in physical activity (young: 104–224 arbitrary units, older: 90–243 arbitrary units).

Systemic $\dot{V}O_{2\text{ peak}}$. As expected, $\dot{V}O_{2\text{ peak}}$ was significantly lower in the older compared with younger subjects, whether the data were expressed in absolute or relative terms (Table 2). Similarly, peak minute ventilation (\dot{V}_E ; l/min), respiratory exchange ratio, and ratings of perceived exertion were lower in older compared with young subjects (Table 2). In the case of $\dot{V}O_{2\text{ peak}}$ (l/min) and peak minute ventilation, women were also lower than men. The age-by-gender interactions suggest these gender effects were due primarily to the low values of the older women. The percentage of maximum predicted heart rate reached during the exercise was similar in all groups.

In the group of postmenopausal women, there was a tendency for $\dot{V}O_{2\text{ peak}}$ to be higher in those women on estrogen replacement therapy (27.4 ± 1.3 ml·kg⁻¹·min⁻¹) compared with those not on any form of this therapy (22.5 ± 2.0 ml·kg⁻¹·min⁻¹; $P = 0.056$). There was no effect of estrogen status on any other

study measure (data not shown). Thus it is likely that this tendency was observed by chance.

Skeletal muscle oxidative capacity and force. In the resting tibialis muscle, P_i /PCr, PCr (mM), and pH were all similar between young and old subjects, with no gender effects (Table 3). At the end of exercise, there were no age or gender effects on the extent to which PCr had depleted. There was a difference in pH at the end of exercise, with the older adults being alkalotic relative to the young subjects. However, the magnitude of this difference was small, and neither group experienced acidosis to an extent that might be expected to influence the rate of PCr recovery (1). The $t_{1/2}$ of PCr recovery was similar in young and older subjects ($P = 0.774$; Fig. 1 and Table 2). The 95% confidence interval for this comparison was -5.61 – 3.97 . Interestingly, there was a trend toward a faster PCr recovery in women compared with men ($P = 0.065$). There was a significant correlation between $\dot{V}O_{2\text{ peak}}$ and PCr recovery time for all subjects combined ($r = 0.38$, $P = 0.02$; $n = 36$), with $r = 0.53$ ($P = 0.02$) for the young group and $r = 0.39$ ($P = 0.12$) for the older group.

At the onset of the contraction, the men generated more force than the women (i.e., were stronger) and the young generated more than the older adults (data not shown). There were no age or gender effects on the amount of fatigue developed during the 15-s MVC. Force fell to ~77% of the initial level in all groups. This degree of fatigue is consistent with a maximal effort during the contraction and indicates that all subjects experienced a similar exercise stimulus.

DISCUSSION

The primary result of this study was the observation that, when matched for similar habitual physical activity levels, a locomotor muscle of healthy older men and women had no deficit in oxidative capacity compared with their younger counterparts. This result suggests that decreased skeletal muscle oxidative capacity is not a de facto consequence of aging in humans. Furthermore, any possible effect of age on the rate of PCr recovery was insignificant compared with the wide range in PCr recovery values observed in both the young and older subjects. An important aspect of this study was the selection of subjects who were healthy yet had comparable, relatively low, activity levels.

Table 1. *Subject characteristics*

Measure	Young Women ($n = 9$)	Older Women ($n = 9$)	Young Men ($n = 10$)	Older Men ($n = 9$)
Age, yr	33.2 ± 4.6	75.3 ± 4.6	33.4 ± 5.2	75.7 ± 4.7
Height, cm	169.2 ± 7.9	161.7 ± 6.8	174.0 ± 8.0	182.1 ± 5.8
Weight, kg	73.4 ± 22.3	59.4 ± 9.7	78.1 ± 15.0	87.3 ± 13.2
Activity				
Accelerometer, arbitrary units/day	149.6 ± 32.9	164.9 ± 50.8	176.1 ± 31.3	143.5 ± 48.4
7-Day recall, kcal·kg ⁻¹ ·day ⁻¹	33.6 ± 1.2	36.2 ± 3.8	36.6 ± 7.6	34.1 ± 1.9

Values are means \pm SD; *n*, no. of subjects. These descriptive data are presented by age and gender groups to aid interpretation. Men were taller and heavier than women, but there were no age effects on height or weight. There were no age or gender effects on physical activity.

Table 2. Peak values obtained at the end of the treadmill test

Measure	Young Women	Older Women	Young Men	Older Men
RER	1.20 ± 0.02	1.11 ± 0.01	1.17 ± 0.02	1.15 ± 0.01
%Heart rate maximum	100.4 ± 1.4	103.2 ± 2.4	99.0 ± 2.0	103.2 ± 3.0
RPE	8.8 ± 0.8	7.8 ± 0.6	9.1 ± 2.0	7.4 ± 0.7
$\dot{V}_{E_{peak}}$, l/min	91.4 ± 3.8	58.7 ± 3.2	131.2 ± 9.9	98.3 ± 7.3
$\dot{V}_{O_{2peak}}$, l/min	2.21 ± 0.90	1.47 ± 0.89	3.22 ± 0.20	2.38 ± 0.57
$\dot{V}_{O_{2peak}}$, ml·kg ⁻¹ ·min ⁻¹	32.6 ± 2.2	25.0 ± 1.4	41.3 ± 1.4	27.6 ± 0.2

Values are means ± SE. RER, respiratory exchange ratio; RPE, rating of perceived exertion; $\dot{V}_{E_{peak}}$, peak minute ventilation; $\dot{V}_{O_{2peak}}$, peak oxygen consumption. $\dot{V}_{O_{2peak}}$, $\dot{V}_{E_{peak}}$, RER, and RPE were all lower in older compared with young subjects. There was a gender effect for absolute $\dot{V}_{O_{2peak}}$ and $\dot{V}_{E_{peak}}$, an age-by-gender interaction for $\dot{V}_{E_{peak}}$, and a tendency for an age-by-gender interaction for $\dot{V}_{O_{2peak}}$ ($P = 0.055$). There was no gender effect on RPE, and there were no age or gender effects in the percent predicted heart rate maximum.

A review of the literature indicates that the issue of whether skeletal muscle oxidative capacity declines with age remains controversial. Evidence both supporting (6, 7, 21, 22, 24) and refuting (5, 28, 31) this decline may be found. A range of subject populations, from frail individuals to athletes, has been studied.

Meredith et al. (24) reported that vastus lateralis muscle oxidative capacity (by biopsy) was reduced in older (65 yr) compared with younger untrained men and women but that this difference disappeared after training. Interestingly, the pretraining difference in $\dot{V}_{O_{2peak}}$ remained between the young and older groups (24). A series of studies of the gastrocnemius muscle, in which both biopsy and MRS techniques were used, have indicated that oxidative capacity is reduced in older volunteers (6, 7, 21, 22). PCr recovery time was slowed in the plantar flexors of both healthy (67 yr) and impaired (82 yr) older compared with young adults (22). Oxidative enzyme activities were decreased in the lateral gastrocnemius muscles of older (64 yr) sedentary but healthy men and women (7). Follow-up studies that combined MRS and biopsy techniques indicated oxidative capacity was lower in the gastrocnemius muscles of older compared with younger subjects, regardless of their training status (6, 21).

In contrast to these and other studies, a number of investigators could find no age-related difference in skeletal muscle oxidative capacity. In an early MRS study, Taylor and colleagues (31) found no effect of age (70–80 yr) on PCr recovery rate after handgrip exercise. The oxidative enzyme capacities of type I and IIa vastus lateralis muscle fibers were similar in older (57 yr) compared with younger trained subjects (28). More recently, Chilibeck et al. (5) found no age-related difference in PCr recovery kinetics in the gastrocnemius

muscle of moderately active younger and older (67 yr) adults. Our study provides further evidence of unimpaired oxidative capacity in the skeletal muscle of older adults, in this case in relatively sedentary, but still healthy, subjects.

Thus evidence is available to both support and refute the concept of a necessary decline of skeletal muscle oxidative capacity with aging. It seems, however, that much of the conflict concerning this issue may be due to differences in the activity of the muscles or populations studied. The previous studies reporting lower oxidative capacity in older subjects included little or no quantitative control for the level of overall physical activity or the activity of the muscle studied. In the study by Meredith and co-workers (24), skeletal muscle oxidative capacity in the older group returned to the level of the younger subjects after training. Similarly, Proctor and colleagues (28) could find no oxidative deficit in older trained subjects. These results imply a primary role of disuse in the decline of oxidative capacity, rather than an inherent age-related defect in oxidative metabolism.

To focus on age, and minimize the effect of activity on our results, we endeavored to control both the quantity and quality of muscle use in our study subjects. By selecting groups with similar overall activity habits, we attempted to control for the quantity of activity in which the muscle was engaged. In addition to the similar activity levels recorded in the young and older groups in the present study, the low $\dot{V}_{O_{2peak}}$ values confirm their relatively sedentary status. Previously, our laboratory observed slowed PCr recovery in the tibialis anterior muscle of volunteers with multiple sclerosis compared with healthy controls (17). Because multiple sclerosis is a central nervous system

Table 3. Indices of peripheral skeletal muscle metabolism

Measure	Young Women	Older Women	Young Men	Older Men
Preexercise P _i /PCr	0.09 ± 0.02	0.08 ± 0.02	0.08 ± 0.02	0.06 ± 0.02
Preexercise PCr, mM	39.2 ± 0.6	39.4 ± 0.6	39.4 ± 0.6	40.0 ± 0.6
Preexercise pH	7.09 ± 0.01	7.06 ± 0.03	7.11 ± 0.02	7.08 ± 0.04
End-exercise PCr, %rest	31.6 ± 4.9	33.1 ± 5.0	33.9 ± 6.0	41.9 ± 5.4
End-exercise pH	7.04 ± 0.03	7.14 ± 0.02	7.01 ± 0.03	7.09 ± 0.04
$t_{1/2}$ PCr recovery, s	19.9 ± 2.6	21.0 ± 2.5	26.0 ± 1.7	23.6 ± 2.3

Values are means ± SE. PCr, phosphocreatine; $t_{1/2}$, postexercise PCr recovery time. With the exception of end-exercise pH, there were no age effects on any measure. There was a tendency toward faster PCr recovery in women compared with men. There were no other gender effects.

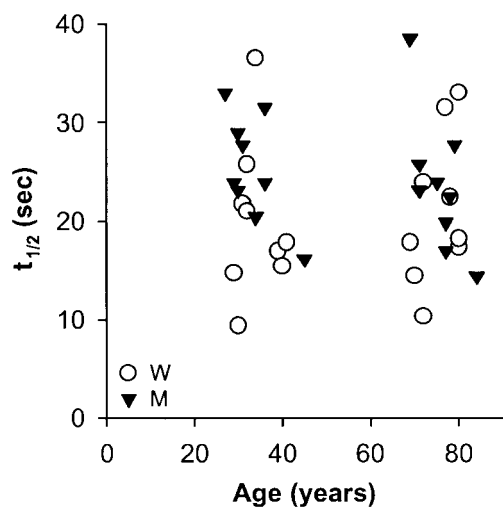


Fig. 1. Individual values for postexercise phosphocreatine recovery time ($t_{1/2}$) for young and older women (W) and men (M). There were no age or gender differences in this variable, although there was a tendency ($P = 0.065$) for the women to recover faster than the men.

disorder, we presumed this to be a secondary effect of reduced physical activity in this group, which was ~35% less active than the sedentary controls (26). Thus the PCr recovery measure is sensitive to changes in oxidative capacity in individuals at the low end of the activity scale. Overall, it appears that the modest activity level observed in our older subjects is adequate to maintain a functional muscle oxidative capacity comparable to that of similarly sedentary younger adults.

By studying a muscle used for locomotion and little else, we also attempted to reduce the variability in oxidative capacity that might be due to the quality of the activity for which the muscle is used. It is likely that the pattern of use of the tibialis muscle was similar in all subjects; it was used primarily for walking. In effect, this minimizes the variability due to differences in the type of activity typically performed. In contrast, other muscle groups that have been studied (e.g., quadriceps and gastrocnemius) can be used both for locomotion and in high-power activities (e.g., jumping, sprinting), which may be more common in younger compared with older people. As a result, the type II fibers in these muscles of the younger subjects might be activated more frequently or forcefully than in the older subjects. It is difficult to imagine a circumstance in which the tibialis anterior might be used for high-power activity; the typically high percentage of type I fibers in this muscle reflects its function (10).

In addition to enrolling only nonsmokers in our study, an effort was made to exclude subjects who might have latent peripheral vascular disease from any other cause. Screening all volunteers for healthy ankle pulses (ratio of ankle to brachial systolic pressure >1.0) may have contributed to our finding of similar recovery times in young and older subjects. Some previous studies indicating age-related differences in oxidative capacity have included older adults

with subclinical claudication or vessel disease, which would have the potential of impairing blood flow and therefore oxygen delivery (22). Under those circumstances, it is expected that PCr recovery would be slowed.

Finally, by studying a relatively small muscle, we were able to assess muscle oxidative capacity without concern that demand on the cardiovascular system during the exercise protocol might have limited peripheral oxygen availability.

The data in Table 3 illustrate that, with the exception of end-exercise pH, the metabolic conditions were similar in all groups at the end of exercise. This is important because acidosis will slow the kinetics of the creatine kinase reaction and therefore delay PCr recovery (1, 33). The slight alkalosis observed in the older subjects at the end of exercise, because of PCr hydrolysis during the exercise, likely had no influence on the rate of PCr recovery (33). Had there been such an effect, it would have shown up as an age effect, which was not observed. A comparable muscle response to exercise is evidenced by the similar magnitude of PCr depletion and fatigue across all groups.

Interestingly, there was a tendency for women to have higher oxidative capacity than men. Although the results of some biopsy studies have suggested gender-related differences in oxidative enzyme capacity (30), further studies will be needed before we may draw any conclusion about this issue. At a minimum, future studies should include a design that is balanced by gender.

Previously, it has been acknowledged that the rate of PCr recovery is an index of the rate of mitochondrial oxidative phosphorylation only under conditions in which the delivery of oxygen is not limited. However, in light of the recent study by Haseler et al. (9), we further interpret the PCr recovery measure as an *in vivo* index of overall, or functional, skeletal muscle oxidative capacity. That is, because the rate of PCr resynthesis is dependent on the adequate delivery of oxygen, and because this delivery may be limiting in healthy individuals under certain conditions (9), it must be emphasized that this is a measure of overall muscle capacity, including the delivery, extraction, and utilization of oxygen.

Despite a similar peripheral muscle oxidative capacity, our older subjects showed the expected age-related decrease in $\dot{V}O_{2\text{ peak}}$ during treadmill walking. It has been argued that $\dot{V}O_{2\text{ peak}}$ in older adults may be limited by three primary mechanisms: 1) lower cardiovascular capacity at peak work rates, 2) smaller absolute muscle mass, and 3) lower oxygen utilization by the working skeletal muscle. Discussion continues in the literature as to which of these mechanisms dominates (cf. Ref. 27). The apparently higher correlation between $\dot{V}O_{2\text{ peak}}$ and PCr recovery in the young ($r = 0.53$) compared with older ($r = 0.39$) groups in the present study is consistent with a more tightly coupled relationship between peripheral and systemic oxidative capacities in young compared with older adults.

We believe that it is unlikely that an age-related difference in lean body mass accounted for all of the difference in $\dot{V}O_{2\text{ peak}}$ in our groups. Proctor and Joyner (27) recently found that, after correction for differences in leg muscle mass measured by dual-energy X-ray absorptiometry, $\dot{V}O_{2\text{ peak}}$ remained $\sim 13\%$ lower in older (61–64 yr) trained men and women compared with young trained adults. In a similar vein, if we “correct” our $\dot{V}O_2$ values for differences in muscle mass (estimated by using the values for anterior compartment fat-free muscle areas previously obtained in comparable groups of young and older women and men; Ref. 16), we are left with age-related deficits in $\dot{V}O_{2\text{ peak}}$ of $\sim 7\%$ for women and $\sim 13\%$ for men, values remarkably similar to those of Proctor and Joyner. Thus our data are consistent with the possibility that, in healthy individuals of similar physical activity habits, the age-related decline in $\dot{V}O_{2\text{ peak}}$ (2) may occur independently from a change in peripheral skeletal muscle oxidative capacity, and may not be fully explained by a loss of muscle mass. Although we do not wish to suggest that the performance of the tibialis anterior limits $\dot{V}O_{2\text{ peak}}$, we do suggest that this locomotor muscle adequately represents the intramuscular metabolic changes that might occur due to aging. By selecting groups with similar activity levels, we focused on the effects of age and gender, with the influence of disuse minimized.

Biopsy studies have demonstrated that, as in other muscles, there is an age-related shift in the tibialis anterior from ~ 75 to $\sim 90\%$ type I fiber composition (19, 20). We cannot rule out the possibility that this shift may mask an effect of age on the oxidative capacity of the muscle. That is, perhaps the additional “oxidative” fiber area might counter a lower oxidative capacity within individual fibers. However, in trained older individuals, there was no oxidative impairment at the single-fiber level (28). Further assessment of single-fiber oxidative capacity, in groups controlled for usual activity level, will be necessary to address this question.

Many of the previously reported deficits in oxidative capacity, therefore, may have arisen because of secondary changes in the muscle. It seems possible to explain nearly all of the previous evidence of reduced capacity by differences in the health, patterns of muscle use or physical activity status of the study subjects. Although it may be that skeletal muscle oxidative capacity is lower in some older individuals, we conclude that, on the basis of the current literature and the results of the present study, a decrease in the functional oxidative capacity of the muscle is not a necessary consequence of aging, at least through the seventh decade. The likelihood is that oxidative capacity is exquisitely sensitive to changes in use, and it therefore may be an excellent marker for early, secondary, changes in skeletal muscle function with aging.

We acknowledge the assistance of Dr. Kirsten Johansen, Hung T. Dao, Julie W. Doyle, and Dr. Brian Soher in the acquisition and analysis of the data. We thank the subjects for their participation in this study. We also thank Dr. Milton Hollenberg for consultation in

reference to the electrocardiograph tests and Dr. John Neuhaus for statistical advice.

This work was supported by National Institute on Aging Grant R29 AG-12819.

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