Vascular and metabolic response to isolated small muscle mass exercise: effect of age

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Lawrenson, L., J. G. Poole, J. Kim, C. Brown, P. Patel, and R. S. Richardson. Vascular and metabolic response to isolated small muscle mass exercise: effect of age. Am J Physiol Heart Circ Physiol 285: H1023–H1031, 2003.—To determine the effect of age on quadriceps muscle blood flow (QMBF), leg vascular resistance (LVR), and maximum oxygen uptake (QV\text{O}_2\text{max}), a thermal dilution technique was used in conjunction with arterial and venous femoral blood sampling in six sedentary young (19.8 ± 1.3 yr) and six sedentary old (66.5 ± 2.1 yr) males during incremental knee extensor exercise (KE). Young and old attained a similar maximal KE work rate (WR_{max}) (young: 25.2 ± 2.1 and old: 24.1 ± 4 W) and QV\text{O}_2\text{max} (young: 0.52 ± 0.03 and old: 0.42 ± 0.05 l/min). QMBF during KE was lower in old subjects by ~500 ml/min across all work rates, with old subjects demonstrating a significantly lower QMBF/W (old: 174 ± 20 and young: 239 ± 46 ml·min\(^{-1}·\text{W}\^{-1}\)). Although the vasodilatory response to incremental KE was ~142% greater in the old (young: 0.0019 and old: 0.0046 mmHg·min\(^{-1}·\text{W}\^{-1}\)), consistently elevated leg vascular resistance (LVR) in the old, ~80% higher LVR in the old at 50% WR and ~40% higher LVR in the old at WR_{max} (young: 44.1 ± 3.6 and old: 31.0 ± 1.7 mmHg·min\(^{-1}·\text{W}\^{-1}\)), dictated that during incremental KE the LVR of the old subjects was never less than that of the young subjects. Pulse pressures, indicative of arterial vessel compliance, were ~36% higher in the old subjects across all work rates. In conclusion, well-matched sedentary young and old subjects with similar quadriceps muscle mass achieved a similar WR_{max} and QV\text{O}_2\text{max} during incremental KE. The old subjects, despite a reduced QMBF, had a greater vasodilatory response to incremental KE. Given that small muscle mass exercise, such as KE, utilizes only a fraction of maximal cardiac output, peripheral mechanisms such as consistently elevated leg vascular resistance and greater pulse pressures appear to be responsible for reduced blood flow persisting throughout graded KE in the old subjects.

Vascular resistance; quadriceps; pulse pressures; O\text{2} conductance

THE AGE-RELATED DECLINE in vascular function may be responsible for reductions in blood flow to active skeletal muscle (27, 29, 35, 49) and has been documented in both clinical and research settings manifesting as decreased compliance in arteries and arterioles, chronic high blood pressure, and coronary disease (8). The mechanisms responsible for attenuated skeletal muscle blood flow with increasing age have been investigated utilizing several variables, such as exercise modality, baseline fitness level, and varying age ranges to test specific theories that link age to decreased perfusion of skeletal muscle. Because of the complexity and interdependence of both central and peripheral changes that occur with advancing age, a consensus concerning the mechanisms has not been reached.

Studies (3, 35, 49) of whole body exercise have documented ~20–30% lower blood flow during cycle exercise in elderly males (55–74 yr). Poole et al. (33) recently reported that old sedentary subjects (69.3 ± 2.0 yr) had an increasing blood flow deficit in comparison with young control subjects during cycle exercise from ~50% of the maximal work rate (WR_{max}). Conversely, small muscle mass experiments have shown preserved perfusion in recreationally active older males. Specifically, similar blood flows were recorded in active young and a wide range of active middle-aged to old (44–69 yr) males during one-legged exercise (26), and similar perfusion and vasodilatory capacity were reported in older (60–74 yr) subjects immediately after dynamic handgrip exercise (21). Together, these findings suggest that in aging populations, blood flow to skeletal muscle is limited by central factors and is therefore preserved during small muscle mass exercise. Casting doubt on these interpretations are data indicating that many peripheral vascular and metabolic factors decline with age, such as decreased reactivity to infused vasodilatory stimuli (9) and increased pulse pressures indicative of arterial vessel stiffening (8). Given that blood flow regulation has been reported to match oxygen demand and local metabolic requirements of skeletal muscle (2), others have implicated factors such as attenuated muscle mass that leads to reduced metabolic demand from chronically inactive muscle (13), decreased mitochondrial density, reduced oxidative capacity (7), and reduced citrate synthase activity (6) for the attenuated skeletal muscle blood flow with age.

The relative contributions of central versus peripheral factors in modulating blood flow are still contested, and both systems are known to decline with age. Therefore, the purpose of this study was to use the knee extensor exercise (KE) modality to study isolated dynamically exercising skeletal muscle in both young...
and old subjects, thereby investigating the consequences of aging on quadriceps muscle blood flow (QMBF) without the contribution of central factors. Specifically, we had several hypotheses. First, old subjects will demonstrate attenuated skeletal muscle blood flow, increased leg vascular resistance, and decreased vasodilatory capacity due to an age-related decline in vascular function. Second, for any given submaximal WR, maximum quadriceps O₂ consumption (QV0₂max) will be similar for young and old subjects. Third, the reduced peripheral blood flow will result in either a compensatory increase in arterial-venous (A-V) O₂ difference or a reduction in WRmax and muscle QV0₂max in the old.

METHODS

Subjects. Subjects consisted of six young (18–27 yr) and six old (61–77 yr) randomly selected healthy non-smoking sedentary males of similar physical activity level (Table 1). As part of the initial subject screening, incremental cycle ergometry tests were performed from WRmin of 50 + 25-W increments (young) and 30–50 + 20-W increments (old) until the subjects became fatigued. All subjects were determined to be sedentary by an interview questionnaire similar to that presented in previous work by Jacobs et al. (20) and were excluded from participation if they reported any exercise on a work-related, recreational, or competitive basis. The subjects’ sedentary lifestyle was confirmed by the preliminary cycle data revealing a low pulmonary VO₂max in both groups (Table 1). Health histories and physical examinations were completed. Subjects were not allowed to participate if they were found to be taking any medications that would alter blood flow responsiveness. Informed consent was obtained according to the University of California-San Diego Human Subjects Protection Program requirements.

Exercise modality and exercise protocol. Single-leg KE was performed that limited work to the quadriceps muscle group, as originally described by Andersen and Saltin (1), and more recently documented by Richardson et al. (38). The ergometer was adjusted so that contraction of the quadriceps muscles turned a flywheel producing a 90°–170° arc of the lower leg. To provide progressive levels of resistance to the quadriceps muscle, tension was incremented by increasing friction on a belt surrounding the subject’s body and the quadriceps muscle, tension was incremented by increasing friction on a belt surrounding the subject’s body temperature at each WR.

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Old</th>
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<tbody>
<tr>
<td>Age, yr</td>
<td>19.8 ± 1.3</td>
<td>66.5 ± 2.1</td>
</tr>
<tr>
<td>Height, cm</td>
<td>174.5 ± 4.2</td>
<td>174.4 ± 2.1</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85.2 ± 5.2</td>
<td>76.9 ± 5.0</td>
</tr>
<tr>
<td>Quadriceps muscle mass, kg</td>
<td>2.23 ± 0.09</td>
<td>2.17 ± 0.06</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.8 ± 0.6</td>
<td>25.2 ± 1.2</td>
</tr>
<tr>
<td>Cycle VO₂ max, ml·min⁻¹·kg⁻¹</td>
<td>31.6 ± 2.3</td>
<td>20.3 ± 1.8</td>
</tr>
</tbody>
</table>

Values are means ± SE. VO₂ max, maximal O₂ consumption. Body mass index determined by weight/height². Quadriceps muscle mass determined by anthropometrical measurements. *P < 0.05, significant difference between young and old subjects.
(17, 41) based on a proposal by Wagner (48) with the assumption of a homogeneously perfused muscle. Briefly, the drop in PO₂ along a capillary is calculated using Fick’s law of diffusion (Eq. 1)

\[
\frac{\Delta V_{O_2}}{\Delta x} = D_{mO_2} \left( P_{\text{capaO}_2} - P_{\text{mitoO}_2} \right)
\]

where \( P_{\text{mitoO}_2} \) is mitochondrial PO₂, which is set at 0 mmHg, only slightly less than that measured in the cytoplasm of canine muscle fibers (14) and in vivo measurements in human muscle (39). \( D_{mO_2} \) is an expression of all phenomena that facilitate O₂ unloading at the muscle and is useful as a comparison among conditions and subject populations for gas exchange analyses (18, 19).

**Thigh volume measurement**. With the use of thigh length, circumference, and skinfold measurements, thigh volume was calculated to allow an estimate of quadriceps femoris muscle mass, as suggested by Jones and Pearson (22), and utilized originally by Andersen and Saltin (2).

**Statistical analysis**. Data were analyzed post hoc with the use of regression analysis with paired and unpaired t-tests. Statistics were performed with the use of commercially available software (GraphPad, San Diego, CA, and SPSS Software, version 10.1). The data were subjected to a power analysis resulting in a β-value ≈ 0.8 in the majority of variables (e.g., \( V_{O_2,\text{max}} \), \( \beta = 0.74 \)). All data are expressed as means ± SE. Significance was established at an α-level of \( P \leq 0.05 \).

**RESULTS**

**Preliminary testing and subject matching.** Both young and old subjects revealed similar height, weight, and activity level (Table 1). In addition, quadriceps muscle mass was not different between young and old, thereby permitting the comparison of data that are not adjusted for muscle mass. Preliminary cycle ergometry testing revealed a significant difference in whole body power output, \( W_{\text{max}} \) (young: 181 ± 4 W and old: 131 ± 12 W) and pulmonary \( V_{O_2,\text{max}} \) (young: 31.6 ± 2.3 and old: 20.3 ± 1.8 ml·min⁻¹·kg⁻¹). In contrast, during small muscle mass KE, the young and old subjects were equally matched in terms of quadriceps \( W_{\text{max}} \) (young: 27.0 ± 2.5 W and old: 24.1 ± 4.0 W; Table 2).

**QMBF and vascular pressures.** QMBF was initially lower in the old subjects, yet the aging subjects showed a greater vasodilatory response to incremental KE (Fig. 1A and 2C). Specifically, at the initial KE (2.1 W), QMBF was attenuated in the old (old: 958 ± 52 ml/min and young: 1,711 ± 143 ml/min). While the quadriceps muscles were challenged by progressive increases in KE WR, the corresponding increase in QMBF per watt (≈115 ml·min⁻¹·W⁻¹) was not different between young and old subjects (Fig. 1A). Although the vasodilatory response to incremental KE (change in vascular resistance per watt) was ≈142% greater in the old (Fig. 2C), at no point was this response sufficient to overcome the elevated initial LVR in the old, as LVR remained ≈80% higher in the old at WR-50%, and ≈40% higher at \( W_{\text{max}} \) (young: 30.1 ± 1.7 mmHg/ml and old: 44.1 ± 3.6 mmHg/ml; Fig. 2C). MAP was not different between young and old subjects at maximal KE. The driving force on blood across the muscle bed (MAP–MVP) was not different between young and old subjects throughout incremental KE, and both groups showed a similar and gradual increase in A-V pressure with increasing work (Fig. 2A). Pulse pressures, a measure of arterial vessel compliance, were ≈36% higher in the old subjects, and the rate of increase throughout incremental KE was similar in both groups (Fig. 2B).

**Leg oxygen consumption.** At each incremental WR, \( V_{O_2,\text{max}} \) was slightly reduced in the old subjects, which did not achieve statistical significance, and was more apparent at WRs <50% of \( W_{\text{max}} \). Although not statistically significant, the old subjects tended toward a lower y-intercept (young: 0.13 ± 0.02 l/min and old: 0.05 ± 0.01 l/min; Fig. 1B). Both groups revealed a similar rise in \( V_{O_2,\text{max}} \) per watt (slope: young, 0.014 ± 0.001; and old, 0.018 ± 0.002 l·min⁻¹·W⁻¹; Fig. 1B). Finally, both groups achieved similar \( V_{O_2,\text{max}} \) values (young: 0.52 ± 0.03 l/min and old: 0.42 ± 0.05 l/min; Table 2).

**A-V O₂ difference.** Elevated A-V O₂ difference was recorded in the old subjects at 3.6 W (young: 11.1 ± 0.8 ml/dl and old: 12.8 ± 1.0 ml/dl), more clearly illustrated by the increased y-intercept (young: 10.7 ± 0.73 ml/dl and old: 12.9 ± 0.68 ml/dl; Fig. 1C). Similar to the increasing A-V O₂ seen in trained athletes, younger subjects increased O₂ extraction as the wattage was incremented during KE. Although not statistically different from that of the young, the old subjects revealed a more constant A-V O₂ difference (slope: young, 0.045 ± 0.01; old, 0.046 ± 0.02 ml·dl⁻¹·W⁻¹; Fig. 1C).

**Table 2. Maximal blood gas and exercise variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Young</th>
<th>Old</th>
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<tbody>
<tr>
<td>Work, watts</td>
<td>27.0 ± 2.5</td>
<td>24.1 ± 4.0</td>
</tr>
<tr>
<td>Quadsricps muscle blood flow, l/min</td>
<td>3.95 ± 0.10</td>
<td>3.32 ± 0.32*</td>
</tr>
<tr>
<td>Quadsricps muscle VO₂, l/min</td>
<td>0.92 ± 0.3</td>
<td>0.42 ± 0.05</td>
</tr>
<tr>
<td>pHₐ</td>
<td>7.38 ± 0.01</td>
<td>7.38 ± 0.01</td>
</tr>
<tr>
<td>pHₐ</td>
<td>7.23 ± 0.01</td>
<td>7.23 ± 0.01</td>
</tr>
<tr>
<td>Hb, g/dl</td>
<td>14.1 ± 0.4</td>
<td>15.1 ± 0.6</td>
</tr>
<tr>
<td>CaₐO₂, ml/dl</td>
<td>19.7 ± 0.52</td>
<td>20.9 ± 0.81</td>
</tr>
<tr>
<td>CVₐO₂, ml/dl</td>
<td>6.5 ± 0.8</td>
<td>8.3 ± 0.6</td>
</tr>
<tr>
<td>PAO₂, mmHg</td>
<td>123 ± 6</td>
<td>116 ± 3</td>
</tr>
<tr>
<td>VENO₂, mmHg</td>
<td>24.0 ± 1.5</td>
<td>27.7 ± 1.5</td>
</tr>
<tr>
<td>SaO₂, %</td>
<td>98.8 ± 0.2</td>
<td>98.3 ± 0.2</td>
</tr>
<tr>
<td>SvO₂, %</td>
<td>32.2 ± 4.2</td>
<td>39.1 ± 2.8</td>
</tr>
<tr>
<td>O₂ del l/min</td>
<td>0.78 ± 0.02</td>
<td>0.69 ± 0.06</td>
</tr>
<tr>
<td>(CAO₂ – CV₀₂), ml/dl</td>
<td>13.2 ± 0.9</td>
<td>12.7 ± 0.8</td>
</tr>
<tr>
<td>Lactate outflow, mmol/min</td>
<td>5.5 ± 1.6</td>
<td>4.2 ± 1.1</td>
</tr>
<tr>
<td>Leg vascular resistance, mmHg·min⁻¹·ml⁻¹</td>
<td>27.2 ± 2.0</td>
<td>43.1 ± 4.5*</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>136 ± 7</td>
<td>138 ± 6</td>
</tr>
<tr>
<td>Arterial-venous pressure, mmHg</td>
<td>120 ± 4</td>
<td>121 ± 7</td>
</tr>
<tr>
<td>PcaO₂, mmHg</td>
<td>42.5 ± 0.9</td>
<td>46.3 ± 2.1</td>
</tr>
<tr>
<td>DmO₂, l/min·mmHg⁻¹</td>
<td>12.5 ± 1.0</td>
<td>10.4 ± 1.0</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 young and 6 old subjects. [Hb], total hemoglobin concentration; CV₀₂, total oxygen content of arterial blood; CV₀₂, oxygen concentration of venous blood; SaO₂, arterial oxygen saturation; SV₀₂, venous oxygen saturation; PAO₂, arterial PO₂; VENO₂, venous PO₂; PcaO₂, mean capillary PO₂; DmO₂, O₂ diffusional conductance. Subscripts a and v denote arterial and venous, respectively. Blood gas measurements from femoral arterial and venous sampling during maximal single leg dynamic knee extensor exercise; quadriceps blood flow measured by thermodilution method. *P < 0.05, significantly different between young and old subjects.
Major blood-related variables. Arterial PO2, O2 saturation, [Hb], and therefore, arterial O2 content were not different between young and old. O2 delivery was not different between young and old across all WRs and at WRmax (Table 2). PcapO2 and DmO2 were similar between the young and old.

DISCUSSION

There are several major findings of this study. First, QMBF measurements during KE revealed a consistently attenuated blood flow (~500 ml/min) in old sedentary subjects when compared with young sedentary subjects of similar quadriceps muscle mass. Second, LVR was elevated in the old throughout KE, and, as the driving force on blood across the muscle bed (A-V pressure) was similar for both groups, elevated LVR was responsible for reduced QMBF in the old subjects. Third, the vasodilatory response to incremental KE (fall in LVR W−1) was elevated in the old subjects, indicating that the vasodilatory pathways activated in response to incremental KE are capable of producing a greater change in LVR from the initial WR of 3 W to WRmax. These changes, however, were insufficient to overcome the initially elevated LVR in the old subjects, who therefore always had a greater absolute LVR than the young subjects. Finally, old and young sedentary subjects of equal quadriceps muscle mass achieved similar WRmax and QV̇O2 max during small muscle mass KE. During cycle exercise, the old subjects revealed lower WRmax and pulmonary V̇O2 max, indicating an age-related central limitation to maximal whole body exercise. When taken together, these findings indicate that when central limitations are minimized during small muscle mass KE, peripheral factors usually associated with declining vascular function, including elevated LVR, elevated pulse pressures, and reduced QMBF persist in the old subjects throughout KE. Perhaps in compensation for the initially reduced QMBF and elevated LVR, the old subjects revealed a greater vasodilatory response to incremental KE, which, when coupled with the elevated A-V O2 difference documented in the old subjects, facilitate the attainment of equal O2 uptake and power output to the young subjects during maximal isolated skeletal muscle exercise.

Attenuated QMBF in old subjects throughout KE. QMBF was consistently lower (~500 ml/min) in the old subjects during KE. These data differ from previous findings obtained with a similar KE model that revealed similar perfusion between young and middle-aged to older subjects (26). This disparity in findings is perhaps explained by the difference in age range and activity levels between the subjects in Magnusson’s study compared with the present research. Whereas Magnusson studied a wide range (44–69 yr) of middle-aged to old men who were regularly physically active, the current study focused on sedentary old subjects (66 ± 2.5 yr).

Findings from the current study also revealed that at maximal KE, older subjects have attenuated QMBF. This is not in agreement with the data presented by Jasperse et al. (21), who reported similar perfusion
between young and old subjects immediately after sub-maximal and maximal dynamic handgrip exercise. The subjects in the Jasperse study were reported to be “chronically physically active” possibly increasing forearm vascular conductance and accounting for the similarities in conductance and the equalization of blood flow. On the basis of mounting evidence implicating endurance exercise in modifying certain aspects of vascular function, such as improved vessel compliance (46) and improved vascular reactivity to infused pharmacological agents (9), one should use caution when comparing data from trained subjects and sedentary subjects. In addition, blood flow measurements presented by Jasperse et al. (21) were made directly after each level of exercise and may not be representative of the pathways controlling blood flow that are activated during dynamic exercise. It is also possible that the vasculature in the upper and lower extremities respond differently to the aging process.

The current data, however, are in accordance with previous studies (23, 49) that have documented reductions in skeletal muscle blood flow in aging subjects during exercise. In a related study from our laboratory, Poole et al. (33) reported an attenuated increase in blood flow to leg muscles in sedentary aging subjects during whole body cycle exercise from 50% of WRmax to WRmax, suggestive of a progressive maldistribution of blood flow with increasing exercise intensity, which was responsible for the attenuated leg blood flow in the old subjects. If central limitations were solely responsible for reduced muscle perfusion during cycle exercise in the old, it would be expected that when these central limitations are minimized (as in KE) perfusion in the old subjects should reach equal values to young

![Fig. 2. A: mean arterial pressure (MAP)-mean venous pressure (MVP) measured with femoral arterial and venous pressure transducers. B: pulse pressures measured in femoral artery. C: leg vascular resistance calculated as (MAP – MVP)/QMBF versus WR. All values recorded during incremental single leg knee extensor exercise. *Significantly different slope and y-intercept between young and old subjects.](http://ajpheart.physiology.org/)

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subjects at the same WR. The finding of a lower QMBF suggests that in the old subjects, peripheral vascular limitations during isolated small muscle mass exercise persist and are responsible for the attenuated blood flow in the old subjects. Possible mechanistic explanations for these observations may be the previously documented augmentation of $\alpha$-adrenergic vasoconstriction (11) and/or the decreased ability of insulin to alter blood flow to skeletal muscle (30). Although resting QMBF data were not collected in the current study, we cannot discount the possibility that low resting QMBF resulting from attenuated vasodilatory factors at rest in the old subjects (e.g., nitric oxide via an endothelial nitric oxide synthase mechanism) may persist during exercise and may be responsible for the consistently attenuated QMBF recorded throughout incremental KE (12, 15, 50).

Elevated LVR and pulse pressures in old subjects. The driving force on blood through the muscle bed (MAP – MVP) was not different in the old subjects. Similarly, MAP at WR max was not different between young and old. LVR was elevated in the old subjects throughout incremental KE and is therefore responsible for decreased QMBF in the old subjects. LVR is largely determined by two age-dependent factors, arteriolar cross-sectional area, and compliance of the arterial wall. Previous studies have documented multiple factors that contribute to elevated vascular resistance in aging populations, including decreased arterial and arteriolar diameter as a result of arterial wall thickening (10), arterial stiffening (25), insulin resistance (30), age-related reductions in tonic nitric oxide-mediated vasodilation (31, 44), and increases in endothelin-1-mediated vasoconstriction (4). Offering further mechanistic insight into elevated LVR in the old are the elevated pulse pressures seen throughout KE. Elevated pulse pressures are indicative of large artery stiffness (8, 25) and decreased vessel conductance both leading to reduced QMBF. These findings of elevated pulse pressures in the old are supported by research presented by Dinenno et al. (10), who concluded that age-associated femoral arterial wall thickening was due to increased $\alpha$-adrenergic vasoconstriction. In addition, Kass et al. (24) implicated glycation end products and their interference with long-lived arterial collagen and elastin fibers as a mechanism underlying age-associated vessel wall stiffening.

Greater reduction in LVR to graded KE in old subjects. Our findings of increased vasodilatory response to KE in the old subjects are in accordance with studies conducted by Jasperse et al. (21), which revealed greater peak increases in forearm vascular conductance in the old subjects. Because the vasodilatory pathways are responding more dramatically in old subjects, it appears that a basal limitation to QMBF is continually and equally dampening the vasodilatory efforts of the smooth muscle reactive pathways across all WRs (Fig. 2C). Because the old subjects begin with a high LVR, it is perhaps simply by necessity that they have a greater reduction in LVR than the young subjects, permitting the required blood flow response to achieve an equal WR max.

The present data, documenting an increased vasodilatory response to incremental KE (Fig. 2C), may at first appear to conflict with the findings of several other research groups who have reported age related declines in endothelium-dependent vasodilation (5, 9, 45). However, it must be remembered that much of this research has been performed at rest when the role of the endothelium in mediating vasodilation may be most significant. During exercise, as in the current study, diminished endothelial function may be overcome by other vasodilatory mechanisms such as metabolite concentrations. In addition, when data presented by DeSouza et al. (9) are examined more closely, it appears that from baseline to the intra-arterial infusion of 1 $\mu$g ACh/100 ml tissue there is a difference between the vasodilatory response in young and old. However, from this point on, the slopes of the two lines (change in conductance per microgram of ACh infusion) are remarkably similar for young and old subjects suggestive of similar vasodilatory capabilities in young and old subjects. This result was not recognized in the study by DeSouza et al. (9). Although resting pharmacological intervention studies have contributed significantly to the current understanding of blood flow regulation by offering a specific insight into select pathways, they may produce different results from the current study because they are designed to evoke responses from a specific pathway from the many regulatory mechanisms that may govern blood flow during exercise and cannot account for the complex combination of mechanical and metabolic changes that influence vascular resistance during exercise. Finally, studies involving dynamic muscle contraction reveal how muscle blood flow is affected by the combination of naturally occurring stimuli in a situation...
much more akin to those occurring in everyday life, and, in such a scenario, the older subjects do not reveal a diminished vasodilatory response to incremental KE (Fig. 2C).

Limitations to maximal exercise. A hallmark of the aging process appears to be a fall in maximal exercise capacity (3, 33, 35). Although this attenuation of maximal exercise was apparent in the current subjects during the prescreening bicycle exercise testing (Table 1), when exercise was isolated to a relatively small muscle mass in the form of KE, the difference between young and old was lost. In support of these findings, variables reflecting relative stress, such as venous lactate outflow and pH, were nearly identical between young and old subjects during submaximal and maximal KE (Table 2). These findings are in agreement with Jasperse et al. (21), who documented a similar WR\textsubscript{max} in young and old physically active males during small muscle mass dynamic handgrip exercise. However, it should be recognized that a statistical analysis of QVO\textsubscript{2}\textsubscript{max} revealed marginally acceptable power \(\beta = 0.74\) and a \(P\) value of 0.14 (two-tailed paired \(t\)-test). Thus the potential of a type II error as a consequence of the limited sample size cannot be ruled out.

In terms of convective \(\text{O}_2\) transport, the old subjects demonstrated a consistently reduced QMBF, but the tendency toward an elevated \(\text{CaO}_2\) resulted in a similar \(\text{O}_2\) delivery in the young and old subjects. Thus both the young and old achieved the same WR\textsubscript{max} A-V \(\text{O}_2\) difference, and QVO\textsubscript{2}\textsubscript{max}. These findings are starkly different from the 30\% reduction in both WR\textsubscript{max} and pulmonary VO\textsubscript{2}\textsubscript{max} exhibited by the same old subjects during the bicycle exercise test. These data suggest a central limitation in aging persons resulting in disparities between young and old subjects during centrally taxing exercise (e.g., maldistribution of cardiac output), which are resolved during a small dynamic muscle mass exercise such as KE.

The diffusional component of \(\text{O}_2\) transport is assessed by the calculation of a normoxic Dm\textsubscript{O}_2, and the young and old subjects appear similar in terms of the movement of \(\text{O}_2\) from blood to muscle cell (Fig. 3). Recently published data (33) collected in our laboratory during maximal cycle exercise in nine sedentary young and nine sedentary old subjects revealed a significantly lower maximal quadriceps muscle Dm\textsubscript{O}_2, pulmonary VO\textsubscript{2}\textsubscript{max} and QVO\textsubscript{2}\textsubscript{max} in the old subjects. It is possible that the decreased Dm\textsubscript{O}_2 and QVO\textsubscript{2}\textsubscript{max} reported during cycle exercise results from central limitations (e.g., inappropriate distribution of a finite cardiac output) that are not present when the quadriceps muscle bed is now the sole muscle with high metabolic demand. It is noteworthy that both the young and old subjects show a greatly reduced Dm\textsubscript{O}_2 compared with data collected from young endurance trained subjects performing KE in our laboratory (37; Fig. 3). These findings suggest that both Dm\textsubscript{O}_2 and QVO\textsubscript{2}\textsubscript{max} are much more strongly associated with a sedentary lifestyle rather than simple age.

The finding of similar quadriceps mass, WR\textsubscript{max} and QVO\textsubscript{2}\textsubscript{max} appears to disagree with reports that normal aging brings about a general reduction in muscle mass of up to 25–30\% by age 70 (6, 13, 42) and a concomitant 30–40\% reduction in muscle strength (34). In addition, others have shown ~50\% lower oxidative capacity per unit volume resulting from decreased ATP per mitochondria recorded during MRI twitch studies (7) and decreased muscle metabolic capacity, as represented by an age-related decline in pulmonary VO\textsubscript{2}\textsubscript{max}, citrate synthase, and phosphocreatine (28). On the basis of these latter findings, it would be expected that for a similar muscle mass, aging subjects should have ~50\% lower WR\textsubscript{max} and QVO\textsubscript{2}\textsubscript{max}. Perhaps resolving this disparity are studies showing that typically persons >50 years of age remain the most sedentary segment of the population, with persons >70 years of age being extreme examples of this inactive group (43), and that this progressive decline in activity level causes the concomitant fall in strength, blood flow, metabolic capacity, etc. Typically, young sedentary volunteers are most likely more active than their older counterparts due to daily routine and leisure activities, tending to magnify the apparent aging effect. The subject selection criteria for this study were strict and many young subjects were rejected for participation in any exercise, even if only on an occasional recreational basis.

In summary, six equally matched sedentary young and old subjects who differed significantly in terms of maximal cycle exercise capacity achieved similar QVO\textsubscript{2}\textsubscript{max} and WR\textsubscript{max} when tested during KE. Submaximally, the old subjects revealed an elevated A-V \(\text{O}_2\) difference, and attenuated QMBF, yielding a similar QVO\textsubscript{2}\textsubscript{max} to the young subjects across all WRs. Elevated LVR is likely responsible for the attenuation in QMBF in the old subjects and may be the result of factors present at rest, which persist during incremental KE, such as decreased arterial cross-sectional area, decreased vasodilatory stimuli, such as endothelial nitric oxide, increased \(\alpha\)-adrenergic vasoconstriction, and decreased arterial compliance resulting in increased pulse pressures that contribute to the obstruction of blood flow in the old subjects. However, these differences did not hinder the vasodilatory response to incremental KE (measured as a change in LVR per watt), which was greater in the older subjects. In addition, diffusional \(\text{O}_2\) transport in this small muscle mass condition appeared to be uncompromised in the old subjects.

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DISCLOSURES

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