Age and sex influence the balance between maximal cardiac output and peripheral vascular reserve

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Submitted 1 September 2009; accepted in final form 27 November 2009

It has been more than three decades since Clausen’s original report (3) highlighting a significant inverse relationship between systemic maximal oxygen uptake (VO2max) and the decrease in peripheral vascular resistance during maximal exercise in humans. This relationship has been interpreted to reflect a matching between maximal aerobic capacity and peripheral vasodilatory capacity. Since this original observation, studies have demonstrated that VO2max is also correlated with other indexes of peripheral vascular reserve; most often examined is the peak vascular conductance response of the calf musculature, which exhibits a positive linear association with VO2max (32). The relationship between VO2max and peak calf conductance is particularly robust when examined in aerobically trained populations (22, 32) or when plotted across a broad range of aerobic fitness levels (15, 17, 23, 31). However, close inspection of plots that combine individuals of different age and/or sex reveals considerable between-group variation, with some subgroups exhibiting a significantly blunted or absent relationship (23).

One explanation for the apparent between-group variation is that the relationship between VO2max and peripheral vascular reserve can be altered in conditions that induce a mismatch between central and peripheral vascular adaptations (11). For example, with advancing age women and men experience similar relative declines in maximal cardiac output and VO2max (2, 4, 7, 13, 25). However, men may exhibit a preserved peripheral vascular reserve with age as suggested by modest (18) to no decrement (28) in peak leg blood flow during isolated muscle mass exercise in older men compared with younger men. Conversely, in women, peripheral vascular reserve may be reduced with age as demonstrated by lower peak leg blood flow and vascular conductance in older women relative to younger individuals (28). These sex-specific vascular adaptations with aging may alter both the relationship between maximal aerobic capacity and peripheral vasodilatation as well as the cardiovascular determinants of peak exercise capacity.

Accordingly, the aim of the present study was to test the hypothesis that the relationship between central and peripheral vascular reserve is altered with aging in a sex-specific manner. Maximal flow-generating capacities of the heart (cardiac output) and leg muscles (peak leg blood flow) were assessed via graded treadmill and single-leg knee extensor exercise, respectively, because these modalities yield the highest achievable estimates of systemic and active skeletal muscle blood flow and perfusion in humans (1).

METHODS

Participants. Sixty-five participants between 20–35 yr of age (19 younger men, 17 younger women) and 60–79 yr of age (12 older men, 17 older women) completed this study. All participants were normotensive (≤140/90 mmHg), apparently healthy, nonsmokers and abstained from caffeine, aspirin/ibuprofen, and herbal supplements for at least 12 h before exercise testing. Younger women were studied in days 1–7 of their menstrual cycle only during the study visit involving knee extensor exercise to standardize the influence of sex hormones on vasodilator function. All participants gave their written informed consent to participate. This study was approved by the Office for Research Protections and the Institutional Review Board at The Pennsylvania State University and is in accordance with the guidelines set forth by the Declaration of Helsinki.

Body composition and muscle mass. Total and regional body composition were measured using dual-energy X-ray absorptiometry (DXA; Hologic QDR 4500W) as described previously (29). Quadriceps muscle mass was estimated from thigh volume as previously described (16, 28).

Treadmill exercise testing. Participants performed graded treadmill exercise tests to peak effort using a modified Balke protocol. The
protocol consisted of a 2-min warm-up at 2.5 mph followed by adjustment of the speed to elicit ~75% of age-predicted peak heart rate after which the intensity of exercise (2% increase in elevation) increased every 2 min until the participants reached volitional fatigue. Blood pressures were measured via brachial auscultation during the second minute of each exercise stage until participants indicated an effort level of 15 (“Hard”) or above on the Borg 6–20 rating of perceived exertion. Blood pressure measurements were not attempted during peak effort to enable participants to fully engage both arms and give maximum effort without disturbance. However, in a subgroup of participants (younger men, n = 9; older men, n = 7; younger women, n = 8; older women, n = 9) the last blood pressure measured was at a time that corresponded to ~90% peak oxygen uptake (VO₂peak) and therefore was used as peak blood pressure for data analyses. Pulsatory oxygen uptake (VO₂) was measured using analysis of expired gases by a Parvomedics metabolic cart (Sandy, UT).

Cardiac output measurement. The open-circuit acetylene uptake method was used for determination of cardiac output. This technique has been validated against the direct Fick technique (14) and has proven reliable for measurement of cardiac output during exercise in both older and younger adults (2).

Graded knee extensor exercise. Single-leg knee extensor exercise was performed as described previously (28). Exercise stages were 3 min in duration, and work rate increased by 8 W in men and 4.8 W in women to produce similar time to exhaustion in all groups (28). A Doppler ultrasound machine (HD1 5000, Philips, Bothell, WA) was used to measure mean blood velocity and vessel diameter of the left common femoral artery. During knee extensor exercise, signals were recorded at a sampling frequency of 400 Hz and stored using a Powerlab system (AD Instruments, Castle Hill, Australia). Diameter measurements were analyzed using edge-detection software (Brachial Analyzer Software, Medical Imaging Applications; Iowa City, IA). Femoral blood flow and vascular conductance were calculated as the average over the last minute of each stage. Peak femoral blood flow are displayed in Fig. 1 for men (younger: 97% predicted and a respiratory exchange ratio (RER) > 1.09, indicating maximal effort by all participants during treadmill exercise.

The effects of age on hemodynamic responses to maximal treadmill exercise are generally consistent with previously published data for non-aerobically trained men and women (23). Maximal cardiac output was higher in men than women (P < 0.05) and was significantly reduced by an average 25–30% with age in both sexes (P < 0.05). Group averages for femoral hemodynamic responses to knee extensor exercise are consistent with our previously published data in non-aerobically trained men and women (28). Peak femoral blood flow was similar between younger and older men (P = 0.54) but was 26% lower in older women compared with younger women (P = 0.001). Similar findings were found for peak vascular conductance (see Table 2).

Relationships between central and peripheral vascular reserve. Relationships between maximal cardiac output and peak femoral blood flow were displayed in Fig. 1A for men and Fig. 1B for women. Maximal cardiac output was positively correlated with peak absolute femoral blood flows (l/min) in men (younger: r = 0.55, P = 0.02; older: r = 0.74, P < 0.01) but not in women (younger: r = 0.34, P = 0.22; older: r = 0.10, P = 0.90). Similarly, VO₂max was correlated to peak femoral blood flow in men (younger: r = 0.56; older: r = 0.62; P < 0.05) but not in women (younger: r = 0.11; older: r = 0.11; P > 0.6). These relationships held true when femoral vascular conductance was used as an index of peripheral vascular reserve such that a significant positive correlation was found between maximal cardiac output and peak femoral vascular conductance in men (younger: r = 0.48; older: r =

Table 1. Anthropometric characteristics for healthy younger and older men and women

<table>
<thead>
<tr>
<th></th>
<th>Younger Men (20–32 yr old)</th>
<th>Older Men (61–79 yr old)</th>
<th>Younger Women (20–30 yr old)</th>
<th>Older Women (61–73 yr old)</th>
<th>Age × Sex Interaction</th>
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<tr>
<td>n</td>
<td>19</td>
<td>12</td>
<td>17</td>
<td>17</td>
<td></td>
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<tr>
<td>Age, yr</td>
<td>25 ± 4</td>
<td>68 ± 3*</td>
<td>24 ± 3</td>
<td>67 ± 4*</td>
<td>P = 0.5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>179.6 ± 6.2</td>
<td>175.7 ± 8.2</td>
<td>164.3 ± 6.6</td>
<td>160.7 ± 6.1</td>
<td>P = 0.2</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>80.1 ± 7.3</td>
<td>78.4 ± 11.3</td>
<td>60.9 ± 8.7</td>
<td>64 ± 8.2</td>
<td>P = 0.3</td>
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<tr>
<td>BMI, kg/m²</td>
<td>24.8 ± 2.2†</td>
<td>25.4 ± 2.8</td>
<td>22.5 ± 2.5</td>
<td>24.8 ± 2.8</td>
<td>P = 0.3</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>19.9 ± 4.8†</td>
<td>22.4 ± 3.6*</td>
<td>29.1 ± 6.1</td>
<td>35 ± 4.9</td>
<td>P = 0.3</td>
</tr>
<tr>
<td>Quadriceps mass, kg</td>
<td>1.9 ± 0.2†</td>
<td>1.7 ± 0.2*</td>
<td>1.5 ± 0.2</td>
<td>1.4 ± 0.3*</td>
<td>P = 0.9</td>
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Values are means ± SE; n = no. of subjects. BMI, body mass index. *Significant age difference within same sex group (P < 0.05). †Significant sex difference within same age group (P < 0.05).

RESULTS

Physical characteristics. Anthropometric characteristics of the participants are presented in Table 1. Effects for an age-sex interaction were insignificant, suggesting that the age group differences in overall body size and composition were similar between men and women.

Peak exercise responses. Table 2 displays group average data for peak exercise responses by mode of exercise. During treadmill exercise, VO₂max was higher in younger vs. older individuals in both sexes (P < 0.05), even when normalized to body weight and appendicular muscle mass (i.e., index of active muscle mass). Younger men and women were of average fitness level while older participants were slightly less fit than their younger counterparts (P < 0.05). Despite this age difference, on average all groups achieved maximal heart rates > 97% predicted and a respiratory exchange ratio (RER) > 1.09, indicating maximal effort by all participants during treadmill exercise.

The effects of age on hemodynamic responses to maximal treadmill exercise are generally consistent with previously published data for non-aerobically trained men and women (23). Maximal cardiac output was higher in men than women (P < 0.05) and was significantly reduced by an average 25–30% with age in both sexes (P < 0.05). Group averages for femoral hemodynamic responses to knee extensor exercise are consistent with our previously published data in non-aerobically trained men and women (28). Peak femoral blood flow was similar between younger and older men (P = 0.54) but was 26% lower in older women compared with younger women (P = 0.001). Similar findings were found for peak vascular conductance (see Table 2).
Peak femoral blood flow persisted in women (younger: r = 0.38, older: r = 0.39, p < 0.05) but not in men (younger: r = 0.32; older: r = 0.21; p < 0.2) (Fig. 1, C and D).

Normalization of maximal cardiac output to appendicular muscle mass and peak femoral blood flow to quadriceps muscle mass abolished the correlation between these variables in younger men (r = 0.30, P = 0.21) while the positive correlation remained in older men (r = 0.68, P < 0.05) (Fig. 2A). The lack of relationship between maximal cardiac output and peak femoral blood flow persisted in women (younger: r = 0.06, P = 0.8; older: r = 0.38, P = 0.13) after normalization of these variables to muscle mass (Fig. 2B).

Last, in a subgroup of participants in whom treadmill blood pressures at peak exercise (~90% VO2max) were available, we examined the relationship between systemic vascular resistance and peak femoral blood flow during knee extensor exercise (Fig. 3). No associations were found in the younger groups (men: r = 0.16, P = 0.67; women: r = 0.43, P = 0.34). In the older groups, associations were found that were significant and directionally opposite with the men having a negative correlation (r = −0.81, P = 0.02) and the women exhibiting a positive correlation (r = 0.68, P = 0.04). While indirect, and limited to a small subsample of the present participants, these results suggest a fundamentally different relationship between the local capacity for exercise-induced hyperemia and the systemic vasodilatory response to intense whole body treadmill exercise.

DISCUSSION

The postulated link between systemic aerobic capacity and peripheral vascular reserve has been largely based on studies in men, with limited attention to intersubject variation or between-group differences in this relationship (i.e., age or sex comparisons), particularly among healthy, non-aerobically trained populations. In the present study we measured maximal cardiac output, a chief determinant of aerobic capacity, and assessed the peak blood flow and conducting capacity of the contracting knee extensor muscles to gain further insight into this balance and possible sex-dependent alterations with normal aging. The principal new findings are 1) maximal cardiac output is significantly correlated with peak knee extensor exercise blood flow and conductance in average fit men but not in women, and 2) sex differences in the balance between central and peripheral vasodilatory capacity appear more pronounced in older adults. These findings suggest sex- and potentially age-dependent differences in systemic cardiovascular regulation during whole body exercise such that leg vascular reserve influences peak achievable oxygen delivery and uptake in men but not women.

Associations observed in men. There generally exists a positive linear association between maximal aerobic capacity (VO2max in ml·kg⁻¹·min⁻¹) and peak calf vascular conductance in men (15, 23, 31, 32). Our finding of a significant positive correlation between maximal cardiac output and peak femoral blood flow (and conductance) in average fit men is consistent with these previous reports and extends our understanding of this relationship to a model that includes multiple vasomotor stimuli (e.g., endothelium-derived factors, metabolites, sympathetic activity) present during muscular contraction. Interestingly, the link between systemic oxygen transport and peripheral vascular reserve was markedly stronger in older men, and in fact persisted in this group but not in younger men when peak femoral blood flow was normalized to quadriceps mass. The stronger relationship found in older men may reflect an ability to utilize a greater fraction of their capacity for leg vasodilation during exercise relative to other groups.

The modest correlations between these variables in younger men are consistent with several reports in the literature showing lower or nonsignificant correlations between VO2max and peak calf conductance in normal-fit compared with endurance-trained younger men (11, 31, 32). We did not include endurance-trained participants in the present study so we cannot

### Table 2. Exercise capacity data for healthy younger and older men and women

<table>
<thead>
<tr>
<th></th>
<th>Younger Men (20–32 yr old)</th>
<th>Younger Women (20–30 yr old)</th>
<th>Older Men (61–79 yr old)</th>
<th>Older Women (61–73 yr old)</th>
<th>Age × Sex Interaction</th>
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<td>n</td>
<td>19</td>
<td>17</td>
<td>12</td>
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<tr>
<td><strong>Treadmill exercise</strong></td>
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<tr>
<td>VO2max, l/min</td>
<td>3.4 ± 0.5†</td>
<td>2.2 ± 0.4†</td>
<td>2.2 ± 0.4</td>
<td>1.4 ± 0.2*</td>
<td>P = 0.01</td>
</tr>
<tr>
<td>VO2max, ml·kg⁻¹·min⁻¹</td>
<td>45.8 ± 4.1†</td>
<td>30.2 ± 4.1†</td>
<td>38.1 ± 5.4</td>
<td>23.5 ± 2.9*</td>
<td>P = 0.7</td>
</tr>
<tr>
<td>VO2max, ml·ApMM⁻¹·min⁻¹</td>
<td>126.1 ± 11.3</td>
<td>91.8 ± 9.9*</td>
<td>135.5 ± 14.8</td>
<td>91.1 ± 7.9*</td>
<td>P = 0.2</td>
</tr>
<tr>
<td>VO2max, percentegle</td>
<td>56.5 ± 17.9</td>
<td>31.3 ± 15.4†</td>
<td>58.4 ± 19.1</td>
<td>33.2 ± 16.1†</td>
<td>P = 0.9</td>
</tr>
<tr>
<td>Maximal heart rate, beats/min</td>
<td>190 ± 9.2</td>
<td>152.8 ± 12.0*</td>
<td>191.8 ± 9.8</td>
<td>154.5 ± 0.9*</td>
<td>P = 0.9</td>
</tr>
<tr>
<td>Maximal heart rate, %predicted</td>
<td>101.4 ± 4.3</td>
<td>97.3 ± 7.5</td>
<td>101 ± 5.4</td>
<td>97.4 ± 4.5</td>
<td>P = 0.8</td>
</tr>
<tr>
<td>Maximal cardiac output, l/min</td>
<td>23.6 ± 2.7</td>
<td>17.4 ± 3.5*</td>
<td>17.7 ± 1.9</td>
<td>12.1 ± 1.6*</td>
<td>P = 0.3</td>
</tr>
<tr>
<td>Maximal stroke volume, ml/beat</td>
<td>142.5 ± 18.2†</td>
<td>134.3 ± 22.3†</td>
<td>103.2 ± 15</td>
<td>97.8 ± 12.8</td>
<td>P = 0.4</td>
</tr>
<tr>
<td>RER</td>
<td>1.12 ± 0.04</td>
<td>1.09 ± 0.05</td>
<td>1.13 ± 0.06</td>
<td>1.10 ± 0.05</td>
<td>P = 0.9</td>
</tr>
<tr>
<td>RPE</td>
<td>19 ± 1</td>
<td>19 ± 1</td>
<td>19 ± 1</td>
<td>19 ± 1</td>
<td>P = 0.6</td>
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<td><strong>Knee extensor exercise</strong></td>
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<tr>
<td>Peak power output, W</td>
<td>40.4 ± 6.8†</td>
<td>33.3 ± 8.8†</td>
<td>24.9 ± 4.2</td>
<td>21.2 ± 4.2*</td>
<td>P = 0.2</td>
</tr>
<tr>
<td>Peak power output, W/kg QMM</td>
<td>16.2 ± 3.3†</td>
<td>15.3 ± 4.6</td>
<td>12.6 ± 2.1</td>
<td>12.8 ± 3.3</td>
<td>P = 0.4</td>
</tr>
<tr>
<td>Peak leg blood flow, l/min</td>
<td>2.1 ± 0.5</td>
<td>2.2 ± 0.7†</td>
<td>1.9 ± 0.4</td>
<td>1.4 ± 0.4*</td>
<td>P = 0.03</td>
</tr>
<tr>
<td>Peak leg perfusion, l·min⁻¹·kg QMM⁻¹</td>
<td>0.8 ± 0.2</td>
<td>1.0 ± 0.3</td>
<td>1.0 ± 0.2</td>
<td>0.9 ± 0.3</td>
<td>P = 0.04</td>
</tr>
<tr>
<td>Peak leg conductance, ml·min⁻¹·mmHg⁻¹</td>
<td>18.5 ± 3.6</td>
<td>21.0 ± 7.5†</td>
<td>20.9 ± 6.2</td>
<td>13.6 ± 4.4*</td>
<td>P &lt; 0.01</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = no. of subjects. VO2max, maximal oxygen uptake; RER, respiratory exchange ratio; RPE, rating of perceived exertion; ApMM, appendicular muscle mass; QMM, quadriceps muscle mass. *Significant age difference within same sex group (P < 0.05). †Significant sex difference within same age group (P < 0.05).
address how higher fitness levels might influence the relationship between maximal cardiac output and peak femoral blood flow. However, we speculate that the central (cardiac output and $V_{\text{O}2\text{max}}$) and peripheral (vasodilatory capacity) adaptations accompanying endurance training would only strengthen the relationships found in the present study as demonstrated previously using peak calf vascular conductance (22, 32).

**Lack of association observed in women.** In contrast to the results for men, the present study found no significant correlations between these variables in younger or older women regardless of how the vascular data were expressed (peak blood flow or conductance) or normalized (absolute or relative to quadriceps mass). The deviation from the relationship between aerobic capacity and peripheral vascular reserve also differed in women based on age. Specifically, younger women had a lower maximal cardiac output than would be predicted from their peak femoral blood flow and conductance relative to younger men. In contrast, older

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**Fig. 1.** Peak cardiac output during treadmill exercise vs. peak quadriceps blood flow during knee extensor exercise: ▲, younger men ($n = 19$); △, older men ($n = 12$) (A); ●, younger women ($n = 17$); ○, older women ($n = 17$) (B). Peak cardiac output during treadmill exercise vs. femoral artery conductance during peak knee extensor exercise: ▲, younger men; △, older men (C); ●, younger women; ○, older women (D).

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**Normalized Peak Cardiac Output vs. Normalized Peak Femoral Blood Flow**

**Fig. 2.** Peak cardiac output during treadmill exercise normalized to appendicular muscle mass vs. femoral blood flow during peak knee extensor exercise normalized to quadriceps muscle mass: ▲, younger men ($n = 19$); △, older men ($n = 12$) (A); ●, younger women ($n = 17$); ○, older women ($n = 17$) (B).
women had a lower peak femoral blood flow than would be predicted from their maximal cardiac output relative to older men. This interpretation suggests that in women peripheral adaptations with age is a factor contributing to the altered balance between systemic aerobic capacity and peripheral vasodilation.

Possible sex differences in the relationship between maximal aerobic capacity and calf vasodilatory capacity have not been explicitly discussed in the literature because, to our knowledge, only one study differentiated responses in women and men (23). Close inspection of that report suggests a weak relationship exists between these variables in women, particularly in those who are older. Collectively these studies [the present study and that of Martin et al. (23)] suggest that in women, systemic aerobic capacity bears a relatively weak association with measures of leg vasodilator reserve.

The mechanisms contributing to the sex-specific differences in the association between aerobic capacity and local vascular reserve are unknown. Relative aerobic fitness level and maximal effort during treadmill testing are unlikely explanations given the similarity in lean body mass-normalized VO$_{2\max}$ between women and men of a similar age group and the consistent use of VO$_{2\max}$ criteria across groups (Table 2). It is possible that the factor(s) underlying this apparent sex-specific dichotomy differ depending on age. This is suggested by the fact that normalizing peak femoral blood flow to estimates of active muscle (quadriceps mass) abolishes the sex-specific association between these variables in the younger groups but not in the older groups (Fig. 2).

Disparate associations between older men and women: potential implications. Sex-based differences in the relationships between peak femoral blood flow and both maximal cardiac output and minimum systemic vascular resistance were most evident between older women and men, suggesting a more pronounced sex difference with increasing age. This is consistent with other studies describing disparate alterations in cardiovascular regulation at rest (9, 10, 24) and during orthostatic challenges (5, 6, 33) with advancing age and/or between men and women. We cannot determine the precise mechanism(s) underlying the exercise-specific alterations identified in the present study. Although the ability to reduce systemic vascular resistance appeared to be impaired in older compared with younger groups (Fig. 3), it is important to note that both older men and older women did exhibit significant reductions in systemic vascular resistance during graded whole body exercise (across percent VO$_{2\max}$; data not shown). Thus, despite the disparate associations between peripheral vascular reserve and systemic hemodynamics in older women vs. men, the overall ability to reduce systemic vascular resistance during whole body exercise appears similarly affected by the normal aging process in both sexes. This may suggest disparate vascular control strategies are used by older men and women to regulate systemic blood pressure during exercise. For example, sex-specific alterations in muscle sympathetic nerve activity (24) and/or buffering of sympathetic outflow (26) with advancing age could influence the mechanisms by which older adults decrease vascular resistance during intense whole body exercise. It is also possible that the vascular reserve capacity of the leg muscles in older women (as reflected during knee extensor exercise) may have less impact on systemic blood pressure responses when large increases in cardiac output (intense treadmill exercise) are sufficient to offset the reduction in systemic vascular resistance.

Experimental considerations. The correlative approach taken in the present study assumes that mode-specific differences including body posture, contraction patterns/ rates, respiratory muscle activity, thermoregulation, and possibly baroreflex modulation of sympathetic muscle activity do not alter our interpretation of the balance between peripheral vasodilator function and maximal cardiac output. Aerobic fitness level differed between younger and older groups in the present study. We do not believe this influenced our primary findings since previous studies show the relationship between peripheral vascular reserve and VO$_{2\max}$ to be strengthened with endurance training (22, 32). Therefore, it is reasonable to speculate that our findings in men would be exaggerated if we had examined older men at a higher fitness level that was similar to the younger men. We would expect no difference in our findings in higher fit older women since younger women did not exhibit a significant correlation.

Additionally, peak femoral blood flows measured in our participants are lower than values reported in previous studies (1, 18, 20, 21). Thermodilution estimates of peak femoral blood flow during knee extensor exercise typically exceed 5 L/min in men while the present study measured peak flows up
to 3 l/min in young and older men. Although our femoral blood flow values with respect to external work rate are comparable to other studies using Doppler ultrasound (8, 12, 19, 27, 28), we believe several factors can explain the discrepancy in peak femoral blood flow between thermodilution-based studies and the present study. First, the contraction frequency used in the present study (40 kicks per minute (kpm)) is lower than other studies (60 kpm) that report higher peak blood flow (1, 18, 30). Second, participants in the present study performed exercise in a nearly supine position, which may influence exercise performance and driving pressure for blood flow. Last, our participants were low to moderately fit and the classic thermodilution-based studies generally included highly-trained individuals. Together, these differences likely explain the lower peak quadriceps power output in our men (30–40 W) compared with previous studies (>55 W), and consequently, the lower peak femoral blood flow estimates reported herein. As such, the peak femoral flows in the present study represent reasonable estimates of the hyperemic capacity of the contracting knee extensor muscles, in men but not women.

**Conclusions.** Our findings indicate that systemic aerobic capacity (maximal cardiac output and \( \dot{V}_O^{2max} \)) was positively correlated with peripheral vascular reserve, as measured by peak blood flow and conducting capacity of the contracting knee extensor muscles, in men but not women. This relationship was most pronounced in older men, regardless of how peripheral vasodilatory capacity was expressed or normalized. The disparate balance between maximal cardiac output and peripheral vascular reserve suggests different cardiovascular regulatory mechanisms and/or limitations during whole body exercise in men and women, particularly with aging.

**ACKNOWLEDGMENTS**

We thank the participants, Ian McKelvey for assistance with data collection, Allen Kanselman for assistance with statistical analysis, and the General Clinical Research Center (GCRC) at University Park for assistance with subject screening and clinical support.

**GRANTS**

This research was supported by National Institute on Aging Grant R01-AG-018246 (to D. N. Proctor) and Division of Research Resources Grant M01 RR-10732 (to GCRC).

**DISCLOSURES**

No conflicts of interest were declared by the authors.

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