Forearm blood flow follows work rate during submaximal dynamic forearm exercise independent of sex

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Gonzales JU, Thompson BC, Thistlethwaite JR, Harper AJ, Scheuermann BW. Forearm blood flow follows work rate during submaximal dynamic forearm exercise independent of sex. J Appl Physiol 103: 1950–1957, 2007. First published October 11, 2007; doi:10.1152/japplphysiol.00452.2007.—To test the hypothesis that sex influences forearm blood flow (FBF) during exercise, 15 women and 16 men of similar age [women 24.3 ± 4.0 (SD) vs. men 24.9 ± 4.5 yr] but different forearm muscle strength [women 290.7 ± 44.4 vs. men 509.6 ± 97.8 N; P < 0.05] performed dynamic handgrip exercise as the same absolute workload was increased in a ramp function (0.25 W/min). Task failure was defined as the inability to maintain contraction rate. Blood pressure and FBF were measured on separate arms during exercise by auscultation and Doppler ultrasound, respectively. Muscle strength was positively correlated with endurance time (r = 0.72, P < 0.01) but the women had a shorter time to task failure than men (450.5 ± 113.0 s vs. 831.3 ± 272.9 s; P < 0.05). The percentage of maximal handgrip strength reached at task failure was similar between sexes (14% maximum voluntary contraction). FBF was similar between women and men throughout exercise and at task failure (women 13.6 ± 5.3 vs. men 14.5 ± 4.9 ml·min⁻¹·100 ml⁻¹). Mean arterial pressure was lower in women at rest and during exercise; thus calculated forearm vascular conductance (FVC) was higher in women during exercise but similar between sexes at task failure (women 0.13 ± 0.05 vs. men 0.11 ± 0.04 ml·min⁻¹·100 ml⁻¹·mmHg⁻¹). In conclusion, the similar FBF during exercise was achieved by a higher FVC in the presence of a lower MAP in women than men. Still, FBF remained coupled to work rate (and presumably metabolic demand) during exercise irrespective of sex.

DURING TRANSIENT or sustained periods of increased muscle contractile activity, an increase in muscle perfusion must take place to deliver oxygen-rich blood to the active mitochondria as well as to remove metabolic by-products that may lead to muscle fatigue (11). The close coupling between muscle oxygen consumption and blood flow (3, 17) has been used as evidence to suggest that local muscle and/or vascular conditions exert considerable feedback regulation over vascular tone, in addition to the role that sympathetic outflow plays in maintaining mean arterial pressure (46). The matching of muscle perfusion to external work rate has been demonstrated in different muscle groups during isometric and dynamic exercise (1, 16). However, the influence of sex on the blood flow response to exercise has yet to be fully investigated; although sex differences in muscle blood flow have been hypothesized to be a factor contributing to the greater fatigue resistance observed in women compared with men (21).

To date, the studies that have examined muscle blood flow during forearm exercise between women and men have relied primarily on strain-gauge plethysmography (26, 29). For example, it has been reported that women have higher muscle perfusion and vascular conductance than men following 4 min of sustained isometric handgrip exercise (26). It has been postulated that women experience less compressive force and lower intramuscular pressure on the peripheral vasculature and, hence, less mechanical hindrance to muscle blood flow compared with men during exercise at the same relative contraction intensity (21). However, the sex difference in muscle blood flow is not a consistent finding given that women and men matched or unmatched for strength show similar muscle blood flow and vascular conductance when submaximal isometric handgrip exercise is extended to fatigue (26). In addition, no sex difference in muscle blood flow was observed following 10 min of dynamic handgrip exercise performed at the same relative intensity (29). While strain-gauge plethysmography provides a good estimate of limb blood flow at rest and during the recovery from exercise, in order for exercise blood flow responses to be measured, the subject is required to stop contracting during the exercise (23, 27). Therefore, the extent that the strain-gauge plethysmography approach reflects muscle blood flow during the actual performance of exercise has recently been questioned (4). The controversy is further supported by the results of earlier studies that clearly demonstrate that the occlusion pressure required for obtaining the measurement of blood flow using this technique causes a significant reduction in muscle blood flow (5, 20).

To circumvent the inherent limitations of other techniques, the use of Doppler ultrasound has been used to measure steady-state as well as transient changes in blood flow during exercise with high temporal resolution (18, 22, 39, 48). However, to our knowledge, the application of Doppler techniques to investigate possible sex differences in muscle blood flow has only recently been examined in the leg (36). Therefore, the aim of the present study was to use Doppler ultrasound to test the hypothesis that performing dynamic handgrip exercise at the same work rate (i.e., same absolute intensity but higher relative intensity for women than men) would result in a similar muscle blood flow response to exercise in women and men, consistent with a feedback control mechanism balancing metabolic requirements to muscle blood flow. To avoid the confounding influence of tension development on vascular resis-

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tance and impedance to flow as seen during isometric exercise (2, 42, 45), the subjects performed dynamic muscle contractions with brief periods of mechanical compression followed by relaxation to allow blood flow to perfuse the muscle unimpeded during the relaxation phases between contractions (28, 40).

METHODS

Subjects. Dynamic handgrip exercise was performed in 15 women (age 24.3 ± 4.0 yr) and 16 men (age 25.9 ± 4.5 yr). Subjects reported themselves to be either sedentary or recreationally active, and all subjects reported not having any metabolic, cardiovascular, and pulmonary disease as assessed through a standard medical history questionnaire. The study was approved by the Human Subjects Research Committee at The University of Toledo and is in accordance with guidelines set forth by the Declaration of Helsinki of The World Medical Association. All subjects provided written informed consent after being explained all experimental procedures, the exercise protocol, and possible risks associated with participation in the study. All testing was performed in the Cardiopulmonary and Metabolism Research Laboratory at The University of Toledo.

Experimental protocol. Subjects were asked to refrain from strenuous physical activity for 24 h before each study session, especially physical activities involving the use of the forearm muscles. On a separate day before any exercise testing, anthropometric measurements including forearm volume and maximal forearm muscle strength were measured by water displacement and using a handgrip dynamometer (Takei), respectively. The average of three maximal voluntary isometric contractions (MVC) was used as the value of forearm muscle strength. No less than 2 min of recovery was allowed between each MVC effort to avoid any effects of fatigue.

On the day of exercise testing, subjects rested in the supine position with both forearms at heart level for at least 15 min before resting forearm blood flow (FBF) was measured in the right brachial artery. Handgrip exercise was performed in the supine position with the right forearm extended to a custom-built arm ergometer. The arm ergometer allowed for 10 cm of distance traveled during each concentric contraction phase, which was recorded by a potentiometer incorporated into the pulley system (see Fig. 1A). This allowed for the offline analysis of contraction duty cycle, frequency, and durations (contraction and relaxation time). The exercise protocol consisted of 2 min of unloaded forearm muscle contractions followed by a ramp increase in work load (0.5 kg/min) as applied by the constant flow of water into a bucket at the end of the pulley system that was calibrated before exercise testing. Task failure was defined as the inability of subjects to maintain contraction frequency and/or duty cycle during handgrip exercise. Contraction frequency was set at 30 contractions/min, which subjects followed with an audio metronome, and dynamic contraction duty cycle was set for a short contraction cycle duration that was easily learned and adhered to by the subjects.

Measurements. Instantaneous blood velocity (cm/s) in the right brachial artery was continuously measured using a Doppler ultrasound velocimeter system (model 500-M, Multigon Industries) operating in pulsed mode. The pulsed-wave Doppler transducer, with an operating frequency of 4 MHz and fixed transducer crystal and sound beam angle of 45° relative to the skin, was placed flat on the inside of the right arm 6–10 cm above the inner humeral condyle, above and parallel to the brachial artery. Blood velocity was measured in all subjects by one researcher exhibiting a between-day and test-retest coefficient of variation of 10.4% and 6.4%, respectively. Electrocadiography (ECG) was obtained using a modified three-lead placement. Brachial artery blood velocity was averaged over each cardiac cycle between R-R wave intervals using software described in a previous study (22). The continuous cardiovascular (blood velocity, ECG) and ergometer data (displacement) were digitized (ADInstruments, PowerLab 16SP, Grand Junction, CO) and stored for offline analysis.

Blood pressure was measured manually from the left arm by auscultation at the end of every minute for the purpose of monitoring changes in mean arterial pressure (MAP) with exercise; MAP = diastolic blood pressure + 0.33 (systolic blood pressure – diastolic blood pressure).

In pilot studies, brachial artery diameter was measured in five subjects during ramp exercise similar to the protocol used in the present study. Consistent with the results of others (28, 40, 44), we found no significant increase in brachial artery diameter during dynamic forearm exercise (see Fig. 2); therefore, resting brachial artery diameter for each subject was used to calculate blood flow at rest and during exercise. Brachial artery diameter was measured using a digital beam-forming ultrasound system (Mysono 201, Medison) operating in two-dimensional echo mode with a 7.5 MHz/40-mm linear array probe. Images were recorded on videotape for offline analysis. The vessel diameter was measured with the arm resting at heart level and after the subject had rested in the supine position for 15 min. Brachial artery diameter was determined from longitudinal and cross-sectional views of the vessel from 10 measurements randomly made where the vessel walls were most accurately visualized. The mean of these measurements was then used to calculate an average cross-sectional area (CSA = πr²) of the artery, where r is the radius of the artery, which in turn was multiplied by the appropriate blood velocity to obtain relevant flows (FBF = blood velocity × CSA × 60). In addition to reporting absolute flow through the brachial artery (FBF; ml/min), FBF was also expressed relative to forearm volume (FBF; ml·min⁻¹·100 ml⁻¹). For each subject, blood flow was reduced from beat-to-beat values into 20-s averages for statistical analysis. Forearm vascular conductance (FVC) was calculated as the ratio of FBFR to MAP (ml·min⁻¹·100 ml⁻¹·mmHg⁻¹).

Muscle activity was assessed by surface electromyography (sEMG) obtained from the forearm muscle group using a commercially available data-acquisition system (PowerLab 16SP, ADInstruments). The analog sEMG signal was sampled at a rate of 2,000 Hz, amplified (model 408 Dual Bio Amplifier-Stimulator, ADInstruments), passed through a high-low pass frequency window of 10–500 Hz, and stored on a computer for later analysis. The raw sEMG signal was sampled using bipolar silver-silver chloride electrodes (20-mm-diameter sample area) spaced 40 mm apart on the inside surface of the right forearm over the digit flexor muscles. A reference electrode was placed over the bony surface of the ulna near the elbow joint of the left arm. Electrode sites were shaved and cleaned with alcohol before electrode placement to reduce interelectrode resistance. All wiring attached to the electrodes were secured by athletic wrap to prevent movement artifact, and a notch filter set at 60 Hz was used to minimize noise in the raw sEMG signal. The sEMG signal was checked for motion artifact by moving and tapping the area surrounding the electrode. The site was cleaned again, and a new electrode was applied if any motion artifact was detected. The raw sEMG signal was analyzed in the time domain by the root-mean-square method for examination of motor unit recruitment during exercise. Because of technical difficulties, sEMG could not be measured in one woman and one man.

Statistical analysis. Anthropometric data along with time to task failure, end workload, and contraction durations were compared between women and men by two-sample Student’s t-tests. A two-way ANOVA with one repeated measure (sex by intensity) was performed to compare blood velocity, FBF, MAP, FVC, heart rate, relative contraction intensity, and sEMG within and between women and men throughout forearm exercise. Because of subjects reaching task failure at different times (and work loads), comparisons between women and men were only made at work loads where all subjects contributed to the group mean (i.e., up to 1.5 W or 3 kg). Statistical significance was set a priori at P ≤ 0.05. When a significant main effect or interaction was observed, a Holm-Sidak post hoc test was used to make multiple comparisons. The Holm-Sidak methods applies a “step-down” critical P value approach in determining significance to maximize statistical significance.
power without increasing the risk of making a type I error (14). Values are expressed as means ± SD unless stated otherwise.

RESULTS

Subjects. Subject anthropometric characteristics are presented and compared between women and men in Table 1. There was no sex difference in age, but women were on average shorter, weighed less, had a lower body mass index (BMI), lower forearm muscle mass, and smaller brachial artery diameter than men. Forearm muscle volume and strength was 35% and 43% lower in women than men, respectively. Muscle strength was linearly related to forearm volume ($r = 0.89, P < 0.01$, pooled data) such that subjects with larger forearms produced greater handgrip strength. Brachial artery diameter was also related to forearm volume ($r = 0.61, P < 0.01$, pooled data).

Ramp test performance. The duration of contraction (women $0.27 ± 0.05$ vs. men $0.24 ± 0.03$ s, $P = 0.07$) and the duration of relaxation between contractions (women $1.74 ± 0.05$ vs. men $1.76 ± 0.03$ s, $P > 0.05$) were similar between women and men. On average, women had a shorter time to task failure than men (women $450.5 ± 113.0$ vs. men $831.3 ± 272.9$ s, $P < 0.05$) that resulted in a lower ($P < 0.05$) peak work load at task failure for women ($2.1 ± 0.4$ W; $4.2 ± 0.8$ kg) than men.
Fig. 2. Brachial artery diameter measured in a subgroup of subjects (n = 5, 1 woman, 4 men) during the ramp increase in handgrip workload. ANOVA testing did not find a significant change in brachial artery diameter during exercise (P = 0.81).

(3.6 ± 0.9 W; 7.4 ± 1.9 kg). Despite this difference, women and men reached task failure at a similar percentage of maximal muscle strength (women 14.3 ± 2.5 vs. men 14.2 ± 2.1%MVC, P > 0.05). The time to task failure was correlated to both forearm muscle strength (r = 0.84, P < 0.01, pooled data) and forearm volume (r = 0.69, P < 0.05, pooled data).

**Hemodynamic response to dynamic handgrip exercise.** The effect of dynamic forearm muscle contractions on blood velocity is shown for a representative subject in Fig. 1, along with the FBF response to a ramp increase in work load (Fig. 1D). Mean blood velocity was not different between women and men at rest and throughout the ramp increase in work load except at task failure where men had faster blood velocities than women (Fig. 3A). Similarly, resting FBFa tended to be lower (P = 0.06) in women (17.4 ± 12.4 ml/min) than men (28.2 ± 17.7 ml/min) but was not different between the sexes throughout handgrip exercise (Fig. 3B). At task failure, FBFa was lower in women compared with men (women 109.8 ± 39.7 vs. men 185.8 ± 69.0 ml/min, P < 0.05) because of the higher work load achieved by men at end exercise. A significant positive correlation was observed between FBFa and workload at end exercise (r = 0.48, P < 0.05, pooled data).

When FBF was expressed relative to forearm volume, no sex difference was present in FBFr at rest (women 2.0 ± 1.2 vs. men 2.1 ± 0.9 ml·min⁻¹·100 ml⁻¹, P > 0.05), throughout handgrip exercise, or at task failure (women 13.6 ± 5.3 vs.

Table 1. Anthropometric data for women and men

<table>
<thead>
<tr>
<th></th>
<th>Women (n = 15)</th>
<th>Men (n = 16)</th>
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</thead>
<tbody>
<tr>
<td>Ag, yr</td>
<td>24.3±4.0</td>
<td>24.9±4.5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>163.9±6.3*</td>
<td>178.0±7.3</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>61.5±9.2*</td>
<td>79.5±11.5</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.8±2.5*</td>
<td>25.0±2.6</td>
</tr>
<tr>
<td>Forearm muscle mass, kg</td>
<td>0.26±0.05*</td>
<td>0.40±0.09</td>
</tr>
<tr>
<td>Forearm muscle volume, ml</td>
<td>836.9±185.7*</td>
<td>1,291.9±282.6</td>
</tr>
<tr>
<td>Isometric MVC, N</td>
<td>290.7±44.4*</td>
<td>509.6±97.8</td>
</tr>
<tr>
<td>Brachial artery diameter, cm</td>
<td>0.37±0.05*</td>
<td>0.42±0.04</td>
</tr>
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</table>

Values are means ± SD. BMI, body mass index; MVC, maximum voluntary traction. *Value significantly lower in women than men (P < 0.05).

men 14.5 ± 4.9 ml·min⁻¹·100 ml⁻¹, P > 0.05) (Fig. 3C). No sex difference was found in resting heart rate or the heart rate response to dynamic handgrip exercise. In contrast, MAP was lower (P < 0.05) in women than men at rest and throughout handgrip exercise although the percent increase in MAP from rest was not different between sexes during handgrip exercise except for task failure where men showed a greater percent increase in MAP than women (Table 2). To normalize FBFr to the sex difference in MAP, FVC was calculated and found to be similar between women and men at rest (women 0.02 ± 0.01 vs. men 0.02 ± 0.01 ml·min⁻¹·100 ml⁻¹·mmHg⁻¹, P > 0.05) but was higher in women than men during handgrip exercise (Table 2). No sex difference was found in FVC at task failure (women 0.13 ± 0.05 vs. men 0.11 ± 0.04 ml·min⁻¹·100 ml⁻¹·mmHg⁻¹, P > 0.05).
Relative contraction intensity, forearm muscle activity, heart rate, blood pressure response, and forearm vascular conductance changes during a ramp increase in handgrip work load for women and men

<table>
<thead>
<tr>
<th>Relative intensity, %MVC</th>
<th>Rest</th>
<th>0.25 W</th>
<th>0.50 W</th>
<th>0.75 W</th>
<th>1.0 W</th>
<th>1.25 W</th>
<th>1.50 W</th>
<th>Task Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>1.7±0.2</td>
<td>3.4±0.5</td>
<td>5.2±0.7</td>
<td>6.9±0.9</td>
<td>8.6±1.2</td>
<td>10.3±1.4</td>
<td>14.3±2.5</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.0±0.2</td>
<td>2.0±0.5*</td>
<td>3.0±0.7*</td>
<td>4.0±0.9*</td>
<td>5.0±1.2*</td>
<td>6.0±1.4*</td>
<td>14.2±2.1</td>
<td></td>
</tr>
<tr>
<td>sEMG, %UC</td>
<td>155±45</td>
<td>184±57</td>
<td>198±68</td>
<td>247±90</td>
<td>315±134</td>
<td>351±136</td>
<td>425±149</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>160±50</td>
<td>197±87</td>
<td>222±93</td>
<td>250±116</td>
<td>289±149</td>
<td>319±158</td>
<td>528±302</td>
<td></td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Women</td>
<td>64±5</td>
<td>68±9</td>
<td>75±10</td>
<td>76±9</td>
<td>80±10</td>
<td>82±8</td>
<td>87±9</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>61±12</td>
<td>68±13</td>
<td>70±13</td>
<td>71±11</td>
<td>72±11</td>
<td>74±11</td>
<td>93±14</td>
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<tr>
<td>MAP, mmHg</td>
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<td></td>
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<tr>
<td>Women</td>
<td>83±6</td>
<td>87±9</td>
<td>89±9</td>
<td>90±9</td>
<td>92±8</td>
<td>93±9</td>
<td>96±8</td>
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<tr>
<td>Men</td>
<td>96±11†</td>
<td>99±10†</td>
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<td>103±9†</td>
<td>104±10†</td>
<td>106±10†</td>
<td>108±10†</td>
<td>124±12†</td>
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<tr>
<td>MAP, %change from rest</td>
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<td></td>
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<tr>
<td>Women</td>
<td>4.4±4.8</td>
<td>6.6±4.8</td>
<td>8.1±4.2</td>
<td>9.9±4.6</td>
<td>11.6±5.6</td>
<td>14.9±5.9</td>
<td>24.7±8.0</td>
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<tr>
<td>Men</td>
<td>3.4±3.2</td>
<td>5.3±5.5</td>
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<td>FVC, ml·min⁻¹·100 ml⁻¹·mmHg⁻¹</td>
<td></td>
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<tr>
<td>Women</td>
<td>0.02±0.01</td>
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<td>0.08±0.03</td>
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<tr>
<td>Men</td>
<td>0.02±0.01</td>
<td>0.04±0.02</td>
<td>0.05±0.02</td>
<td>0.06±0.02*</td>
<td>0.07±0.02*</td>
<td>0.08±0.03*</td>
<td>0.09±0.03*</td>
<td>0.11±0.04</td>
</tr>
</tbody>
</table>

Values are means ± SD. UC, unloaded contraction; MAP, mean arterial pressure; FVC, forearm vascular conductance. *Value significantly higher in women than men (P < 0.05). †Value significantly lower in women than men (P < 0.05).

**Forearm muscle activity.** The increase in sEMG was significantly correlated with exercise work load (r = 0.52, P < 0.05, pooled data); hence, no sex difference was found in forearm muscle activity during dynamic handgrip exercise (Table 2). At task failure, women and men demonstrated a similar increase in sEMG when expressed as a percent change from unloaded contractions (women 425.6 ± 149.1% vs. men 528.8 ± 302.9%, P > 0.05).

**DISCUSSION**

The aim of the present study was to test the hypothesis that sex differences influence muscle blood flow during exercise. To this end, Doppler ultrasound was used to measure FBF in women and men during progressive dynamic handgrip exercise to fatigue where the slope of the ramp function was the same for both sexes (i.e., same absolute task but lower relative task for men than women). In agreement with our original hypothesis, the significant findings of the present study suggest that muscle blood flow remains well-matched to work rate and presumably the metabolic demand of the exercising muscle in a manner independent of sex. First, FBF during submaximal exercise, expressed either as conduit flow (FBFa, ml/min) or muscle perfusion relative to forearm volume (FBFr, ml·min⁻¹·100 ml⁻¹), was not different between women and men, despite considerable differences in forearm muscle size and strength. Second, in contrast to the similar FBF responses, FVC was greater in women than men during submaximal exercise, which can be attributed primarily to the lower MAP in women compared with men. Finally, since FBFa matched work rate during submaximal exercise, FBFa was higher in men than women at task failure because of the greater absolute work load achieved by men at task failure. Additionally, FBFr appears to be coupled to the relative contractile demands of muscle as indicated by the similar muscle pressure measured in women and men at task failure when both sexes ended exercise at the same relative contraction intensity (i.e., ~14% of their respective MVCs). The speculation that sex differences in relative contraction intensity, and hence vascular occlusion to muscle blood flow during exercise, are partly responsible for sex differences in exercise tolerance is not supported by the results of the present study.

**Forearm blood flow is similar between women and men.** The regulation of skeletal muscle blood flow during exercise is controlled by central and peripheral factors, including the metabolic requirements of the active muscle. Since metabolic demands are proportional to exercise work rate, it is reasonable to assume that the similar slope of the ramp function used in the present study for women and men yielded a similar increase in work rate as resistance was progressively added. The results of the present study demonstrated a close coupling between FBFa and the increase in metabolic demand of the forearm muscles and that this association was similar for women and men. These findings are in agreement with previous studies demonstrating a close matching between oxygen consumption and muscle blood flow during exercise (1, 3, 16, 17), and suggests that metabolic requirements may outweigh any potential hemodynamic advantage women may have due to sex differences in contraction-induced changes in intramuscular pressure or local vasomotor control factors such as nitric oxide bioavailability (12).

Forearm blood flow, when expressed as conduit flow (FBFa, ml/min), exhibits a close coupling to absolute work load as demonstrated by two findings. First, a significant correlation was present between FBFa and exercise work load such that FBFa increased in a linear fashion with the progressive increase in handgrip work load. Second, FBFa was higher in men than women at task failure, which is consistent with the higher work load achieved by the men compared with the women. On the other hand, blood flow expressed relative to forearm volume (FBFr, ml·min⁻¹·100 ml⁻¹), was not correlated with absolute work load but was associated with the relative contraction intensity. Evidence for this relationship can be found in the similar FBFr between women and men at task failure where both sexes ended exercise at 14% MVC. The similar relative increase in forearm muscle activity at task failure suggests that FBFr follows muscle mass recruitment during...
exercise irrespective of absolute work load. Together, these findings indicate that FBFa increases in proportion to the intensity of muscular activity, and presumably metabolic rate, while FBFr increases with muscle mass recruitment during exercise.

Our findings of a similar FBFa response between women and men during handgrip exercise is in partial agreement with the results of a recent study that examined sex differences in femoral artery blood flow during incremental single-leg knee extension exercise. Parker et al. (36) found femoral blood flow to be similar between sexes at low work loads (<15 W) but was higher for women than men at moderate to high work loads (15–40 W). The authors attributed the sex difference in femoral blood flow in part to a proportionately larger increase in femoral artery diameter during exercise in women than men. Also, it was reasoned that a lower hemoglobin concentration in women than men may have contributed to the higher exercise hyperemia consequent to the lower arterial oxygen content of the blood. In contrast to these findings, the results of our pilot studies indicate that brachial artery diameter remains relatively unchanged from resting values, at least at the relatively low work loads (<5 W) achieved by our subjects. It is possible that sex differences in FBF may be elicited if higher work loads could be achieved during dynamic handgrip exercise before fatigue.

In the present study, the increase in sEMG was not significantly different between women and men during dynamic exercise. In contrast to dynamic exercise, Hunter et al. (24) has shown men to have a higher rate of increase in sEMG than women during static isometric exercise, although the total increase in sEMG at task failure was similar between sexes. This sex difference in the pattern of muscle activity indicates that muscle mass recruitment is different between women and men during isometric exercise. Since the increase in sEMG during isometric exercise is associated with increased intramuscular pressure (9), it follows that sex differences in motor unit recruitment would result in different levels of muscle perfusion during exercise since intramuscular pressure is known to reduce muscle perfusion during exercise (42). In this manner, we believe the lower muscle perfusion in men than women reported by Hunter et al. (26) is the result of sex differences in the muscle mass recruited at the time of blood flow measurement (4 min into an isometric handgrip contraction). This is in agreement with a recent study by Thompson et al. (47) that reported similar FBF and sEMG responses between women and men during static isometric handgrip exercise at a low contraction intensity. The similar rise in forearm muscle activity along with FBFr between women and men in the present study supports this relationship.

Vascular conductance is greater in women than men. A significant sex difference was found in FVC such that women had a higher FVC than men during dynamic handgrip exercise. This difference was in the presence of a lower MAP in women than men. Sex differences in MAP are not a consistent finding although men are frequently reported to have a higher resting blood pressure, particularly systolic blood pressure, than women (32, 33). This sex-related difference in blood pressure may be due to sex differences in body mass (34), a lower tonic sympathoadrenal activity in women than men (7), or the effect of sex hormones (estrogen and progesterone) on blood pressure regulation (41). In the present study, men had significantly higher resting systolic and diastolic blood pressure than women (group average systolic/diastolic blood pressure: men 128/82 vs. women 108/72), although both sexes were normotensive. On the basis of the equation we used to calculate MAP, we believe the higher resting MAP in men than women in the present study was due to the significant sex difference in diastolic blood pressure.

Despite the sex difference in absolute MAP, the percent increase in MAP from rest was not different between women and men during handgrip exercise. Only at task failure when men exercised longer and achieved a higher exercise work load was the percent increase in MAP higher in men than women. This suggests that brachial artery control during dynamic handgrip exercise involved sympathetic outflow to the artery that adjusted MAP in proportion to exercise intensity in an identical fashion between women and men. Considering that the contractile demand and forearm muscle activity was the same between women and men in the present study, it is reasonable to speculate that comparable levels of muscle metabolites were produced by women and men during exercise, which would lead to reflex sympathetic activation (8). In contrast to autonomic vasoconstrictor signals, the higher FVC in women compared with men suggests that vasodilatory signals within the forearm microcirculation (local vasodilation) may have been greater or the vasculature more sensitive to these signals in women than men during exercise. This may be a sex difference found in other limbs considering that women have also been shown to have a greater vascular conductance in the femoral artery during incremental knee extension exercise (36). Evidence for sex differences in vascular reactivity is provided by studies that report a greater flow-mediated vasodilation and vasoconstriction in women than men (6, 31). Animal research also reports sex differences in the sensitivity of the vasculature to endothelial-dependent agonists that vary between arteries (30). Nevertheless, the higher FVC allowed women to achieve the same FBF response as men during exercise. This information adds to the literature by demonstrating sex differences in the control of muscle blood flow during dynamic handgrip exercise, which recent studies suggest may vary with age (38).

Sex differences in exercise tolerance. Time to task failure was ~85% longer in men than women during dynamic handgrip exercise performed in a ramp function (0.5 kg/min). Our findings are in agreement with previous literature reporting muscle strength to be positively related to absolute endurance time during dynamic exercise. Using bench press exercise, Shaver (43) found muscle strength to be significantly related ($r = 0.93$) to the number of repetitions subjects could perform with a common work load set at 75% of the group’s mean MVC force. However, when work load was set relative to each subject’s maximal strength (i.e., 75% of each individual’s MVC), muscle strength was no longer significantly correlated to the number of repetitions completed ($r = -0.19$). In the same manner, the present study found forearm muscle strength to be significantly correlated with time to task failure ($r = 0.84$) for exercise performed with a common increase in absolute work load. However, if exercise tolerance were to be defined as the percentage of maximal force capacity achieved at task failure, then muscle strength would no longer be associated with exercise tolerance since the contractile force measured at task failure correspond to ~14% MVC for both
sexes. This indicates that exercise tolerance, if expressed relative to maximal capacity, was similar between women and men during dynamic forearm exercise. Indeed, muscle strength may play a minor role in determining exercise tolerance during intermittent contractions. Recently, Wigmore et al. (50) reported that muscle strength accounted for only 5% of the variability in dorsiflexor muscle fatigue during intermittent isometric contractions. In that study, muscle strength and volume were not correlated to exercise tolerance as defined by the time when force attained was 5% MVC below target force. Moreover, comparisons of women and men matched for muscle strength have found women to exercise longer than men during intermittent isometric contractions (13, 25), although this may be dependent on the muscle group examined (15).

The longer exercise endurance time in men is in contrast to the greater exercise tolerance frequently reported for women during sustained isometric handgrip exercise (21, 26, 49). The difference in exercise tolerance between isometric and dynamic handgrip exercise may be related to contraction duration and its influence on muscle blood flow. Barnes (2) has shown FBF to become limited in high-strength men with as little as 20% MVC during static isometric handgrip contractions of at least 15 s. This would have likely increased the potential for greater muscle fatigue and shortened endurance time as been shown to occur during limited blood flow conditions (37). In the present study, women and men performed intermittent dynamic handgrip contractions that when summed over minute were on average a total of 6 s per minute of exercise. This duration is too short to significantly limit the delivery of oxygen or removal of metabolic by-products from the working forearm muscles during exercise. Moreover, intermittent contractions allow for a hyperemic response between contractions (28, 40), which minimizes the effect of the mechanical compression placed on muscle vasculature, thereby preventing a contraction-induced reduction of muscle blood flow during exercise.

Study limitations. A limitation of the present study is the absence of sEMG measurements during MVC testing, which prevents estimating the amount of muscle mass recruited as a percentage of the total amount of muscle mass available. It is possible that men recruited a larger percentage of their available motor units to generate a greater absolute force compared with women, which would result in a lower muscle perfusion relative to the number of active muscle fibers. However, we believe this to be unlikely since the specific tension for males and females is quite similar (35) and thus the proportion of muscle recruited for a given force would also be expected to be similar between the sexes. Nevertheless, the change in muscle activity normalized to unloaded contractions showed the pattern of motor unit recruitment to be similar between sexes and related to FBFr during dynamic forearm exercise.

A second limitation of the present study was that the association between FBF and muscle fatigue, which is typically defined as the inability to maintain either the required or expected force (10), was not directly examined. Instead, exercise tolerance was defined and compared between sexes based on the inability of the subjects to maintain contraction frequency and/or duty cycle. Although it is reasonable to speculate that the physiological mechanisms underlying muscle fatigue contributed significantly to the slowing of muscle contraction rates as the individual approached task failure, the contractile force deficit was not assessed. Nonetheless, FBFa increased with an increase in work load up to task failure and was not different between women and men. The absence of a plateau or decrease in FBF during handgrip exercise suggests that FBF was not a factor limiting exercise tolerance. This is in agreement with a recent report that found the onset of muscle fatigue, as assessed by periodic measurements of MVC force, to occur before the plateau in blood flow occurred during intermittent isometric dorsiflexor exercise (50).

Last, menstrual cycle phase was not controlled for in the women tested in this study. Although menstrual cycle phase (i.e., estrogen levels) has a significant influence on vascular reactivity (19), recent studies suggest that menstrual cycle phase may not significantly influence the response of muscle blood flow to exercise in humans. For instance, Hunter et al. (26) recently reported no association between the day of the menstrual cycle in women and measures of forearm blood flow and vascular conductance taken at rest and postcontraction from isometric handgrip exercise. Furthermore, Lynn et al. (32) did not find the increase in femoral blood flow following cycling exercise at 60% of peak O2 consumption to be different between menstrual cycle phases or between women and men. On the basis of these results, we do not believe that menstrual cycle phase played a significant influence on our study results. Still, vascular reactivity to a flow-mediated stimulus has been shown to be dependent on menstrual cycle phase and differ between sexes (19); therefore we cannot discount the possibility that menstrual cycle phase had an influence on the study findings.

Conclusions. The experimental approach used in the present study required women and men to exercise at the same absolute work rate and, presumably, metabolic demand. Our results find that FBF, whether expressed as conduit artery flow or normalized to forearm volume, was not different between women and men during dynamic handgrip exercise. The similar FBF response to exercise was achieved by a higher FVC in the presence of a lower MAP in women than men. Last, the sex difference in time to task failure despite the similar FBF response to exercise suggests that muscle blood flow does not determine exercise tolerance during this dynamic handgrip exercise.

GRANTS

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