Forearm blood flow responses to fatiguing isometric contractions in women and men

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Thompson BC, Fadia T, Pincivero DM, Scheuermann BW. Forearm blood flow responses to fatiguing isometric contractions in women and men. Am J Physiol Heart Circ Physiol 293: H805–H812, 2007. First published April 27, 2007; doi:10.1152/ajpheart.01136.2006.—Previous studies suggest that women experience less vascular occlusion than men when generating the same relative contractile force. This study examined forearm blood flow (FBF) in women and men during isometric handgrip exercise requiring the same relative force. Thirty-eight subjects [20 women and 18 men, 22.8 ± 0.6 yrs old (means ± SE)] performed low- and moderate-force handgrip exercise on two occasions. Subjects performed five maximum voluntary contractions (MVC) before exercise to determine 20% and 50% MVC target forces. Time to task failure (TTF) was determined when the subject could not maintain force within 5% of the target force. Mean blood velocity was measured in the brachial artery with the use of Doppler ultrasonography. Arterial diameter was measured at rest and used to calculate absolute FBF (FBFa; ml/min) and relative FBF (FBFr; ml·min⁻¹·100 ml⁻¹). Women generated less (P < 0.05) absolute maximal force (208 ± 10 N) than men (357 ± 17 N). The TTF was longer (P < 0.05) at 20% MVC for women (349 ± 32 s) than for men (230 ± 23 s), but no difference between the sexes was observed at 50% MVC (women: 69 ± 5 s; men: 71 ± 8 s). FBFa and FBFr increased (P < 0.05) from rest to TTF in both women and men during 20% and 50% MVC trials. FBFr was greater in women than in men at ≥30% TTF during 50% MVC. At exercise durations ≥60% of TTF, FBFa was lower (P < 0.05) in women than in men during handgrip at 20% MVC. Despite the longer exercise duration for women at the lower contraction intensity, FBFa was similar between the sexes, suggesting that muscle perfusion is matched to the exercising muscle mass independent of sex.

Muscle fatigue; electromyography; muscle contraction; endurance

Evidence from previous studies (2, 26) indicate that a large muscle mass can generate greater absolute force during a muscle contraction, which in turn may lead to increased intramuscular pressure, occlusion of blood flow, metabolite accumulation, and impaired delivery of oxygen to the exercising muscle. Because women generally have less muscle mass and generate less absolute force during the same relative task than men, it might be expected that women will exhibit greater muscle endurance than men because they experience less intramuscular pressure and therefore less vascular occlusion (2, 11). Consistent with this view, Hunter and Enoka (16) reported that the exercise pressor response was lower in women than in men, not matched for strength, and that endurance time was inversely related to the change in mean arterial pressure. Although there are a number of possible explanations for the differences in the exercise pressor responses between women and men, these findings suggest that differences in muscle perfusion may contribute significantly to the reduced exercise tolerance in stronger individuals. This view is supported by the results of a recent study (24) demonstrating that sex differences in the magnitude of muscle fatigue during dorsiflexion exercise were eliminated by inducing muscle ischemia. These findings are in agreement with an earlier study that indicated that sex differences in muscle fatigability may be associated with a greater reliance on aerobic metabolism in women than in men under normal free-flow conditions (19).

Despite the known effects of muscle contraction on intramuscular pressure and vascular occlusion, muscle blood flow has not been directly compared between women and men during isometric exercise. Hunter et al. (17) recently demonstrated, using venous occlusion plethysmography, that the reactive hyperemic response after a sustained isometric contraction was similar between women and men; however, the time to task failure was significantly longer for women than for men. Although the results of this study are of interest, muscle blood flow could only be assessed during periods of relaxation following exercise and could not be directly measured during exercise. In addition, using this approach to estimate muscle blood flow assumes that the magnitude of reactive hyperemia is inversely proportional to muscle perfusion (and/or occlusion) during the muscle contraction (17). Although there is a good association between the duration of muscle contraction and the reactive hyperemic response (6, 13), there is little evidence to indicate that this approach can be used to estimate the magnitude of vascular occlusion between individuals, particularly those with appreciably different forearm volumes. Furthermore, the results of previous studies have shown that the occlusion pressure required to use the venous occlusion plethysmography approach significantly reduces muscle blood flow (3, 12), and thus the extent that muscle perfusion is either similar or different in women and men during performance of an isometric contraction has not been resolved.

The results of previous investigations have shown that, with increasing contraction intensity, the time to reach fatigue is either greater for women than for men (29) or the difference between the sexes is diminished (21). Although these conflicting findings may be a consequence of the different muscle groups examined in these studies (21, 29), the effect of increasing muscle contraction intensity on vascular occlusion in women compared with men has not been previously examined. Therefore, the purpose of the present study was to elucidate the...
interaction between muscle tension development and muscle blood flow in women and men while they performed fatiguing isometric handgrip exercise at the same relative intensity. Doppler ultrasound techniques were used to directly assess brachial artery blood flow during exercise, and measures of forearm volume were made to determine relative blood flow responses (i.e., muscle perfusion) during isometric handgrip exercise at two different contraction intensities. It was hypothesized that, because the absolute tension development would be less for women than for men (i.e., same relative task), women would experience less vascular occlusion during exercise, leading to sufficient muscle perfusion, and therefore would exhibit improved exercise tolerance vs. that shown for men. Second, it was hypothesized that, as contraction intensity increased, differences in muscle blood flow between the sexes would be reduced, resulting in no difference in contraction duration.

METHODS

Subjects. Subjects for this study included 18 adult men (means ± SE; age = 22.7 ± 0.6 yr, height = 179.3 ± 1.6 cm, mass = 80.7 ± 4.0 kg) and 20 women (age = 22.7 ± 0.8 yr, height = 161.8 ± 1.3 cm, mass = 55.2 ± 1.4 kg), all in good health. The women reported no irregular menstrual cycles, oral contraceptive use, or pregnancy in the year preceding the study; all experimental sessions were performed during the luteal phase of the menstrual cycle. Individuals with any hand dysfunction or any reported history of cardiovascular or pulmonary disease, orthopedic pathology, or diabetes mellitus or individuals who were currently taking any prescription medications were excluded from participating in this study. Before participants performed any exercise, written, informed consent was obtained and the experimental protocol and risks associated with participating in the exercise were described to each subject. This study was approved by the Human Subjects Research Review Committee at The University of Toledo and were in accordance with the Declaration of Helsinki.

Experimental protocol. All subjects participated in three separate experimental sessions. During the first session, anthropometric data (body height, body mass, and forearm volume) were obtained, as well as brachial artery diameter. The remaining two experimental sessions consisted of fatiguing isometric handgrip exercise with the dominant arm, performed on separate days with a minimum of 48 h between sessions. Subjects were instructed to maintain their customary level of physical activity during the period between the sessions but to refrain from any strenuous exercise or work requiring strong handgrips for at least 24 h before they arrived at the laboratory. To ensure familiarization with the equipment and experimental procedures, subjects were provided instructions and were required to perform a series of submaximal handgrip practice sessions before the first experimental session.

Isometric handgrip exercise and fatigue protocol. Handgrip force and muscle fatigue were measured with a handgrip dynamometer (MLT 003/D; ADInstruments, Colorado Springs, CO), with the subjects supine. Subjects were positioned on a standard treatment table with their head supported and arms extended and slightly abducted, with the wrist placed midway between forearm pronation and supination. The subjects were instructed to squeeze the handgrip dynamometer maximally [maximum voluntary contraction (MVC)] for 5 s after a series of submaximal familiarization contractions. Each MVC was performed by having the subject increase their force from resting to their maximal level, with the maximal force held for 3 s. Concurrent visual feedback of force level was provided to the subjects on a computer monitor, as well as verbal encouragement, to elicit their maximal effort. Subjects performed a total of five MVCs, with at least 2 min of rest between each contraction. The average of the individual subject’s three highest MVCs in each experimental session was used as an estimate of their maximal voluntary effort and to determine the target force for the subsequent fatiguing contractions.

After determination of the MVC, an isometric contraction was then performed to the predetermined target force of either 20% or 50% MVC until task failure. Task failure was defined as the time at which the subject could no longer sustain the target force within 5% of the target level for more than 2 s. The submaximal contractions were performed on a separate day in a randomized order. The absolute force at the target level was displayed on a monitor, and subjects were required to match their generated force tracing to the target level for as long as possible. All subjects were provided verbal encouragement throughout the isometric contraction to maintain handgrip force at the target requirement. Subjects were not provided any feedback regarding their performance (i.e., time to task failure) before the conclusion of the study.

Brachial artery blood flow and cross-sectional area measurements. Continuous measurements of blood velocity in the brachial artery of the dominant arm were obtained by Doppler ultrasound velocimetry (500-V; Multigon Industries), operating in pulsed mode. The Doppler transducer, with an operating frequency of 4 MHz and a fixed-angle crystal of 45° relative to the skin, was placed flat on the medial aspect of the upper arm ~6–10 cm proximal to the antecubital fossa and parallel to the brachial artery. The ultrasound gate was adjusted to the total width of the artery to ensure complete insonation of the brachial artery. An audio demodulator, calibrated according to the manufacturer’s specifications, was used to convert the frequency spectrum of Doppler audio signals to an instantaneous mean blood velocity. The analog blood velocity signal from the Doppler system was recorded at 100 Hz (PowerLab 16SP; ADInstruments, Colorado Springs, CO) and stored on computer for later off-line analysis. Mean brachial artery blood velocity was determined as the area under the curve for each cardiac cycle (i.e., triggered by the detection of each R-wave-to-R-wave interval), with blood velocities expressed per minute (i.e., cm/min) by multiplying the cardiac cycle-by-cycle values by the corresponding heart rate (HR) (Matlab Release 11.1, The Mathworks).

On a separate day, the cross-sectional area of the brachial artery was determined by echo-Doppler sonography, using a multifrequency linear array probe (5–9 MHz; center frequency of 7.5 MHz) operating in two-dimensional echo mode (Mysono 201, Medison, CA) (18, 28). Brachial artery diameter was determined with the subject in a supine position over 10–15 cardiac cycles at peak systole and end diastole from a cross-sectional view of the artery at the level used to measure blood velocity. The measurement of arterial diameter was only performed on cardiac cycles that provided well-defined arterial borders. The average artery diameter for each subject was then used to calculate the cross-sectional area by approximating the artery to a circle. Changes in brachial artery diameter were examined in a subgroup of 10 healthy, young subjects (5 women and 5 men) while performing an isometric contraction at 20% MVC. Brachial artery diameter, which was determined as the average value measured over 10–15 cardiac cycles, was measured at rest, at the onset of muscle contraction, and 30 s before task failure. Consistent with previous reports in the literature (20), our findings indicated that brachial artery diameter did not change appreciably from rest (0.36 ± 0.03 cm), to the onset of exercise (0.36 ± 0.02 cm), to task failure (0.37 ± 0.02 cm); therefore, resting arterial diameters were used to calculate forearm blood flow (FBF). FBF (ml/min) was calculated beat by beat as the product of mean blood velocity and cross-sectional area. In addition to examining the absolute blood flow through the conduit artery, we measured forearm volume using the water displacement technique to determine relative blood flow responses (i.e., muscle perfusion; ml·min⁻¹·100 ml tissue⁻¹) to exercise. For each subject and contraction intensity, resting blood flow was averaged over a 30-s window; blood flow responses during the isometric contraction were analyzed by normalizing exercise duration from 0% to 100% of time.
to task failure and subsequently partitioning the cardiovascular responses into equal bins of 10%.

Measurement of surface electromyography. Surface EMGs were obtained from the wrist and finger flexor muscle groups, using two sets of disposable, circular surface snap electrodes (Ag/AgCl; 1.4 cm diameter, 2.0 cm interelectrode distance; Noraxon Dual Electrodes, Noraxon, AZ). Before electrode placement, the skin was shaved and cleaned with isopropyl alcohol to reduce skin impedance and to ensure good adhesion of the electrodes. The electrodes were placed over the belly of the finger flexor muscle group, located approximately over the middle one-third of the anterior forearm. After completion of the first trial, an outline of the electrodes was traced onto a transparent sheet placed over the subjects’ forearm in an effort to record EMG activity from a similar site during subsequent visits to the laboratory. The reference electrode was placed over the olecranon process of the nondominant arm.

The raw EMGs were sampled at 2,000 Hz by a differential biopotential amplifier [common mode rejection (CMR) \( \leq 60 \text{ dB at 1 kHz} \); gain \( = 5,000 \)] (PowerLab, ADInstruments) and saved to computer disk for offline analyses. The raw EMG signals were band-pass filtered (20–500 Hz), full-wave rectified, and integrated over the middle 3 s of each of the MVC trials and over incrementing bins of 10% during the sustained muscle contractions. Each integrated EMG (iEMG) value was subsequently divided by the duration of the analyzed sample to obtain a 1-s value. Each time-normalized value was then expressed as a percentage of the averaged EMG values obtained for the three highest MVCs.

Statistical analysis. A two-way ANOVA (sex by trial day) with one repeated measure was performed for the average of the three highest MVCs. The time to task failure was analyzed by two-way ANOVA (sex by intensity) with one repeated measure. A two-way repeated-measures ANOVA (20% vs. 50% MVC) was used to compare cardiovascular variables (FBF and HR) and iEMG. At task failure, differences in FBF between sexes were analyzed by one-way repeated-measures ANOVA (20% vs. 50% MVC). The Student-Newman-Keuls multiple comparison post hoc analysis was used to test for differences between means where appropriate. Data are reported as means ± SE unless otherwise indicated. Statistical significance was accepted at \( P \leq 0.05 \).

RESULTS

Subjects. Subject characteristics are summarized in Table 1. Resting FBF across the two trials were as follows: day 1 = 21.8 ± 2.4 ml/min and day 2 = 21.4 ± 2.5 ml/min [intraclass correlation coefficient (ICC) = 0.78]. Average MVC forces across the 2 days were 275 ± 8 and 284 ± 7 N (ICC = 0.94). The average iEMG obtained for MVC performed each day demonstrated good reliability across the two experimental sessions (day 1 = 0.41 ± 0.05 V, day 2 = 0.37 ± 0.03 V; ICC = 0.81).

As expected, the mean forearm volume was considerably less for women (\( P < 0.05 \)) than for men (Table 1); therefore, initial comparisons in muscle blood flow between sexes were examined after being normalized to forearm volume (i.e., relative changes expressed as ml·min\(^{-1}·100 \text{ ml tissue}^{-1}\)). In addition, absolute changes in FBF (i.e., ml/min) through the brachial artery were also compared between the sexes, independent of differences in forearm volume, in an effort to gain further insight into the interaction between muscle contraction and vascular occlusion.

FBF at 20 and 50% MVC: relative changes. The group means for women and men showing the changes in relative FBF (FBFr) during isometric handgrip exercise to task failure

![Fig. 1. Relative forearm blood flow (FBF; ml·min\(^{-1}·100 \text{ ml}^{-1}\)) group means for women (○) and men (●) during fatiguing isometric handgrip exercise at 20% maximum voluntary contraction (MVC) (top) and 50% MVC (bottom). There were no significant differences in relative FBF between sexes at 20% MVC. Male volunteers experienced less relative FBF than the female volunteers from 30 to 100% time to task failure (TTF). *Significantly different from results for female volunteers (\( P < 0.05 \)).](http://ajpheart.physiology.org/content/293/7/1532/F1)

Table 1. Subject characteristics, absolute force production, and time to task failure during sustained isometric contractions at 20% and 50% MVC

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>( n )</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Age, yr</td>
<td>22.7±0.8</td>
<td>22.7±0.6</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>55.2±1.4</td>
<td>80.7±4.0*</td>
</tr>
<tr>
<td>Height, cm</td>
<td>161.8±1.3</td>
<td>179.3±1.6*</td>
</tr>
<tr>
<td>Arterial diameter, cm</td>
<td>0.29±0.01</td>
<td>0.38±0.01*</td>
</tr>
<tr>
<td>Forearm volume, cm(^3)</td>
<td>767.5±25.1</td>
<td>1313.2±52.8*</td>
</tr>
</tbody>
</table>

20% MVC trial

| MVC Force, N              | 206±10 | 357±17* |
| 20% MVC target force, N   | 41±2   | 68±4*  |
| 20% MVC time to task failure, s | 349±32 | 230±23* |

50% MVC Trial

| MVC force, N              | 209±9  | 364±15* |
| 50% MVC target force, N   | 104±5  | 180±7*  |
| 50% MVC time to task failure, s | 69±3   | 71±8   |

Values are means ± SE. MVC, maximum voluntary contraction. *Statistically different from results for female volunteers (\( P < 0.05 \)).
at 20 and 50% MVC are presented in Fig. 1. A significant time main effect \((P < 0.05)\) was observed for FBFr at 20% MVC; however, there was no main effect for sex or sex-by-time interaction, indicating that FBFr was well matched to muscle volume in both women and men. At task failure, FBFr was not significantly different between women \((7.4 \pm 0.7 \text{ ml}\cdot\text{min}^{-1}\cdot100 \text{ ml}^{-1})\) and men \((6.7 \pm 0.8 \text{ ml}\cdot\text{min}^{-1}\cdot100 \text{ ml}^{-1})\) during exercise at 20% MVC.

At 50% MVC, a significant main effect for time \((P < 0.05)\) and main effect for sex \((P < 0.05)\) were observed for FBFr. Post hoc analysis revealed that FBFr was higher \((P < 0.05)\) in women than in men from 30 to 100% of the time to task failure (Fig. 1). At task failure, FBFr was lower \((P < 0.05)\) for women during exercise at 50% than at 20% MVC. Similarly, in men, FBFr at task failure was lower \((P < 0.05)\) during exercise at 50% MVC than at exercise at 20% MVC. Furthermore, the proportional decrease in FBFr at task failure with the increase in contraction intensity from 20 to 50% MVC was considerably greater \((P < 0.05)\) for men \((35.0 \pm 1.1%)\) than it was for women \((11.3 \pm 0.4%)\).

**FBF at 20 and 50% MVC: absolute changes.** Male and female group mean results for absolute FBF (FBFa) during isometric handgrip exercise to task failure at 20 and 50% MVC are presented in Fig. 2. Analysis of the blood flow at 20% MVC revealed significant time \((P < 0.05)\) and sex main effects, as well as a time-by-sex interaction \((P < 0.05)\). Post hoc analysis indicated that FBFa was lower \((P < 0.05)\) in women than in men from 60 to 100% of time to task failure (Fig. 2). At task failure, the FBFa was lower \((P < 0.05)\) in women \((57.5 \pm 6.0 \text{ ml/min})\) than in men \((84.5 \pm 9.3 \text{ ml/min})\) at contraction intensities corresponding to 20% MVC.

A significant time main effect \((P < 0.05)\) was observed for FBFa during exercise at 50% MVC; no significant sex main effect or sex-by-time interaction was observed. Consistent with this finding, FBFa was similar between women \((50.7 \pm 6.5 \text{ ml/min})\) and men \((56.7 \pm 10.3 \text{ ml/min})\) at task failure during exercise at 50% MVC. For the men, FBFa at task failure was higher \((P < 0.05)\) during exercise at 20% MVC than at 50% MVC. However, no difference in FBFa was observed for women between the exercise intensities.

**Heart rate.** Resting HR was similar between women and men before exercise for both 20% MVC \((72 \pm 3 \text{ and } 66 \pm 2 \text{ beats/min for women and men, respectively})\) and 50% MVC \((72 \pm 3; \text{ and } 69 \pm 2 \text{ beats/min for women and men, respectively})\) trials. There was a significant time main effect at 20% and 50% MVC \((P < 0.05)\) for HR, but no significant sex main effect or time-by-sex interaction was detected for either the 20% or 50% MVC trials. The increase in HR at task failure was greater \((P < 0.05)\) for both sexes during 50% MVC \((99 \pm 4 \text{ and } 104 \pm 4 \text{ beats/min for women and men, respectively})\) compared with 20% MVC \((92 \pm 4 \text{ and } 93 \pm 3 \text{ beats/min for women and men, respectively})\), but there was no difference in HR responses between women and men.

**MVC and endurance time.** The time to task failure was longer \((P < 0.05)\) for women \((349 \pm 32 \text{ s})\) than for men \((230 \pm 23 \text{ s})\) during exercise at 20% MVC (Table 1). There was no difference between women \((69 \pm 5 \text{ s})\) and men \((71 \pm 8 \text{ s})\) for time to task failure during exercise at 50% MVC (Table 1). The relationship between target force and the time to task failure for women and men is presented in Fig. 3. The nonlinear regression demonstrates that the time to task failure decreases as a function of the absolute target force, indicating that those individuals with a higher target force tend to fatigue earlier than those with a lower target force. Additionally, this relationship between target force and time to task failure was not appreciably different between women and men (Fig. 3). The women exhibited lower maximal strength than the men when the MVCs were examined over the 2 days of testing \((P < 0.05)\) (Table 1). When expressed relative to forearm volume, there was no difference in MVC force between women \((0.27 \pm 0.2 \text{ N/ml})\) and men \((0.27 \pm 0.2 \text{ N/ml})\). As shown in Fig. 3, a linear relationship between forearm volume and absolute force was observed for both the women and men (pooled data, \(r = 0.74)\).

**Sustained submaximal contraction iEMG.** A significant main effect for time \((P < 0.05)\) but no significant sex main effect for time-by-sex interaction for handgrip muscle iEMG at 20% MVC was observed. Handgrip muscle iEMG increased significantly during the sustained contraction in an equivalent pattern between women and men (Fig. 4). Similar results were observed for handgrip muscle iEMG at 50% MVC (Fig. 4), which demonstrated a significant time main effect \((P < 0.05)\) but no significant sex main effect or time-by-sex interaction.

Fig. 2. Absolute FBF (ml/min) group means for women (○) and men (★) during isometric handgrip exercise at 20% MVC (top) and 50% MVC (bottom). Men experienced greater FBF than women from 60 to 100% TTF during the 20% MVC fatiguing contraction, whereas no significant difference was observed at 50% MVC. *Significantly different from results for female volunteers \((P < 0.05)\).
DISCUSSION

The purpose of the present study was to examine the interaction between muscle tension development and FBF in women and men as they performed a fatiguing isometric handgrip contraction requiring the same relative intensity. It was hypothesized that the absolute tension development would be lower for women than for men, resulting in less vascular occlusion, and thus brachial artery blood flow would be higher in women than in men. In addition, we speculated that this sex difference in blood flow may account for the greater resistance to fatigue for women than for men, which has been previously reported (14, 16). In contrast with our original hypothesis, we found that FBF, when expressed relative to forearm volume, was similar between women and men at contraction intensity corresponding to 20% but not 50% MVC. It is interesting to note, however, that absolute blood flow through the brachial artery was appreciably lower in women than in men during contraction intensities corresponding to 20% and 50% MVC. When considered together, these observations suggest that FBFr, which may reflect muscle perfusion, was sufficient for the muscle mass recruited during the isometric contraction, at least at the lower contraction intensity, and that this response is independent of sex. In agreement with previous studies (16, 17), the time to task failure was significantly longer for women than for men during exercise at 20% MVC; however, this difference was not apparent during exercise at 50% MVC. Because FBFr was similar between women and men, and there was a difference in time to task failure, the results of the present study suggest that sex differences in FBF may not be an underlying mechanism explaining the observed differences in muscle fatigability (4, 16, 24).

FBF. The results of the present study demonstrated that, despite the lower absolute force generated by women at each of the contraction intensities, the FBFa was lower in women than it was in men at 20% MVC and was not different from men at 50% MVC. The extent to which muscle contractions lead to vascular occlusion and reductions in FBF is dependent on the force of contraction and the subsequent change in intramuscular pressure (2, 23, 26). Thus the amount of muscle mass activated during a contraction may contribute significantly to the development of vascular occlusion. Given that women typically have less muscle mass than men (22), they will generate lower absolute tensions (16) for the same relative

Fig. 4. Integrated EMG (iEMG) responses during exercise at 20% MVC (top) and 50% MVC (bottom) for women (○) and men (●). Both sexes experienced significant time main effect (P < 0.05) at the 2 intensities, but there was no significant sex main effect.

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Fig. 3. Top: an exponential decay \( y = 39.8 + 163.3e^{-0.008x} \), \( r = 0.74 \); pooled data] was observed for target force (as %MVC) and the TTF for both women (○) and men (●). Bottom: a linear relationship (\( y = 0.21x + 54.7, r = 0.73 \); pooled data) was observed between forearm volume (cm\(^3\)) and force (N), for both women (○) and men (●).
task, thereby reducing the demand for blood flow at the same relative contraction intensity. Forearm volume was significantly correlated with maximum force generation for women and men, at both 20 and 50% MVC. In addition, there was a significant correlation between target force and the time to task failure in the sexes. When taken together, these results suggest that muscle mass, rather than sex, may factor prominently in the development of muscle fatigue. As already indicated, FBFa was lower for women than for men at contraction intensities corresponding to 20% MVC, which is consistent with the results of previous studies indicating that vascular occlusion may not significantly impede muscle blood flow until contraction intensities exceed ~20% MVC (1, 2). However, the observation that FBFr was similar between the sexes at 20% MVC suggests that muscle perfusion was sufficient and well matched to the muscle mass recruited since the demand for blood flow would presumably be proportional to force development and therefore the muscle mass recruited (30).

The absolute force generated by a contracting muscle has been correlated to the mass of that contracting muscle (16). As the amounts of force and muscle mass increase to perform a given task, an increase in vascular occlusion and subsequent impediment to muscle blood flow may occur (2, 23). A comparison of the blood flow response as a function of contraction intensity indicated that, at task failure, FBFr was significantly reduced at 50% MVC compared with 20% MVC in men but not in women. Furthermore, the men exhibited a proportionately greater decrease in FBFr and FBFa at task failure (i.e., from 20 to 50% MVC) than the women (i.e., FBFr decreased by ~11% in women, whereas FBFr decreased by ~35% in the men) despite the increase in relative contraction intensity being similar between the sexes. Although changes in intramuscular pressure were not measured in the present study, the more pronounced decrease in FBFr with increasing contraction intensity in the men may be indicative of greater vascular occlusion occurring in the men than in women. This finding would suggest that vascular occlusion during muscle contraction may be influenced to a greater extent by muscle volume (i.e., greater muscle mass) and/or absolute force production rather than by relative force requirements, consistent with the results of an earlier study (2).

**FBF and exercise tolerance.** In the present study, the time to task failure was significantly longer for women than for men at the lower intensity, but not at the higher exercise intensity examined. Because FBFr was similar between the sexes at the lower intensity and increasing the contraction intensity had relatively little impact on FBFr in the women than the men, it is not possible to conclude with certainty that a limitation in blood flow may have contributed to the sex difference in fatigability as previously suggested (16), at least at the lower exercise intensity. Evidence against sex differences in muscle blood flow leading to longer endurance times in women than in men has been previously reported in the literature. For example, West et al. (29) reasoned that, because longer endurance times in women persisted throughout a range of contraction intensities from 20 to 80% MVC, muscle blood flow could not explain the sex differences in time to task failure since blood flow should have been maximally occluded in both women and men at the higher contraction intensities. However, these findings are inconsistent with those of Russ and Kent-Braun (24) who demonstrated that sex differences in the fatigability of the dorsiflexor muscles could be eliminated by occluding muscle blood flow. Using a similar approach, Clark et al. (4) demonstrated that occlusion of blood flow to the knee extensors during an isometric contraction of 25% MVC resulted in a similar time to task failure between sexes, which was initially longer for women during the nonoccluded trial. It should be noted that, although women exhibited less muscle fatigue than men under the free-flow condition (i.e., normal muscle blood flow), the reduction in MVC at end exercise was similar for women and men during the ischemic condition (refer to Fig. 1 of Ref. 24). Similarly, a reduction in blood flow to the knee extensor muscles in the latter study (4) had a relatively small effect on the time to task failure in men (i.e., a difference of 4 s between normal and occluded conditions) but had an appreciable effect in the women (i.e., a difference of 35 s between normal and occluded conditions). The reasons for this apparent difference in time to task failure between the sexes in response to blood flow occlusion is not readily discernable from these studies (4, 24), but these findings are consistent with the view that differences in muscle metabolism may be associated with sex differences in muscle fatigability (4, 25).

**Time to task failure.** The results of the present study demonstrated a significantly longer time to task failure for women than for men at a contraction intensity corresponding to 20% MVC. Although consistent with some (21) but not all studies (29), the time to task failure was not different between the sexes at contraction intensities requiring 50% MVC. Although consistent with some (21) but not all studies (24), the time to task failure was not different between the sexes at contraction intensities requiring 50% MVC. Despite this discrepancy, the results of another study (16) that also observed a similar response suggesting that the relationship between absolute force development and muscle size is a better predictor of the time to task failure than differences between the sexes. In addition, the responses of the women and men (pooled data shown in Fig. 3) are distributed along the same regression line, indicating that there was no appreciable difference between the sexes for this relationship.

**iEMG responses.** During submaximal isometric contractions, the neuromuscular system attempts to maintain force production primarily by increasing the recruitment of additional unfatigued motor units and the firing frequency of already recruited motor units (7, 8). It has been suggested that differences in neuromuscular activation patterns between the sexes may contribute to the differences observed in muscle fatigability between women and men (5). For example, the results of previous studies indicate that, compared with women, men experience a greater reduction in neuromuscular activation after fatiguing heavy-resistance exercise (9), a greater increase in descending neural drive to the contracting muscles during intermittent and isometric contractions (14, 15, 24), and a nonaltered pattern of muscle activation after pro-
longed limb immobilization (27), consistent with the view that differences in motor unit recruitment strategies between women and men may contribute to differences in muscle fatigability. A previous study (4) did demonstrate that, although there were significant sex differences in neuromuscular activation patterns during sustained knee extension exercise at 25% MVC, these differences were not associated with the time to task failure. The associations between sex, neuromuscular activation patterns, and muscle fatigability have been questioned by others as well (10). A comparison between the sexes in the present study indicated that neuromuscular activation is similar between women and men. Despite the efforts by each subject to maintain the target force, iEMG progressively increased with contraction duration to task failure. However, similar to a previous report (29), the iEMG value at task failure did not achieve the value attained for the prefatigue MVC. The reason(s) for this inability to maximally activate all of the motor units, at least to the extent that they were activated during the prefatigue MVC, is not known, although it is evident that there was no appreciable difference between the sexes.

During contractions at 20% MVC, increases in iEMG and FBFr, with increasing contraction duration, were observed for both women and men. The increase in FBFr appears to be coupled to the increase in iEMG, in agreement with the notion that blood flow is well matched to muscle activation, at least at contraction intensities requiring 20% MVC (and presumably less). Although we were not able to determine at what contractile force blood flow and muscle activation tend to dissociate, it is evident from the results of the present study that blood flow was reduced at 50% MVC (compared to 20% MVC), whereas iEMG continued to increase.

**Conclusions.** In summary, despite the greater FBFa in men compared with women during performance of the same relative muscle contraction (i.e., 20% MVC), the increase in FBFr was similar between the sexes, suggesting that muscle perfusion was well matched to the muscle mass recruited, at least at the lower exercise intensity. The similar FBFa between men and women during the higher contraction intensity (i.e., 50% MVC) together with the proportionately greater reduction in muscle blood flow for the men vs. the women at task failure is consistent with the higher absolute forces generated by the men resulting in greater vascular occlusion. In agreement with the results of others, the extent that muscle blood flow represents a limitation to exercise tolerance appears to be independent of sex.

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