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Sex Differences in Time to Task Failure and Blood Flow for An Intermittent Isometric Fatiguing Contraction

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Abstract

The purpose of this study was to compare the time to task failure, postcontraction hyperemia, and vascular conductance of young men and women for a submaximal intermittent fatiguing contraction performed with the handgrip muscles. Twenty men and 20 women (mean \pm SD: 22 \pm 4 years) performed an isometric contraction at 50% of maximal voluntary contraction (MVC) (6-s contraction, 4-s rest) until task failure. Forearm venous occlusion plethysmography was used to estimate the peak blood flow (after 10-min occlusion) and blood flow at rest after 6-s submaximal contractions of varying intensities, and during an intermittent fatiguing contraction at 1-min intervals and task failure. The time to task failure was longer for the women compared with the men (408 \pm 205 s vs. 297 \pm 57 s, $P < 0.05$). Postcontraction hyperemia and vascular conductance were greater for men than for women after nonfatiguing 6-s submaximal contractions performed at 20%, 40%, 50%, 60%, and 80% of MVC force ($P < 0.05$). In contrast, hyperemia and vascular conductance were similar for both genders when measured at 50 s into the fatiguing contraction, at each minute thereafter, and at task failure. Regression analysis indicated that the rate of electromyographic activity and perceived exertion were the significant predictors of the time to task failure. The longer time to task failure for women compared with men for an intermittent fatiguing contraction with handgrip muscles was not explained by postcontraction hyperemia or vascular conductance with fatigue.

Young women are less fatigable than men for isometric contractions performed at the same relative intensity during sustained and intermittent tasks.¹¹ The sex difference in muscle fatigue for isometric tasks may involve factors associated with perfusion.^{6, 18, 32} For example, the sex difference in muscle fatigue was not exhibited when blood flow was occluded during intermittent maximal contractions of the ankle dorsiflexor muscles³² and a sustained submaximal contraction of the quadriceps muscles.⁶ For sustained submaximal contractions, the sex difference in time to failure is related to the strength of the subject.^{14, 15, 18} Presumably, stronger individuals (usually men) sustain greater absolute forces when the relative target force is based on maximal strength. Greater absolute forces are associated with increased intramuscular pressures and occlusion of blood flow.^{1, 34, 35} Therefore, they probably lead to more rapid accumulation of metabolites, impairment of oxygen delivery to the muscle, and a more rapid rate of muscle fatigue.¹⁴ Accordingly, when men and women were matched for strength, the time to task failure was similar in young men and women for sustained submaximal contractions of the elbow flexor and finger flexor muscles.^{15, 18} Differences in perfusion appear to explain some but not all of the sex difference in time to task failure for a sustained submaximal contraction.^{18, 36}

In contrast to sustained contractions, young women exhibit a longer time to task failure than men for an intermittent isometric contraction, even when the sexes are matched for strength.^{9, 16} Because the difference in muscle fatigue between men and women is not exhibited under ischemic conditions for an intermittent task,³² the sex difference involves a perfusion-dependent mechanism that is not related to strength. Accordingly, women have greater limb vasodilation in response to pharmacological and physiological stimuli during dynamic exercise of the legs and sustained contractions.^{18, 21, 24, 27} One possible explanation for the sex difference in muscle fatigue is that there is a sex difference in perfusion and clearance of metabolites and consequent greater fatigue resistance in women compared with men during an intermittent task. Accordingly, metabolic byproducts of muscle fatigue that also act as vasodilators⁷ differ between men and women.^{20, 33} Women exhibited greater vasodilation than men during a sustained isometric contraction¹⁸ and also during graded dynamic exercise.²⁷ For sustained isometric contraction, the greater vasodilation of the women did not explain the sex difference in the time to task failure.¹⁸ In healthy young men, the limitation of blood flow to ankle dorsiflexor muscles was not a factor in impaired force production during intermittent contractions.⁴⁰ The contribution of muscle perfusion to the longer time to failure of an intermittent isometric fatiguing contraction for women compared with men, however, is not understood.

The purpose of this study was to compare the time to task failure, postcontraction hyperemia, and vascular conductance before, during, and at task failure of a submaximal intermittent isometric contraction performed by young men and women in handgrip muscles. Postcontraction (reactive) hyperemia was quantified using venous occlusion plethysmography^{19, 39} along with blood pressure measurements to calculate vascular conductance. This technique is a well-established and reliable method for determining increased blood flow (hyperemia) immediately after isometric contractions.¹⁹ It is inversely associated with muscle perfusion during brief contractions.^{13, 39} Therefore, those individuals who have greater hyperemia and vascular conductance immediately after an isometric contraction are likely to have less perfusion during the contraction.

We quantified postcontraction hyperemia and calculated vascular conductance to understand the hemodynamics of men and women after: (1) a series of brief nonfatiguing submaximal isometric contractions at various intensities; (2) each minute of an intermittent fatiguing contraction maintained at 50% of maximal strength; and (3) task failure. An intermittent contraction with 6-s contractions followed by 4-s rest was chosen, because we had previously observed differences in postcontraction hyperemia and vascular conductance when men were stronger than women after brief 6-s submaximal contractions.¹⁸ We hypothesized that women would have less postcontraction hyperemia and vascular conductance than men following brief contractions, and this would be associated with a longer time to task failure.

METHODS

Twenty young men (22.3 ± 5.2 years) and 20 young women (20.9 ± 3.3 years) volunteered to participate in this study. All subjects were healthy with no known neurological or cardiovascular diseases, and they were naive to the protocol. Prior to participation in the study, each subject provided informed consent. The institutional review board at Marquette University approved the protocol.

The physical activity level for each subject was assessed with a questionnaire²² that estimated the relative kilocalorie expenditure per week. None of the subjects had a recent history of strength training. The day of the menstrual cycle on which the experimental protocol was performed was recorded for each female participant.

Mechanical Recording.

Subjects were seated upright in an adjustable chair with the nondominant arm abducted approximately 80° at the shoulder and the elbow resting on a padded support. The elbow joint was flexed so that the forearm was horizontal to the ground. The hand was placed slightly above heart level with the wrist resting on a padded support, and the hand gripped a custom-designed and adjustable handgrip dynamometer. The handgrip dynamometer recorded the forces exerted by the finger flexors and was mounted on a rigid restraint so that the subject's hand and forearm were midway between pronation and supination. The forces detected by the transducer (SBO-200; Transducer Techniques, Temecula, California) were recorded on-line using a Power 1401 A-D converter [Cambridge Electronic Design (CED), Cambridge, UK] and Spike2 software (CED). They were displayed on a monitor located 1.6 m in front of the subject. The force signal was digitized at 1000 samples/s.

Electrical Recordings.

Surface EMG was recorded to ensure that each subject performed no forearm contraction during measurement of blood flow and to give a global measure of muscle activation of the finger flexor muscles during the intermittent fatiguing contraction. The EMG signal was recorded with bipolar surface electrodes (Ag–AgCl, 8-mm diameter, 16 mm between electrodes) placed over the belly of the finger flexor muscles (anterior forearm) about one third of the distance of the forearm distal to the antecubital fossa. The electrodes were placed proximal to the plethysmographic strain gauge, which was used to measure hyperemia. A reference electrode was placed on a bony prominence at the elbow. Care was taken to standardize electrode locations between subjects. The electromyographic (EMG) signal was amplified (1000×) and band-pass filtered (13–1000 Hz) with a

bioamplifier (Coulbourn Instruments, Allentown, Pennsylvania) prior to being recorded directly to computer using the A-D converter. The EMG signal was digitized at 2000 samples/s.

Cardiovascular Measurements.

Blood pressure was monitored during measurement of resting and peak forearm blood flow, throughout the fatiguing contraction, and during postcontraction hyperemia with an automated beat-to-beat blood pressure monitor (Finapres 2300; Ohmeda, Madison, Wisconsin). The blood pressure cuff was placed around the middle phalanx of the middle finger of the relaxed, dominant hand with the arm placed on a table adjacent to the subject at heart level. Manual blood pressure was taken at the brachial artery to confirm the readings with the Finapres when the hand was placed at heart level. The blood pressure signal was recorded on-line to the computer at 500 samples/s.

Forearm Blood Flow.

The subject was seated in the same position as for the mechanical recordings for all blood flow measurements. Each subject was seated as described for measurements of force, and the arm was slightly above heart level.

Resting Measurements.

Forearm blood flow was measured noninvasively using venous occlusion plethysmography.^{19, 28} A double-stranded mercury-in-silastic strain gauge was positioned around the largest circumference of the forearm and connected to an electrically calibrated and self-balancing plethysmograph (EC-6; D.E. Hokanson, Inc., Bellevue, Washington). Data from the plethysmograph were sampled at 200 HZ (1401 Plus; CED) and recorded directly to the computer. A venous occlusion cuff was positioned proximal to the elbow joint and connected to a rapid and adjustable cuff inflator air source (E-20 Rapid Cuff Inflator and AG-101 Air Source; D.E. Hokanson, Inc., Bellevue, Washington). A wrist cuff was manually inflated to 300 mm Hg at 1 min prior to the resting blood flow measurements to prevent blood flow to the hand. The wrist cuff remained inflated throughout the measurement of each blood flow and deflated at the end of the measurement. Resting forearm blood flow was measured repeatedly over 3 min by inflating the venous occlusion cuff to 50 mm Hg for 8 s and deflating for 7 s. Thus, 12 resting blood flow measurements were obtained. Blood pressure was monitored continuously, and the venous occlusion cuff pressure was maintained at lower than diastolic blood pressure. A cuff pressure of 50 mm Hg was chosen, because it resulted in the most linear slope.²⁸

Passive Arterial Occlusion.

Passive arterial occlusion of the forearm was used to determine peak blood flow and vascular conductance.²⁸ Occlusion was administered by inflating the occlusion cuff to suprasystolic pressures (200 mm Hg) for 10 min. At 9 min of occlusion, the wrist cuff was inflated to 300 mm Hg. At 10 min, the occlusion cuff was deflated and rapidly inflated to 50 mm Hg for 8 s followed by deflating for 7 s. Forearm blood flow was then measured every 15 s for 3 min with the first measurement being obtained within 10 s of cuff deflation. The wrist cuff remained inflated throughout the measurement of each blood flow and was deflated at the end of the 3 min of blood flow measurements.

Experimental Protocol.

Each subject visited the laboratory for an introductory session to become familiar with the equipment and to practice performance of maximal voluntary contractions (MVCs). They returned for one additional experimental session on another day. The protocol for the experimental session involved: (1) measurement of resting blood flow; (2) measurement of peak blood flow after 10 min of occlusion with an inflatable cuff around the upper arm; (3) assessment of the MVC force for the handgrip muscles after full recovery from the occlusion; (4) performance of submaximal isometric tasks for determination of the hyperemic response and EMG–force relations for 6-s contractions sustained at 20%, 40%, 50%, 60%, and 80% of MVC force; (5) performance of an

intermittent fatiguing contraction (6-s contraction, 4-s rest) at 50% of MVC until task failure, with post-contraction hyperemia measured every minute and immediately following the fatiguing contraction; and (6) an MVC performed with the handgrip muscles within 20 s of completing the fatiguing contraction.

MVC Force.

Each subject performed three MVC trials with the handgrip muscles. The MVC task consisted of an increase in force from zero to maximum of over 1–2 s, and the maximal force was held for 2–3 s. The force exerted by the hand was displayed on a monitor, and each subject was verbally encouraged to achieve maximal force. There was a 60-s rest between trials. If the peak forces from two of the three trials were not within 5% of each other, additional trials were performed until this was accomplished. The greatest force achieved by the subject was taken as the MVC force and used as the reference to calculate the target level for the brief submaximal contractions at 20%, 40%, 50%, 60%, and 80% MVC force and the 50% MVC intermittent contraction.

Brief Submaximal Contractions.

Each subject performed a sustained constant-force contraction with the handgrip muscles for ~6 s at target values of 20%, 40%, 50%, 60%, and 80% of MVC force. At 4 s, a cuff placed at the wrist of the arm performing the contraction was inflated to 300 mm Hg to occlude blood flow to the hand.²⁸ The subject was then asked to relax, and the upper arm cuff was inflated to 50 mm Hg to determine the reactive hyperemic response to the brief contraction. The cuff was inflated within 2 s after completion of the contraction. The contractions were performed in a randomized order, and the subject was given a 60-s rest between each contraction. These submaximal contractions were performed to:

1. Determine the post-contraction hyperemia and vascular conductance in the men and women in the nonfatigued state at various relative intensities of contraction.
2. Record the EMG activity of the finger flexor muscles so that the EMG–force relation could be compared between the men and women in the nonfatigued state. The EMG signal was also examined to ensure that the subject was relaxed during the measurement of blood flow. These relations for the men and women were also examined to ensure that changes in EMG, postcontraction hyperemia, and vascular conductance during the fatiguing contraction and at task failure represented physiological adjustments rather than differences in recording conditions between groups.

Fatiguing Contractions.

An intermittent fatiguing contraction of the finger flexor muscles was performed at a target value of 50% MVC force until failure. The subject was required to match the target force as displayed on the monitor and was verbally encouraged to sustain the force during the intermittent contractions. The subject was cued by the investigator to perform repeated 6-s isometric contractions at 50% MVC force followed by 4-s rest (Fig. 1). An MVC was performed once every minute during the 6-s contraction period with an increase in force from zero to maximum for the first 1–2 s, and the maximal force was held for the remaining 4 s. MVCs were performed to determine the magnitude of muscle fatigue (reduction in MVC force) during the intermittent task.² The fatiguing task was terminated when the force declined by 10% of the 50% target value for greater than ~5 s despite strong verbal encouragement. Neither the subject nor the investigator who terminated the task knew the time during the task.

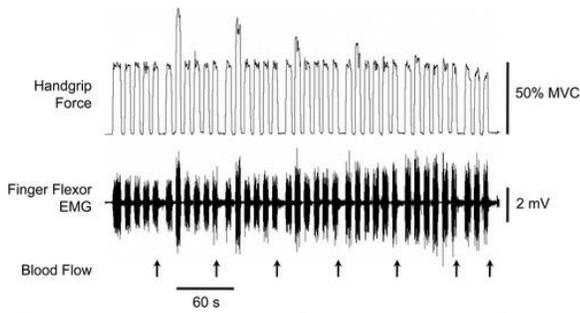


Figure 1 Representative fatiguing protocol. Handgrip force (top panel) and the interference EMG of finger flexor muscles (lower panel) of a woman for the fatiguing intermittent contraction. Maximal voluntary contraction (MVC) force was assessed every minute during the protocol, and it declined until task failure. Arrows at bottom show the time points blood flow was measured using venous occlusion plethysmography during the intermittent protocol. Note that the duration of the rest period during blood flow measurement was longer so that a meaningful measure of flow could be obtained. Blood flow was also measured at task failure.

Postcontraction hyperemia was measured every minute during the fatiguing contraction and at task failure after a 6-s contraction sustained at 50% of initial MVC force. The first measurement was made after the fifth contraction, which was ~ 50 s into the fatiguing task (Fig. 1). As for the brief submaximal contractions, a wrist cuff was inflated to 300 mm Hg during the 6-s contraction, and subjects were asked to completely relax their forearm and hand immediately after contraction. At this time, the upper arm cuff was inflated to 50 mm Hg during an extended rest period of ~ 8 s.

During the fatiguing contractions, an index of perceived effort, the rating of perceived exertion (RPE), was assessed with the modified Borg 10-point scale.³ The subjects were instructed to focus the assessment of effort on the forearm muscles performing the task. The scale was anchored so that 0 represented the resting state, and 10 corresponded to the strongest contraction that the forearm muscles could perform. The RPE was measured at 30-s intervals during the fatiguing contraction.

Data Analysis.

The blood flow data, handgrip force, mean arterial pressure (MAP), and EMG activity collected during the experiments were analyzed off-line using the Spike2 data analysis system (CED, Ltd., Cambridge, UK).

The MVC force was quantified as the peak value achieved during the MVC. Similarly, the maximal EMG was determined as the average value over a 0.5-s interval centered about the peak rectified EMG. The rectified EMG of the constant-force contractions performed at 20%, 40%, 50%, 60%, and 80% of MVC force was averaged over the first 3 s of the 6-s contraction. The EMG activity during the fatiguing contraction was quantified as averages of the rectified EMG (AEMG) during the first 6-s contraction; the 6-s contraction nearest in time to 25%, 50%, and 75% of the time to failure; and during the last 6-s contraction. The EMG was normalized to the peak EMG obtained during the MVC.

MAP was recorded from the on-line blood pressure signal during the fatiguing contraction and analyzed by comparing ~ 6 -s averages at the following time-points: during the first 6-s contraction; during 6-s contractions nearest in time to 25%, 50%, and 75% of the time to failure; and during the last 6-s contraction.

The rate of increase in EMG activity, RPE, and MAP for each subject was calculated as the difference in values between the start and end of the fatiguing contraction divided by the time to failure. Similarly, the rate of decline in MVC force for each subject was calculated as the difference between the MVC before the fatiguing contraction and the force at task failure divided by the time to failure.

Blood Flow Analysis.

Blood flow analysis was performed as previously reported.²⁸ Blood flow was analyzed (Spike2, CED) from the slope of the initial, linear portion of the plethysmographic signal. For resting measurements, this included the entire portion of the signal, whereas, for forearm blood flow following passive arterial occlusion, the 6-s submaximal contractions, and the intermittent fatiguing contraction, the initial 2–4 heart beats contained the linear portion of the signal. All blood flow data were analyzed by placing two cursors around the linear portion of plethysmographic signal, and the corresponding slope was calculated using a data analysis software program. Forearm blood flow (BF, ml min⁻¹100 ml) was derived using the following equation:

$$\text{BF} = \text{slope (V s}^{-1}\text{)} \cdot \text{calibration factor} \times [(\text{ml} \cdot 100 \text{ ml}^{-1}) \cdot 1 \text{ V}^{-1}] \cdot (60 \text{ s min}^{-1}).$$

Vascular conductance (ml min⁻¹·100 ml⁻¹·mm Hg⁻¹) was calculated as BF/MAP. For resting measurements, this included averaging the 12 blood flow measurements obtained divided by the average MAP during the 3-min collection period. Forearm vascular conductance after contraction was calculated by dividing each blood flow measurement by the average of MAP that occurred over a 10-s time period that started and ended 1 s on either side of the 8-s cuff inflation. Peak vascular conductance was the highest calculated value of the blood flow per 10-s average of MAP following cuff deflation. Peak conductance occurred within the first 45 s or the first blood flow measurements following release of the cuff after 10-min occlusion. The highest blood flow and vascular conductance measured after 10-min occlusion were used as peak blood flow and peak vascular conductance, respectively.

Statistical Analysis.

Data are reported as mean values (\pm SD) in the text and tables and displayed as means (\pm SE) in the figures. Separate analyses of variance (ANOVAs; SPSS, version 15) were used to compare the time to task failure and percent decline in MVC force after the fatiguing contraction for the men and women. Repeated-measures ANOVAs were used to compare the following dependent variables across time and between men and women: forearm blood flow and vascular conductance at 1-min intervals during the fatiguing contraction and at task failure, and MAP, RPE, and EMG activity during the fatiguing contraction. Repeated-measures ANOVAs were used to compare the following dependent variables across contraction intensities and between men and women: EMG activity and forearm blood flow, and vascular conductance after the nonfatiguing 6-s constant-force contractions. Independent *t*-tests were used to compare the sexes for the decline in MVC force across the fatiguing task and the rates of change in various dependent variables as a function of absolute time. Associations were determined between some variables using Pearson's correlation analysis. Because of the expected multivariate correlations of dependent with independent variables and among dependent variables, stepwise linear regression was used to gain insight into the predictive nature and contribution of dependent variables to the total variation of the time to task failure (SPSS, version 15). For all analyses, a significance level of $P < 0.05$ was used to identify statistical significance.

RESULTS

The young men were taller than the young women and had greater body mass (Table 1). The reported level of physical activity was variable, but it was similar for men and women (Table 1).

Table 1. Physical characteristics and handgrip strength of the men and women.*

Variable	Men (<i>n</i> = 20)	Women (<i>n</i> = 20)	<i>P</i> -value
Height (cm)	173 \pm 11	165 \pm 12	0.02
Body mass (kg)	78 \pm 10	65 \pm 10	<0.001
Physical activity (Met·hour/week)	59 \pm 65	44 \pm 32	0.29

MVC (N)	504 ± 97	354 ± 70	<0.001
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MVC, maximum voluntary contraction.

* Data expressed as mean ± SD.

MVC Force.

Maximal handgrip force for men was greater than for women (70% of men) when performed prior to the intermittent fatiguing contraction (Table 1). Thus, men exerted greater absolute force than women when the brief contractions were performed at 20%, 40%, 60%, and 80% of MVC force and during the intermittent fatiguing contraction performed at 50% of MVC force. The MVC performed ~10 s after completion of the fatiguing contraction was similarly reduced ($P < 0.001$) for men and women ($39 \pm 10\%$ vs. $42 \pm 7\%$, respectively, $P = 0.39$). The rate of decline in MVC force, however, was greater for men than women (41.4 ± 15.3 N/min vs. 26.3 ± 13.7 N/min, respectively, $P = 0.002$).

Time to Task Failure.

The time to task failure was longer for women (408 ± 205 s) compared with men (297 ± 57 s, $P = 0.02$). There was no relation between absolute force exerted during the contractions and the time to failure for the intermittent fatiguing contraction ($r = -0.27$, $P = 0.10$).

Blood Flow and Vascular Conductance.

Resting.

Men and women had similar resting values of MAP (85 ± 10 mm Hg vs. 85 ± 7 mm Hg, respectively, $P = 0.96$), forearm blood flow, and vascular conductance (Table 2).

Table 2. Resting and peak forearm blood flow and vascular conductance for the men and women.*

Variable	Men	Women	P-value
Resting blood flow ($\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ ml}^{-1}$)	2.6 ± 0.9	2.9 ± 1.5	0.45
Resting vascular conductance ($\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ ml}^{-1} \cdot \text{mm Hg}^{-1}$)	0.032 ± 0.011	0.035 ± 0.019	0.48
Peak blood flow ($\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ ml}^{-1}$)	45.0 ± 10.3	40.3 ± 5.9	0.10
Peak vascular conductance ($\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ ml}^{-1} \cdot \text{mm Hg}^{-1}$)	0.52 ± 0.14	0.46 ± 0.08	0.12

* Data presented as mean ± SD.

Peak.

Peak blood flow and vascular conductance were determined in response to 10 min of passive occlusion. Peak blood flow and peak vascular conductance of the forearm were also similar for men and women (Table 2).

After 6-s Submaximal Contractions.

Postcontraction hyperemia and vascular conductance were assessed in response to 6-s contractions performed at 20%, 40%, 50%, 60%, and 80% of MVC force. There was a main effect of sex, because women had less blood flow compared with men after the brief isometric contractions at each relative force level (Fig. 2A; $P = 0.01$). Blood flow was progressively greater with the increase in force for both men and women after each contraction ($P < 0.001$), and there was no interaction of sex and intensity of contraction.

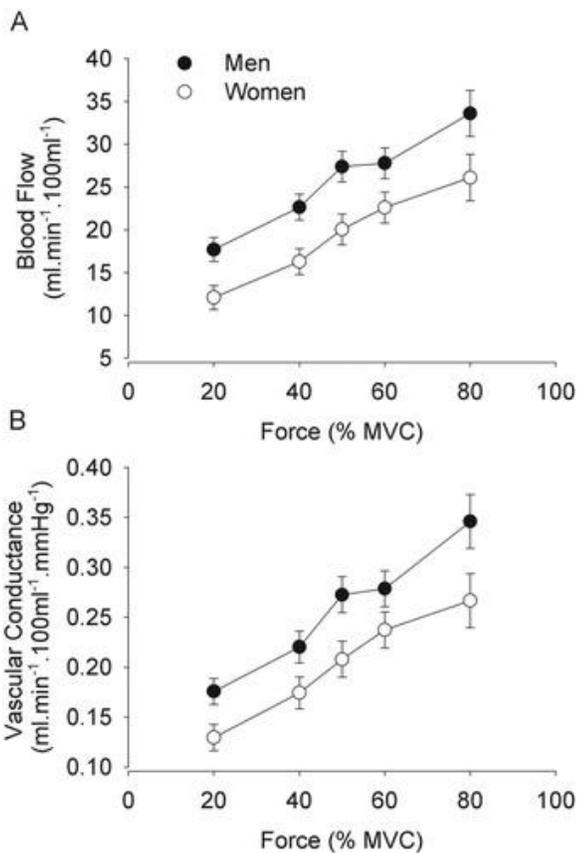


Figure 2 Forearm blood flow (**A**) and vascular conductance (**B**) after submaximal contractions maintained at 20%, 40%, 50%, 60%, and 80% of MVC force for 6 s by men (filled circles) and women (open circles). Data show mean (\pm SEM) values. The men had greater postcontraction hyperemia and vascular conductance after compared with women ($P < 0.05$).

Similarly, women had less vascular conductance after the submaximal contractions compared with men for each contraction force (main effect of sex, $P = 0.03$) (Fig. 2B). Similar to that for blood flow, forearm vascular conductance was progressively greater with the increase in force for both men and women ($P < 0.001$), and there was no interaction of sex and intensity of contraction.

Fatiguing Contraction.

Men and women had similar blood flow and vascular conductance at task failure ($P = 0.86$). The blood flow after the task-failure contraction for men was $40.2 \pm 10.8 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1}$ ($92 \pm 15\%$ of peak flow), and for women it was $39.6 \pm 11.1 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1}$ ($93 \pm 34\%$ of peak flow, $P = 0.90$). Similarly, forearm conductance was similar for men ($0.361 \pm 0.093 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1} \cdot \text{mm Hg}^{-1}$, $72 \pm 16\%$ of peak conductance) and women ($0.340 \pm 0.086 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1} \cdot \text{mm Hg}^{-1}$, $73 \pm 19\%$ of peak conductance) at task failure ($P = 0.53$).

Blood flow and vascular conductance were estimated at 1-min intervals during the 50% MVC fatiguing contraction with the first measurement assessed at 50 s into the protocol. When first assessed during the fatiguing contraction (50 s), postcontraction hyperemia was similar for men ($31.4 \pm 14.7 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1}$, $71 \pm 25\%$ of peak flow) and women ($26.2 \pm 11.5 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1}$, $63 \pm 25\%$ of peak flow, $P = 0.26$). Similarly, vascular conductance did not differ after 50-s-duration fatiguing contraction for men ($0.284 \pm 0.139 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1} \cdot \text{mm Hg}^{-1}$, $56 \pm 21\%$ of peak conductance) and women ($0.258 \pm 0.108 \text{ ml}\cdot\text{min}^{-1} \cdot 100 \text{ ml}^{-1} \cdot \text{mm Hg}^{-1}$, $55 \pm 22\%$ of peak conductance, $P = 0.53$). There was no sex difference in blood flow and vascular conductance at any of the 1-min intervals thereafter (Fig. 3).

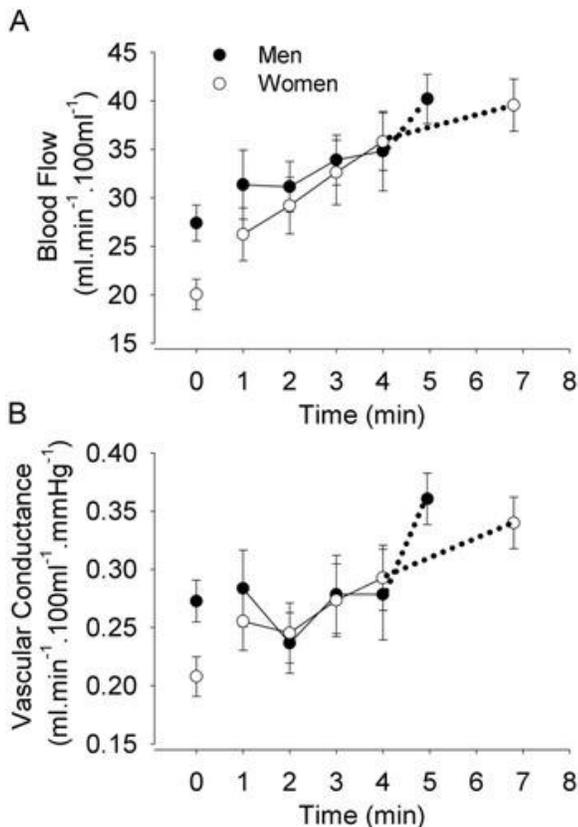


Figure 3 Forearm blood flow (**A**) and vascular conductance (**B**) measured before, during, and after failure of the 50% MVC fatiguing contraction for men (filled circles) and women (open circles). Blood flow and vascular conductance were measured at 1-min intervals with the first measurement starting at 50 s into the task (shown as the first minute in the figure). The mean values (\pm SEM) are shown after a brief contraction at 50% MVC before the fatiguing contraction (time 0), at 1-min intervals until 4 min, and at task failure. The dotted line between 4 min and task failure indicates that the time varied among subjects. There were sex differences in blood flow and vascular conductance during the 6-s nonfatiguing contraction measured before the start of the fatiguing contraction (shown at time 0), but not at any of the 1-min intervals during the fatiguing contraction, or at task failure ($P > 0.05$).

There was an association between the force exerted at 50% of MVC with postcontraction hyperemia ($r = 0.51$, $P < 0.001$) and vascular conductance ($r = 0.45$, $P < 0.01$) immediately after the brief nonfatiguing 50% MVC. These associations had disappeared after 50 s of the fatiguing contraction for postcontraction hyperemia ($r = -0.17$, $P = 0.33$) and vascular conductance ($r = 0.11$, $P = 0.52$). Furthermore, there were no associations between time to task failure and postcontraction hyperemia ($r = -0.21$, $P = 0.21$) or vascular conductance ($r = -0.22$, $P = 0.19$) immediately after the brief nonfatiguing 50% MVC. There was no association between time to task failure and postcontraction hyperemia ($r = -0.17$, $P = 0.34$) or vascular conductance ($r = -0.16$, $P = 0.36$) measured after 50 s into the fatiguing contraction. There were also no correlations between time to failure and any measure of hyperemia when men and women were considered separately.

There was no association between the day of the menstrual cycle for the women and any of the blood flow or vascular conductance measures taken at rest, after 10 min of occlusion, and postcontraction ($P > 0.05$). Furthermore, there was no association between day of menstrual cycle with the time to task failure, nor with the strength of women ($P > 0.05$).

Stepwise linear regression analysis was performed to determine the predictors of time to task failure. Significant predictors of the time to task failure did not involve any measure of cardiovascular function or blood flow. The

significant predictors of time to task failure were the rate of increase in perceived exertion (RPE) and EMG activity. The rate of increase in RPE explained 42% of the variance in time to failure ($r = 0.64$, $P < 0.001$), and together the rate of increase in RPE and EMG activity accounted for 51% of the variance ($r = 0.71$, $P < 0.05$). Other dependent variables that were entered into the model but were not significant included: rate of change in hyperemia and vascular conductance during the fatiguing contraction; post-contraction hyperemia; and vascular conductance after the brief nonfatiguing 50% MVC contraction and at task failure of the fatiguing contraction; height; weight; physical activity levels; MAP; and absolute forces exerted during the contraction.

MAP during the Fatiguing Contraction.

Mean arterial pressure increased from rest during the fatiguing contraction ($P < 0.001$; Fig. 4) for both men and women. There was a sex difference ($P = 0.01$) and an interaction of sex and time ($P = 0.04$), because men and women had similar MAPs at the start of the contraction. Men had greater increases in MAP and greater MAP at the end of the contraction compared with women.

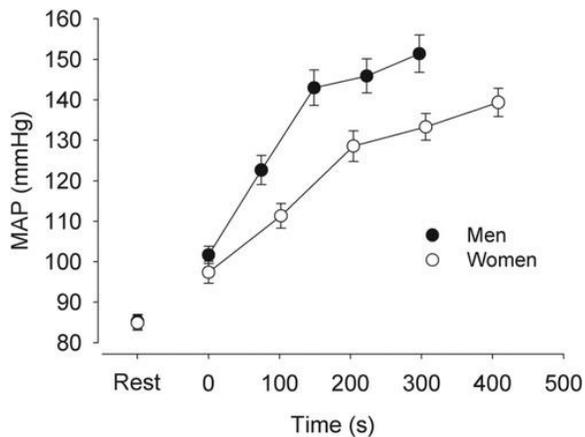


Figure 4 The mean arterial pressure (MAP) during the fatiguing contraction for men and women. Data show mean (\pm SEM) values of 4–6-s intervals during target force contractions closest to 25% increments of the time failure. The men and women had similar MAPs at rest and at the start of the fatiguing contraction, but men had higher values than the women at task failure ($P < 0.05$).

Rating of Perceived Exertion.

RPE increased during the fatiguing contraction ($P < 0.001$), but it was similar for men and women at the beginning and end of the fatiguing contraction held to task failure ($P = 0.69$; Fig. 5A). The RPE values for the men and women progressed from 3.2 ± 1.5 and 2.5 ± 1.3 , respectively, at the start of the contraction to 9.7 ± 0.6 and 9.6 ± 0.9 , respectively, at task failure. The rate of increase in RPE (normalized to absolute contraction time) did not differ significantly between the men and women (1.3 ± 0.4 vs. 1.1 ± 0.4 RPE/min, respectively, $P = 0.12$).

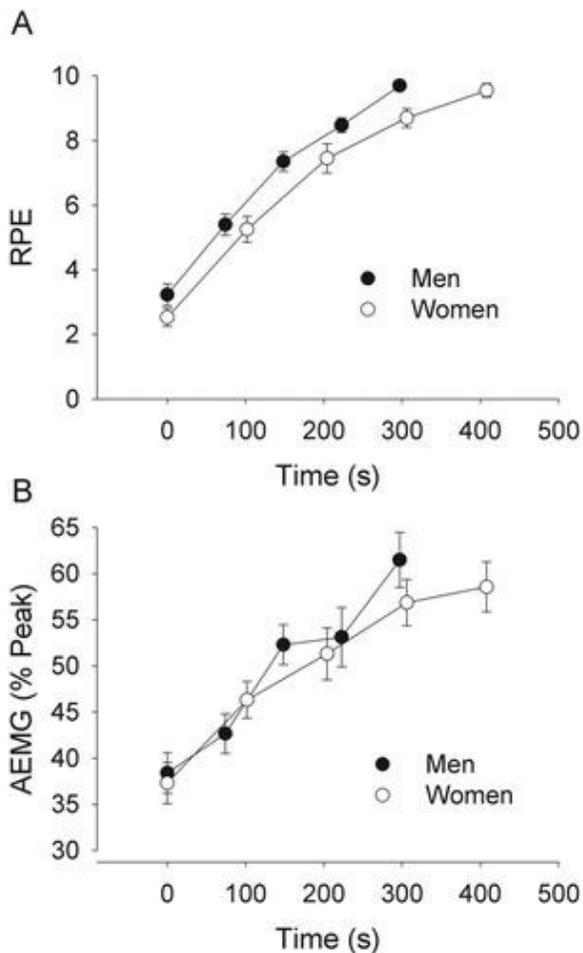


Figure 5 Rating of perceived exertion (RPE) (**A**) and EMG activity of the finger flexors muscles (**B**) during the fatiguing contraction for men and women. Data show mean (\pm SEM) values during target force contractions closest to 25% increments of the time failure. (**A**) The increase in the RPE did not differ between men and women ($P > 0.05$). (**B**) The increase in the average of the rectified EMG (AEMG, % peak during the MVC) was greater for men than for women ($P < 0.05$). The rates of increase in RPE and EMG activity were significant predictors of the time to task failure.

EMG Activity.

EMG–Force Relation.

The average rectified EMG (AEMG; % peak EMG) for the finger flexor muscles was determined during 6-s isometric contractions held at 20%, 40%, 50%, 60%, and 80% of MVC force. AEMG increased with contraction intensity ($P < 0.001$). There was no sex difference in the AEMG ($P = 0.41$) and no interaction of sex and intensity ($P = 0.82$). The AEMGs for men and women were similar for each intensity of contraction: 20% ($13 \pm 4\%$ vs. $13 \pm 3\%$, respectively); 40% ($29 \pm 9\%$ vs. $28 \pm 7\%$, respectively); 50% ($38 \pm 7\%$ vs. $36 \pm 9\%$ respectively); 60% ($51 \pm 11\%$ vs. $48 \pm 10\%$ respectively); and 80% ($70 \pm 15\%$ vs. $67 \pm 10\%$, respectively) of MVC force.

Average EMG during the Fatiguing Contraction.

The amplitude of the AEMG (% MVC EMG) for finger flexor muscles increased during the fatiguing contraction for men and women ($P < 0.001$, Figs. 1 and 5B). There was no sex difference ($P = 0.86$) and no interaction of sex and time ($P = 0.21$). The AEMG was similar at the start and end of the fatiguing contraction for both sexes: the AEMG was $38 \pm 10\%$ for the men and $37 \pm 10\%$ for the women at the start, and $61 \pm 13\%$ for the men and $59 \pm 12\%$ for the women at the end of the fatiguing contraction. Consequently, the rate of increase in EMG activity

(normalized to absolute contraction time) was greater for men ($5.0 \pm 3.6\%/min$) compared with women ($3.3 \pm 2.2\%/min$, $P = 0.04$).

DISCUSSION

To understand the role of muscle perfusion in the sex difference of time to task failure for an intermittent submaximal contraction we compared the postcontraction hyperemia and vascular conductance of men and women during an isometric fatiguing contraction performed with the handgrip muscles. The new findings were that postcontraction hyperemia and vascular conductance were greater for men compared with women after brief nonfatiguing submaximal contractions, but they were similar after 50 s of fatiguing contraction, at 1-min intervals thereafter, and at task failure. Thus, the longer time to task failure for women compared with men for the isometric intermittent task was not due to differences in postcontraction hyperemia or vascular conductance. Regression analysis indicated that postcontraction hyperemia and vascular conductance were not significant predictors of the time to task failure. Significant predictors of time to task failure included the rate of increase in RPE and EMG activity.

Sex Differences in Hyperemia and Vascular Conductance after Brief Submaximal Contractions.

Postcontraction hyperemia and vascular conductance following the brief submaximal contractions were greater for men compared with women at intensities of between 20% and 80% of MVC force. In addition, increases in contraction intensity resulted in larger postcontraction hyperemia and vascular conductance for both sexes. As we found in this study, and have previously shown, postcontraction hyperemia and vascular conductance were greater for the stronger men compared with the women after brief submaximal contractions, but they were similar when the sexes were matched for strength.¹⁸ Consistent with our findings, strong men had greater hyperemia than weak men,¹ indicating that strength rather than the sex of the subject influences postcontraction hyperemia during brief non-fatiguing contractions. Accordingly, we found associations between postcontraction hyperemia for the brief contraction at 50% MVC and the absolute target force that was exerted for the fatiguing contraction. The sex difference in flow and conductance, therefore, is in part due to a strength-associated difference in the intramuscular pressure and mechanical compression of vessels within the muscle.^{1, 23, 35} Greater strength exerted by men involved greater intramuscular pressure and greater vascular occlusion. Because perfusion of the muscle is inversely related to postcontraction hyperemia,³⁹ the vasculature of women was likely less compressed and more perfused compared with the stronger men who exerted greater absolute force during each of the brief contractions. Postcontraction hyperemia after brief submaximal contractions may also be influenced by a sex difference in vasodilation that is independent of strength and muscle mass²⁷ and mediated by long-term exposure to estrogen.^{27, 30} Our study could not distinguish between the contribution of mechanical compression and vasodilation, but it confirmed that women appear to have less postcontraction hyperemia and vascular conductance than men for brief submaximal isometric contractions.

Postcontraction Hyperemia Similar in Men and Women during an Intermittent Fatiguing Contraction.

We sought to determine whether the sex difference in postcontraction hyperemia that we observed during brief isometric contractions in this study, and in another investigation,¹⁸ persisted throughout the fatiguing contraction and contributed to the sex difference in time to task failure. Within 1 min (measured at 50 s) of performing the intermittent contractions, however, men and women had similar levels of postcontraction hyperemia and vascular conductance. These levels continued to increase each minute thereafter until task failure and did not differ between the sexes. The increase in active hyperemia is related to the increasing metabolic demands of muscle. As a fatiguing contraction increases in duration, motor units are recruited and are

reflected as an increase in EMG activity. The intramuscular pressure likely increases,^{13,34} and therefore postcontraction hyperemia increases. Vasodilation also occurs upon contraction, as metabolic byproducts of muscle fatigue accumulate in the muscle.^{7,38}

Our results suggest, therefore, that the influence of vasodilation on postcontraction hyperemia and vascular conductance were similar for men and women after about 1 min of intermittent fatiguing contraction, because we showed no sex difference in these variables. Furthermore, the sex difference in postcontraction hyperemia and vascular conductance we observed during the brief contractions were diminished with increased fatigue. This suggests that the contribution of vasodilation was greater than mechanical compression as the fatiguing task progressed. Gonzales and colleagues¹⁰ also found no sex difference in forearm blood flow during a fatiguing dynamic handgrip task when men and women performed contractions at similar workloads.¹⁰ For a sustained isometric contraction at a low force, however, women showed greater vasodilation, even when they were matched for strength during the fatiguing contraction.¹⁸ Nevertheless, the sex difference in the time to task failure was not explained by postcontraction hyperemia in our earlier study¹⁸ nor the present study. Wigmore and colleagues also found that the magnitude of fatigue experienced by men during an intermittent protocol of the dorsiflexor muscles was not explained by a limitation in blood flow to the muscle.⁴⁰

Accordingly, our regression analysis indicated that postcontraction hyperemia and vascular conductance recorded before or throughout the intermittent protocol were not significant predictors of time to task failure in men and women. Thus, sex differences in metabolism during isometric tasks,^{20,33} and the metabolic byproducts that potentially cause vasodilation,⁷ did not result in measurable sex differences in perfusion during the intermittent fatiguing contraction at 50% of MVC force. One possible explanation is that venous occlusion plethysmography was not sufficiently sensitive to detect a sex difference in blood flow during the fatiguing contraction despite a detectable sex difference for brief contractions before the fatiguing task. A limitation of venous occlusion plethysmography is that blood flow is assessed after the contraction (hyperemic response) rather than during the contraction. There is good association between the hyperemic response and the contraction duration,¹³ but other measures that directly quantify blood flow during the contraction, such as ultrasonography, are required to confirm our findings for an intermittent task.

The sex difference in time to task failure was not related to any other measure of hyperemia or vascular conductance taken throughout the protocol. Postcontraction hyperemia and vascular conductance were similar at task failure, as shown previously by our group¹⁸ and recently by Thompson and colleagues.³⁶ The resting and peak levels of flow and conductance were also similar for men and women as we have also shown before.¹⁸ Thus, hyperemia and vascular conductance assessed using venous occlusion plethysmography did not influence the sex difference in time to task failure for the intermittent fatiguing contraction.

What Explains the Sex Difference in Time to Task Failure for a Submaximal Intermittent Contraction?

This study has confirmed that the following factors do not explain the sex difference in time to task failure for an intermittent contraction: (1) contraction hemodynamics despite differences during brief nonfatiguing contractions; and (2) strength of the subject.^{9,16} Regression analysis, however, showed that the significant predictors of time to task failure for the intermittent task included the rate of increase in perceived exertion and the rate of increase in EMG activity. The increase in motor unit recruitment significantly contributes to increased EMG activity during a fatiguing contraction in men and women,^{4,26} as the already active muscle fibers fatigue and are not able to generate the required force. Both RPE and EMG activity are influenced by feedforward descending drive and peripheral feedback mechanisms.^{5,8,12}

We also found that mean arterial pressure increased at a lower rate for women compared with men during the contraction, and it was less at task failure for women. The increase in mean arterial pressure during contraction (pressor response) is due to central command and peripheral feedback from the muscle (mechanoreflex and metaboreflex via group III and IV afferents).³¹ Because men fatigued more quickly than women, the women likely had less afferent feedback via the metaboreflex from the handgrip muscles or reduced feedforward input to the cardiovascular centers in the ventral medulla.³¹ There is a lack of evidence, however, of sex differences in feedforward mechanisms that influence voluntary activation and a sex difference in muscle fatigue for flexor muscles.¹⁷ A sex difference in glycolytic metabolism,³³ fiber-type composition,^{25, 29, 37} and the change in twitch relaxation rate and twitch amplitude during a fatiguing contraction¹⁷ suggest that a sex difference in muscular mechanisms may have contributed to the sex difference in the time to task failure. Any sex difference in muscular mechanisms for the time to task failure, however, did not influence a measurable difference between men and women in postcontraction hyperemia or vascular conductance assessed using venous occlusion plethysmography.

In conclusion, the time to task failure for a moderate-force intermittent fatiguing contraction with the handgrip muscles was longer for women than for men. Although men had greater postcontraction hyperemia and vascular conductance than women during brief nonfatiguing contractions, this sex difference disappeared within 1 minute of the intermittent fatiguing contraction and did not explain the longer time to failure of the women compared with the men. Time to failure was explained by rates of perceived effort and EMG activity and was also associated with mean arterial pressure, which increased at a lower rate for women than for men during the fatiguing contraction. Therefore, the longer time to failure for women compared with men for an intermittent fatiguing contraction with handgrip muscles was not due to a sex difference in postcontraction hyperemia or vascular conductance.

Acknowledgements

This study was funded by a Marquette University, College of Health Sciences faculty development award to S.K.H.

Abbreviations

AEMG, average of the rectified electromyography; ANOVA, analysis of variance; BF, blood flow; DBP, diastolic blood pressure; EMG, electromyography; MAP, mean arterial pressure; MVC, maximal voluntary contraction; RPE, rating of perceived exertion; SBP, systolic blood pressure

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