Muscle Strength Influences Pressor Responses to Static Handgrip in Men and Women

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Abstract

NOTAY, K., J. B. LEE, A. V. INCIGNITO, J. D. SEED, A. A. ARTHURS, and P. J. MILLAR. Muscle Strength Influences Pressor Responses to Static Handgrip in Men and Women. Med. Sci. Sports Exerc., Vol. 50, No. 4, pp. 778–784, 2018. Purpose: Whether differences in absolute muscle strength affect blood pressure (BP) responses to relative intensity static exercise remains controversial but could contribute to known sex-based differences and influence the interpretation of cross-sectional data. Methods: One hundred thirty-two healthy participants (66 men and 66 women; age, 22 ± 3 yr) underwent continuous seated measurements of BP (Finometer) and heart rate (electrocardiography) during baseline rest and 2 min of static handgrip (30% maximal voluntary contraction (MVC)). BP and heart rate responses were quantified in 30-s epochs during exercise and compared between men and women with and without statistical adjustment (ANCOVA) for differences in baseline BP (or heart rate), forearm girth, and handgrip MVC. Within each sex, BP and heart rate responses were compared also between tertiles of handgrip MVC (n = 22 per group). Results: Men had larger systolic, diastolic, and mean arterial pressure responses during static handgrip than did women (interaction term, all P < 0.0005), although heart rate responses were similar (interaction term, P = 0.25). These sex-based BP differences persisted after statistical adjustment for differences in baseline BP or forearm girth; however, controlling for handgrip MVC abolished differences in BP responses during static handgrip exercise between men and women (interaction term, all P > 0.35). In men, BP responses were smaller within the lowest tertile of handgrip MVC (interaction term, all P < 0.006), whereas in women, BP responses were larger within the highest tertile of handgrip MVC (interaction term, all P < 0.04). Conclusions: Our findings suggest an important between- and within-sex role of absolute handgrip strength in mediating the BP response to static handgrip exercise and highlight the importance of controlling for interindividual differences in future work. Key Words: HEMODYNAMIC, SEX DIFFERENCES, MAXIMAL VOLUNTARY CONTRACTION, MUSCLE MASS, EXERCISE

Exercise is considered a valuable, noninvasive perturbation to uncover physiologically relevant differences in cardiovascular or autonomic function between groups that are not apparent at rest (1,2). One of the most studied exercise modes involves submaximal static handgrip contractions (i.e., 20%–50% of maximal volitional contraction (MVC)) completed for a set duration (e.g., 1–3 min) (3–10) or until failure (11–19). Static exercise produces reproducible increases in heart rate and blood pressure (BP) through cardiac parasympathetic withdrawal and sympathetic activation (20,21), although large interindividual variability in pressor responses exists (9).

The magnitude of cardiovascular responses to static exercise are thought to be governed primarily by both the relative intensity and the duration of the contraction, independent of the amount of contracting muscle mass or absolute tension generated (22). However, the latter assertions remain controversial as numerous small-scale studies have reported differences in BP responses during similar relative intensity static handgrip and leg exercise (i.e., differences in muscle mass) (23–25) or within participants when comparing the dominant to the nondominant leg with different absolute strength (24). Sex-based differences in absolute muscle strength (26) also parallel observations that men demonstrate larger BP responses to fixed-duration (e.g., 2–3 min) 30% MVC static handgrip contractions compared with women (3–7). Unfortunately, prior studies examining sex comparisons did not address specifically whether controlling for baseline differences in muscle mass or strength ameliorated differences between men and women in hemodynamic responses during static handgrip exercise. In addition, men and women routinely present with different resting BP values (15), which may affect responses due to regression to the mean (27).
Supporting an important contribution of muscle strength in determining hemodynamic responses to static handgrip exercise, interindividual differences in relative force are negatively correlated with static handgrip time to failure (12–14). As a result, even when completing a static contraction at the same relative intensity, those with higher target forces will fatigue earlier causing intensity differences between participants during prolonged contractions. In prior work, normalizing for static handgrip time to failure has abolished sex-based differences in BP responses during 20%–40% MVC static handgrip exercise in some (12,14,16,18,19) but not all (11,13,15,17) studies. A major limitation of assessing static handgrip time to failure is that it can be influenced by perception of effort through somatosensory, neurocognitive (e.g., learned experience), psychological, and hedonistic (e.g., forearm discomfort/pain) inputs (28–30). Early termination of a contraction prior to true physiological failure (due to disinterest or discomfort) would confound normalization of BP and heart rate responses.

Therefore, the purpose of the study was to investigate, in a large cohort of 132 healthy young men and women, potential sex differences in hemodynamic responses to 30% MVC static handgrip exercise, with and without adjustment for differences in resting baseline BP, forearm girth, and handgrip strength. To further probe the confounding role of handgrip strength, we compared, within each sex, the hemodynamic responses to static handgrip exercise within tertiles of handgrip MVC. We hypothesize that 1) men will have larger BP responses to static handgrip than women but that these differences will be abolished after adjustment of baseline covariates, and 2) within each sex, differences in BP responses will be detected across tertiles of muscle strength.

**METHODS**

**Participants.** One hundred thirty-two young healthy recreationally active men (n = 66) and women (n = 66) were studied between January and August 2017 after providing informed written consent. All of the women self-reported that they possessed a regular 28-d menstruation cycle and 5). If women reported taking oral contraception (e.g., forearm discomfort/pain) inputs (28–30). Early termination of a contraction prior to true physiological failure (due to disinterest or discomfort) would confound normalization of BP and heart rate responses.

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**Participants.** One hundred thirty-two young healthy recreationally active men (n = 66) and women (n = 66) were studied between January and August 2017 after providing informed written consent. All of the women self-reported that they possessed a regular 28-d menstruation cycle and were studied during the early follicular phase (between days 1 and 5). If women reported taking oral contraception (n = 29), they were studied similarly during the first 5 d of their placebo pills to align with the early follicular phase. All participants were free of known cardiovascular or metabolic disease and did not consume any chronic medications other than oral contraception. The University of Guelph Research Ethics Board approved all procedures.

**Experimental protocol.** Before the testing visit, participants were asked to refrain from caffeine, alcohol, and vigorous exercise for a minimum of 24 h. Participants were studied for a single visit in a light- and temperature-controlled laboratory. After voiding and collection of anthropometric measurements, participants were positioned upright on a comfortable chair with their feet up on an ottoman for the measurements, participants were positioned upright on a laboratory. After voiding and collection of anthropometric characteristics between men and women were assessed using mathematical transformation to achieve normality. Baseline cardiovascular and metabolic variables during static handgrip exercise both between sexes, and within male and female tertiles separately. Similar two-way ANOVAs were used to compare directly heart rate and BP responses between men and women matched for handgrip MVC. Significant main effects and interactions were probed using Bonferroni post hoc tests. To control for sex differences in baseline BP (or heart rate), forearm girth, and/or handgrip MVC on heart rate and BP responses to static handgrip exercise, data were analyzed using an ANCOVA. We completed three ANCOVA models to test the effects of each covariate independently. Model 1 was used to covariate baseline BP (or heart rate); model 2, to covariate forearm girth; and model 3, to covariate handgrip MVC. Significance...
RESULTS

Baseline participant characteristics comparing men and women are found in Table 1. Participants were matched for age, body mass index, diastolic BP, and mean arterial pressure (all P > 0.05), although height, body weight, handgrip MVC, and forearm girth were all larger in men (all P < 0.0001). Compared with women, men also had higher resting systolic BP (P = 0.0009) and lower resting heart rate (P < 0.0001).

Effect of sex. Heart rate and BP increased during static handgrip exercise (time effect, all P < 0.0001). Systolic BP responses were different between men and women at 60 s (P = 0.003), 90 s (P < 0.0001), and 120 s (P < 0.0001); diastolic BP responses were different at 90 s (P = 0.0005) and 120 s (P = 0.0001); and mean arterial pressure responses were different at 60 s (P = 0.04), 90 s (P = 0.0001), and 120 s (P < 0.0001). Heart rate responses were not different between men and women (interaction term, P = 0.25; Fig. 1).

Table 2 displays P values for the main effect of sex and the interaction term after adjusting for baseline differences in baseline BP (or heart rate), forearm girth, or handgrip MVC. Statistical adjustment for baseline BP and forearm girth had no effect on the observed differences in BP responses between men and women. In contrast, adjustment for handgrip MVC abolished all sex-based differences in BP responses. To confirm this observation, we matched the 12 weakest men and 12 strongest women (MVC: 37 ± 3 kg vs 36 ± 2 kg, P = 0.54) and found no significant main effects of sex (all P > 0.16) or sex–time interactions (all P > 0.35) for heart rate and BP responses to static handgrip exercise.

Across the entire cohort, handgrip MVC was positively associated with systolic BP (r = 0.42; P < 0.0001), diastolic BP (r = 0.37; P < 0.0001), mean arterial pressure (r = 0.40; P < 0.0001), and to a lesser extent heart rate (r = 0.22; P = 0.01).

Influence of handgrip MVC on static handgrip responses in men. In men, the mean handgrip MVC was 39 ± 4 kg (range, 32–43 kg) in the first tertile, 46 ± 2 kg (range, 43–49 kg) in the second tertile, and 58 ± 7 kg (range, 50–75 kg) in the third tertile. Systolic BP responses were larger in tertiles 2 and 3 compared with tertile 1 at 60 s (P = 0.01 and P = 0.005, respectively), 90 s (P = 0.003 and P = 0.001,
respectively), and 120 s (both \( P < 0.0001 \)). Diastolic BP responses were higher in tertile 2 compared with tertile 1 at 60 s (\( P = 0.04 \)), whereas both tertiles 2 and 3 were greater than tertile 1 at 90 s (\( P = 0.002 \) and \( P = 0.006 \), respectively) and 120 s (both \( P < 0.0001 \)). Mean arterial pressure responses were higher in tertiles 2 and 3 compared with tertile 1 at 60 s (\( P = 0.01 \) and \( P = 0.02 \), respectively), 90 s (both \( P = 0.001 \)), and 120 s (both \( P < 0.0001 \)). Heart rate responses were also greater in tertiles 2 and 3 at 90 s compared with tertile 1 (both \( P = 0.02 \)), and tertile 3 was greater than tertile 1 at 30 s (\( P = 0.02 \)), 60 s (\( P = 0.03 \)), and 120 s (\( P = 0.01 \)). There were no differences between tertiles 2 and 3 for any variable (Fig. 2).

**Influence of handgrip MVC on static handgrip responses in women.** In women, the mean handgrip MVC was 21 ± 4 kg (range, 13–25 kg) in the first tertile, 27 ± 1 kg (range, 25–29 kg) in the second tertile, and 34 ± 3 kg (range, 29–41 kg) in the third tertile. Systolic BP responses were greater in tertile 3 compared with tertile 2 at 60 s (\( P = 0.001 \)), and greater than both tertiles 1 and 2 at 90 s (\( P = 0.03 \) and \( P < 0.0001 \), respectively) and 120 s (\( P = 0.001 \) and \( P < 0.0001 \), respectively). Diastolic BP responses were higher in tertile 3 compared with tertile 2 at 60 s (\( P = 0.02 \)) and 90 s (\( P = 0.008 \)), and greater than both tertiles 1 and 2 at 120 s (\( P = 0.02 \) and \( P = 0.01 \), respectively). Mean arterial pressure responses were higher in tertile 3 compared with tertiles 1 and 2 at 60 s (\( P = 0.048 \) and \( P = 0.005 \), respectively) and 120 s (\( P = 0.002 \) and \( P = 0.003 \), respectively). In addition, tertile 3 had a greater mean arterial pressure response compared with tertile 2 at 90 s (\( P = 0.0009 \)). Heart rate was not different between any of the tertiles. There were no differences between tertiles 1 and 2 for any variable (Fig. 3).

**DISCUSSION**

The present study sought to examine the effect of sex on BP and heart rate responses to static handgrip exercise with and without statistical adjustment for differences in baseline BP (or heart rate), forearm girth, and handgrip MVC. In support of our hypothesis, men had greater BP responses to static handgrip exercise than did women, although no differences in heart rate responses were observed. After controlling for differences in baseline BP or forearm girth, these sex-based differences in BP responses persisted. However, after adjustment for differences in handgrip MVC, the differences in BP

**TABLE 2.** \( P \) values of unadjusted and adjusted models for sex (group) and sex-time (interaction) effects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
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<td>-0.0001</td>
<td>-0.0001</td>
<td>-0.0001</td>
</tr>
<tr>
<td>Diastolic BP</td>
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<td>0.0005</td>
<td>0.002</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
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<td>-0.0001</td>
<td>0.0003</td>
<td>-0.0001</td>
</tr>
<tr>
<td>Heart rate</td>
<td>0.53</td>
<td>0.25</td>
<td>0.78</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Model 1 covariates baseline BP or heart rate; model 2 covariates forearm circumference; model 3 covariates handgrip MVC. Bold values indicate statistical significance (\( P < 0.05 \)).

FIGURE 2—Systolic BP (A), diastolic BP (B), mean arterial pressure (C), and heart rate (D) responses during 2 min of 30% MVC static handgrip in men (\( n = 66 \)) divided by tertiles of handgrip MVC (\( n = 22 \) in each group). *\( P < 0.05 \); **\( P < 0.01 \); ***\( P < 0.0001 \) vs tertile 3. †\( P < 0.05 \); ††\( P < 0.01 \); †††\( P < 0.001 \); ††††\( P < 0.0001 \) vs tertile 2. Mean ± SEM.
responses between men and women were abolished. The examination of a large data set also permitted a novel examination of the effect of handgrip MVC on within-sex BP and heart rate responses. These results demonstrate that, in men, BP responses were smaller within the lowest tertile of handgrip MVC compared with the two stronger groups, whereas in women, BP responses were larger in the strongest tertile of handgrip MVC compared with the two weaker groups. Overall, these results demonstrate the importance of absolute muscle strength in determining the pressor response to static handgrip exercise and emphasize the need to control for interindividual differences.

Prior studies investigating the effect of sex on hemodynamic responses between men and women during fixed-duration static handgrip exercise failed to account for differences in baseline BP, muscle strength, or muscle mass, and in some cases restricted analysis to only mean arterial pressure or failed to account for different phases of the menstrual cycle in women (3–7). Each of these studies concluded that men demonstrate greater BP responses during static handgrip compared with women. In an effort to control for confounding effects of muscle strength, a number of studies have normalized data to account for differences in baseline BP, muscle strength, or muscle mass, and in some cases restricted analysis to only mean arterial pressure or failed to account for different phases of the menstrual cycle in women (3–7). Each of these studies concluded that men demonstrate greater BP responses during static handgrip compared with women. In an effort to control for confounding effects of muscle strength, a number of studies have normalized data to account for differences in static handgrip time to failure, which in some studies has eliminated these sex differences (12,14,16,18,19), though inconsistently as others reported that larger BP responses in men persisted (11,13,15,17). In addition, in two studies, women did not possess longer static handgrip time-to-failure responses, although they had a lower absolute handgrip MVC than did men (15,19). In one of these studies, men demonstrated a greater BP response (15), whereas the other study showed no BP differences between men and women (19). This inconsistency in results, combined with time-to-failure exercises not being comfortable and requiring great motivation to reach true fatigue (28), potentially makes handgrip to fatigue a nonideal measure for normalizing between groups.

The primary finding in the present study was that adjustment for handgrip MVC, but not baseline BP or forearm girth, abolished sex-based differences in BP responses during a 30% MVC 2-min static handgrip contraction. This finding emphasizes the importance of absolute strength on BP responses when performing a relative intensity fixed-duration static handgrip contraction between men and women. Moreover, a second novel finding was that within both sexes, BP responses differed on the basis of tertile groupings of handgrip MVC. This finding further supports the notion that absolute strength can affect BP responses during static handgrip. Interestingly, examination of the strength-based tertiles across the entire cohort identified three distinct bands of BP responses: the first band consisting of the two weakest female tertiles, the second consisting of the strongest women and weakest men, and the third consisting of the two strongest male tertiles. The present study did not investigate the mechanism(s) responsible for the confounding effects of handgrip MVC on BP responses; however, we speculate that differences in skeletal muscle fiber-type distribution may be involved. In support of this hypothesis, a higher proportion of fast-twitch brachioradialis muscle fibers was correlated positively with mean arterial pressure responses ($r = 0.89$) at the end of a 2-min 40% MVC static handgrip contraction (32). Similarly, the diastolic BP response to 2 min of electrically evoked static plantar flexion at 30% MVC was related to fast isomyosin content of

![FIGURE 3—Systolic BP (A), diastolic BP (B), mean arterial pressure (C), and heart rate (D) responses during 2 min of 30% MVC static handgrip in women ($n = 66$) divided by tertiles of handgrip MVC ($n = 22$ in each group). *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$ vs tertile 1. †$P < 0.05$; ††$P < 0.01$; †††$P < 0.001$; ††††$P < 0.0001$ vs tertile 2. Mean ± SEM.](http://www.acsm-msse.org)
the lateral gastrocnemius and soleus (33). Fast-twitch muscle fibers have been associated with higher rates of metabolite production during static exercise (32,34), which would stimulate metabolically sensitive group III/IV skeletal muscle afferents (32,35) that relay peripheral afferent feedback to increase central sympathetic outflow and ultimately BP (20,21).

The present findings have important implications for the interpretation of past and future studies, demonstrating a critical need to control for muscle strength when performing cross-sectional designs with between-group differences in handgrip MVC. Studies drawing conclusions from groups with different handgrip MVC may show attenuated hemodynamic responses or underestimate a true difference in responses between groups. For example, attenuated BP responses during a 2-min static handgrip at 30% MVC were reported in individuals with Down syndrome, although this group had lower absolute handgrip MVC (11.6 ± 1.6 kg) compared with the control group (27.4 ± 2.8 kg) without Down syndrome (10). Whether a true physiological attenuation in BP responses exists may be confounded by the difference in absolute strength between the two groups. In contrast, Sterns et al. (8) reported no differences in BP responses during 2 min of static handgrip at 30% MVC between patients with heart failure and a healthy control group. The heart failure group again had weaker absolute handgrip MVC (38 ± 3 kg) compared with the healthy controls (45 ± 2 kg). This difference in absolute strength may ultimately underestimate the true difference in BP responses between these two groups. Therefore, on the basis of the findings from the present study, controlling for differences in absolute handgrip MVC is essential when comparing between participants.

We acknowledge several limitations in the present study. We studied only young healthy men and women, which may limit the generalizability to older or diseased cohorts. Similarly, whether BP responses to larger muscle mass exercise exhibit the same patterns as small muscle mass handgrip exercise warrants further work. The specific duration and intensity may also affect the observed findings. We selected the 2-min, 30% MVC static handgrip contraction because it represents one of the most commonly used exercise modes in the literature (3,4,6,8,10); however, whether similar findings are present with alternative protocols is unclear. Future studies are required to test BP responses to a variety of relative and absolute intensities to confirm these results. We also acknowledge that circumferential measurements of forearm girth provide an indirect estimate of muscle mass (36). Finally, using handgrip MVC to determine each individual’s relative exercise intensity may not be the best indicator of underlying metabolic activity (37), and future studies should consider the use of forearm critical force. Nevertheless, the present results demonstrate that the use of already collected MVC data may suffice in controlling for interindividual differences in handgrip strength.

In conclusion, our results demonstrate that the larger BP responses to static handgrip exercise observed consistently in men compared with women are abolished after adjustment for handgrip MVC but not baseline BP or forearm girth. Furthermore, we show that differences in handgrip MVC also are associated with variability in BP responses within both men and women separately. These findings underscore the importance of controlling for interindividual differences in absolute muscle strength when examining cardiovascular responses to exercise.

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