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High cardiovascular reactivity and muscle strength attenuate hypotensive effects of isometric handgrip training in young women: A randomized controlled trial

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ABSTRACT

Objective: Isometric resistance training may reduce resting blood pressure (BP); however, the magnitude of this effect varies among individual subjects and few studies attempted to predict it. This study aimed to investigate the potential hypotensive effects of isometric training and their association with cardiovascular reactivity to acute isometric exercise and muscle strength in young women.

Methods: In this randomized trial, twenty young women were randomly assigned to either the training (n = 10) or control (n = 10) group. Women from the training group performed unilateral isometric handgrip sessions for 8 weeks (4 × 2 min at 25% of maximal voluntary contraction [MVC]; 3 days/week). Cardiovascular reactivity to acute isometric exercise and MVC were measured at baseline. Resting BP was assessed during and after the intervention.

Results: Resting systolic BP significantly lowered only in the training group. The change in resting systolic BP following an 8-week intervention was significantly associated with the systolic BP and diastolic BP reactivity to the acute exercise at baseline during set 3 and 4 (P < .05). The handgrip MVC was associated with changes in systolic BP (r = 0.79, P = .007), diastolic BP (r = 0.68, P = .032), and mean arterial pressure (r = 0.79, P = .006). These results indicated that high cardiovascular reactivity and strength attenuate the hypotensive effects following isometric training in young women.

Conclusions: The hypotensive effects following isometric training may be identified by BP reactivity to acute isometric exercise or handgrip strength in young women.

Introduction

Hypertension is one of the most important risk factors for cardiovascular disease (1). Exercise training has been recommended as a non-pharmacological intervention to reduce resting blood pressure (BP) (2). Recently, some studies showed that isometric exercise training (IET) produces significant hypotensive effects in normotensive subjects and hypertensive patients (3). The American Heart Association also suggests that IET may be used as an effective alternative to BP-lowering treatments (Class IIb, Level of Evidence C) (4). However, the mechanism of BP reduction induced by IET remains elusive, and further investigations are required to establish the efficacy and safety of IET as antihypertensive therapy (4). Therefore, more data about the hypotensive effects of IET are required to validate IET for exercise prescription.

Previous studies showed that IET decreases resting BP (5–8); conversely, few studies have demonstrated interindividual variability or the lack of IET effect on BP (9,10). Three studies that aimed to predict resting BP reduction induced by IET showed that the assessment of cardiovascular reactivity to acute isometric exercise or serial subtraction would be useful (11–13). Temporary elevation of BP from resting value during acute isometric exercise or serial subtraction was found to be associated with the reduction of resting BP in middle-older aged adults (11,12). In young subjects, two studies investigated the relationship between the BP reactivity to acute isometric exercise and lowering effects of the IET on resting BP (13,14). One of these studies showed a significant relationship among them (13), whereas the other study found no association (14). It remains unclear whether hypotensive effects due to IET could be predicted before intervention in young adults. Identification of hypotensive effects due to IET in young adults fits with the concept of primary intervention for the prevention of hypertension, according to the global emphasis of the World Health Organization (15). Especially, BP control is crucial in women. For instance, elevated BP is associated with a stronger risk factor of left ventricular hypertrophy in women than in men (16). Moreover, premenopausal systolic BP was an independent predictor of future vascular calcification (17). While IET has the potential for reducing BP in young women, there was limited investigation (3). Consequently, we investigated the potential of lowering the BP by IET and predictive factors in young women.

The BP reactivity to one set of isometric handgrip exercise in young women exhibits low and small interindividual variability compared with that in young men (13). On the other hand, repeated exercise augments BP reactivity than one set of
isometric exercise (18). Therefore, we examined the relationship between the BP reactivity to acute isometric exercise using repeated exercise and hypotensive effects by the IET in young women. We also focused on muscular strength as a predictive factor for lowering the BP by IET before the intervention, because muscular strength affects the BP reactivity to acute isometric exercise (19) and can be easily measured. Thus, the purpose of the present study was to identify whether 1) IET reduces resting BP, and 2) cardiovascular response to acute isometric exercise or muscle strength is associated with the hypotensive effects following IET in young women.

Materials and methods

Study design and subjects

This study was a two-armed, parallel-group, randomized controlled trial (RCT) conducted at the Japan Women’s University. We adopted an RCT design to evaluate the effect of the 8-week isometric handgrip training on resting BP against a control group with 5 measurement periods (baseline, 2 weeks, 4 weeks, 6 weeks, and 8 weeks). The study recruited women who were aged 18–22 years with a BMI of <25 kg/m² through social media. Exclusion criteria were the use of medication potentially influencing blood pressure and nonroutine events scheduled during the intervention period. Participants were randomized (1:1 allocation ratio) to the control group or training group by permuted blocks randomization (sizes of two to six). Participants undertook a complete preliminary session where they were familiarized with the measurement of resting BP, handgrip MVC, and anthropometric parameters.

During the second visit between day 2 and day 7 after the first visit, resting BP was measured and the training group performed the first isometric handgrip (IHG) training with cardiovascular reactivity measured. After the second visit, the training group continued IHG training 3 times/week for 8 weeks. The control group maintained their normal routine.

All participants were required to attend the laboratory every 2 weeks for measurement of the resting BP. Handgrip MVC was also monitored every 2 weeks in the training group. After 8 weeks, resting BP and anthropometric measurements were conducted between day 2 and day 7 after the last training session.

Twenty Japanese young women between 18 and 22 years of age participated in this study. Most of the subjects played recreational sports (i.e., swimming, running, baseball) approximately two times per week. None of the subjects smoked or received any medication. Subjects were randomly assigned to either the control (n = 10) or the training (n = 10) group. Based on the assumption of a similar response of systolic BP compared to that of the previous study of isometric training (20), sample size was calculated to detect the difference in systolic BP between the two groups (control and training groups) over time (five measurements at baseline, 2, 4, 6, and 8 week) with baseline systolic BP as covariate (repeated measures analysis of covariance). The sample size was determined with G*Power 3.1 (input parameters: $f = 0.4$, $\alpha = 0.05$, power = 0.8, numerator df = 4, groups = 10, covariates = 1), which found that 8 participants per group were required to detect the differences. The institutional ethics committee approved the study protocol, and the study was conducted according to the ethical standards of the Helsinki Declaration. All subjects provided written informed consent prior to participation.

Isometric handgrip training

Participants from the training group performed IHG exercise using a handgrip dynamometer (S-14145, Takei Scientific Instrument, Japan). Participants completed 4 sets of handgrip exercise, using their left (non-dominant) hand, at 25% MVC lasting 2 min separated by a 3 min rest period. The target force was displayed on the handgrip device. Training intensity was adjusted every 2 weeks if MVC increased. All subjects maintained a training diary, recording the time of day, rating of perceived exertion (21) at the last set, training force, and implementation status. Participants were instructed to breathe normally during exercise for preventing the Valsalva maneuver.

Measurements

Anthropometric measurement

Height was measured to the nearest 0.1 cm using an analog stadiometer. Bodyweight was measured to the nearest 0.2 kg with a digital scale (TBF-310, Tanita, Japan). Maximal forearm girth was assessed at the widest part of the forearm using the mean of two measurements.

Cardiovascular measurement

Systolic BP (SBP), diastolic BP (DBP), and heart rate (HR) were measured in a seated position on the brachial artery of the right upper arm using an automated brachial oscillometer (HEM-907, Omron Healthcare, Japan) that passed the international validation protocol (22). SBP, DBP, and HR measurements were obtained 3 times at a 1-min interval after sitting in the chair for 15 min, and the latter 2 data sets (measurement 2 and 3) were averaged for the analysis. If the measurements 2 and 3 showed a difference >5 mmHg, 2 additional measurements were obtained and the average of the last 4 data sets was used (23). The same investigator performed all the measurements. The mean arterial pressure (MAP) was calculated using the formula: DBP + 1/3 (SBP – DBP). Pulse pressure (PP) was calculated as an arithmetic difference between SBP and DBP. The subjects refrained from caffeine or alcohol intake 12 hours before testing and avoided any vigorous exercise in the last 24 hours, and all tests were performed a minimum of 4 hours post-prandial. All tests were conducted in a quiet, darkened, and temperature-controlled laboratory (23–25°C). All repeat tests were conducted at the same time of the day or within 2 hours of the initial baseline testing time.

Static contraction

Participants maximally squeezed a handgrip dynamometer 2 times using the left hand for 4 s a minute apart. The highest generated value was used for the MVC.
Cardiovascular response to exercise

The cardiovascular reactivity to acute IHG exercise was measured continuously using a Finapres device via an inflatable finger cuff placed on the right hand’s middle finger with the hand positioned at the heart level. Data were recorded by a data acquisition system (MP150, Biopac Systems, Inc., USA). Each data set was averaged every 30 s using a proprietary software (AcqKnowledge, Biopac Systems Inc., USA). The SBP, DBP, and HR response to the exercise were evaluated using the delta changes from the 30 s before the onset of exercise to the last 30 s of exercise in each set as used in previous studies for measurement of cardiovascular responses to isometric exercise (24,25).

Statistical analysis

All statistical analyses were performed with IBM SPSS version 25. All values are expressed as mean ± SD. Differences in the resting BP and HR changes between the training and control group were analyzed at baseline (before training) and over the course of 8 weeks using a 2-way repeated-measures ANOVA (group × time) with Bonferroni’s post hoc tests. A previous study revealed that initial SBP could affect the hypotensive degree (26); therefore, we used analysis of covariance (ANCOVA) for change in SBP with baseline BP as the covariate. Residualized change scores obtained by regressing the change in SBP following interventions on pre-intervention SBP were used for SBP (11,13). A paired t-test was used for analyzing pre- and post-training changes in forearm girth and body weight. Pearson’s r correlation coefficients were determined to assess relationships among pre- to post-training changes in resting BP and cardiovascular reactivity during isometric exercise, and MVC at baseline. The alpha level was set at 0.05 (two-sided).

Results

Thirty-two subjects were assessed for eligibility and 12 refused to participate. Twenty participants were randomized to the training group (n = 10) and control group (n = 10) and completed all measurements as presented in Figure 1. At baseline, no significant differences were observed in any measurement between the training and control groups (Table 1). All participants from the training group completed the 8-week training. There were no reported adverse events. There were no significant changes in body weight and forearm girth between pre- and post-training measurements in either group.

Resting blood pressure and heart rate

Following the 8-week intervention, no interaction of the SBP changes was observed between the training and control groups (P = .155), however, IHG training significantly reduced the SBP at 6 weeks from baseline (mean difference [MD] −3.4 mmHg, 95% confidence interval [CI] −6.58 to −0.22, P = .034); more reduction was obtained at 8 weeks, although not statistically significant (MD −4.7 mmHg, 95% CI −11.36 to 3.01, P = .279) (Figure 2). The control group indicated no changes in the resting SBP following the 8-week intervention (e.g., 6 weeks: MD −0.4 mmHg, 95% CI −5.48 to 6.28, 8 weeks: MD −1.6 mmHg, 95% CI −7.18 to 4.18, P > .05). DBP indicated no significant effects (time, group, and time × group; P > .05); the mean difference in values following 8 weeks was −3.0 mmHg (95% CI −9.36 to 3.28) and −1.6 mmHg (95% CI −9.04 to 5.78) in the training and control groups, respectively. MAP indicated a trend for an interaction effect (P = .08) between the training (MD −3.6 mmHg, 95% CI −9.23 to 2.09) and the control groups (MD −1.6 mmHg, 95% CI −7.99 to 4.71) following 8 weeks of training. There were no significant changes in PP and HR between the groups (P > .05).
Cardiovascular reactivity as a predictor of isometric handgrip training effectiveness

The residualized change in resting SBP following 8 weeks of IHG training was associated with the SBP and DBP reactivity to acute isometric exercise during set 3 and 4 (Table 2). There were no associations between HR reactivity to acute exercise and the SBP regarding the hypotensive effects.

Maximum voluntary contraction as a predictor of isometric handgrip training effectiveness

Pre-training handgrip MVC was associated with residualized changes of SBP, delta changes of DBP, and MAP following 8 weeks of IHG training (Figure 3). There were no associations between handgrip MVC and delta changes of PP, and HR following 8 weeks of IHG training.

Discussion

Prevention strategies applied early in life may provide the greatest protection against the development of hypertension later in life (27). Several studies have revealed that IHG training lowers the resting BP using 30% or 50% MVC in

Table 2. Baseline cardiovascular reactivity and the relationship with resting systolic blood pressure change by isometric training.

<table>
<thead>
<tr>
<th>Reactivity</th>
<th>Δ SBP (mm Hg)</th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Δ DBP (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Δ MAP (mm Hg)</td>
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<td></td>
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<tr>
<td></td>
<td>Δ PP (mm Hg)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Δ HR (bpm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 set</td>
<td>10 (12)</td>
<td>0.40</td>
<td>.250</td>
</tr>
<tr>
<td>2 set</td>
<td>9 (13)</td>
<td>0.35</td>
<td>.320</td>
</tr>
<tr>
<td>3 set</td>
<td>13 (11)</td>
<td>0.64</td>
<td>.047*</td>
</tr>
<tr>
<td>4 set</td>
<td>15 (20)</td>
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<tr>
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<tr>
<td>2 set</td>
<td>7 (7)</td>
<td>0.32</td>
<td>.360</td>
</tr>
<tr>
<td>3 set</td>
<td>9 (5)</td>
<td>0.67</td>
<td>.034*</td>
</tr>
<tr>
<td>4 set</td>
<td>12 (11)</td>
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<tr>
<td>1 set</td>
<td>9 (9)</td>
<td>0.48</td>
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<tr>
<td>2 set</td>
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</tr>
<tr>
<td>3 set</td>
<td>11 (7)</td>
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<td>.016*</td>
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<tr>
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</tr>
<tr>
<td>4 set</td>
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<td>-0.12</td>
<td>.753</td>
</tr>
</tbody>
</table>

Values are displayed as mean (SD). SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate. *P <.05.

Picture 2: Blood pressure changes in isometric handgrip training and control groups. Results are presented as mean ± SD. CON, control; IHG, isometric handgrip; SBP, systolic blood pressure. *P <.05 vs. baseline.

Figure 2.

Figure 3. Correlation analysis of handgrip maximal voluntary contraction prior to training period and changes in (a) systolic blood pressure (residualized changes), (b) diastolic blood pressure, and (c) mean arterial pressure following isometric handgrip training.

Figure 3.
young adults (8,13,20,26). We used 25% MVC because it was difficult for some subjects to maintain the 30% MVC handgrip exercise in our pilot study. In the present study, significant hypotensive effects in SBP were obtained in the training group even if 25% MVC (not 30% MVC) was used. The level of hypotensive effects shown at 6 weeks (−3.4 mmHg) of training was comparable to those reported by a previous study (13), however, some studies obtained higher hypotensive effects (20,26) in young women. There were no significant changes at 8 weeks (−4.7 mmHg) of training despite the mean reduction value being greater at 6 weeks. These results showed that the responses to the training were affected by interindividual and intraindividual variability of response to IET, which was also noted by a previous study (10). It remains unknown whether the participants who exhibited less hypotensive effects were unresponsive to the IET or the exercise program was not appropriate for hypotensive effects. Future research is required to identify whether modified methods (i.e., intensity, duration) of exercise protocols could reduce resting BP which was not altered following IET using the most common isometric exercise protocols (i.e., 30% MVC × 2 min).

As mentioned above, the hypotensive effects following isometric training showed interindividural variability in the present study. The novel finding of this study was that the hypotensive effects following IHG training were associated with BP reactivity to acute IHG exercise and handgrip MVC. It may be useful to identify the response to the IHG training before training intervention is decided. The identification of hypotensive effects by IET is not well known, however, some studies focused on showing the association between hypotensive response to IET and BP reactivity to acute isometric exercise or serial subtraction (11–14). These studies showed that the elevation of BP from resting value to stress task was associated with the reduction of resting BP in middle-aged women at rest and young adults (11–13), except one study which indicated no relationship among them (14). Interestingly, our results, which measured the BP during the repeated exercise, indicated that the exaggerated BP reactivity to acute IHG exercise could attenuate the hypotensive effects. These data, however, contradicted those reported by previous research (13). The mechanism of this relationship could not be explained based on the present study findings. Further studies are needed to investigate the effects of high BP reactivity to acute isometric exercise and MVC on the responsiveness of the hypotensive factors (e.g., endothelial-dependent vasodilation, autonomic nervous system, oxidative stress) (28).

There were several limitations to our study. First, it was the lack of menstrual cycle control. However, previous studies have shown that that cycle induces no effect on resting BP (29,30), BP reactivity to the isometric exercise (29,31,32), and MVC (31–33). Therefore, the menstrual cycle probably did not influence our findings. Second, the sample size of the present study may be considered small by some standards. A post-hoc power analysis using SBP as the primary measure indicated a power of 0.73 with the achieved sample size of n = 20. Third, although we used a randomized study, baseline BMI appeared higher in the training group than in the control group. It might affect our results, although no changes in BMI were observed following the intervention in each group. Fourth, this study was not designed to elucidate the mechanism of hypotensive effects following IET. Future studies are necessary to reveal the mechanism and examine the most efficacious methods for lowering BP following IET.

In conclusion, resting BP can be reduced by IHG training in young women. The BP reactivity to acute isometric exercise and handgrip MVC at pre-training is associated with the change in resting BP induced by isometric training. This suggests that the hypotensive response in young women can be identified by the BP reactivity and MVC before training, if the traditional method that sets the relative intensity (e.g., 30% MVC) is used.

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Declaration of Interest Statement

The authors declare that they have no conflict of interest.

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