Effects of Watermelon Supplementation on Aortic Hemodynamic Responses to the Cold Pressor Test in Obese Hypertensive Adults

Arturo Figueroa, Alexei Wong, and Roy Kalfon

BACKGROUND
Cold-induced increases in aortic blood pressure (BP) may cause adverse cardiac events in hypertensives by increasing ventricular afterload. L-citrulline supplementation reduces BP at baseline and during the cold pressor test (CPT), but the effect on wave reflection (augmentation pressure (AP) and index (AIx)) is controversial. Our aim was to assess the effect of L-citrulline–rich watermelon supplementation on aortic hemodynamic responses to CPT in hypertensive adults.

METHODS
Brachial systolic BP (bSBP) and aortic systolic BP (aSBP), AP, AIx, AIx adjusted to 75 beats/min (AIx75), reflection time (Tr), first (P1) and second systolic peak (P2; wave reflection magnitude), heart rate (HR), and systolic time index (STI; myocardial oxygen demand) at baseline and during CPT and magnitude of the response from baseline to CPT were evaluated in 13 individuals (10 women; 57 ± 1 year; bSBP 151 ± 5 mm Hg). Participants were randomized to a 6-week watermelon or placebo supplementation in a crossover design.

RESULTS
Watermelon reduced (P < 0.05) bSBP, aSBP, P1, and P2 at baseline and CPT compared with placebo; thus, increases from baseline to CPT were unaffected. Watermelon did not affect AP, AIx, AIx75, and STI at baseline but decreased (P < 0.05) AP and STI during CPT and the increases in AP (~5 mm Hg) and AIx75 (~7.3%) from baseline to CPT.

CONCLUSIONS
Watermelon supplementation reduced aortic BP and myocardial oxygen demand during CPT and the magnitude of the cold-induced increase in wave reflection in obese adults with hypertension. Watermelon may provide cardioprotection by attenuating cold-induced aortic hemodynamic responses.

CLINICAL TRIALS REGISTRATION
Clinicaltrials.gov register, NCT01185041

Keywords: aortic blood pressure; augmented pressure; augmentation index; blood pressure; hypertension; myocardial oxygen demand.

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Cold exposure is associated with impaired aortic hemodynamics and increased risk for adverse coronary events in older adults. Cold-induced sympathetic-mediated vasoconstriction causes an increase in wave reflection from peripheral arteries to the aorta, leading to increased left ventricular (LV) afterload (aortic blood pressure (BP) and augmentation index (AIx)) and myocardial oxygen (MO) demand in hypertensive adults. Although the magnitude of the BP response during cold exposure does not appear to be influenced by BP or adiposity category, a higher aortic BP during cold exposure may confer a greater risk for adverse cardiac events in adults with obesity and hypertension.

The cold pressor test (CPT) and whole-body cold exposure have been used to evaluate the efficacy of antihypertensive substances on brachial BP and aortic hemodynamics in normotensive and hypertensive adults. L-citrulline supplementation has reduced the cold-induced increase in brachial and aortic systolic BP (SBP) in young healthy men. Recent evidence indicates that short-term L-citrulline and watermelon supplementation reduce brachial and aortic SBP at thermoneutral temperature (baseline). Antihypertensive drug treatment reduced the increase in brachial SBP during cold exposure in hypertensive adults as a result of decreased baseline SBP. Consequently, the simultaneous decrease in SBP at baseline and during cold exposure leads to no significant effect of the treatment on the magnitude of the cold-induced hypertension. Since watermelon and L-citrulline supplementation do not reduce AIx at baseline or during CPT, the benefit of watermelon supplementation on AIx could be evident on the magnitude of the increase from baseline to CPT.

The purpose of the study was to evaluate the effects of watermelon supplementation on the cold-induced alterations in aortic hemodynamics in obese hypertensive adults. We hypothesized that watermelon supplementation would attenuate the BP response during CPT and the magnitude of the AIx response from baseline to CPT.
METHODS

Participants

Thirteen middle-aged adults (10 women and 3 men) with hypertension (brachial SBP ≥140 mm Hg, confirmed on 2 separate days), obesity (body mass index (BMI) ≥30 kg/m²), and a sedentary lifestyle (defined as <60 min of regular exercise per week in the last year) were enrolled in the study. Participants were recruited through various sources, including local newspaper advertisements and flyers placed on public boards at the university and in the general community. All women were postmenopausal, defined as the absence of menstruation for at least 1 year. All participants were non-smokers without evidence of cardiovascular or metabolic disease as determined by medical history. Exclusion criteria included regular (more than 2 days/week) consumption of L-citrulline/L-arginine–rich foods and use of L-citrulline/L-arginine supplements or hormone therapy. Participants were not taking antihypertensive medication and were advised to seek treatment or follow-up after the study. The Florida State University Institutional Review Board approved the experimental procedures. All participants signed an approved informed consent document prior to data collection.

Study design

In a double-blind, crossover design, participants were randomly assigned to either watermelon supplementation or placebo in a 1:1 ratio for 6 weeks. Laboratory personnel were blind to the supplementation assignments. Supplementation was separated by a 2-week washout period because vascular effects of L-citrulline or watermelon supplementation do not persist after 2 weeks. Participants were familiarized with the study tests and procedures, which were performed in a quiet, temperature-controlled room (23°C), after an overnight fast and abstinence from caffeinated drinks, alcohol, and intense or prolonged physical activity for at least 24 hour before testing. After 20 minutes of supine rest, brachial BP was recorded using an automated oscillometric device (HEM-705CP; Omron Healthcare, Vernon Hill, IL). Brachial BP, electrocardiogram, and aortic hemodynamic measures were collected before (baseline) and during the second minute of CPT. Before and after 6 weeks, the tests were conducted in the morning at the same time each day (±1 hour) to avoid potential diurnal cardiovascular variations. Participants were instructed not to modify their physical activity and diet throughout the study.

Watermelon and placebo supplementations

Watermelon powder was provided by Milne Fruit Products (Prosse, WA) and contained sieved and freeze-dried watermelon extract. The daily watermelon intake (4 g L-citrulline and 2 g L-arginine/day divided into 3 doses) in this study was equivalent to ~2.3 pounds of raw red watermelon. Placebo powder consisted of maltodextrin with sucrose, glucose, and fructose (2:2:1) to match the carbohydrate composition of the watermelon powder. The participants mixed the supplements in water. The last dose of the supplement was consumed ~24 hours before the cardiovascular tests. A powder bag count was conducted at the end of each supplementation period to assess compliance.

Cold pressor test

The CPT was done by introducing the participant’s right hand up to the wrist in ice-cold water (4°C) for 2 minutes. Subjects were encouraged to maintain a constant rate and depth of breathing throughout the test.

Cardiovascular measurements

Applanation tonometry was used to record arterial waveforms using a high-fidelity transducer (Millar Instruments, Houston, TX). Radial waveforms were obtained and calibrated with brachial SBP and diastolic BP (DBP). Aortic pressure waveforms were derived using a generalized validated transfer function (SphygmoCor; AtCor Medical, Sydney, Australia). Pulse pressure (PP) was calculated as SBP–DBP. The aortic pressure wave is composed of a forward wave (P1), caused by stroke volume ejection, and a reflected wave (P2) that returns to the aorta from peripheral sites. Augmented pressure (AP) was defined as the difference between the second (P2) and first (P1) systolic peaks (AP = P2 – P1). Alx was defined as AP expressed as a percentage of the aortic PP. Alx adjusted to 75 beats/min (Alx75) was calculated. Transit time of the reflected wave (Tr) indicates the round-trip travel of the forward wave to the peripheral reflecting sites and back to the aorta. Subendocardial viability ratio (SEVR) was calculated as diastolic time index (DTI)/systolic time index (STI). Two high-quality measurements (operator index ≥80%) of aortic hemodynamics were collected, and the average was used in the analysis. In our laboratory, the intraclass correlation coefficients for aortic hemodynamics at baseline and during CPT, calculated on 2 separate days, are ≥0.94. Heart rate (HR) was assessed by a continuous electrocardiogram sampled by a data acquisition system (Biopac, Santa Barbara, CA).

Anthropometry and body composition

Height was measured to the nearest 0.5 cm using a stadiometer and body weight was measured to the nearest 0.1 kg using a scale (Sunbeam Products, Boca Raton, FL). BMI was calculated as weight, in kilograms, divided by height, in meters. Total fat and lean mass were determined from whole-body dual-energy X-ray absorptiometry (GE Lunar DPX-IQ, Madison, WI).

Statistical analysis

The Shapiro-Wilk test was used to confirm normality. Possible between-group differences in all parameters before the supplementations were analyzed with unpaired t tests. Two-way analysis of variance (ANOVA) with repeated measures was used to determine differences in cardiovascular parameters at baseline, CPT, and the magnitude of the changes from baseline to CPT before and after both
supplementation. When ANOVA produced a significant treatment-by-time interaction, post-hoc comparisons with paired t tests were used to evaluate the within-group difference between before and after the supplementation. Pearson correlation was used to determine the relationship between changes in aortic hemodynamics. Based on previous data, sample size was calculated to include 13 participants in order to provide 80% power in detecting a 65%–7% decrease in aortic SBP. Values are presented as means ± standard error. Statistical significance was defined as P < 0.05. Statistical analyses were performed with SPSS, version 20.0 (SPSS, Chicago, IL).

RESULTS

No withdrawals or adverse events occurred during the study. Participant characteristics are presented in Table 1. Weight and body composition did not change throughout the study. Compliance (mean ± standard deviation) with placebo and watermelon supplementation was 97.7 ± 2.6% and 97.4 ± 4.0%, respectively.

Hemodynamic responses to CPT before watermelon supplementation

There were significant (P < 0.05) increases in brachial SBP (21.5 ± 5 mm Hg), brachial DBP (14.3 ± 3 mm Hg), brachial PP (8.2 ± 2 mm Hg), aortic SBP (27.6 ± 6 mm Hg), aortic DBP (15.7 ± 7 mm Hg), aortic PP (12.2 ± 2 mm Hg), aortic AP (10.2 ± 2 mm Hg), aortic AIx (9.0 ± 2.5%), aortic AIx75 (12.1 ± 2.8%), P1 (17.6 ± 6 mm Hg), P2 (27.5 ± 5 mm Hg), STI (934 ± 172 mm Hg/s/min), DTI (374 ± 242 mm Hg/s/min), and HR (5 ± 2 beats/min), with decreases in Tr (14 ± 7 msec) and SEVR (25.7 ± 5.2%) from baseline to CPT.

Effects of watermelon supplementation on hemodynamics

Table 2 summarizes the cardiovascular and aortic hemodynamic parameters at baseline before and after the

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n = 13)</th>
<th>Watermelon (n = 13)</th>
<th>Mean difference (95% CI) at 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial SBP, mm Hg</td>
<td>146 ± 5</td>
<td>151 ± 5</td>
<td>138 ± 41b</td>
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<tr>
<td>Brachial DBP, mm Hg</td>
<td>84 ± 4</td>
<td>87 ± 4</td>
<td>81 ± 41b</td>
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<td>Brachial PP, mm Hg</td>
<td>61 ± 3</td>
<td>64 ± 3</td>
<td>56 ± 33a</td>
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<td>Aortic SBP, mm Hg</td>
<td>138 ± 5</td>
<td>139 ± 4</td>
<td>130 ± 41a</td>
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<td>Aortic DBP, mm Hg</td>
<td>87 ± 4</td>
<td>87 ± 4</td>
<td>82 ± 41a</td>
</tr>
<tr>
<td>Aortic PP, mm Hg</td>
<td>51 ± 3</td>
<td>51 ± 3</td>
<td>47 ± 3</td>
</tr>
<tr>
<td>Tr, msec</td>
<td>138 ± 6</td>
<td>141 ± 6</td>
<td>134 ± 7</td>
</tr>
<tr>
<td>AP, mm Hg</td>
<td>16 ± 2</td>
<td>16 ± 2</td>
<td>17 ± 3</td>
</tr>
<tr>
<td>AIx, %</td>
<td>30.8 ± 2.4</td>
<td>30.3 ± 2.3</td>
<td>30.1 ± 1.9</td>
</tr>
<tr>
<td>AIx75, %</td>
<td>26.7 ± 2.2</td>
<td>25.6 ± 2.2</td>
<td>26.2 ± 1.9</td>
</tr>
<tr>
<td>P1, mm Hg</td>
<td>122 ± 4</td>
<td>123 ± 4</td>
<td>113 ± 41a</td>
</tr>
<tr>
<td>P2, mm Hg</td>
<td>138 ± 5</td>
<td>139 ± 4</td>
<td>130 ± 41a</td>
</tr>
<tr>
<td>STI, mm Hg/s/min</td>
<td>2,738 ± 135</td>
<td>2,729 ± 127</td>
<td>2,776 ± 129</td>
</tr>
<tr>
<td>DTI, mm Hg/s/min</td>
<td>3,792 ± 156</td>
<td>3,826 ± 179</td>
<td>3,848 ± 158</td>
</tr>
<tr>
<td>SEVR, %</td>
<td>141 ± 6</td>
<td>143 ± 7</td>
<td>134 ± 7</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>67 ± 2</td>
<td>70 ± 3</td>
<td>68 ± 3</td>
</tr>
</tbody>
</table>

Values are mean ± standard error.
Abbreviations: AIx, augmentation index; AIx75, augmentation index adjusted to 75 beats/minute; AP, augmented pressure; CI, confidence interval; DBP, diastolic blood pressure; DTI, diastolic time index; P1, first systolic peak pressure; P2, second systolic peak pressure; PP, pulse pressure; SBP, systolic blood pressure; SEVR, subendocardial viability ratio; STI, systolic time index; Tr, time of reflection.

*P < 0.05, †P < 0.01, ‡P < 0.001 different from before (within treatment paired t test).
*P < 0.01, †P < 0.001 different from placebo (analysis of variance with repeated measures).
supplementations. Watermelon supplementation decreased \((P < 0.05)\) brachial SBP, brachial DBP, brachial PP, aortic SBP, aortic DBP, P1, and P2 compared with no changes after placebo. Watermelon supplementation did not affect aortic PP, Tr, AP, Alx, Alx75, STI, DTI, SEVR, and HR.

During CPT (Table 3), watermelon supplementation decreased \((P < 0.05)\) brachial SBP, brachial PP, aortic SBP (Figure 1A); aortic PP, P1, P2 (Figure 1B); aortic AP (Figure 1C); and STI (Figure 1D) compared with placebo. Aortic DBP, Tr, Alx, Alx75, DTI, SEVR, and HR during CPT were not affected by watermelon supplementation. Changes in STI during CPT were correlated with changes in aortic SBP \((r = 0.840, P < 0.001)\), P2 \((r = 0.840, P < 0.001)\), and aortic Alx75 \((r = 0.572, P < 0.01)\).

Watermelon supplementation reduced the magnitude of the increase in aortic AP \((P < 0.05)\), Alx \((P = 0.056)\), and Alx75 \((P < 0.05)\) compared with placebo (Figure 2) but it did not affect the magnitude of the BP responses from baseline to CPT.

**DISCUSSION**

In the present study, CPT elicited increases in brachial and aortic BP. Sympathetic overactivity\(^4\) induced by 2–3 minutes CPT (4°C) resulted in modest increases in brachial SBP (13–19 mm Hg) but greater increases in aortic SBP (21–31 mm Hg) in young normotensive adults.\(^6,15,16\) Similarly, whole-body and facial cooling caused a higher aortic response than brachial SBP response.\(^3,17\) Despite the type, cold exposure (CPT, whole-body, or facial) induces an early return of the reflected wave to the aorta, which increases aortic SBP and Alx (11%–20%).\(^3,6,15,17\) Since CPT involves sympathetic-mediated pain stimulation,\(^3,18\) BP responses can be higher during CPT than whole-body cold exposure.\(^18\) The magnitude of the aortic SBP, AP, and Alx responses to CPT in the present study are consistent with responses to 15–20 minutes of whole-body cold exposure observed in middle-aged and older adults.\(^3,19\)

Whole-body cold exposure acutely decreases SEVR by 10% in middle-aged hypertensives,\(^3\) mainly through an increase in MO2 demand (9.5%–10%).\(^20,21\) Because whole-body cold exposure decreases HR in older adults, the increase in LV afterload (SBP) induces an increase in MO2 demand (calculated as rate-pressure product = HR \(\times\) SBP),\(^3,20,21\) which could be attenuated by HR reduction. Although no increase in HR during CPT at 4°C is a common finding in young adults,\(^6,15\) some studies have shown a modest increase in HR (~8 beats/min) during CPT at 0°C,\(^4,22\) suggesting that water temperature is an important factor for the HR response to CPT. In the present study, SEVR decreased by 27% due to an increase in STI (34%), indicating that CPT increased MO2 demand. This response to CPT has been attributed to an increased aortic SBP, wave reflection magnitude, and HR.\(^22\) In the present study, HR was slightly increased (~5 beats/min) during CPT.

### Table 3. Hemodynamic parameters during cold pressor test before and after placebo and watermelon supplementation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n = 13)</th>
<th>Watermelon (n = 13)</th>
<th>Mean difference (95% CI) at 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>Brachial SBP, mm Hg</td>
<td>169 ± 6</td>
<td>171 ± 7</td>
<td>172 ± 6</td>
</tr>
<tr>
<td>Brachial DBP, mm Hg</td>
<td>99 ± 5</td>
<td>98 ± 4</td>
<td>101 ± 5</td>
</tr>
<tr>
<td>Brachial PP, mm Hg</td>
<td>70 ± 4</td>
<td>72 ± 4</td>
<td>71 ± 4</td>
</tr>
<tr>
<td>Aortic SBP, mm Hg</td>
<td>162 ± 6</td>
<td>163 ± 7</td>
<td>166 ± 6</td>
</tr>
<tr>
<td>Aortic DBP, mm Hg</td>
<td>102 ± 5</td>
<td>101 ± 4</td>
<td>104 ± 5</td>
</tr>
<tr>
<td>Aortic PP, mm Hg</td>
<td>61 ± 4</td>
<td>62 ± 3</td>
<td>62 ± 4</td>
</tr>
<tr>
<td>Tr, msec</td>
<td>126 ± 3</td>
<td>125 ± 4</td>
<td>124 ± 3</td>
</tr>
<tr>
<td>AP, mm Hg</td>
<td>24 ± 3</td>
<td>25 ± 3</td>
<td>25 ± 3</td>
</tr>
<tr>
<td>Alx, %</td>
<td>38.0 ± 2.2</td>
<td>38.8 ± 2.5</td>
<td>39.1 ± 2.2</td>
</tr>
<tr>
<td>Alx75, %</td>
<td>37.5 ± 2.5</td>
<td>37.2 ± 2.8</td>
<td>38.2 ± 2.3</td>
</tr>
<tr>
<td>P1, mm Hg</td>
<td>138 ± 5</td>
<td>138 ± 5</td>
<td>140 ± 5</td>
</tr>
<tr>
<td>P2, mm Hg</td>
<td>162 ± 6</td>
<td>163 ± 7</td>
<td>166 ± 6</td>
</tr>
<tr>
<td>STI, mm Hg.s/min</td>
<td>3,638 ± 193</td>
<td>3,605 ± 209</td>
<td>3,710 ± 189</td>
</tr>
<tr>
<td>DTI, mm Hg.s/min</td>
<td>4,129 ± 189</td>
<td>4,121 ± 167</td>
<td>4,222 ± 168</td>
</tr>
<tr>
<td>SEVR, %</td>
<td>116 ± 5</td>
<td>117 ± 6</td>
<td>116 ± 5</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>74 ± 2</td>
<td>71 ± 3</td>
<td>71 ± 2</td>
</tr>
</tbody>
</table>

Values are mean ± standard error.

Abbreviations: Alx, augmentation index; Alx75, augmentation index adjusted to 75 beats/minute; AP, augmented pressure; CI, confidence interval; DBP, diastolic blood pressure; DTI, diastolic time index; P1, first systolic peak pressure; P2, second systolic peak pressure; PP, pulse pressure; SBP, systolic blood pressure; SEVR, subendocardial viability ratio, STI, systolic time index; Tr, time of reflection.

\(^{ap}P<0.05, ^{bp}P<0.1, ^{cp}P<0.01\) different from before (within treatment paired t test).

\(^{ap}P<0.05, ^{bp}P<0.01\) different from placebo (analysis of variance with repeated measures).
Attenuation of Wave Reflection Responses to Cold

in hypertensive adults, which can be explained by reduced cardiovascular baroreflex sensitivity associated with increased aortic stiffness (pulse wave velocity (PWV)). The increased LV afterload, HR, and STI observed during CPT may have been influenced by an enhanced sympathetic activity related to pain, adiposity, and hypertension as well as altered coronary hemodynamics related to aging. The age-related arterial stiffening might be an important factor underlying the increases in aortic SBP and AIx during cold exposure in older adults.

The present findings show that brachial and aortic SBP and DBP before CPT (baseline) were significantly decreased by watermelon supplementation, while baseline AP, AIx, and AIx75 were unaffected. There is some evidence of the beneficial effects of L-citrulline and watermelon supplementation on BP and brachial-ankle PWV in normotensive and prehypertensive or hypertensive adults at thermoneutral temperature. However, L-citrulline and watermelon supplementation have not been able to decrease AIx in normotensive men and obese hypertensive postmenopausal women. In this study, a concurrent decrease in P2 and P1 explains the lack of impact of watermelon supplementation on baseline AP and AIx.

It was suggested that greater aortic SBP and LV afterload during whole-body cold exposure may increase the risk for cardiovascular complications in hypertensives. In the present study, watermelon supplementation reduced aortic SBP, DBP, PP, AP, P1, and P2 during CPT due to the concurrent reduction at baseline. Consistent with the present findings, reductions in aortic SBP (4 mm Hg) and PP (3 mm Hg) during CPT were observed in young normotensive men following 4 weeks of L-citrulline supplementation with no effect on AIx. Recently, Sanchez-Gonzalez et al. observed reductions in AP (3 mm Hg) during 30 minutes of whole-body cold exposure (4°C) following L-citrulline supplementation. It is important to consider that AP is the difference between P2 and P1 and that AIx is the AP relative to aortic PP. In the present study, AP during CPT decreased by 4 mm Hg

Figure 1. Changes in (A) aortic systolic blood pressure (ΔSBP), (B) second systolic peak pressure (ΔP2), (C) augmented pressure (ΔAP), and (D) systolic time index (ΔSTI) during cold pressor test after placebo and watermelon supplementation. Values are presented as mean ± standard error. *P < 0.05 and †P < 0.001 different than before; ‡P < 0.05 and §P < 0.01 different than placebo.
due to a greater decrease in P2 than P1, indicating that the effect on AP was mediated via a reduction in wave reflection magnitude. However, when AP was expressed as a percent of a reduced aortic PP, AIx during CPT was not significantly reduced.

In agreement with our findings, the concurrent decrease in BP at baseline and during whole-body cold exposure following antihypertensive treatment leads to no effect on the magnitude of the increase in BP from baseline to cold in hypertensive adults. A novel finding of the present study is that watermelon supplementation lowered the magnitude of the AP (5.2 mm Hg) and AIx75 (7.3%) responses from baseline to CPT. Although it may appear that the slightly elevated AIx or AIx75 at baseline (~4%) contributed to this attenuation, Hinstala et al. indicated that the magnitude of the AIx response to whole-body cold exposure is independent of the baseline value. Thus, a similar magnitude of the AIx response to CPT at 0 and 6 weeks would be expected without watermelon supplementation. A possible explanation for the attenuated increase in wave reflection responses to CPT is that baseline AP and AIx75 were not reduced by watermelon supplementation. Because increased AP is a predictor of negative cardiovascular outcomes in patients with coronary artery disease, attenuation of the cold-induced increase in AP may decrease the propensity for adverse cardiovascular events in high-risk individuals.

We found that watermelon supplementation reduced STI during CPT without affecting the baseline value. This decrease in STI was strongly related to reductions in CPT-induced increases in aortic SBP, P2, and AIx75, which are markers of LV afterload influenced by the vasomotor tone. Reduced cold-induced peripheral arterial vasoconstriction after watermelon supplementation may have attenuated the increase in the reflected wave magnitude (P2), leading to a reduction in aortic SBP and AIx75 responses. Because HR was not affected by watermelon supplementation, HR may have not contributed to the reduction in STI during CPT. It has been shown that a cold-induced rise in SBP plays a main role on the increase in MO\textsubscript{2} demand in older adults. Therefore, watermelon supplementation may reduce cold-induced MO\textsubscript{2} demand by decreasing aortic SBP and wave reflection magnitude.

The mechanism underlying the attenuation of aortic hemodynamic responses during CPT is unclear. However, it may involve an increased production of endothelial nitric oxide and subsequent reduction in the vasomotor tone as previously observed with L-citrulline or watermelon supplementation. We did not observe changes in Tr (estimate index of aortic PWV) at baseline after watermelon supplementation, which is consistent with the lack of effect of watermelon supplementation and antihypertensive drugs on aortic PWV. Our finding of an unaltered Tr reduction during CPT suggests that watermelon supplementation may not affect the increase in aortic PWV induced by CPT. Thus, it is possible that the attenuation in wave reflection magnitude during CPT may be attributed to a reduced vasomotor tone of peripheral arteries.

The cold-induced increases in aortic wave reflection, aortic PWV, and MO\textsubscript{2} demand in older adults may be important risk factors for coronary events during cold weather.
Although the peak BP during whole-body cold exposure is reduced by antihypertensive drugs, the magnitude of the BP response is not attenuated in hypertensives. Thus, attenuation of aortic wave reflection magnitude leading to a decrease in MO\textsubscript{O}, demand during CPT may be of clinical relevance in older adults with hypertension exposed to cold temperatures. Some potential limitations of this study can be mentioned. First, our sample size was relatively small; however, it was appropriate for observation of the significant effects of watermelon supplementation on hemodynamic responses to CPT. Second, participants were primarily women; higher BP responses to CPT may occur in young women than in men, but this differential response is not present in older adults. Third, we were unable to measure bioactive substances in plasma. However, previous studies have shown increased L-arginine and nitric oxide following L-citrulline and watermelon supplementation. Fourth, the diet was not controlled during the study, but participants were told to avoid consumption of food rich in citrulline/L-arginine (e.g., nuts, melons, tuna, and beans). To avoid the acute effect of increased L-arginine, which persists for <1 hour, hemodynamics were measured in the fasted state at least 24 hours after the last watermelon dose. Last, hemodynamic responses to CPT may differ from other cold exposure types.

In conclusion, the new findings of the present study are that watermelon supplementation attenuated the aortic wave reflection magnitude and MO\textsubscript{O}, demand responses to CPT in obese middle-aged adults with hypertension. Therefore, watermelon supplementation may provide some cardioprotective effect by attenuating the cold-related increases in aortic hemodynamics in older adults with hypertension.

ACKNOWLEDGMENTS

We are grateful to Milne Fruit Products for providing the watermelon extract and placebo supplements.

DISCLOSURE

The authors declared no conflict of interest.

REFERENCES


