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ORIGINAL RESEARCH

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Acute effects of energy drink on arterial stiffness and endothelial function in young male bodybuilders with habitual caffeine consumption

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Abstract

Elite bodybuilders consume energy drink (ED) immediately before or during strength training. However, the effects of ED on cardiovascular responses have not been fully understood. In this study, the carotid-femoral pulse wave velocity (cfPWV) and flow-mediated dilation (FMD), which are indices of arterial stiffness and endothelial function in response to acute ED consumption, were examined. Forty-five young men (30.0 $\pm$ 3.9 years) were investigated: sedentary (CON, n = 15), physically active (PA, n = 15), and bodybuilders (BD, n = 15). After they consumed commercial ED, their vascular function was analyzed at the following time points: pre, post, 30 min and 60 min. At baseline, the age, height and systolic and diastolic blood pressure of the groups did not significantly differ; conversely, their weight, body mass index, lean mass, fat percent and grip strengths significantly differed ($p < 0.05$). After ED consumption, central and peripheral blood pressure markedly increased in the PA and CON groups ($p < 0.05$) but not in the BD group. cfPWV, augmentation index and wave reflection were not different among the groups and did not change at any time point ($p > 0.05$). However, FMD notably differed among the groups after ED consumption. The FMD of the BD group increased sharply and significantly after ED consumption at post-time points (pre, 6.5% $\pm$ 1.7%; post, 13.1% $\pm$ 2.6%; 30 min, 10.7% $\pm$ 2.9%; 60 min, 8.9% $\pm$ 2.4%, $p = 0.001$). The FMD markedly increased after ED consumption in the PA group ($p = 0.004$), but it did not change in the CON group ($p > 0.05$). ED consumption acutely triggered the increase in endothelial function in the BD and PA groups. Therefore, these findings helped elucidate the distinct cardiovascular responses to ED intake among different populations with varying physical activity or training levels.

Keywords

Caffeine; Strength training; Pulse wave velocity; Flow-mediated dilation

1. Introduction

Cardiovascular disease (CVD) is the main cause of death worldwide. Its development and an unexpected cardiac arrest may be associated with excessive energy drink (ED) intake, especially in young adults such as elite bodybuilders who engage in regular high-intensity resistance exercise [1]. Exercise plays a critical role in affecting arterial stiffness, which is a major determinant of CVD. For example, regular aerobic exercise improves arterial stiffness, whereas resistance training or weightlifting increases arterial stiffness. Strenuous resistance exercise induces exceptionally high systolic and diastolic blood pressure, which can be as high as 480/350 mmHg [2]. Chronic exposure to high blood pressure during vigorous resistance exercise leads to left ventricular hypertrophy because of a high afterload [3]. Furthermore, such conditions in elite bodybuilders may result in vascular remodeling and subsequently alter arterial stiffness because of their extreme training regimens [4]. Therefore, studies have further explored how EDs affect the cardiovascular system in these populations.

EDs have become increasingly popular, but concerns on their effects on the human body have been raised [5]. They are often used as effective beverages in temporarily enhancing arousal, weight loss, concentration, athletic performance and energy level [6]. They typically contain high amounts of caffeine, along with sugar, taurine, vitamin B complex, guarana and ginseng. Although these substrates, particularly caffeine, have the potential to induce an increase in heart rate and blood pressure, their effects are generally short lived and negligibly detrimental to healthy individuals but not to people with cardiovascular disorders [7].

The unfavorable effects of resistance exercise on arterial stiffness rely on training intensity. Some studies have suggested that arterial stiffness is increased by high-intensity resistance exercise, but it is decreased by low-intensity resistance training [8]. Other studies have demonstrated that arterial

stiffness decreases notably irrespective of resistance training intensity [8]. This inconsistent finding leads to the discrepancy in performing resistance training on arterial stiffness. Furthermore, few studies have been performed on elite bodybuilders who perform chronic high-intensity resistance exercises on arterial stiffness.

Elite bodybuilders often consume EDs with a high caffeine content immediately before and during training sessions since caffeine is a well-known stimulant that can positively influence their physical performance by increasing their alertness, reducing perceived exertion, and delaying the onset of fatigue [2]. High-caffeine-content EDs have the potential to enhance fat oxidation and increase motivation during resistance exercise; consequently, endurance/strength/power improves, and training sessions become more productive. Ra and colleagues [9] showed that taurine supplementation decreases the delayed rise in arterial stiffness following eccentric exercise, which is likely influenced by exercise-induced oxidative stress in healthy young men. *Panax ginseng* supplementation does not affect arterial stiffness and endothelial function for 12 weeks in individuals with hypertension and type 2 diabetes [10]. Thus, results may vary in different studies, and more robust clinical evidence from other substances in EDs may be required. Previous studies also demonstrated that ingesting commercially available EDs acutely elevates blood pressure and arterial stiffness; furthermore, it impairs endothelial function in healthy populations [11, 12]. Indeed, available evidence supports the claim that EDs deform the vasoconstrictor-vasodilator balance in favor of vasoconstriction, which may impede baroreflex-mediated vasodilatory responses that will otherwise prevent an increase in blood pressure and arterial stiffness [4]. The consumption of high-dosage caffeine with sugar-sweetened beverages acutely increases arterial stiffness and endothelial dysfunction [4]. Therefore, the incidence of CVDs among elite bodybuilders can be increased because of the synergistic effects of rigorous resistance training and the consumption of EDs, leading to sudden changes in cardiovascular hemodynamics.

However, to our best knowledge, evidence is insufficient to suggest that distinct vascular adaptations occur at rest among elite bodybuilders, who chronically engage in high-intensity strength training and habitually consume EDs containing substantial amounts of caffeine compared with their counterparts. In addition, studies have yet to clarify whether the acute vascular responses of elite bodybuilders to EDs with high caffeine doses differ from those of their counterparts. Hence, the present study aimed to compare the baseline hemodynamics and examine the acute effects of EDs with a significant caffeine content on arterial stiffness and endothelium-dependent vasodilation. This study aimed to provide insights into the potential mechanisms underlying the vascular responses and adaptation induced by EDs in elite bodybuilders with habitual caffeine consumption.

2. Materials and methods

2.1 Participants

An a priori power analysis was performed with G-Power (ver. 3.1.9.7, Heinrich-Heine-Universität, Düsseldorf, Germany) [13] to determine the sample size. A power analysis with an F-test for repeated two-way analysis of variance (ANOVA) was conducted with an effect size of 0.25, α-level of 0.05, and power level of 0.91 ($1 - \beta$). Therefore, 15 participants in each group were established as a sufficient sample size. Forty-five young men (30.0 $\pm$ 3.9 years) were recruited for this study through flyers, advertisements, word of mouth, and participants residing in or around Seoul, South Korea. They were assigned into their corresponding groups based on their reported physical activity: sedentary young males (CON, n = 15), physically active young males (PA, n = 15), and young male bodybuilders (BD, n = 15). According to the results of screening with a questionnaire, bodybuilders had been exercising for at least 5 years and participating in competitions before the study. The registration of the athletes in Korean Sport & Olympic Committee was also double-checked. For the last 3 months (at least), the participants were either sedentary (no participation in regular physical activity) or physically active ($\geq$3 h/week of aerobic and/or resistance exercise). All participants self-reported that they were healthy and non-obese; had no history of cardiovascular, kidney, autonomic, or metabolic disease; and were not taking any medications. However, habitual ED use was not considered in either the inclusion or exclusion criteria of this study. The characteristics of the participants are presented in Table 1.

2.2 Study protocol

A cross-sectional and quasi-experimental study design was used in this study. The participants refrained from food, caffeine and smoking for at least 8 h before the experiments and reported to our laboratory in the morning. All procedures were performed by the three groups at the same time of the day. Physically active young males and bodybuilders were examined at least 24 h after their last exercise session to avoid the acute effects of exercise on the normal physiological state. The participants were also observed under quiet, comfortable, and ambient laboratory (~24 °C) conditions. All vascular measurements were performed using automated equipment to minimize investigator bias.

Following instrumentation, the participants rested quietly in a supine position for 20 min. Afterward, steady-state hemodynamic data as the pre-consumption baseline were obtained for 5 min, and the carotid-femoral pulse wave velocity (cfPWV) and flow-mediated dilation (FMD) were determined. Next, the participants were instructed to be in a semi-recumbent position and given 1 min to drink 473 mL of Monster Energy (Monster Beverage, Corona, CA, USA), which contains caffeine, glucose, taurine, *P. ginseng*, L-carnitine, glucuronolactone, inositol, guarana extract, B vitamins, maltodextrin [14]. Monster Energy was chosen because it is one of the most popular EDs among commercially available soft drinks [3]. Their drinking duration was 3.2 $\pm$ 1.1 min. After drinking a can of Monster Energy, the participants returned to the supine position, and their hemodynamics (*e.g.*, BP and heart rate), cfPWV and FMD were measured at the following time

TABLE 1. Characteristics of the selected subjects.

Variables	CON (n = 15)	PA (n = 15)	BD (n = 15)	*p*-value
Age (yrs)	29.0 ± 3.5	29.5 ± 4.2	32.1 ± 3.5	0.093
Height (cm)	173.4 ± 5.0	174.6 ± 4.7	177.8 ± 8.0	0.148
Weight (kg)	72.3 ± 8.8	80.6 ± 8.0*	85.6 ± 11.7*	0.003
BMI (kg/m^2)	24.1 ± 3.0	26.5 ± 2.0*	27.0 ± 3.0*	0.011
Lean mass (kg)	31.5 ± 3.7	38.3 ± 3.5*	42.3 ± 4.6*,†	0.001
Fat percent (%)	22.7 ± 4.8	17.2 ± 3.8*	14.1 ± 6.5*	0.001
WHR	0.88 ± 0.05	0.84 ± 0.03	0.85 ± 0.04	0.056
Seated SBP (mmHg)	111.5 ± 9.4	114.3 ± 11.2	117.5 ± 14.7	0.424
Seated DBP (mmHg)	73.6 ± 8.4	71.1 ± 9.6	70.0 ± 10.6	0.593
Seated HR (bpm)	73.6 ± 12.9	68.1 ± 9.3	73.0 ± 14.5	0.423
Cigarette Smokers, n (%)	6 (40)	3 (20)	3 (20)	
Caffeine consumption, n (%)	15 (100)	15 (100)	15 (100)	
Rarely	-	-	-	
Occasionally	-	-	-	
Frequently	3	2	3	
Daily	12	13	12	
Right grip strength (kg)	27.7 ± 4.6	33.5 ± 5.8*	37.9 ± 4.5*	0.001
Left grip strength (kg)	24.7 ± 4.6	32.8 ± 5.6*	36.5 ± 4.3*	0.001
Right relative grip strength (kg/kg)	38.4 ± 5.3	41.2 ± 5.1	44.9 ± 7.1*	0.024
Left relative grip strength (kg/kg)	34.4 ± 6.1	40.5 ± 5.3*	43.3 ± 7.0*	0.002
Training careers (yrs)	-	4.8 ± 2.8	14.5 ± 6.4	

*Data are presented as mean ± standard deviation; CON, control; PA, physically active; BD, bodybuilder; BMI, body mass index; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; *$p < 0.05$ vs. CON; †$p < 0.05$ vs. PA. Rare caffeine consumption was defined as <1 caffeine-containing beverage per month; occasional caffeine consumption was defined as 1–3 beverages per month; frequent caffeine consumption was defined as 1–6 caffeine-containing beverages per week; and daily caffeine consumers were defined as ≥1 caffeine-containing beverage per day.*

points: post-consumption, 30 min and 60 min [3]. These time points were selected because ED consumption increases blood pressure 30 min after consumption during supine rest under normal conditions and then lasts ~120 min for observation following ED consumption [15]. If needed, the participants were permitted to urinate between the measurement time points of 30 and 60 min. The graphical representation of the study design and procedures is displayed in Fig. 1.

2.3 Anthropometry and body composition

The participants' height was measured using a scale (Seca 213, Seca, Hamburg, Germany). Their body mass (kg) was divided by their height (m) squared (kg/m^2) to determine the body mass index (BMI). Body composition was assessed using a bioelectrical impedance device (Inbody 270, Inbody, Seoul, South Korea). During the body composition test, the participants were instructed to hold still in a standing position on the board of the device.

2.4 Peripheral blood pressure

BP was measured in duplicate by using an automatic device (UM-211, A & D, Tokyo, Japan) on the right arm after 5 min of rest in a seated position with the arm at the heart level.

2.5 Grip strength

A grip strength dynamometer was used to assess the maximal handgrip strength of both arms (HD BTA, Vernier Software & Technology, Beaverton, OR, USA). Grip strength was divided by the body weight (kg/kg) to calculate the relative grip strength.

2.6 Central arterial stiffness and blood pressure

Arterial stiffness was used to measure cfPWV by sequentially recording the participants' electrocardiogram-gated carotid and femoral artery pressure waveforms (SphygmoCor XCEL, AtCor Medical, Sydney, Australia). The transit distance between the carotid and femoral artery measurement locations was calculated as the surface distance from the suprasternal notch to the carotid and femoral recording sites measured

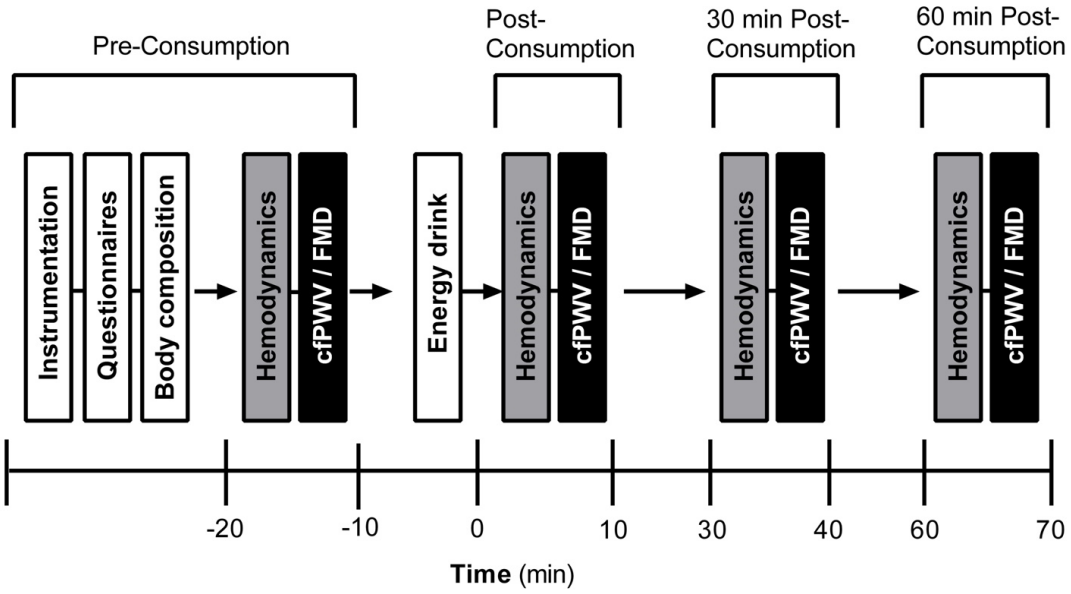

FIGURE 1. Schematic of the study design. cfPWV, carotid-femoral pulse wave velocity; FMD, flow-mediated dilation.

with a flexible measuring tape. Carotid and femoral recording sites were marked with indelible ink on the first assessment to ensure that measurements were made from the same location at each time point.

As a secondary analysis, a central aortic pressure waveform was acquired from pulse waves obtained at the brachial artery by using a brachial cuff. Noninvasive central blood pressure measurements such as central aortic systolic blood pressure, central pulse pressure, and aortic augmentation index (AIx) were also reported. All applanation tonometry measurements for each participant were performed by the same investigator during the experimental trials.

2.7 Endothelial vasodilatory function

Endothelium-dependent reactivity, measured by the FMD of the brachial artery, was determined using a noninvasive Doppler ultrasonography system equipped with online computer-assisted semi-automatic analysis software (UNEX EF-38G, UNEX Co., Ltd., Nagoya, Japan) and a 10 MHz linear array transducer. Shear stress-induced vasodilation was produced by inflating a sphygmomanometer cuff 2 cm below the antecubital fossa to occlude the artery at 50 mmHg above the resting systolic blood pressure for 5 min. An automated probe, which was self-adjusted to provide a crisp longitudinal image of the artery and to record the baseline data, was used to capture the cross-sectional images of the artery by analyzing B-mode ultrasound. After cuff deflation, brachial artery diameters were acquired *via* B-mode ultrasound images for 2 min. The FMD was calculated as the maximum percentage of the increase in the brachial artery diameter over the baseline. Brachial artery recording sites were marked with indelible ink on the first assessment to ensure that measurements were made from the same location at each time point. These procedures were performed in accordance with previously described methods [16].

2.8 Statistical analysis

Data were reported as the mean and standard deviations of each primary dependent variable. The normality of the distribution of all outcome variables was verified using a Kolmogorov-Smirnov test. Two-way ANOVA (group $\times$ time) with repeated measures was used to analyze the effects of ED consumption on each dependent variable. If a significant interaction effect was found, a Tukey method *post-hoc* test was conducted to identify within-group changes over time. One-way ANOVA with repeated measures was performed to compare pre-, post-, 30 min- and 60 min-consumption values of the dependent variables in each group. Data were analyzed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA), and graphs were designed using GraphPad Prism (version 8, GraphPad Software, La Jolla, CA, USA). A priori statistical significance was set at $p \leq 0.05$.

3. Results

3.1 Peripheral and central hemodynamics

Table 2 shows the baseline and changes in the peripheral and central hemodynamics of the three groups before and after ED consumption. The baseline (pre-stage) hemodynamic characteristics were largely similar among the three groups; however, the central and peripheral systolic blood pressure (SBP) of the BD group were slightly higher than those of the two other groups. The peripheral SBP and diastolic blood pressure (DBP) measured immediately after ED intake markedly increased in the CON (at 60 min) and PA (post, 30 min and 60 min) groups throughout the time course. Consistently, the central SBP, DBP, and mean arterial pressure (MAP) profoundly increased in the CON and PA groups during the observation period. The central pulse pressure (PP) was significantly increased only in the PA group. However, noteworthy changes in peripheral and central hemodynamics were not found in the BD group compared with the baseline measurements.

TABLE 2. Time course of the changes in peripheral and central hemodynamics before and after ED consumption.

	Pre-Consumption	Post-consumption	30 min post-consumption	60 min post-consumption	*p*-value
Brachial SBP (mmHg)					
CON	117.9 ± 6.4	125.1 ± 7.1	124.8 ± 9.8	129.9 ± 10.4*	Time: 0.001†
PA	115.4 ± 7.5	127.6 ± 14.2*	141.4 ± 16.5*	128.3 ± 12.9*	Group: 0.043†
BD	130.3 ± 11.6	135.0 ± 12.6	138.8 ± 16.4	134.2 ± 16.2	Interaction: 0.004†
Brachial DBP (mmHg)					
CON	69.9 ± 5.6	75.1 ± 6.7	76.5 ± 7.3*	76.2 ± 6.2*	Time: 0.001†
PA	67.9 ± 11.2	74.6 ± 13.1	79.8 ± 11.8*	74.7 ± 8.8	Group: 0.970
BD	73.4 ± 8.0	73.2 ± 9.2	73.0 ± 9.4	74.8 ± 10.6	Interaction: 0.023†
HR (bpm)					
CON	64.9 ± 11.8	60.7 ± 10.2	64.0 ± 8.3	65.4 ± 8.9	Time: 0.007†
PA	61.9 ± 7.9	57.9 ± 6.3	62.7 ± 10.1	65.7 ± 12.5	Group: 0.804
BD	67.7 ± 11.8	62.6 ± 9.3	63.0 ± 8.0	65.1 ± 9.2	Interaction: 0.600
Aortic SBP (mmHg)					
CON	102.8 ± 6.4	109.6 ± 8.1	109.6 ± 8.1	113.0 ± 8.2*	Time: 0.001†
PA	101.4 ± 7.8	111.8 ± 13.1	123.4 ± 15.5*	110.8 ± 12.5	Group: 0.180
BD	113.2 ± 8.2	116.1 ± 9.9	117.4 ± 13.7	114.7 ± 13.1	Interaction: 0.001†
Aortic DBP (mmHg)					
CON	68.8 ± 11.5	75.1 ± 6.7	77.5 ± 7.1*	77.6 ± 6.1*	Time: 0.001†
PA	68.9 ± 11.1	74.6 ± 13.1	80.9 ± 12.1*	75.6 ± 9.0	Group: 0.998
BD	75.0 ± 8.3	73.2 ± 9.1	74.7 ± 10.1	76.6 ± 11.5	Interaction: 0.600
Aortic PP (mmHg)					
CON	32.0 ± 5.1	33.6 ± 6.1	32.1 ± 5.5	35.4 ± 7.9	Time: 0.014†
PA	32.6 ± 4.9	35.7 ± 7.3	42.6 ± 9.1*	37.4 ± 9.9	Group: 0.005†
BD	38.2 ± 6.1	42.1 ± 7.1	42.8 ± 6.5	38.1 ± 5.3	Interaction: 0.600
Aortic MAP (mmHg)					
CON	83.5 ± 5.9	88.8 ± 5.9	89.8 ± 7.1*	91.5 ± 6.6*	Time: 0.001†
PA	81.0 ± 9.9	89.2 ± 11.1*	97.8 ± 12.9*	89.3 ± 11.1*	Group: 0.862
BD	89.7 ± 8.2	89.9 ± 9.4	90.3 ± 12.7	91.1 ± 13.2	Interaction: 0.002†

*Data are mean ± standard deviation. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; PP, pulse pressure; MAP, mean arterial pressure; CON, control; PA, physically active; BD, bodybuilder. *$p < 0.05$ vs. pre-consumption; †significant interaction or main effect.*

3.2 Arterial stiffness, wave reflection, and endothelial function

Fig. 2 illustrates the arterial stiffness and endothelial vasodilatory function (represented by flow-mediated vasodilation; FMD) of the three groups at pre- and post-ED administration time points. cfPWV of the elite bodybuilders was considerably higher than that of the other counterparts at baseline. However, AIx, AIx@75, forward magnitude, reflection magnitude, reflected wave magnitude, and FMD did not differ among the groups at baseline and after ED consumption (Table 3, $p > 0.05$). These findings were consistent with our inference, which suggested that the supplementation and training regimens of elite bodybuilders might not alter the vascular remodeling and resting endothelial function at baseline and the subsequent time points after ED consumption. Shear stress-mediated endothelial vasodilation (FMD) was considerably enhanced across the time points after ED consumption compared with the pre-condition in the PA and BD groups, but this observation was not evident in the CON group. Changes in cfPWV from pre-consumption did not differ among the groups (Fig. 2C). However, the change in FMD from pre-consumption to 60 min was significantly higher in the BD group than in the other groups (post, CON: −0.6 ± 2.8%; PA: 2.2 ± 1.6%; BD: 6.6 ± 2.4%; $p < 0.001$, 30 min, CON: −1.0 ± 3.7%; PA: 2.6 ± 1.9%; BD: 4.2 ± 3.6%; $p < 0.001$, 60 min, CON: −1.8 ± 3.9%; PA: 1.5 ± 1.5%; BD: 2.4 ± 3.5%, $p = 0.002$, Fig. 2D).

4. Discussion

In this quasi-experimental design, the baseline and acute hemodynamic responses to consuming a commercially available

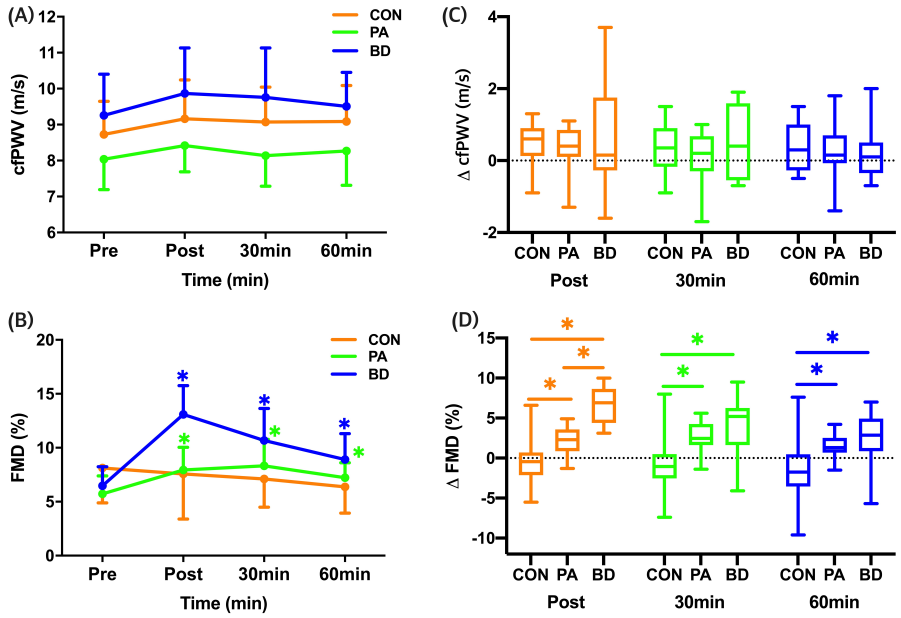

FIGURE 2. Time course of the changes in vascular responses before and after ED consumption. (A) Carotid-femoral pulse wave velocity, (B) flow-mediated dilation, (C) change in carotid-femoral pulse wave velocity from pre-consumption to post-consumption, 30 min post-consumption, and 60 min post-consumption, (D) change in flow-mediated dilation from pre-consumption to post-consumption, 30 min post-consumption, and 60 min post-consumption. All significant differences were preceded by a significant group × time interaction. *$p < 0.05$ compared with the pre-condition within groups or CON between groups. CON, control; PA, physically active; BD, bodybuilder; cfPWV, carotid-femoral pulse wave velocity; FMD, flow-mediated dilation.

TABLE 3. Time course of arterial stiffness indices before and after ED consumption.

	Pre-consumption	Post-consumption	30 min post-consumption	60 min post-consumption	*p*-value
AIx (%)					
CON	6.4 ± 9.4	5.6 ± 9.2	5.1 ± 8.4	4.3 ± 11.8	Time: 0.002†
PA	7.2 ± 5.9	8.7 ± 10.9	12.4 ± 10.3	2.3 ± 13.6	Group: 0.693
BD	8.3 ± 10.6	8.1 ± 11.3	2.6 ± 9.4	−1.0 ± 10.1	Interaction: 0.059
AIx@75 (%)					
CON	1.4 ± 9.5	−1.1 ± 9.2	−0.1 ± 9.3	−0.3 ± 11.6	Time: 0.037†
PA	1.1 ± 8.1	0.3 ± 10.5	6.2 ± 11.6	−2.4 ± 12.2	Group: 0.900
BD	4.8 ± 12.6	2.1 ± 11.7	−3.3 ± 10.8	−5.2 ± 10.5	Interaction: 0.043†
Forward wave magnitude (mmHg)					
CON	27.3 ± 4.7	26.4 ± 4.1	28.1 ± 5.7	29.3 ± 4.4	Time: 0.096
PA	31.6 ± 9.3	30.8 ± 5.4	32.7 ± 4.8	31.9 ± 5.2	Group: 0.009†
BD	29.1 ± 7.1	33.2 ± 7.4	38.3 ± 16.2	30.6 ± 6.2	Interaction: 0.205
Reflected wave magnitude (mmHg)					
CON	12.7 ± 3.2	12.7 ± 2.2	13.4 ± 3.0	13.5 ± 2.4	Time: 0.221
PA	14.6 ± 4.4	15.2 ± 2.9	15.8 ± 3.2	14.5 ± 2.9	Group: 0.035†
BD	15.4 ± 3.9	16.1 ± 3.7	16.2 ± 3.5	14.1 ± 3.6	Interaction: 0.551
Reflection magnitude (%)					
CON	46.5 ± 7.2	46.0 ± 13.0	47.8 ± 5.8	46.7 ± 6.2	Time: 0.168
PA	46.6 ± 6.1	49.4 ± 5.8	48.0 ± 5.0	45.5 ± 5.7	Group: 0.525
BD	53.2 ± 6.6	48.3 ± 5.1	48.5 ± 4.6	45.7 ± 5.3	Interaction: 0.133

Data are mean ± standard deviation. AIx, augmentation index; AIx@75, heart rate-corrected augmentation index. †significant interaction or main effect; CON, control; PA, physically active; BD, bodybuilder.

ED (including 160 mg of caffeine) were investigated in elite bodybuilders with habitual caffeine intake and compared with their counterparts. Although endothelium-dependent vasodilation was significantly improved after ED consumption at different time points in the PA and BD groups, central arterial stiffness was not altered in all groups. However, the central and peripheral SBP, DBP and MAP following ED administration increased in the PA and CON groups but not in the BD group.

Studies have comprehensively explored the effects of ED on cardiovascular health. Specifically, its effect on CVD and vascular function in healthy populations has been investigated using data on arterial stiffness and endothelial function parameters [11, 14, 17]. In the present study, the central and peripheral blood pressure after ED consumption in the PA and CON groups significantly increased with time, but these findings were not observed in the BD group. These results were consistent with previous findings, which showed that the BP at rest and during a cold pressor test considerably increased after healthy young adults consumed soft drinks [18]. A meta-analysis reported that ED intake ($\geq$200 mg of caffeine) significantly causes an acute increase in SBP and DBP by 4.4 and 2.7 mmHg, respectively [12]. However, similar to our findings on DBP that did not change at any time point in the BD group, the literature has some contradictory information on the immediate effects of EDs on DBP in healthy young women [19, 20]. Several trials have also reported unaltered DBP findings 60 min after ED consumption [21, 22]. Therefore, similar to previous studies, our research demonstrated that SBP and DBP significantly increased after ED intake in the CON and PA groups, but these parameters did not differ in the BD group. These findings are distinct because they include bodybuilders in the evidence showing the effect of ED on BP. They may also be consistent with previous results, which demonstrated that the caffeine intake of hypertensive individuals produces an acute increase in BP after 60 min [23]. These varying and controversial results could be attributed to confounding factors such as the use of different ED volumes and ingredients, the variability of study methods (*e.g.*, time points), and the demographic under investigation. Additionally, various methodological techniques, including sphygmomanometry and continuous beat-by-beat hemodynamic monitoring, were used in such investigations to measure blood pressure.

EDs cause an increase in cardiovascular morbidity and mortality [24, 25]. The risks of cardiovascular morbidity and mortality are independently increased by high arterial stiffness [26]. Arterial stiffness is determined by structural and physiological changes in arterial walls [27]. In the present study, which used an experimental design involving acute intervention, changes in the vascular structure after a single instance of ED intake were not expected. As such, we could propose several physiological rationales to elucidate why we did not observe any changes in arterial stiffness and/or wave reflection in all groups. First, transient elevations in blood pressure have the potential to induce arterial stiffness. Previous studies demonstrated that the acute consumption of coffee and ED leads to an increase in systolic blood pressure [28] and pulse wave velocity in healthy adults [29]. Thus, we expected that blood pressure would increase after ED consumption in our study. Partially consistent with previous results [29], our findings revealed that the central and peripheral blood pressure increased at various post-ED consumption time points in the CON and PA groups. However, we did not observe this pattern at any point following ED ingestion in the BD group. Although the factors contributing to such inconsistent blood pressure perturbations between groups are largely unclear, these inconsistencies could be attributed to the insufficient dosage of ED used in the current study; consequently, it failed to induce a pressor response in the BD group. In general, $>$90 mg of caffeine is associated with a persistent increase in blood pressure [30], while a dose of 250 mg or more leads to an increase in arterial stiffness [4, 31]. In our study, the participants consumed 160 mg of caffeine and other substances in 473 mg (16 oz) of Monster Energy [32]. Nevertheless, none of the previous studies were consistent with our findings that blood pressure did not increase in the BD group. Regarding this issue, the amounts (160 mg) of caffeine and other ingredients in ED in this study might be inadequate to affect hemodynamics significantly. This observation is particularly relevant considering that elite bodybuilders commonly consume $>$400 mg of caffeine daily (overdose; 10 mg/kg or 750 mg for an average person) [33]. Furthermore, the participants in the BD group were verified to regularly and habitually consume ED containing considerable doses of caffeine before and after their training sessions.

Second, arterial stiffness is independently linked to the activation of the sympathetic nervous system [34]. Caffeine is regarded as a drug that can stimulate the central nervous system [32]; as such, the increase in the heart rate is attenuated by a β-adrenoreceptor antagonist [35]. Moreover, sucrose, which is produced by the combination of glucose and fructose in Monster Energy beverages, increases the heart rate [36]. In the present study, the heart rate was slightly higher at 60 min post-consumption in the PA group, but it did not significantly change at any time point in all groups. Our results were consistent with previous evidence, which showed that the heart rate is not affected by caffeine consumption [37]; another study revealed that the heart rate and its variability (*e.g.*, high-frequency component) are significantly increased by caffeine ingestion [38]. However, studies have yet to clarify whether the consumption of ED with a combination of caffeine and sucrose triggers this sympathetic nervous activation of the heart rate. Thus, given that the heart rate of the groups did not change at any time points, direct and indirect evidence was insufficient to demonstrate substantial sympathetic activation after ED ingestion in our population. This lack of evidence was pertinent to the absence of remarkable changes in the central and peripheral arterial stiffness in response to ED intake in all groups. In line with cfPWV, AIx and wave reflection did not change after ED consumption in all groups. Given that AIx and wave reflection, which are determined by additional vascular and hemodynamic characteristics, are merely a proxy for vascular tone, the unchanged arterial stiffness did not correspond to AIx and wave reflection [4, 29].

Endothelial dysfunction refers to the mechanical impairment of the endothelium's ability by regulating vascular resistance. An impaired endothelial function is closely associated with atherosclerosis, coronary artery disease, and decreased ni-

tric oxide bioavailability [39]. Endothelial function is determined using a gold standard of measurement that involves the non-invasive method of vascular ultrasound for endothelium-dependent flow-mediated vasodilation [16]. However, previous studies showed inconsistent findings on the effect of EDs on endothelial function [39–41]. Higgins *et al.* [39] found that endothelial function worsens 90 min after young adults consume an ED, but another study showed that ED consumption improves endothelial function after 90 and 240 min [41]. Considering endothelial function, we demonstrated that the acute effects of ED consumption varied in terms of FMD. In the BD and PA groups, ED consumption favorably affected FMD, but opposite results were observed in the CON group. To our knowledge, this study is the first to reveal that endothelial function in elite bodybuilders could be improved after ED consumption.

As the main component of EDs, caffeine is a well-known vasoconstriction substance, which is an adenosine receptor antagonist. Adenosine is an adenosine triphosphate breakdown product that induces vasodilation in most vessels [42]. Although ED consumption did not change the FMD in the CON group, FMD responses to ED were significantly increased in the BD and PA groups. These results were consistent with previous findings showing that acute caffeine and ED ingestions increase endothelium-dependent vasodilation in healthy young adults [41, 43, 44]. Caffeine also targets vascular smooth muscle cells in the cardiovascular system, and the most commonly observed effect is a triggered intracellular Ca^{2+} (iCa^{2+}) concentration. The activation of ryanodine receptors in the sarcoplasmic reticulum, which also causes a transient contraction, is the initial mechanism by which the iCa^{2+} concentration increases [45]. However, caffeine increases endothelium-dependent vasodilation by promoting nitric oxide synthesis in the endothelium through the release of Ca^{2+} from the endoplasmic reticulum *via* the activation of the ryanodine-sensitive Ca^{2+} channel [46]. The "caffeine paradox" likely exists in the association of ED consumption with endothelial function [47]. Thus, we speculated that caffeine in ED stimulated vasodilation through endogenous nitric oxide production in the endothelium by releasing more Ca^{2+} in the PA and BD groups; otherwise, caffeine in ED triggered vasocontraction that increased the iCa^{2+} concentration in vascular smooth muscle cells.

Some of Monster's ingredients, alone or in combination, may ameliorate endothelial function probably because the amount of other components, which include nitric oxide donors such as taurine, niacin, ginseng, guarana and B-vitamins, is larger than that of caffeine in Monster [41]. For instance, taurine supplements may help the cardiovascular system by reducing oxidative stress [48]. In addition to caffeine, other components such as antioxidants in Monster beverages contributed to the increase in the FMD of the PA and BD groups. However, this finding remained questionable because the CON group might experience an unfavorable effect or not show any effect after ED consumption. As such, further studies should be performed to elucidate the detailed responses of ED ingredients and physical activity status.

The observed disparate effects of EDs on endothelial function can be attributed to strength training. In general, aerobic exercise enhances endothelial function by increasing shear stress on the endothelium during exercise [49]. However, strength training may increase hemodynamic stress because it causes excessive vascular tension and mechanical compression in blood vessels during strength exercise [5]. That is, vascular compression caused by resistance training deteriorates vascular endothelial function. Strength training may worsen endothelial function although several studies have found an increased endothelial function after strength training [50, 51]. The mechanical compression of resistance vessel walls during exercise, followed by blood flow release after exercise, results in a substantial increase in vessel wall shear stress [52]. This phenomenon is considered the most likely explanation for the enhanced endothelium-dependent vasodilation in strength training. Thus, to our best knowledge, bodybuilders who chronically undergo strength training may have a favorable dose response to ED in terms of endothelial function, potentially reflecting the elevated vascular reserve; they also largely consume caffeine, which may lead to caffeine tolerance. However, in the present study, these groups differently responded to acute ED consumption; further studies may elucidate the effects of ED on fitness level.

This investigation has limitations notwithstanding the nature of our study design. First, only male participants were included; thus, further research should be performed to determine whether or not these findings also apply to female participants. Second, we did not further identify the detailed mechanisms on how ED affected the vascular functions of vasoconstrictors and the sympathetic nervous system, including angiotensin II, endothelin-1 and catecholamine. Third, bodybuilding training may be divided into three seasons: off-season, pre-competition and competition [7]. We did not control the seasons because they differently focus on training, nutrient intake and mental stress. As such, this variation likely affected the results of this study. Fourth, we did not measure the effect of ED consumption on vascular function during resistance exercise. Further studies should be conducted on such subjects to observe any possible effects on vascular function. Lastly, even though we could not identify whether the acute effects of ED exhibited short- or long-term influence on cardiovascular events in bodybuilders, our findings could serve as preliminary details describing how such occurrences could be elucidated.

5. Conclusions

ED may induce favorable acute cardiovascular effects on the endothelial vasodilatory function of bodybuilders. However, after ED consumption, peripheral and central arterial stiffness (*e.g.*, cfPWV) did not change in all groups, whereas peripheral and central blood pressures significantly increased in all groups except elite bodybuilders. Further research should be performed to evaluate the vascular function of individuals with more chronic exposures to EDs.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

AUTHOR CONTRIBUTIONS

WP and KH—designed the research study and wrote the manuscript. DL and HJB—performed the research and analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All participants in this study were informed about the experimental procedures before they provided their written consent. Protocols and informed consent forms were approved by the Institutional Review Board of Chung-Ang University in South Korea (1041078-202107-HRSB-233-01). All study procedures were performed in compliance with the Declaration of Helsinki.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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