Autoregulated and Non-Autoregulated Blood Flow Restriction on Acute Arterial Stiffness

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ABSTRACT
This study aimed to investigate the acute effects of autoregulated and non-autoregulated applied pressures during blood flow restriction resistance exercise to volitional fatigue on indices of arterial stiffness using the Delfi Personalized Tourniquet System. Following a randomized autoregulated or non-autoregulated blood flow restriction familiarization session, 20 physically active adults (23 ± 5 years; 7 females) participated in three randomized treatment-order sessions with autoregulated and non-autoregulated and no blood flow restriction training. Participants performed four sets of dumbbell wall squats to failure using 20% of one repetition maximum. Blood flow restriction was performed with 60% of supine limb occlusion pressure. Testing before and post-session included an ultrasonic scan of the carotid artery, applanation tonometry, and blood pressure acquisition.

Carotid-femoral pulse wave velocity increased in the non-autoregulated and no blood flow restriction training groups following exercise while carotid-radial pulse wave velocity increased in the no blood flow restriction training group (all p < 0.05). Carotid-femoral pulse wave velocity exhibited an interaction effect between autoregulated and non-autoregulated blood flow restriction in favor of autoregulated blood flow restriction (p < 0.05). Autoregulated blood flow restriction training does not influence indices of arterial stiffness while non-autoregulated and no blood flow restriction training increases central stiffness.
Introduction

Low-load resistance exercise with blood flow restriction (BFR) is becoming increasingly employed in rehabilitation [1] because of the similar musculoskeletal benefits it confers compared to traditional heavy load strength training, including muscle hypertrophy [2] and strength [3]. However, despite BFR’s growth as an alternative exercise approach, there are still concerns regarding its safety profile [4, 5].

While peripheral hemodynamics (i.e. brachial BP measures) have been a focus of research in elucidating the safety profile of BFR resistance exercise, less is known regarding the central hemodynamic responses (i.e. aortic BP and stiffness measures). A recent systematic review [6] highlighted significant heterogeneities that exist in the limited body of literature in this area, including differences in BFR prescriptive factors and repetition schemes, as well as the absence of the “gold standard” pulse wave velocity (PWV) assessment, for arterial stiffness in acute resistance exercise investigations. PWV measures the difference in time delay of the systolic waveform between a central (i.e. aorta) and peripheral (i.e. radial or tibial artery) site and provides a measure of stiffness associated with the central and peripheral arterial apparatus, respectively [7]. Significantly stiffer arteries may predispose exercisers to a higher risk of cardiovascular events [7] during acute bouts of exercise. Of potential significance are that daily transient increases of arterial stiffness in aggregate can elevate the risk for CVD [8]. In addition, there is evidence acute reductions in arterial stiffness can lower risk of cardiovascular disease and mortality [9], emphasizing the importance of continual investigations.

Evidence indicates that chronically elevated PWV independently predicts the presence of cardiovascular risk factors (i.e. atherosclerosis) and hypertension [7], as well as morbidity and mortality [10]. As such, it is prudent to understand the impact that an acute resistance exercise session with BFR may play on PWV, particularly as BFR is becoming more utilized in populations with hypertension [11], obesity [12] and heart failure [13].

While research on PWV appears to indicate a deleterious effect on health when chronically elevated, acute measures of central arterial stiffness (including PWV) following resistance exercise appear to vary based on whether the exercise was performed with the upper or lower body [14], the contraction type (i.e. concentric versus eccentric) [15], the repetition scheme used [16], the exercise cadence employed [17], and the load used (i.e. 30% 1-rep max versus 70–80% 1-rep max) [18]. Arterial stiffness measures tend to increase acutely post-resistance exercise and a rule of thumb is that chronic PWV elevations of 1 m/s increases all-cause mortality [19], although the relative importance of acute increases is less established, particularly in the BFR literature. Therefore, understanding the impact of resistance exercise with BFR on acute measures of arterial stiffness is important but is currently understood.

As BFR becomes more widely implemented in different practice settings [1], the availability of BFR equipment for consumer purchase has increased. However, there is a dearth of research available on the different types of BFR devices used, as well as features marketed to enhance its safety, tolerability, and/or efficacy during application [20]. One of those features is autoregulation of applied BFR pressures, whereby the applied pressure to the exercising limb from the BFR cuff is kept relatively constant compared to a manually inflatable (non-autoregulated) cuff that does not adjust and, therefore, may heighten cardiovascular and perceptual exercise responses [21]. Autoregulation of applied pressures is likely of practical importance due to the interaction of the cuff and the underlying musculature, as well as its potential impact on modulating acute exercise-related responses. In the concentric portion of the exercise, the cross-sectional area of the limb enlarges as the muscle fibers within shorten. Under non-autoregulated conditions, the diameter of the cuff does not change during the concentric phase, theoretically creating greater pressures inside the limb. Autoregulated BFR devices accommodate for increases in limb diameter during the concentric phase, and may afford similar limb pressures in both phases of muscular contraction [21]. Studies using cuffs capable of autoregulation of applied BFR pressures have been implemented in healthy [22] and clinical populations [23]. Conversely, cuffs that are unable to autoregulate have also been used in healthy [24] and clinical populations [25]. Both forms of pressure regulation appear to be safe [5], but it is currently unknown whether autoregulation further enhances the safety profile and tolerance of BFR exercise compared to non-autoregulated pressure application, as well as impact measures of performance.

A recent study highlighted the potential for autoregulation of applied BFR pressures to enhance the safety of BFR exercise compared to non-autoregulated cuff applications. Jacobs et al. [26] showed a near 3x risk reduction in minor adverse events (i.e. light-headedness) in the autoregulated compared to the non-autoregulated cuff condition when performing the same exercise series. This study provided the first direct evidence that autoregulation may enhance the acute safety profile of BFR exercise. However, the hemodynamic (i.e. brachial blood pressures) and perceptual responses (i.e. rate of perceived exertion/discomfort) to exercise between conditions were largely the same, indicating the influence of other factors not measured. A potential factor may be acute changes in central arterial stiffness. It is important to also note a majority of BFR devices on the market today do not have the ability to autoregulate, but the impact of blood flow restriction on central stiffness has yet to be investigated. Thus, much is unknown regarding the impact of autoregulation of applied pressures on arterial stiffness.

This study aimed to assess the acute impact of autoregulation of applied pressures on arterial stiffness in a cohort of healthy, physically active adults during wall squat exercise to volitional fatigue. In accordance with the results from previous studies using both types of pressure regulation during BFR exercise that promote similar long-term musculoskeletal benefits, we hypothesized that differences in acute measures of arterial stiffness would be observed between the autoregulated and non-autoregulated BFR cuff conditions, and autoregulated and low-load resistance exercise without BFR.

Materials and Methods

Participants

Twenty-five physically active males and females were recruited at an institution affiliated with one of the authors via a flyer and email outreach. Each female participant served as their own control and
their phases of menstrual cycle followed normal patterns and were not controlled throughout the study period. Previous investigations have concluded variations in menstrual phases and use of hormonal contraceptives have little to no influence on indices of arterial stiffness (our primary outcome measure) [27–29]. Physically active was characterized as consistently exercising for greater than 6 months of ≥ 1,000 MET/min/week. Participants were initially screened for study eligibility (Table 1) and, if they met inclusion criteria and did not display any exclusion criteria, they were scheduled for a familiarization session. None of the participants reported tobacco use, however, potential exposure to secondhand smoke was not controlled. Each participant signed an informed consent document in accordance with the Declaration of Helsinki acknowledging potential risks and harms.

### Study design

This intervention assessed differences in arterial stiffness following lower body blood flow restriction (BFR) in exercise performed to volitional fatigue using two different applied pressure settings (autoregulated [AR-BFR] versus non-autoregulated [NAR-BFR]) in a sample of healthy, physically active participants. In this crossover, randomized-controlled study, each participant reported to the lab for four sessions. During the initial session (familiarization), each participant was randomized to AR-BFR or NAR-BFR using a randomization software (www.random.org/lists) and the exercise protocol was performed without assessing outcomes. Following the familiarization session, each participant was randomized into AR-BFR, NAR-BFR or No-BFR by the same software and performed the identical exercise protocol as in the familiarization session (Fig. 1), and the outcome variables were assessed.

Each session was separated by at least 7 days to reduce the potential impact on exercise recovery and from soreness [30]. Participants were instructed to avoid caffeine and alcohol for 24 hours, and fully void before all sessions. They were advised to continue their normal training activities while avoiding exercise-related activities 24 hours before each session, including the familiarization session. All testing occurred within ± 1 hour week-to-week to minimize diurnal variations in responses. Measurements were conducted in the Exercise Physiology Research Lab at an institution affiliated with one of the authors after a 4-hour fast between 06:00 to 12:00 hours. Ambient temperature was set at 21°C (70°F) for all testing sessions. The study was approved by the institutional ethics committee.

### Testing protocol

Initially, participants had their one repetition maximum (1-RM) determined and then underwent a familiarization session to acclimate them to the sequencing of data collection and the BFR stimulus. In all sessions, four sets to volitional fatigue of dumbbell wall squats were performed using ~20% 1-RM (to the nearest 5-pound increment) with (AR-BFR) or without (NAR-BFR) autoregulation of applied pressures, in addition to a No-BFR condition. Dumbbells were held with arms fully extended and the shoulder flexed at 0°. Due to the synthetic ice pad (Snipers Edge, Minneapolis, MN) mounted on the wall, drag was minimized during the upward and downward phase of each repetition. Rest between sets was 1 minute. Cadence was monitored via a metronome (Seiko, Mahwah, NJ) for a 2-sec concentric and a 2-sec eccentric phase, with range of motion set to 90° of knee flexion at the bottom and full extension at the top. Volitional fatigue for each set was determined as the inability to perform the technique to specifications (i.e. maintaining back flat against the wall), inability to maintain appropriate cadence, and/or desire to stop. A verbal warning was given upon the first technique violation, and then the set was stopped with a second violation.

Ultrasoundography of the carotid artery, applanation tonometry, and BP acquisition were completed before and 10 minutes post-exercise for all training sessions when the cuffs were not inflated. We selected 10 minutes post-exercise due to feasibility and that a recent meta-analysis concluded data collection periods between 0–14 minutes post-exercise yield similar PWV values [31]. Rate of perceived exertion (RPE), rate of perceived discomfort (RPD), and a subjective measure of participant enjoyment of the session were assessed immediately post-exercise in all training sessions while cuffs were inflated, as well as adverse events monitored. In addition, total training volume and repetitions were recorded for all trials (Fig. 2).

### BFR settings – autoregulation and limb occlusion pressure

For the AR-BFR or NAR-BFR familiarization and BFR exercise trials, two 11.5 cm variable contour pneumatic BFR cuffs (Delfi Personalized Tourniquet Systems, Vancouver, Canada) were placed around the most proximal portion of each thigh. Following a 10-min supine rest, limb occlusion pressure (LOP) was determined in the supine position and subsequently set at 60% LOP for the duration of exercise in accordance with practice recommendations [32] and within the pressure recommendations of a recent paper [33] that indicate a positive impact in reducing repetitions to fatigue in comparison with load-matched free-flow exercise. We acknowledge that there is a body of growing evidence indicating that LOP changes as a function of position (supine < sitting < standing in the legs) [34, 35]. However, to the authors’ knowledge, no study exists indicating that the differences in %LOP significantly influence the acute responses to BFR exercise when obtained in the position of exercise (i.e. standing) or in another position (i.e. supine or sitting). Thus, we elected to assess LOP in supine to increase reliability and align with most of the published literature on BFR exercise.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tr>
<td>• Age 18-40 years old</td>
<td>• Resting BP &gt; 140/90 mmHg</td>
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<tr>
<td>• Physically active (&gt; 6 months) of ≥ 1,000 MET/min/wk</td>
<td>• BMI &gt; 40 kg/m2</td>
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<tr>
<td>• Weight stable for previous 6 months (± 2.5 kg)</td>
<td>• Recent surgery (&lt; 2 months)</td>
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<tr>
<td>• Female subjects reported regular menstrual cycles for the last 2 years</td>
<td>• Past or current history of CHD, stroke, or major CVD events. Reported sleep apnea.</td>
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<td>• Active renal or liver disease</td>
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To minimize potential discrepancies, each participant used 34-inch length cuffs. The Delfi Personalized Tourniquet device has been previously validated for its accuracy in determination of LOP compared to doppler ultrasound [36] and has the capacity to adjust the applied pressure (i.e., autoregulate) and cuff diameter to the exercising limb to maintain a relatively consistent pressure despite changes in muscle volume during exercise [21]. Furthermore, it has been shown to be the only commercially available BFR device capable of maintaining set-interface pressure during BFR exercise compared to four other BFR devices [37]. Conversely, during NAR-BFR training, the cuff diameter does not adjust to the phase of muscle contraction during exercise, possibly increasing cuff pressure on the limb above 60% LOP. NAR-BFR was performed by enabling a function that disabled autoregulation of applied pressures while the cuff was still tethered to the device with an air tube. BFR was applied continuously in both conditions, inflating prior to the first set, and deflating after completion of the 4th set following subjective assessments. Total time under tension was recorded for both BFR sessions. Participants were blinded to the presence of autoregulation for all trials but were not blinded when exercising in the No-BFR condition as no cuffs were applied to the exercising limbs. A No-BFR training session utilizing the same failure scheme and load but without the pneumatic cuffs applied to the legs was also performed in a randomized order.

Fig. 1 Schematic of study protocol. AR-BFR, Autoregulated BFR pressures; NAR-BFR, Non-autoregulated BFR pressures; No-BFR, Low-load exercise without BFR.

Fig. 2 Schematic of all treatment sessions. SBP, systolic blood pressure; DBP, diastolic blood pressure; RPE, rating of perceived exertion; RDP, rating of perceived discomfort; Perform again, 10-point Likert scale assessing desire to perform exercise again; HR, heart rate; RPP, rate pressure product.
Familiarization session

A maximal dumbbell wall squat strength test (one-repetition maximum, 1-RM) was completed prior to the familiarization session in the recreational center at an institution affiliated with one of the authors in accordance with the guidelines from the National Strength and Conditioning Association [38], All 1-RMs were determined within five attempts. Afterward, participants walked to the laboratory and sat quietly with legs uncrossed for 10 minutes prior to seated BP measurements following standard guidelines [39]. Height, weight and body composition assessment followed. Participants then rested supine on the examination table for 10 minutes. Lastly, carotid ultrasound scans and arterial tonometry were performed, which completed all pre-training assessments. For all central arterial and peripheral assessments, the examiners were not blinded to the group condition due to limitations in personnel. Participants were then provided instructions on RPE, RPD, and shown a 1–10 Likert scale assessing likelihood of performing the training again during the familiarization session. The RPE scale ranged from 0 “no exertion” to 10 “maximal effort” and participants were cued with the same question, “How hard do you think you’re working?” every time before answering. Similarly, the RPD scale ranged from 0 “no discomfort” to 10 “maximal discomfort” and participants were asked “How much discomfort do you feel?” every time before responding. Participants were informed that these would be assessed immediately post-exercise during sessions 2–4. Each participant was then randomized into AR-BFR or NAR-BFR and performed the exercise protocol as described above.

Outcome measures

Anthropometrics

Total body mass and height were measured during the familiarization session on a medical scale and stadiometer (Detecto 439 Physician Beam Scale) accurate to ± 0.1 kg and stadiometer between 0600 and 1200 after a void and 4-hour fast. Participants wore standard shorts and t-shirts at the time of weighing. Air displacement plethysmography (BOD POD) (Cosmed Metabolic Company, Rome) measured fat and fat-free body mass. Participants wore tight clothing and sat quietly inside the BOD POD during three sequential measurements.

Brachial Blood Pressure

Seated and supine brachial BP measurements were taken under quiet, ambient (~21°C) conditions. All BP measurements adhered strictly to American Heart Association guidelines [39]. After a 5–10 minute rest period, both seated and supine measurements were auscultated from the right brachial artery using an automated sphygmomanometer (Welch, Allyn, New York). Systolic (SBP) and diastolic (DBP) BPs were recorded every 2 minutes, and average SBP and DBP readings were tabulated using 3 sequential measurements within 6 mmHg of each other.

Carotid Artery Ultrasonography

A doppler ultrasound machine probe (Terason T3300, Burlington, MA) was placed approximately 2 cm distal from the carotid bulb after a 10-min supine rest. Longitudinal B-mode images of the right common carotid artery were recorded in 10-sec increments and measured manually offline. The distance between the apical surface of the tunica media of the near and far wall was used to determine systolic (maximal) and diastolic (minimal) diameters. Three measurements of the systolic and diastolic diameters were recorded and averaged.

Arterial Applanation Tonometry and Pulse Wave Velocity

Using a high-fidelity transducer (Complior Analytic Tonometer, Alam Medical, Vincennes, France), right carotid arterial pressure waveforms and amplitudes were recorded after a 10-min supine rest. The right brachial supine SBP and DBP (explained above) and carotid waveforms were used to equate carotid SBP (cSBP), DBP (cDBP) and mean arterial pressure (cMAP) through a proprietary transfer function. All tonometry recordings were taken by the same experienced researcher with excellent reproducibility (r > 0.90; p < 0.05) for β-stiffness, PWV and arterial compliance (AC).

Detailed procedures on PWV have been described elsewhere [40]. Briefly, after a 10-min supine rest for conventional steady state conditions, three high-fidelity tonometers (Complior Analytic Tonometer, Alam Medical, Vincennes, France) simultaneously recorded and averaged 10 waveforms from the right side carotid site lateral from the laryngeal prominence, radial site distal of the scaphoid bone, and the femoral site at the most proximal portion of the leg distal from the inguinal ligament. Distances between the arterial sites were measured in the supine position with a caliper to the nearest 0.5 cm. Carotid-femoral PWV (CF-PWV) and carotid-radial PWV (CR-PWV) were calculated by dividing the distance between arterial sites by the foot-to-foot time delay between arterial waveforms (PWV = D (m)/Δt (sec)).

β-Stiffness Index and Arterial Compliance

β-stiffness is an index of arterial stiffness, capturing the nonlinear relationship between pressure and diameter independent of acute changes to BP [7]. A detailed explanation of the procedure can be found elsewhere [7]. Briefly, it was calculated as $\beta = \ln(SBP/DBP)/(\text{systolic diameter-diastolic diameter)/diastolic diameter}$ and expressed in arbitrary units. Carotid systolic and diastolic diameters, cSBP and cDBP, were factored in the β-stiffness calculations. Arterial compliance (AC) is an index of arterial stiffness and is sensitive to acute BP changes (29). AC was calculated as (π(systolic diameter2 - diastolic diameter2) ÷ 4(sBP-DBP)) using carotid diameters and pressures [7].

Perceptual Experience Assessments

Immediately following completion of the final set and with the cuffs still inflated, participants were requested to provide their rate of perceived exertion (RPE) and rate of perceived discomfort (RPD), and were asked to rate the likelihood that they would perform the same exercise again. Participants were asked to anchor their response based on the entire exercise session. Three 8-inch x 10-inch charts were held in front of the participant by the same administrator in the following order: RPE, RPD and a 1–10 Likert scale. RPE and RPD scales were read to the participant in accordance with a previous validation study [41]. Likelihood to perform this exercise again was assessed with the question “on a scale of 1–10, how likely would you perform the same exercise again? 10 being very likely and 0 being not likely at all.” Participants were asked to report any adverse responses in conjunction with the performance of each
exercise bout. Any responses gathered were classified according to a recently published review [5].

Statistical analysis

G Power (Kiel University, Germany) software 3.1.9.7 calculated a sample size of 20 participants using repeated measures analysis of variance (ANOVA) at α = 0.05 & β = 0.80 to detect an effect size of 0.35 [42]. The power calculation is based on data from Stanford et al. [43] using central SBP over time as the dependent variable and it was determined that twenty participants were required for a moderate effect size. To account for the expected attrition rate of 20%, 25 participants 18–40 years of age and racial and ethnic backgrounds meeting the inclusion and exclusion criteria (Table 1) were recruited for the study. Statistical Package for the Social Sciences (IBM SPSS version 28, SPSS Inc., Chicago IL) was used for both descriptive and inferential statistical analyses. Shapiro-Wilk test was performed on variables to assess distribution patterns. Paired samples t-tests assessed baseline (i.e., before treatment) differences. A 3 (group) x 2 (time) two-way ANOVA was used to examine the effects of treatment and the treatment-order interaction on variables of interest. The Greenhouse-Geisser correction was used when there was failure to meet assumptions of sphericity. Post hoc analysis (Tukey HSD) was performed on variables with significant F-ratios. Findings with a p < 0.05 were considered significant, and all data are presented in means ± standard deviation (SD) unless otherwise stated. Effect sizes were reported as Cohen’s d and were defined as: 0.2, small; 0.5, moderate; and ≥ 0.8, large [44].

Results

Participants

Participant characteristics are listed in Table 2. Thirteen males and 7 females completed the study. Attrition of five participants occurred for various reasons, including time constraints, missed appointments, acute illness, and loss of contact but not from BFR (Fig. 1). No injuries or adverse events related to the treatments were reported. There were no significant baseline differences recorded in pre-testing during the familiarization period in arterial stiffness, cardiovascular (Table 3), or performance (Table 4) variables among any of the randomized sessions.

Hemodynamics

Several hemodynamic changes were identified (Table 3). As relative changes (pre- to post-) were similar to absolute changes (pre- to post-), we elected to report only relative changes between conditions in our Table. Central SBP increased (mean difference (MD) = 7 ± 12 mmHg, 95% confidence interval (CI) (2–13), p = 0.004, effect size (ES) = 0.65), central pulse pressure (PP) (MD = 7 ± 12 mmHg, 95% CI (1–13), p = 0.012, ES = 0.55), and central mean arterial pressure (MAP) (MD = 3 ± 7 mmHg, 95% CI (1–6), p = 0.029, ES = 0.45) in No-BFR. Compared to AR-BFR, HR, SBP, and rate pressure product (RPP) were significantly higher immediately following exercise in NAR-BFR (MD HR: 8 ± 12 bpm, p = 0.01, 95% CI (2–13), ES = 0.63; MD RPP: 1297 ± 1973 au, p = 0.01, 95% CI (373–2219), ES = 0.66), and No-BFR (MD HR: 8 ± 14 bpm, 95% CI (2–14), p = 0.01, ES = 0.58; MD SBP: 6 ± 9 mmHg, 95% CI (1–10), p = 0.01, ES = 0.58; MD RPP: 1773 ± 2074 au, 95% CI (819–2726), p < 0.01, ES = 0.87) (Fig. 3 and 4). All groups experienced a significant increase in supine heart rate (HR) and RPP following treatment (all p < 0.05). Additionally, NAR-BFR and No-BFR experienced a significantly greater increase in supine HR (MD NAR-BFR: 4 ± 9 bpm, 95% CI (1–8), p = 0.046, ES = 0.41; MD No-BFR: 7 ± 9 bpm, 95% CI (3–11), p = 0.002, ES = 0.79) and supine RPP (MD NAR-BFR: 560 ± 1215 au, 95% CI (26–1146), p = 0.030, ES = 0.46; MD No-BFR: 1066 ± 1391 au, 95% CI (396–1736), p = 0.002, ES = 0.76) compared to AR-BFR.

Arterial stiffness measures

Following the intervention, CF-PWV significantly increased in NAR-BFR (MD = 0.57 ± 1.12 m/s, 95% CI (0.05–1.09), p = 0.017, ES = 0.51) and No-BFR (MD = 0.63 ± 1.42 m/s, 95% CI (0.04–1.43), p = 0.032, ES = 0.44) (Table 3). Compared to AR-BFR, NAR-BFR experienced a greater increase in CF-PWV (MD = 0.70 ± 1.60 m/s, 95% CI (0.05–1.44), p = 0.034, ES = 0.43) (Table 3). CR-PWV significantly decreased after the intervention in No-BFR (MD = −0.82 ± 1.51 m/s, 95% CI (0.09–1.54), p = 0.015, ES = 0.54). No statistical differences were detected in β-stiffness and AC (Table 3) (all p > 0.05) with the interventions.

Performance

Total reps and training volume were significantly lower in AR-BFR (reps: −29.6 ± 13.9, 95% CI (-23.11–36.08), p < 0.01, ES = 2.13; volume: −1331 ± 855, 95% CI (-931–1731), p < 0.01, ES = 1.55) and NAR-BFR (reps: −31.0 ± 17.9, 95% CI (-22.59–39.40), p < 0.01, ES = 1.73; volume: −1426 ± 999, 95% CI (-958–1893), p < 0.01, ES = 1.42) compared to No-BFR (Table 4). Time under tension was not different between BFR conditions (452 ± 87 vs. 444 ± 74 s in AR-BFR and NAR-BFR, respectively). RPD was significantly greater in AR-BFR (1.2 ± 1.4, 95% CI (0.31–1.9), p < 0.01, ES = 0.86) and NAR-BFR (1.6 ± 1.3, 95% CI (1.0–2.2), p < 0.01, ES = 1.2) compared to
**Table 3** Arterial stiffness, central hemodynamics and muscle swelling responses pre- and post-intervention. Values expressed as mean ± SD; C, carotid; R, radial; F, femoral; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; β-SI, β stiffness index; AC, arterial compliance; HR, heart rate; RPP, rate pressure product. *P<0.05 Within Group; †P<0.05 Between Group Effect with AR-BFR.

<table>
<thead>
<tr>
<th>Variable</th>
<th>AR-BFR PRE</th>
<th>AR-BFR POST</th>
<th>NAR-BFR PRE</th>
<th>NAR-BFR POST</th>
<th>No-BFR PRE</th>
<th>No-BFR POST</th>
<th>Baseline Difference p values</th>
</tr>
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<tbody>
<tr>
<td>CF-PWV, m/s</td>
<td>7.05±1.40</td>
<td>7.12±1.43</td>
<td>7.12±1.15</td>
<td>7.69±1.65†</td>
<td>6.87±1.04</td>
<td>7.51±1.41‡</td>
<td>0.757</td>
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<tr>
<td>CR-PWV, m/s</td>
<td>9.33±3.07</td>
<td>8.33±2.66</td>
<td>9.35±2.50</td>
<td>9.33±2.51</td>
<td>8.91±1.74</td>
<td>8.36±2.18*</td>
<td>0.775</td>
</tr>
<tr>
<td>Central SBP, mmHg</td>
<td>117±15</td>
<td>119±16*</td>
<td>117±15</td>
<td>119±14*</td>
<td>115±12</td>
<td>122±13*</td>
<td>0.629</td>
</tr>
<tr>
<td>Central DBP, mmHg</td>
<td>67±8</td>
<td>65±9</td>
<td>67±8</td>
<td>67±11</td>
<td>67±8</td>
<td>68±9</td>
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<tr>
<td>Central PP, mmHg</td>
<td>50±12</td>
<td>54±13*</td>
<td>50±15</td>
<td>53±13</td>
<td>48±12</td>
<td>55±13*</td>
<td>0.641</td>
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<tr>
<td>Central MAP, mmHg</td>
<td>83±9</td>
<td>83±10</td>
<td>84±8</td>
<td>84±10</td>
<td>83±8</td>
<td>86±9*</td>
<td>0.713</td>
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<tr>
<td>β-SI, U</td>
<td>6.02±2.04</td>
<td>5.42±1.44</td>
<td>5.99±2.31</td>
<td>5.85±1.60</td>
<td>6.45±2.33</td>
<td>6.08±2.93</td>
<td>0.738</td>
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<tr>
<td>AC, mm²/mmHg x 10⁻¹</td>
<td>1.41±0.40</td>
<td>1.41±0.44</td>
<td>1.44±0.68</td>
<td>1.30±0.38</td>
<td>1.31±0.42</td>
<td>1.38±0.58</td>
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<tr>
<td>Supine SBP, mmHg</td>
<td>121±10</td>
<td>128±12*</td>
<td>121±8</td>
<td>129±15*</td>
<td>122±9</td>
<td>131±12*</td>
<td>0.629</td>
</tr>
<tr>
<td>Supine DBP, mmHg</td>
<td>67±8</td>
<td>65±9</td>
<td>67±8</td>
<td>67±11</td>
<td>67±8</td>
<td>68±9</td>
<td>0.840</td>
</tr>
<tr>
<td>Supine PP, mmHg</td>
<td>55±7</td>
<td>63±10*</td>
<td>54±8</td>
<td>63±10*</td>
<td>55±9</td>
<td>63±12*</td>
<td>0.791</td>
</tr>
<tr>
<td>Supine MAP, mmHg</td>
<td>85±8</td>
<td>86±9</td>
<td>85±7</td>
<td>87±11</td>
<td>85±7</td>
<td>89±9*</td>
<td>0.642</td>
</tr>
<tr>
<td>Supine HR, bpm</td>
<td>63±9</td>
<td>79±13*</td>
<td>65±10</td>
<td>83±12*‡</td>
<td>62±11</td>
<td>85±13*‡</td>
<td>0.316</td>
</tr>
<tr>
<td>Supine RPP, au</td>
<td>7409±1426</td>
<td>9474±1966*</td>
<td>7625±1156</td>
<td>9910±1766‡</td>
<td>7051±1026</td>
<td>10415±1749*‡</td>
<td>0.070</td>
</tr>
</tbody>
</table>

**Table 4** Reps, repetitions; TUT, time under tension; RPE, rating of perceived exertion; RDP, rating of perceived discomfort; Perform again, 10-point Likert scale assessing desire to perform exercise again. †P<0.05 Between difference with No-BFR.

<table>
<thead>
<tr>
<th>Variable</th>
<th>AR-BFR</th>
<th>NAR-BFR</th>
<th>No-BFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Reps</td>
<td>53±20†</td>
<td>52±17‡</td>
<td>83±27</td>
</tr>
<tr>
<td>Volume</td>
<td>2436±1263</td>
<td>2341±1020</td>
<td>3767±1771</td>
</tr>
<tr>
<td>TUT, sec</td>
<td>452±87</td>
<td>444±74</td>
<td>N/A</td>
</tr>
<tr>
<td>RPE</td>
<td>8.2±0.8</td>
<td>8.5±1.0</td>
<td>8.2±1.2</td>
</tr>
<tr>
<td>RPD</td>
<td>6.2±2.3</td>
<td>6.6±2.2</td>
<td>5.0±2.4</td>
</tr>
<tr>
<td>Perform again</td>
<td>6.85±2.39</td>
<td>6.95±2.61</td>
<td>7.50±2.50</td>
</tr>
</tbody>
</table>

No-BFR (►Table 4). RPE and the 1–10 Likert scale assessing the likelihood of performing the training again was not different between any conditions (all p>0.05).

**Discussion**

This is the first study to examine the acute responses between AR-BFR, NAR-BFR, and No-BFR exercise on arterial stiffness changes in a lower body resistance protocol to volitional fatigue using a frequently studied BFR training device in healthy, physically active adults. The main findings are (1) AR-BFR blunts exercise-induced central arterial stiffness compared to NAR-BFR and No-BFR, and (2) no differences were observed between perceptual outcomes or volume performed between AR-BFR and NAR-BFR; however, both produced greater discomfort than No-BFR.

**Arterial stiffness, central and peripheral hemodynamics**

AR-BFR blunted the increase in CF-PWV compared to NAR-BFR 10 minutes post-exercise with between-group differences of ~0.70 m/s with a small to moderate effect. We also observed that No-BFR increased CF-PWV 0.63 m/s, although between-group differences with AR-BFR did not reach significance. In addition, supine RPP following exercise was elevated in both NAR-BFR and No-BFR trials above AR-BFR, indicating heightened myocardial workload [45]. We also observed negligible or no between-group differences in central hemodynamics (central SBP/DBP/PP/MAP) and changes in β-stiffness or AC. Explaining the potential reasons why these results may have occurred is challenging, and likely not due to performance or perceptual-related factors, as total volume, time under tension, and RPE/RPD were similar between BFR conditions. Moreover, the increase in post-exercise CF-PWV occurred in No-BFR, where participants performed ~34% more volume, lowering the likelihood that volume modulates the CF-PWV response. There may be a post-exercise temporal buffering effect on central stiffness with the autoregulation feature as it is designed to accommodate...
Ever, we believe our measurement site (i.e. femoral artery) is more suitable for capturing central stiffness changes due to its proximal location compared to the radial artery assessment in the upper extremity. Future studies are needed to clarify the possible influence of thigh cuffs on arterial stiffness in the leg. As this was the first study of its kind, no direct comparisons can be made with the existing body of BFR literature.

Prior research has hypothesized that the acute increases in central stiffness markers following high-intensity resistance exercise may be due to the unique hemodynamics of strenuous exercise [46]. Pierce et al. [46] proposed that large fluctuations in BP and the use of the Valsalva maneuver mechanically compress the vasculature, leading to a heightened pressor response and acute stiffening of the arteries. However, over time (i.e. weeks to months), the central arterial apparatus adapts, leading to negligible changes in central stiffness [18]. Nonetheless, while the relevance of the magnitude of acute changes in CF-PWV speeds are uncertain, the current body of evidence indicates that changes of +1 m/s increase age, sex and risk-factor adjusted cardiovascular events, mortality, and all-cause mortality between 14–15% [47]. As our study evidenced acute increases of 0.6–0.7 m/s in both NAR-BFR and No-BFR, practitioners seeking to minimize adverse events during BFR exercise may choose AR-BFR, as it prevented increases in central arterial stiffness. While the values we report do not exceed what is currently known to be associated with cardiovascular disease (+1 m/s), those looking to reduce central stiffness may opt for AR-BFR, as it mitigated any observable increase in CF-PWV. Although it is important to note that no adverse events were recorded in any group throughout our entire study, necessitating further research on the potential relevancy of our findings, particularly in at-risk populations.

**Performance, perceptual responses and safety**

In this study, AR-BFR and NAR-BFR did not display differences in any of the performance or perceptual measurements assessed. Both displayed similar total repetitions, volume, time under tension, RPE, and RPD. In comparison, No-BFR performed significantly more repetitions and total volume than both BFR conditions with less RPD. These results align with the overall body of literature on No-BFR versus BFR exercise on reducing exercise performance [32], as we observed a volume reduction of approximately 34% in both BFR conditions. However, this partially conflicts with a recent meta-analysis on perceptual demands [48] that indicated RPE/RPD was similar between No-BFR as long as exercise was taken to volitional fatigue. Our study reported high RPD in both BFR conditions compared to No-BFR with equal RPE. Lastly, our results conflict with a recent study investigating autoregulation of applied pressures using another commercially available BFR training device [26], indicating that acute responses to a BFR training program with autoregulation are possibly device-specific [20].

In the only other study directly comparing the impact of AR-BFR on exercise performance with cuffs of similar size, Jacobs et al. [26] had 56 participants perform a series of fixed and failure leg extension BFR exercise protocols in a randomized order using 20% 1-RM. Using the Smartcuffs device (cuff width 10.16 cm) capable of performing both AR-BFR and NAR-BFR, it was observed that during failure protocols, AR-BFR condition performed significantly more volume than NAR-BFR with similar RPE and less RPD (albeit not likely clinically relevant). Interestingly, no clinically relevant differences were observed in heart rate and brachial BP responses between conditions, leaving unanswered questions regarding what could be responsible for the observed differences. In contrast, our study with the Delfi Personalized Tourniquet device did not show performance or perceptual differences between the AR-BFR and NAR-BFR conditions. This observation may be attributable to differences in device autoregulation responsiveness of being able to maintain a consistent pressure between contraction phases, allowing for some reperfusion between repetitions — although this is speculative and requires comparative research in future studies.

In addition, it is important to note that no adverse events were reported in our study despite all exercise sessions (including the familiarization session) being conducted to failure, whereas Jacobs et al. [26] reported an adverse event in 7.14% of trials (n = 16 total) with a risk difference of 7% between NAR-BFR and AR-BFR in favor of AR-BFR. It is challenging to understand why the occurrence of adverse events was higher given that our study protocol had BFR exercise performed to failure in all trials, whereas Jacobs et al. [26] had participants perform a fixed repetition scheme more indicative of recommended practice [32] before performing a failure routine. More research is needed to understand the participant, device and protocol-specific ways to minimize the occurrence of adverse events during BFR exercise.

**Limitations**

This is the first study to investigate the arterial stiffness responses to an acute exercise session to volitional fatigue with and without the presence of autoregulation of applied BFR pressures, but it is not without limitations. First, we sought to include both males and females to have a better representative sampling of healthy, physi-
cally active young adults. However, our study was likely not adequately powered to assess between-sex differences. Recognizing the potential for different responses between sexes, we performed a between-sex analysis. We noted divergent responses in CR-PWV in the NAR-BFR condition in females, as well as a reduced overall volume of exercise performed in all conditions, compared to males. However, nothing else reached significance (Supp ▶ Table 1). Therefore, we cannot say with certainty that the responses between sexes are identical, warranting more research that uses a sample size adequately powered to detect between-sex differences. Second, while different menstrual phases do not appear to influence indices of arterial stiffness, less is known how it impacts pain and perceived effort to exercise. Thus, interpretation of these subjective scores should be viewed with caution. Third, due to not having a leg press, we utilized a wall squat. As this type of exercise is not confined to a predetermined range of motion, there is likely a greater skill component than a traditional leg press and different muscle activation patterns. In addition, participants performed the wall squat leaning into a minimal friction wall, which may have altered the load moved by the lower body. To control for this, we included a familiarization session identical to the one performed in data collection. This likely allowed for some motor learning to occur and potentially reduced the impact of the novel wall squat exercise. Lastly, as participants were healthy, one cannot extrapolate the findings to clinical populations without a degree of caution.

Clinical implications
With more devices available for consumer purchase, it is prudent for research to investigate whether certain features, such as autoregulation of applied pressure, impact the acute response to BFR exercise. Our study provides two main takeaways. The primary takeaway is that autoregulation of applied pressures has the potential to limit the exercise-induced increases in CF-PWV in healthy, physically active men and women. This may have relevance for increasing the safety of BFR exercise as non-autoregulated pressures, as well as low-load exercise to failure, increased CF-PWV to a similar degree. And second, our results on performance and perceptual responses diverge from a recent study on autoregulation [26], supporting that autoregulation may have varying impact on the acute- and potentially long-term responses to BFR exercise. As such, autoregulation of applied BFR pressures is an important feature that warrants consideration in practice and future research, particularly with respect to at-risk populations where attenuating the central stiffness responses may be desired. The use of autoregulation may, therefore, also serve a protective role in mitigating adverse responses to BFR exercise.

Pre-Print
Part of the data collected from this study was published in pre-print on SportRxiv [49].

Acknowledgements
We wish to thank Delfi Medical for loaning us the devices used within this study for research purposes. Delfi Medical did not have any role in the experimental design, data collection, or conclusions drawn from this investigation.

Conflict of Interest
Nicholas Rolnick is the founder of the BFR PROS and teaches BFR training workshops to fitness and rehabilitation professionals using a variety of BFR training devices.

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Notice
This article was changed according to the following Erratum on November 8th 2023.

Erratum
The conflict of interest information of author N. Rolnick were added to the article. This could not be displayed until now due to a technical error.