Arterial Blood Flow at Rest and During Exercise with Blood Flow Restriction

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ABSTRACT

Arterial Blood Flow at Rest and During Exercise with Blood Flow Restriction

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PURPOSE: This study compared arterial occlusion pressure (AOP) of the superficial femoral artery (SFA) between the dominant and nondominant legs and the relationship between blood flow and occlusion pressure at rest and during muscle contractions in males and females. METHODS: The AOP of the SFA was measured using Doppler ultrasound in the dominant and nondominant legs of 35 (16 males, 19 females) apparently healthy, normotensive young adults. Blood flow in the SFA was measured in the resting state (REST) and during plantar flexion exercise (EXC) at occlusion pressures ranging from 0% to 100% of AOP. ANOVA was used to compare AOP between the dominant and nondominant legs and between males and females. Regression analysis was used to evaluate the influence of relevant variables on AOP. A mixed model was used to evaluate the relationship between blood flow and occlusion pressure at REST and during EXC. RESULTS: There was a significant difference in the AOP between the dominant and nondominant legs in males (230 ± 41 vs 209 ± 37 mmHg) and females (191 ± 27 vs 178 ± 21 mmHg), respectively. There was also a significant sex difference in the AOP in the dominant (230 ± 41 vs 191 ± 27 mmHg; p = 0.002) and nondominant (209 ± 37 vs 178 ± 21 mmHg; p = 0.004) legs, respectively. Regression analysis revealed that after accounting for leg circumference, age, sex, blood pressure, and skinfold thickness were not independent predictors of AOP. At REST and during EXC, there was a linear relationship between relative blood flow and occlusion pressure. CONCLUSIONS: Differences in leg circumference contribute to a portion of the differences in AOP between the dominant and nondominant legs and between sexes. The linear relationship between relative blood flow and occlusion pressure suggests that occlusion pressures during blood flow restriction exercise should be chosen carefully. A large variance in blood flow measurements at different occlusion pressures suggests the need for evaluating the reliability of blood flow measurements and standardization of methods.

Keywords: blood flow restriction, arterial flow, arterial occlusion pressure, exercise
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INTRODUCTION

Blood flow restriction (BFR) applied to the arms or legs during resistance training has gained support as an effective alternative to traditional strength training (1-5). Research has shown that loads as low as 20% of an individual’s one-repetition max (1 RM), when combined with partial blood flow occlusion, is as effective as traditional strength training in promoting hypertrophy and increasing or maintaining muscular strength (1, 2, 6, 7). Thus, blood flow restriction exercise (BFRE) is appropriate for use during musculoskeletal rehabilitation in segments of the population in which muscle weakness is evident, such as the elderly, those with chronic diseases that often involve muscle wasting, and rehabilitation following an injury or surgery (7-10). The effectiveness of BFRE to increase muscular strength and hypertrophy has also popularized this method of resistance training among athletes (9, 11).

The intent of BFR is to partially restrict arterial blood flow into the limb and occlude venous blood flow out of the muscle (12-16). Previous studies have utilized a wide range of methods to restrict arterial blood flow. Some studies (17, 18) used elastic wraps to restrict blood flow as a “practical” method of BFRE. The lack of a measure of occlusion pressure could produce inconsistent blood flow restriction between two limbs and between exercise sessions. Most studies use an inflatable cuff to restrict blood flow. Early studies used absolute cuff pressures (13, 14, 19-24) ranging from 50 to 300 mmHg or cuff pressures based on brachial systolic blood pressure (25, 26). Using an absolute pressure to restrict blood flow during BFRE is problematic as it represents different levels of blood flow restriction between individuals. Use of absolute pressures to occlude blood flow brings the results of some studies into question and possibly increases the discomfort and risk to the participants (7, 27-34). The current recommended practice (4) is to measure the pressure required to completely occlude arterial
blood flow and use a percentage of the arterial occlusion pressure (AOP) to restrict blood flow during BFRE (35-37).

Although a review of the literature indicates that over 150 papers have been published on the topic of BFR and BFRE, answers to some questions remain unclear, including the relationship between blood flow and occlusion pressure, sex differences in the AOP, differences in the AOP between dominant and nondominant limbs, and the relationship between blood flow and occlusion pressure. The relationship between cuff pressure and arterial blood flow in the legs is not well represented in the literature. A few authors have reported that the relationship between arterial blood flow and absolute cuff pressure in the leg is linear (13, 14, 19, 38). To the contrary, a recent study reported a nonlinear relationship between cuff pressure (%AOP) and arterial blood flow and a plateau in blood flow at pressures between 40% and 80% AOP (37). Since pain and discomfort are more likely to occur when high cuff pressures are used during BFR (22), the recent data (37) suggests that it may be possible to mitigate the discomfort of BFR by using lower cuff pressures (22, 39, 40) while still eliciting the beneficial skeletal muscle adaptations.

To date, studies have not reported the AOP in the dominant and nondominant limbs. In most of the literature where occlusion pressure is based on a percentage of AOP, dominance of the occluded limb is not reported in unilateral interventions and any differences between limbs were not reported in bilateral studies (8, 28, 39, 41-43). Although the results of one study (44) indicate a statistically significant difference in the AOP between males and females, the small differences of 4–7 mmHg between the sexes were reported to be inconsequential.

Although previous studies have included male and female participants, sex differences in AOP have not been reported. As there may be sex differences in the factors that influence AOP
(e.g., limb circumference, blood pressure), differences in AOP between males and females should be evaluated. In addition, vascular reactivity, resistivity, and blood pressure change across the four phases of the menstrual cycle (45), which could alter the response to BFR in females and potentially create differences in AOP between males and females.

The purposes of this study were to compare: a) femoral artery AOP in the dominant and nondominant legs, and b) femoral arterial blood flow at relative occlusion pressures (0–100% AOP) in the dominant leg at rest and during exercise in young healthy men and women. We hypothesized a direct positive relationship between limb circumference and AOP, a significant difference in AOP between the dominant and nondominant legs, and a significant sex difference in AOP and in the relationship between arterial blood flow and relative occlusion pressure (%AOP) at rest and during exercise.

METHODS

Study Design

This study was a cross sectional study that measured the AOP in both legs and blood flow in the femoral artery of the dominant leg under two experimental conditions: resting (REST) and exercise (EXC). During REST, subjects sat quietly while blood flow measurements were taken. During EXC, subjects performed repetitions of plantar flexion at 20% of their previously determined one repetition maximum (1 RM). During both conditions, blood flow was measured when the cuff was inflated to pressures representing 0%, 20%, 40%, 60%, 80% and 100% of the AOP. The primary variables of interest included the AOP (mmHg) and blood flow (ml/min) at each increment of blood flow restriction (%AOP).
Participants

A total of 35 (16 males, 19 females) apparently healthy, normotensive adults, 18–35 years of age participated in this study. Interested participants were excluded from participation if they had any known risk factors for cardiovascular disease or one or more risk factors for thromboembolism, which include: obesity (BMI ≥ 30 kg/m2), diagnosed Crohn’s disease, a previous fracture of the hip, pelvis, or femur, a major surgery in the last 6 months, varicose veins, a family history of deep vein thrombosis or pulmonary embolism, and on oral birth control (31, 40, 43, 44, 46-49). Individuals were also excluded if a) they had been diagnosed as having or were being treated for cardiovascular disease, renal disease, diabetes, or hypertension, b) their resting blood pressure was categorized as either Stage 1 or Stage 2 hypertension (SBP ≥ 130 or a DBP ≥ 80 mmHg) (50), or c) they were pregnant or less than 6 months postpartum.

Procedures

Subjects were instructed to refrain from eating during the 2 hr prior to their participation, consuming caffeine for the previous 8 hr, and participating in vigorous physical activity the previous 24 hr (31, 48, 51). All procedures for each subject were completed in one 2–3 hr visit to the lab. The methods, expectations, risks, and benefits of the study were explained to each subject after which they voluntarily provided written informed consent. Subjects completed a preparticipation questionnaire that included questions about their current health status, cardiovascular risk factors, signs and symptoms, use of medications, age, sex, pregnancy status, and physical activity levels.

The subject’s height (cm) was measured using a calibrated wall-mounted stadiometer scale (SECA Model 264; SECA, Cino, CA, USA). Body mass (kg) was measured using a digital scale (Ohaus Model CD-33, Ohaus Corporation, Pine Brook, NJ, USA) and BMI (kg/m2) was
calculated from measured height and body mass values. Subjects then sat quietly in a comfortable chair for 5 min with legs uncrossed. Blood pressure was measured on the right arm. The average of two systolic (SBP) and diastolic (DBP) blood pressure measurements was recorded, or if they were not within 5 mmHg of each other, a third measurement was taken and the two closest measurements were averaged. Mean arterial pressure (MAP) was calculated as DBP plus one-third of pulse pressure. The circumference and skinfold thickness of the dominant and nondominant thighs were measured in the standing position using a spring-loaded Gullick measuring tape and a calibrated Lange caliper (Santa Cruz, CA), respectively. Measurements were taken at one-third of the distance between the inguinal crease and the top of the patella (4, 8), which was the anticipated location of the occlusion cuff during blood flow measurements. Skinfold measurements were taken three times and the average of the three measurements was used in the data analysis. Following familiarization with the plantar flexion exercise and apparatus, the participant’s plantar flexion 1 RM was measured on the dominant leg following the American College of Sports Medicine (ACSM) guidelines for determining a 1 RM.

Blood Flow Measurements

All blood flow measurements were performed using a handheld Doppler probe (9 MHz; 55 mm) and GE ultrasound machine with an integrated ECG (GE LOGIQ, GE Healthcare). Blood flow restriction was accomplished using a Hokanson SC10 cuff (10 cm wide; 85 cm long) attached to an E-20 rapid cuff inflator (Hokanson, Bellevue, WA, USA). Blood flow in the femoral artery was measured distal to the occlusion cuff. Color flow mode and pulse wave forms were viewed to determine the presence of blood flow. During the entire time of testing, participants were in a semireclined (15°) position to allow reasonable access to the femoral artery using the ultrasound. Angle of insonation of the ultrasound probe was maintained at 60°.
Measurement of Arterial Occlusion Pressure

The AOP of the dominant and nondominant legs was measured once in a randomized order for each participant. The occlusion cuff was placed on the participant’s thigh one-third of the distance between the inguinal fold and the top of the patella. A handheld Doppler probe was used to detect a pulse wave in the femoral artery distal to the cuff with the cuff uninflated. The cuff was then inflated to 50 mmHg and then gradually increased until arterial flow and pulse waves were no longer detected. The AOP was recorded to the nearest increment possible with the cuff system. Once the AOP was recorded, the cuff was immediately deflated. The cuff was removed and placed on the other leg. The participant rested for 3–5 min (42, 44, 48) with no pressure applied to the cuff after which the process was repeated.

Measurement of Arterial Blood Flow

Arterial blood flow distal to the cuff was measured for 1 min at cuff pressures equivalent to 0%, 20%, 40%, 60%, 80%, and 100% of the individual’s AOP in randomized order. There was a 3-min rest period between measurements with the cuff deflated. Measurements at each of the occlusion pressures were completed at REST prior to measurements during EXC. This was done to minimize the effects of exercise on blood flow in the resting condition. Arterial blood flow was measured in a like manner while the participant was performing repetitions of plantar flexion exercise. A cable extending from a weight machine positioned behind the participant was attached to the foot with a looped strap. During EXC, the participant performed repetitions of plantar flexion against a resistance representing 20% of their 1 RM at a cadence of 30 repetitions per minute using verbal cues and a clock to keep participants on cadence. Repetitions of plantar flexion exercise were performed for 3 min and blood flow measurements were completed during the third minute. This exercise was selected because the exercise could be performed while
keeping the thigh stationary, thereby allowing the measurement of femoral artery blood flow. The resistance was selected because research has shown that loads as low as 20% of an individual’s 1 RM, when combined with partial blood flow occlusion, is as effective as traditional resistance training at promoting hypertrophy and increasing or maintaining muscular strength (1, 2, 6, 7). Preliminary experiments indicated that participants could perform the exercise using a light resistance for at least 3 min. This duration was selected to allow blood flow to reach steady-state. After measurements were completed at each increment in pressure, the cuff was deflated. After 5 min of rest, the cuff was inflated to the next randomly assigned cuff pressure (%AOP) and the measurements were repeated.

One-minute video clips were stored for later analysis. Using the integrated ECG and pulse waves as reference points, femoral artery diameter was measured at two time periods representing the end of diastole and during systole. The first measurement was taken just before the QRS complex of the ECG and the second was taken at the peak of the QRS complex of each heartbeat. The two diameter measurements were averaged for each beat over five 12-s periods. Time averaged blood flow velocity (TAV) over five 12-s periods was recorded. Blood flow (ml/min) was then calculated automatically by the ultrasound machine but is represented as follows:

\[
\text{Blood flow (ml/min), } = \text{Cross sectional area (cm}^2\text{) } \times \text{TAV (cm/s) } \times 60 \text{ s/min}
\]

Data Analysis

Sex differences in age, height, body mass, BMI, and blood pressure measurements were determined using a one-way analysis of variance. We used the Bonferroni’s method for correcting the p value to reduce a type I error because of the multiple comparisons. The adjusted p-value for this analysis was 0.007. Differences in leg circumference, thigh skinfold thickness,
and AOP between the dominant and nondominant legs and between males and females were determined using a 2x2 mixed model analysis of variance (proc mixed). The influence of sex, SBP, DBP, MAP, thigh skinfold and circumference measurements on the AOP was evaluated using regression analysis.

Analysis of arterial blood flow data during the REST condition, expressed as a percentage of unoccluded blood flow, and occlusion pressure, expressed as a percentage of individual AOP (0%, 20%, 40%, 60%, 80%, 100%) presented two major challenges. One challenge was that relative blood flow when there was no occlusion (0% AOP) is represented as 100%. Although each subject’s blood flow in absolute terms (ml/min) is unique, blood flow at 0% AOP in relative terms is 100% for every subject. Thus, at 0% AOP there is no variance in the blood flow data. Second, blood flow at various degrees of occlusion (e.g., 20%, 40%, 60% AOP) for some subjects was higher than when there was no occlusion (0% AOP). Thus, the difficulty in analyzing the blood flow data is that there is one data point (0% AOP) where there is no variance in blood flow and other data points where relative blood flow is greater than 100%. To analyze these data, we first evaluated if relative blood flow at 20% AOP was significantly different from relative blood flow (100%) at 0% AOP. We used a one-sample t-test for this analysis. We found that the average relative blood flow at 20% AOP was 81% (CI = 70.4%–91.6%) of unoccluded blood flow, which was significantly different than 100% (p = 0.0009). We then fit a mixed linear model between relative blood flow and relative occlusion pressure. We used a mixed model to account for within- and between-subject variability since each subject had multiple data points. To further appropriately account for variability when fitting the model, we omitted the blood flow data at 0% AOP due to its lack of variability and only used data at occlusion pressures of 20%, 40%, 60%, 80% and 100% of AOP. The initial analysis revealed
that there was no sex difference in the relationship between blood flow and occlusion pressure. We therefore fit a linear model that did not include sex as a variable. A 95% confidence interval (CI) and prediction interval (PI) were computed for the line of best fit through the data.

A similar process was followed when analyzing arterial blood flow in the EXC condition. In this analysis, blood flow at 20% AOP was 97.2% (CI = 77.4%–117.1%) of unoccluded blood flow at 0% AOP which was not significantly different (p = 0.7688) than 100% blood flow. We then fit a mixed linear model between relative blood flow and relative occlusion pressure, omitting the blood flow data at 0% AOP due to the lack of variability. There was no sex difference in the relationship between blood flow and occlusion pressure so we fit a linear model that did not include sex as a variable. A 95% CI and PI were computed for the line of best fit through the data.

RESULTS

Participant characteristics are shown in Table 1. As expected, males were taller and heavier than the female participants. Males also had higher systolic, diastolic, and mean arterial pressures. In both males and females, the small difference in the circumference between the dominant and nondominant legs was significant (p = 0.0379). There was no significant difference (p = 0.7898) in either of the thigh circumferences between males and females. There was no significant difference (p = 0.5517) in the thigh skinfold thickness between the dominant and nondominant legs of either males or females. Differences in thigh skinfold thickness between males and females approached significance (p = 0.0538).

Arterial Occlusion Pressure

There was a significant difference in the AOP between males and females in both the dominant (230 ± 41 vs 191 ± 27 mmHg; p = 0.002) and nondominant (209 ± 37 vs 178 ± 21 mmHg; p = 0.002) conditions.
mmHg; p = 0.004) legs, respectively. Likewise, there was a significant difference in the AOP between the dominant and nondominant legs in both males (230 ± 41 vs 209 ± 37 mmHg) and females (191 ± 27 vs 178 ± 21 mmHg), respectively. Regression analysis revealed that after leg circumference entered the equation, SBP, DBP, MAP, skinfold thickness, age and sex were not significant independent predictors of AOP. The resulting regression model was:

\[
\text{AOP (mmHg)} = 40.4 + (3.23) \text{ Leg Circumference (cm)}
\]

The relationship between AOP and leg circumference is shown in Figure 1 with 95% CI and 95% PI.

Arterial Blood Flow

In the REST condition, the mixed model analysis revealed a linear relationship between relative blood flow (% unoccluded blood flow) and relative occlusion pressure (%AOP). The resulting equation (R = −0.842; Residual Standard Error = 25.3) was:

\[
\text{Percent Blood Flow} = 99.46 − 0.85(\text{Occlusion Pressure})
\]

In the EXC condition, the resistance used during plantar flexion ranged from 10–25 pounds for males and 5–20 pounds for females. The mixed model analysis revealed the following linear relationship between blood flow and occlusion pressure:

\[
\text{Percent Blood Flow} = 124.8 − 1.14(\text{Occlusion Pressure})
\]

where Occlusion Pressure = 20%, 40%, 60%, 80%, 100% AOP. The relationships between blood flow and occlusion pressure at REST and during EXC are shown in Figure 2 and Figure 3, respectively, with 95% CI and 95% PI.

**DISCUSSION**

This paper adds to the current body of knowledge about BFR and BFRE in that we report, perhaps for the first time, large differences in AOP between males and females and
between the dominant and nondominant legs that are statistically significant and of practical importance. The linear relationship between blood flow and occlusion pressure expressed in relative terms reported in this study was unrelated to sex. We also report a large variance in blood flow data at different levels of occlusion that is not entirely unique to this study but has not been transparent in the literature.

Arterial Occlusion Pressure

We report a large sex difference in AOP in both the dominant and nondominant legs (Table 1). Although other studies have included male and female participants, they have not reported sex differences in AOP. For example, Loenneke et al. (8) measured AOP in both arms and both legs of 171 participants (52 males, 119 females) but did not report the AOP measurements for each arm or leg or sex differences in AOP. Two recent studies reported cuff width (5 cm vs 12 cm) preferences between males and females during arm BFRE (52) and changes in muscle thickness following BFRE (52). Even though AOP was measured in one arm with the 5 cm cuff and the other arm with a 12 cm cuff, AOPs and sex differences in AOP for each cuff size were not reported (52). Most recently, Crossley et al. (37) measured AOP in both legs of 11 males and 12 females but did not report differences in AOP between the two legs or between males and females. To the best of our knowledge, only one previous study has reported a sex difference in AOP. Jessee et al. (44) reported that the AOP of the right arm of females (n = 147) was on the average 4–7 mmHg (p < 0.05) lower than in males (n = 102) across three different cuff sizes (5 cm, 10 cm, and 12 cm). Although significantly different, the authors report that the differences in AOP were inconsequential in prescribing BFRE (44). As such, the authors failed to provide an explanation for the sex differences in AOP with each of the three cuff sizes. Contrary to the conclusions made by Jessee et al. (44), the large sex differences in AOP and the
large difference in AOP between the dominant and nondominant legs reported in this study (Table 1) require further study and are of practical importance when using BFRE in clinical and nonclinical settings.

It is well reported that differences in the AOP are attributed primarily to differences in limb circumference (11, 13, 53). The larger the limb, the greater the pressure required to occlude the blood vessel. Larger limbs have more mass between the skin and the blood vessels that must be compressed in order to occlude the vessel, and higher pressures are required to transmit adequate force to the deeper tissues (8, 42). Hence, it follows that sex differences in AOP may be accounted for by differences in limb circumference. Jessee et al. reported an average sex difference in circumference of the right arm of 5.3 cm (44). The regression analysis reported by Jessee et al. (44) indicated that after accounting for arm circumference, arm length, SBP, and DBP, sex remained a significant independent predictor of AOP and the models accounted for 55% to 65% of the variance in AOP depending on the cuff size. In this study, there was an average difference in circumference of < 1 cm in both the dominant and nondominant legs between and within males and females (Table 1). Despite small differences in leg circumference, there were large differences in AOP between the dominant and nondominant legs within and between males and females (Table 1). It should be appreciated that the leg circumference of the dominant leg is not always larger than that of the nondominant leg. In this study, the dominant leg was larger than the nondominant leg in 20 of the participants and the nondominant leg was larger in 15 of the participants. Likewise, the AOP is not always higher in the larger leg. In this study, the AOP was higher in the larger leg (15 dominant; 5 nondominant) of 20 participants and higher in the smaller leg (9 dominant; 6 nondominant) of 15 participants.
Contrary to the findings of Jessee et al. (44), the regression analysis in this study indicates that after accounting for leg circumference, SBP, DBP, MAP, skinfold thickness, sex, and age were not significant predictors of AOP. The observed sex differences in AOP is largely due to differences in leg circumference. A likely explanation for the differences in the results between this study and that of Jessee et al. (44) is that in this study we measured AOP in both legs and Jessee et al. measured AOP only in the right arm. In addition, we report the AOP of both the dominant and nondominant legs whereas Jessee et al. only reported the AOP of the right arm, rather than the dominant arm.

Limb circumference is the most influential independent variable in the estimation of AOP because it represents the overall mass of the limb that must be compressed to occlude a blood vessel. The composition of the limb may also influence the pressure required to occlude a blood vessel. In this study, the seemingly large sex differences in thigh skinfold thickness approached significance but likely did not enter into the regression equation to estimate AOP because it is included as part of the overall circumference of the leg. It also represents only a portion of the tissue mass that must be compressed to occlude the femoral artery. Using B-mode ultrasound, Loenneke et al. (8) measured fat thickness of the upper arms in 171 participants (52 males, 119 females). Evaluation of regression models to estimate AOP that included SBP, DBP, arm circumference, muscle thickness and fat thickness lead to the conclusion that the absolute size of the arm may be more important than the composition of the arm in predicting AOP. Loenneke et al. (8) also measured circumferences and AOP in both arms and both legs of each participant but did not report the circumference or AOP measurements for each arm or leg or sex differences in AOP.
Arterial Blood Flow at Rest and During Exercise

To date, relatively few studies have reported the relationship between occlusion pressure and blood flow though there is a call to do so (38). Because the AOP and absolute blood flow at any given absolute pressure varies widely between individuals, it is appropriate to express blood flow and occlusion pressure in relative terms. Nevertheless, two early studies (13, 14) reported a linear relationship between absolute blood flow (ml/min) in the femoral artery at various absolute occlusion pressures (100–300 mmHg). The results of this study (Figures 1 and 2) indicate a linear relationship between relative femoral arterial blood flow (% unoccluded blood flow) and relative occlusion pressure (%AOP) in the REST and EXC condition. Our data concur with those of a previous study reporting a linear relationship between relative blood flow and %AOP in the posterior tibial artery at rest (38). A nonlinear stepped relationship between relative blood flow and relative occlusion pressure (%AOP) in a resting condition in the brachial artery was reported by Mouser et al. (54). They reported that blood flow in the brachial artery decreased from 0% AOP to 10% AOP then stayed constant until blood flow decreased again at 40% AOP, and then stayed constant to 90% AOP. Mouser et al. (55) also reported a nonlinear relationship between brachial artery blood flow and occlusion pressure in which blood flow between 50–90% AOP was relatively unchanged. In a similar manner, the results of the Crossley et al. (37) study indicate that there was no significant difference in femoral blood flow at cuff pressures between 30% and 80% AOP. Some difference in methodology between studies could help explain the disparity between our results and those of Crossley et al. (37). Subjects in our study were in a semireclined position, whereas subjects in Crossley et. al. (37) study were in the seated position. Additionally, measurements in the study by Crossley et al. were performed on alternating legs in a randomized order over the course of the study, meaning the AOP and blood
flow reported were a reflection of AOP and blood flow in both legs rather than the dominant versus nondominant leg (37).

Two other recent studies reported blood flow during exercise with BFR. Kilgas et al. (56) reported brachial blood flow at different occlusion pressures (0%, 60%, 80%, 100% AOP) during rhythmic handgrip exercise and Singer et al. (57) reported femoral artery blood flow at the same relative pressures during knee extension exercise. Both studies reported that compared to resting, blood flow increased during exercise at all occlusion pressures, however, compared to 0% AOP, blood flow decreased with increasing levels of occlusion. Neither study directly reported the relationship between blood flow and occlusion pressure.

Whether the relationship between blood flow and occlusion is linear or nonlinear is of practical importance in clinical and nonclinical settings. A nonlinear relationship suggests that use of a lower, more comfortable and potentially safer occlusion pressure (e.g., 40% AOP) would provide an equally effective stimulus during BFRE as at higher occlusion pressures. A linear relationship suggests that the occlusion pressure used during BFRE should be selected more carefully and that further research is required to determine a recommended reduction in blood flow to be used during BFRE.

Variance in Blood Flow Measurements

It is appropriate to express blood flow during BFR as a percentage of unoccluded blood flow. Thus, at 0% AOP, blood flow would be expressed as 100%. One would expect a decrease in blood flow with increasing levels of occlusion and that blood flow at 100% AOP would be expressed as 0%. In this study, we observed a large variation in blood flow at different levels of occlusion. For example, we note that blood flow at higher levels of occlusion was sometimes greater than at lower levels of occlusion or when there was no occlusion (0% AOP). We also
found that some participants had notable blood flow at an occlusion pressure equivalent to the previously measured AOP. Variance in the data presented in this study is apparent in the wide prediction intervals shown in Figures 2 and 3. These observations are suggestive of a robust cardiovascular system that maintains blood flow across various levels of occlusion pressures (55).

Although most previous studies have not discussed the variation in blood flow measurements, evidence of such is present in previous studies. For example, in the table of blood flow data presented by Mouser et al. (54), relative blood flow at 70% AOP was greater than relative blood flow at 60% and 50% AOP. Likewise, although mean brachial artery blood flow values decreased with increasing levels of occlusion, the large standard deviations of data presented by Mouser et al. (55) suggest that in some subjects blood flow at higher occlusion pressures was greater than at lower occlusion pressures. This could be attributed to a cardiovascular response to high occlusion pressures in the absence of exercise (13, 58). It could also be possible that after several applications of BFR there are local responses in the vasculature that alters blood flow or the AOP. Although previous research indicates that blood flow returns to normal within 30 to 90 s after the occlusion is removed (59), there may need to be longer rest periods between sequential blood flow measurements with occlusion. Lastly, although data collected from each subject in this study occurred in a single day, Mouser et al. (55) reported a significant day-to-day variation in resting blood flow that clearly has implications for future research involving blood flow measurement over multiple days and the use of BFRE in clinical and nonclinical settings. Our experiences in measuring blood flow in the superficial femoral artery and close examination of data presented in the literature warrants a call for further studies evaluating the variance and reliability of blood flow measurements during BFR.
Study Limitations

This study had several limitations. Participants were all normotensive college-age coeds without known risk factors for cardiometabolic diseases. Therefore, the results of our study, while valuable in understanding blood flow responses to BFRE, may not be applicable to all populations. In this study, participants performed plantar flexion exercise with the intention of measuring blood flow during exercise. Nevertheless, plantar flexion exercise in the semireclined position does not reflect the way that BFRE would typically be used in a clinical or athletic setting where multijoint seated or standing exercises are favored. In this study the Hokanson SC10 cuff (10 cm wide; 85 cm long) attached to an E-20 rapid cuff inflator (Hokanson, Bellevue, WA, USA) was used for all measurements. Clinicians, researchers, and other practitioners may use different brands of cuffs and inflation systems, different cuff sizes, or other methods to occlude blood flow. All these factors should be taken into consideration when interpreting our results.

Direction for Future Studies

Based on the results of this study, future studies should take several things into consideration when designing their protocols. First, participants should include both male and female participants and there should be full disclosure of limb dominance, limb circumference, AOP, and blood flow data on both limbs in males and females. Based on our results, there is a significant difference in AOP between males and females and between dominant and nondominant legs in both sexes. While it is clear that limb circumference is more influential on AOP than limb composition, the sex differences in thigh skinfold thickness reported in this study and the influence of fat thickness reported by Loenneke et al. (8) lend support for an influence of limb composition on AOP that needs further investigation. Additionally, when reporting
differences between sexes, time in the menstrual cycle should be included for women as blood pressure, vascular reactivity, and vascular resistivity all change depending on phase of the menstrual cycle (45). The large variation of blood flow measurements at different occlusion pressures reported in this and previous studies suggests the need to standardize blood flow measurement methods and investigate the reliability of AOP and blood flow measurements. Additionally, assessments of reliability in measurements of blood flow with and without occlusion between test administrators, within days, and between days needs attention.
REFERENCES


Table 1. Participant Characteristics

<table>
<thead>
<tr>
<th></th>
<th>MALES (n = 16)</th>
<th>FEMALES (n = 19)</th>
<th>COMBINED (n = 35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>23.8 ± 3.6</td>
<td>22.9 ± 3.5</td>
<td>23.3 ± 3.5</td>
</tr>
<tr>
<td>Height (cm) *</td>
<td>177.6 ± 5.3</td>
<td>166. ± 8.7</td>
<td>171.8 ± 9.1</td>
</tr>
<tr>
<td>Body Mass (kg) *</td>
<td>77.4 ± 10.6</td>
<td>63.6 ± 9.6</td>
<td>68.8 ± 11.6</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>23.9 ± 3.6</td>
<td>22.7 ± 2.9</td>
<td>23.3 ± 3.2</td>
</tr>
<tr>
<td>SBP (mmHg) *</td>
<td>126 ± 10</td>
<td>114 ± 5</td>
<td>120 ± 10</td>
</tr>
<tr>
<td>DBP (mmHg) *</td>
<td>76 ± 13</td>
<td>71 ± 7</td>
<td>73 ± 10</td>
</tr>
<tr>
<td>MAP (mmHg) *</td>
<td>93 ± 10</td>
<td>85 ± 5</td>
<td>89 ± 8</td>
</tr>
<tr>
<td>Thigh Skinfold (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominant Leg</td>
<td>25.8 ± 11.0</td>
<td>32.6 ± 9.2</td>
<td>29.5 ± 10.5</td>
</tr>
<tr>
<td>Nondominant Leg</td>
<td>25.9 ± 11.6</td>
<td>32.8 ± 8.8</td>
<td>29.6 ± 10.6</td>
</tr>
<tr>
<td>Thigh Circumference (cm) ^</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominant Leg</td>
<td>48.8 ± 4.2</td>
<td>49.2 ± 4.9</td>
<td>49.0 ± 4.5</td>
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<tr>
<td>Nondominant Leg</td>
<td>47.9 ± 4.5</td>
<td>48.5 ± 4.9</td>
<td>48.3 ± 4.7</td>
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<tr>
<td>AOP * ^</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dominant Leg</td>
<td>230 ± 41</td>
<td>191 ± 27</td>
<td>209 ± 39</td>
</tr>
<tr>
<td>Nondominant Leg</td>
<td>209 ± 37</td>
<td>178 ± 21</td>
<td>192 ± 33</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, MAP = mean arterial blood pressure, AOP = arterial occlusion pressure.

* = significant difference between males and females (p < 0.05).

^ = significant difference between dominant and nondominant leg in both males and females.
Figure 1. Relationship between limb circumference and arterial occlusion pressure in the legs

Solid line = line of best fit. Dashed lines = 95% Prediction Intervals. Dotted lines = 95% Confidence Intervals.
Figure 2. Relationship between arterial blood flow and occlusion pressure at rest

Solid line = line of best fit. Dashed lines = 95% Prediction Intervals. Dotted lines = 95% Confidence Intervals.
Figure 3. Relationship between arterial blood flow and occlusion pressure during exercise

Solid line = line of best fit. Dashed lines = 95% Prediction Intervals. Dotted lines = 95% Confidence Intervals.