

Acute Vascular and Cardiovascular Responses to Blood Flow–Restricted Exercise

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ABSTRACT

DOWNS, M. E., K. J. HACKNEY, D. MARTIN, T. L. CAINE, D. CUNNINGHAM, D. P. O'CONNOR, and L. L. PLOUTZ-SNYDER. Acute Vascular and Cardiovascular Responses to Blood Flow–Restricted Exercise. *Med. Sci. Sports Exerc.*, Vol. 46, No. 8, pp. 1489–1497, 2014. Blood flow-restricted resistance exercise improves muscle strength; however, the cardiovascular response is not well understood. **Purpose:** This investigation measured local vascular responses, tissue oxygen saturation (StO₂), and cardiovascular responses during supine unilateral leg press and heel raise exercise in four conditions: high load with no occlusion cuff, low load with no occlusion cuff, and low load with occlusion cuff pressure set at 1.3 times resting diastolic blood pressure (BFR_{DBP}) or at 1.3 times resting systolic blood pressure (BFR_{SBP}). **Methods:** Subjects ($N = 13$) (men/women, 5/8, 31.8 ± 12.5 yr, 68.3 ± 12.1 kg, mean ± SD) performed three sets of leg press and heel raise to fatigue with 90-s rest. Artery diameter, velocity time integral, and stroke volume were measured using two-dimensional and Doppler ultrasound at rest and immediately after exercise. HR was monitored using a three-lead ECG. Finger blood pressure was acquired by photoplethysmography. Vastus lateralis StO₂ was measured using near-infrared spectroscopy. A repeated-measures ANOVA was used to analyze exercise work and StO₂. Multilevel modeling was used to evaluate the effect of exercise condition on vascular and cardiovascular variables. Statistical significance was set *a priori* at $P < 0.05$. **Results:** Artery diameter did not change from baseline during any of the exercise conditions. Blood flow increased after exercise in each condition except BFR_{SBP}. StO₂ decreased during exercise and recovered to baseline levels during rest only in low load with no occlusion cuff and high load with no occlusion cuff. HR, stroke volume, and cardiac output (\dot{Q}) responses to exercise were blunted in blood flow–restricted exercise. Blood pressure was elevated during rest intervals in blood flow–restricted exercise. **Conclusions:** Our results demonstrate that cuff pressure alters the hemodynamic responses to resistance exercise. These findings warrant further evaluations in individuals presenting cardiovascular risk factors. **Key Words:** BLOOD FLOW–RESTRICTED EXERCISE, ARTERIAL BLOOD FLOW, CARDIOVASCULAR RESPONSE TO RESISTANCE EXERCISE, HEMODYNAMIC RESPONSE TO RESISTANCE EXERCISE

High-load resistance training is the most common and effective mode of increasing muscle strength and size (19). In older, inactive, or unhealthy populations, resistance training can also prevent age-related muscular degeneration and protect against metabolic syndrome by improving glucose metabolism and blood lipid profiles (32).

Unfortunately, some individuals (i.e., those with musculoskeletal weakness from injury/disease or who present high cardiovascular risk factors) cannot safely lift heavy loads because of the resulting mechanical or cardiovascular stresses (25). Low-load resistance training (20%–50% of maximum strength) coupled with a restriction in blood flow to the active muscle has been shown to increase muscular strength and size (16,22,24,41,44). Induction of local ischemia appears to be the main stimulus for the muscular training adaptations associated with low-load blood flow–restricted exercise (BFR) (21,38,40,45); however, the disruption in blood flow to and away from the muscle has only been scarcely examined (39). In addition, the acute vascular and systemic cardiovascular responses to BFR exercise need to be evaluated more completely before it is recommended to individuals with cardiovascular risk factors.

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The specific BFR prescription and equipment vary between studies; however, most use a cuff pressure at or above resting systolic blood pressure (SBP) and three to five sets of exercise with 30–90 s of rest between sets. Maintaining the cuff pressure (i.e., ischemia) throughout the exercise session, including rest periods between exercise sets, seems to be a critical factor in achieving the hypertrophic response (16). Even with a standardized cuff pressure, the magnitude of the reduction in blood flow likely varies between individuals because of a variety of factors including the cuff width, thickness of the layer of soft tissue situated between the cuff and the vessel (i.e., the effective pressure applied to the blood vessel is less than the external cuff pressure), muscle mass, and differences in the systemic cardiovascular response (i.e., blood pressure (BP), HR, and stroke volume (SV)) to exercise (35). Knowledge of hemodynamic and vascular responses can be used to improve comfort and likely safety by identifying the lowest cuff pressure that effectively induces ischemia.

Rather than high-load exercise, cardiac rehabilitation programs most commonly incorporate moderate-intensity resistance training (50%–75% of one-repetition maximum (1RM)). High-load resistance training (greater than 75% of maximum strength) is increasingly recommended for elderly populations; however, it is prescribed cautiously for patients with hypertension or peripheral artery disease because a remarkable increase in systolic and diastolic BP occurs during exercise (23), and these individuals exhibit an exacerbated BP responses to exercise. Furthermore, the resistance training effects on arterial compliance are not clear: elevated and reduced age-related changes in arterial stiffness have been reported in resistance-trained individuals compared with their sedentary counterparts (8,25,28,29). Alternatively, BFR resistance training could elicit improvements in muscle strength and endurance, without the musculoskeletal and cardiovascular stresses associated with high-load resistance exercise.

Given the potential applications of BFR exercise in clinical populations, it is important to characterize the level of ischemia at the exercising muscle and the acute cardiovascular responses, to most efficiently and safely prescribe resistance exercise. The main purpose of this investigation was to measure local arterial blood flow, tissue oxygen saturation (StO_2), and systemic cardiovascular responses during unilateral leg press and heel raise resistance exercise performed under four different conditions that varied by exercise load and cuff pressure: low load with no occlusion cuff pressure (LL), low load with occlusion cuff pressure set at 1.3 times resting diastolic BP (BFR_{DBP}) or set at 1.3 times resting systolic BP (BFR_{SBP}), and high load with no occlusion cuff (HL). This study design allowed for identifying and describing the relation between exercise load, degree of ischemia, and acute cardiovascular responses for each exercise condition. The results from the two different levels of BFR may be used to improve comfort and safety by determining whether a lower cuff pressure can induce a similar level of ischemia. We hypothesized the following: 1) arterial blood flow would be the highest during HL exercise and the lowest

during BFR_{SBP} ; 2) StO_2 would be the lowest during the BFR exercise conditions; and 3) the exercise-induced elevations in HR and BP would not recover during the rest intervals of BFR exercise sessions.

MATERIALS AND METHODS

Subjects. A total of 13 moderately active (self-reported physical activity two to five times per week) men and women between the ages of 20 and 55 yr were selected after screening with a health history questionnaire and physical exam performed by a physician at NASA Johnson Space Center. Subjects were excluded if they had any orthopedic limitations or cardiovascular risk factors or diseases, were currently taking any medications or supplements (including hormonal contraceptives), had a personal or family history of blood clotting disorders, or reported having smoked in the last year. All subjects provided written informed consent before participation. The study was approved by the NASA Johnson Space Center, University of Houston, and Syracuse University institutional review boards.

Experimental protocol. All subjects reported to the NASA Johnson Space Center Exercise Physiology Laboratory on five separate occasions for data collection and at least two times before data collection to practice the leg press and heel raise exercises and for familiarization with the inflation cuff. Thigh and calf circumference were measured before the start of each exercise session while subjects were seated on the leg press with their feet resting on the foot plate. Supine unilateral left leg press and heel raise exercises were performed at all sessions using the Agaton Fitness System® (Agaton Fitness AB, Boden, Sweden). A 1RM for the left leg for leg press and heel raise exercise was determined on the first day of data collection and was used to set the exercise load for the following four data collection sessions. To determine 1RM, subjects performed a warm-up of 8–10 dynamic repetitions at a light to moderate weight. Then single attempts at progressively heavier weights were performed until the heaviest weight that could be lifted for one repetition was found.

At the next four data collection sessions (separated by at least 48 h and no reported muscle soreness), subjects performed supine unilateral left leg press and heel raise exercise under one of four different conditions in a randomized order. The exercise load and/or occlusion cuff pressure for each condition were as follows (load/cuff pressure): HL (80% of 1RM/no cuff), LL (20% 1RM/no cuff), BFR_{DBP} (20% 1RM/ $1.3 \times$ supine resting diastolic blood pressure (DBP)), BFR_{SBP} (20% 1RM/ $1.3 \times$ supine resting SBP). During each exercise session, subjects were asked to complete three sets of supine left leg press and heel raise exercises to volitional fatigue with 90 s of rest between sets. All sets of leg press were completed before starting heel raise exercise. For the BFR sessions, the cuff (6 \times 83 cm SC5 tourniquet cuff inflated using a E20 Rapid Cuff Inflator, D. E. Hokanson Inc., Bellevue, WA) was placed around the

proximal thigh for leg press exercise and above the knee for heel raise exercise. The cuff was inflated to the designated pressure 60 s before the start of exercise, and it remained inflated throughout exercise and rest intervals. During each data collection session, femoral (during leg press) or popliteal (during heel raise) artery diameter, blood flow velocity, velocity time integral (VTI), and vein cross-sectional area (CSA) were measured using two-dimensional and Doppler ultrasound at rest and immediately (within 15 s) after each set of exercise. Thigh StO_2 was measured at rest and continuously during the exercise session using near-infrared spectroscopy (NIRS).

NIRS. The NIRS sensor used in this study was a prototype of the sensor in Ellerby et al. (7) and was calibrated and operated using the same mathematical assumptions. Previous work has demonstrated that the sensor is accurate and reliable in animal and human models (7). Briefly, the NIRS sensor was adhered to the skin overlying the subject's vastus lateralis during leg press exercise with double-sided tape. Care was taken to securely adhere the sensor to the subject's skin so that the sensor did not move during exercise. NIRS data were collected on all subjects; however, four of the subjects were excluded from the analysis because their exercise duration was not sufficient for NIRS data acquisition. The lowest StO_2 value obtained at the end of each exercise set and the average of the last 30 s of rest were reported.

Vessel ultrasound imaging and analysis. Two-dimensional vascular ultrasound images were obtained with the subject in the supine position at rest, at rest with the cuff inflated, and immediately (within 15 s) after each set of exercise. During leg press exercise, ultrasound images were acquired from the superficial femoral artery and vein with the subject's knee bent at approximately 90° and their foot resting on the leg press plate. Doppler images of blood flow were acquired with the probe located distal to the inflated cuff (approximately 4 inches above the medial condyle). For heel raise exercise, ultrasound images were acquired at the popliteal artery and vein with a slight bend in the subject's leg and their foot resting on the leg press foot plate. Doppler images of blood flow were acquired with the probe placed at the back of the leg approximately 2 inches below the knee joint. The images were captured after exercise in the following order: Doppler, arterial diameter, and vein CSA. Two-dimensional and Doppler images were obtained using a commercially available system (Philips CX50; Philips Medical, Andover, MA) with a 12- to 3-MHz linear array probe. The insonation angle was less than 60° during femoral and popliteal blood flow acquisition, and Doppler velocity was corrected for the angle of incidence. Ultrasound images were obtained by trained sonographers, and the same two sonographers performed all imaging throughout the investigation.

All ultrasound analyses were performed offline using ProSolv software (v.3.0) by the same technician. The technician analyzed the images blinded from the condition. Two technicians measured blood flow velocity and VTI from

three different subjects in triplicate to test for reliability and repeatability. Resting flow velocity and VTI were measured by tracing the flow profiles for three cardiac cycles obtained before the start of exercise. Exercise peak flow velocity and VTI were determined by tracing the three flow profiles with the highest velocity captured within 15 s of exercise completion. Arterial diameter was measured from longitudinal vessel images captured at the R-wave of the ECG. The diameters measured at the intima-media border for three images were averaged. Blood flow was calculated in milliliters per minute as $\text{VTI} \times \text{vessel CSA}$. Vein CSA was determined by tracing the circumference of three vessel images and averaging the values.

Echocardiography and analyses. Doppler spectra of the ascending aortic blood flow were obtained at the same time as the vascular images (within 15 s of exercise cessation) by a separate registered sonographer using a commercially available system (Biosound MyLab 30, Indianapolis, IN) with a 2-MHz nonimaging probe directed through the suprasternal window. All data were stored digitally and analyzed offline by a trained technician using a MATLAB (Mathworks, Natick, MA) program specially designed for this analysis. Data blinding and technician repeatability and reliability were verified using the method described for the leg blood flow analysis. The accuracy and reproducibility of the MATLAB program were previously validated against a commercially available analysis software program (ProSolv version 3.0, Indianapolis, IN). Three cardiac cycles were traced and averaged. The time between R-R intervals was measured to determine HR.

SV was calculated as the product of the mean VTI and the CSA of the aortic annulus orifice obtained at baseline using a 3-MHz phased array probe on the same equipment. Echocardiographic Doppler estimates of SV have been validated under experimental conditions similar to those described here (12). Although such measurements tend to systematically underestimate the absolute SV, they accurately reflect changes in SV (14). Cardiac output (\dot{Q}) was calculated from the product of HR and SV.

BP acquisition and analysis. Finger arterial BP was acquired at 200 Hz using photoplethysmography with a laboratory system (Finometer; Finapres Medical Systems, the Netherlands). This technique has been shown to provide accurate measurement of BP changes relative to intraarterial BP (15). BP was digitized and recorded at 250 Hz (Notocord, France). Data were acquired continuously; however, the data collected during the exercise bouts were not usable because of periods of dropout, likely due to subjects moving their arms or clenching fists during exercise. Resting BP measurements were taken at the brachial artery using a standard BP cuff and sphygmometer to verify the accuracy of the finometer data. Data analyses were performed on 90-s segments of data obtained at baseline and during the 90-s rest period after each set of exercise. Offline analyses were performed using a MATLAB code specifically written for this analysis (Mathworks).

Statistical analysis. A 4 × 3 (condition × exercise set) repeated-measures ANOVA was used to analyze the number of repetitions, total work, and StO₂ during exercise. When main effects were significant, Bonferroni *post hoc* tests were conducted for pairwise comparisons. Multilevel modeling, which allows for differences in covariance between each combination of time and condition, was used to determine the effect of exercise condition on the vascular- and cardiovascular-dependent variables. “Exercise condition” and “time” were both entered as level 1 variables (repeated measures), which were nested within “subjects” as the level 2 variable (between group). This analysis was chosen because blood flow can be affected by several external factors, which requires a statistical analysis more robust than traditional multiple regression techniques. Regression analysis was conducted to determine whether cuff pressure, exercise load, and limb circumference could be used to predict blood flow at the femoral artery during leg press.

Preliminary analyses showed no significant difference between the three sets of exercise in ultrasound or echocardiograph measurements; therefore, measurements obtained after each set of exercise were averaged and used for subsequent analyses. Statistical significance was set *a priori* at $P < 0.05$ for all analyses. The SPSS statistical package (version 17.0, Chicago, IL) was used for data analysis. All data are presented as mean and SE unless otherwise noted.

RESULTS

Thirteen subjects passed the screening examination and were admitted into the study (five men, eight women; age, 31.8 ± 12.5 yr; weight, 68.3 ± 12.1 kg; height, 169.1 ± 12.1 cm; thigh circumference, 39.2 ± 4.79 cm; calf circumference, 35.9 ± 3.31 cm, mean \pm SD). 1RM for the left leg press and heel raise exercises was 52.3 ± 6.1 and 86.7 ± 7.9 kg, respectively. The exercise weight for the LL and BFR conditions for leg press was 10.9 ± 1.2 kg and 16.7 ± 5.5 kg for heel raise. For the HL condition, the exercise weights were 40.4 ± 4.6 and 68.7 ± 22.2 kg for leg press and heel raise, respectively. The inflation cuff pressure was set at 95 ± 2 mm Hg for the BFR_{DBP} condition and 146 ± 4 mm Hg for the BFR_{SBP} condition.

Exercise performance. The repeated-measures ANOVA showed significant time–condition interaction effects for the repetitions and total work for leg press and heel raise exercise. Relative to the first set of exercise, subjects performed fewer repetitions ($P < 0.05$) and less work ($P < 0.05$) during the second and third sets of exercise in each condition except HL (Fig. 1).

Leg press repetitions (Fig. 1A) during the first set of exercise were significantly different between all conditions, except the two BFR conditions. In the second and third sets of exercise, the greatest number of repetitions were performed in the LL condition ($P < 0.05$), and no differences

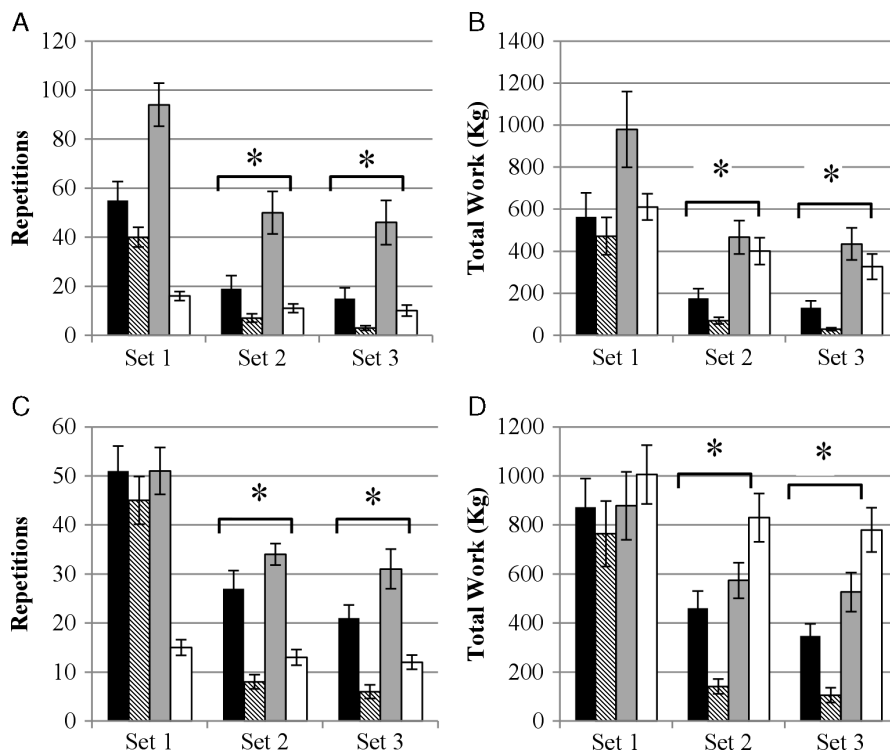


FIGURE 1—Repetitions and total work for leg press and heel raise. Data are mean \pm SE. BFR_{DBP}, low-load blood flow–restricted exercise with cuff pressure set at $1.3 \times$ resting diastolic BP (black bars); BFR_{SBP}, low-load blood flow–restricted exercise with cuff pressure set at $1.3 \times$ resting systolic BP (striped bars); LL, low-load resistance exercise (gray bars); HL, high-load resistance exercise (white bars). A, Leg press repetitions for each set of exercise. B, Leg press total work for each set of exercise. C, Heel raise repetitions for each set of exercise. D, Heel raise total work for each set of exercise. *Different from set 1, $P < 0.05$.

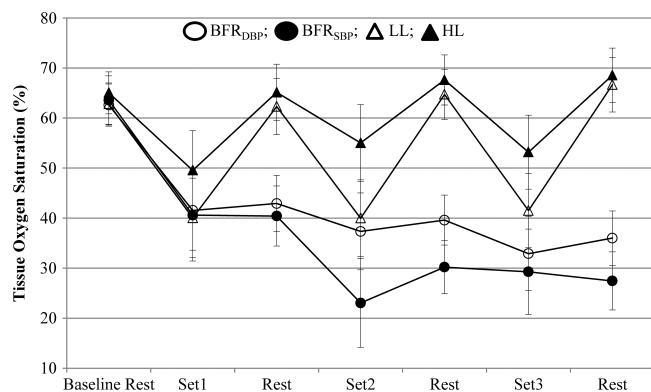


FIGURE 2—Thigh StO₂ during leg press exercise and rest. Data are mean \pm SE. StO₂ during exercise was lower than baseline rest in all conditions ($P < 0.05$). During the rest intervals, StO₂ was lower than baseline rest in the BFR conditions ($P < 0.05$) but not the HL or LL conditions.

were detected between the other three conditions. Leg press total work (Fig. 1B) performed during the first exercise set was greater during the LL condition than during any other condition ($P < 0.05$). No differences were detected between the other three conditions. In the second exercise set, total work was lower in the BFR conditions than that in the LL and HL conditions ($P < 0.05$). In the third set of exercise, total work was greatest in the LL and HL conditions but was only significantly different from BFR_{SBP}.

Heel raise repetitions (Fig. 1C) in the first set of exercise were lower in the HL condition than that in any other condition ($P < 0.05$). In the second and third sets of exercise, more repetitions were performed in the BFR_{DBP} and LL conditions than that in the BFR_{SBP} and HL conditions ($P < 0.05$). Total work (Fig. 1D) was not different between any of the conditions in the first set of heel raise exercise. In the second and third exercise sets, less total work was performed in the BFR_{SBP} condition than that in any other condition ($P < 0.05$), and total work was greater in the HL condition than that in either of the two BFR conditions ($P < 0.05$). No differences were detected between the LL and BFR_{DBP} conditions.

TABLE 1. Blood vessel measurements at rest and exercise.

	Leg Press		Heel Raise	
	Rest	Exercise	Rest	Exercise
Velocity (cm·s ⁻¹)				
BFR _{DBP}	98.54 \pm 6.50	112.90 \pm 7.32*	62.84 \pm 7.80	101.24 \pm 7.71*
BFR _{SBP}	92.46 \pm 6.49	85.85 \pm 11.12	55.84 \pm 6.90	40.13 \pm 7.32*
LL	97.08 \pm 9.04	162.40 \pm 8.65*	64.89 \pm 6.26	135.59 \pm 9.49*
HL	104.28 \pm 8.26	176.37 \pm 12.43*	64.26 \pm 6.26	134.13 \pm 9.66*
VTI (cm)				
BFR _{DBP}	16.84 \pm 1.56	25.63 \pm 2.29*	10.12 \pm 1.74	22.96 \pm 1.85*
BFR _{SBP}	15.35 \pm 1.42	14.60 \pm 1.98	8.51 \pm 1.16	9.86 \pm 2.18
LL	17.00 \pm 1.64	43.28 \pm 3.44*	12.76 \pm 3.11	46.26 \pm 4.00*
HL	18.54 \pm 1.67	55.55 \pm 4.71*	13.04 \pm 1.71	43.31 \pm 4.56*
Vein area (cm ²)				
BFR _{DBP}	0.29 \pm 0.05	0.68 \pm 0.06*	0.34 \pm 0.06	0.76 \pm 0.08*
BFR _{SBP}	0.25 \pm 0.06	0.88 \pm 0.12*	0.35 \pm 0.07	0.97 \pm 0.08*
LL	0.27 \pm 0.06	0.38 \pm 0.05*	0.34 \pm 0.05	0.51 \pm 0.05*
HL	0.27 \pm 0.05	0.38 \pm 0.05*	0.32 \pm 0.06	0.53 \pm 0.06*

*Different from baseline, $P < 0.05$.

Data are mean \pm SE. BFR_{DBP}, low-load blood flow–restricted exercise with cuff pressure set at 1.3 times resting diastolic BP; BFR_{SBP}, low-load blood flow–restricted exercise with cuff pressure set at 1.3 times resting systolic BP; LL, low-load resistance exercise; HL, high-load resistance exercise.

NIRS. The NIRS data (Fig. 2) showed a significant time effect for StO₂ at the vastus lateralis during the exercise sessions ($P < 0.05$). StO₂ decreased during exercise by approximately 50% in the BFR conditions, and by 35% and 20% in the LL and HL conditions, respectively. At the end of the 90-s rest periods, StO₂ returned to baseline levels in the conditions without the cuff, but it did not recover in the BFR conditions.

Blood flow. At baseline (rest), femoral and popliteal artery diameter, blood flow velocity, VTI, blood flow over time, and vein CSA were not different between conditions. Artery diameter did not change from baseline to 15 s postexercise in any condition (leg press, 0.502 \pm 0.057 cm; heel raise, 0.537 \pm 0.015 cm). Resting superficial femoral and popliteal artery diameters and femoral blood flow are similar to those previously reported (30,43). The resting popliteal artery blood flow measurements are higher than those previously reported in literature (42); however, this is likely due to the location of the measurement (close to the knee joint) and because our resting measurements occurred after the completion of leg press exercise.

The mixed model showed a significant time–condition interaction for femoral and popliteal blood flow velocity ($P < 0.001$), VTI ($P < 0.001$), blood flow ($P < 0.001$), and vein CSA ($P < 0.001$). The measured ultrasound variables are presented in Table 1, and the calculated blood flow (mL·min⁻¹) results are shown in Figure 3. Blood flow immediately after leg press and heel raise exercise was different between all conditions ($P < 0.05$) except HL and LL. In addition to less blood flow during the BFR_{SBP} condition, the flow profiles were more variable from one cardiac cycle to the next than they were in HL or LL. Femoral and popliteal vein CSA increased from baseline to exercise in all conditions, but the vein CSA after exercise was larger in the conditions performed with the cuff than that in those performed without it ($P < 0.05$).

The multiple regression model with all three predictors (cuff pressure, exercise load, and limb circumference) produced $R^2 = 0.367$, $P = 0.016$. Cuff pressure was a significant

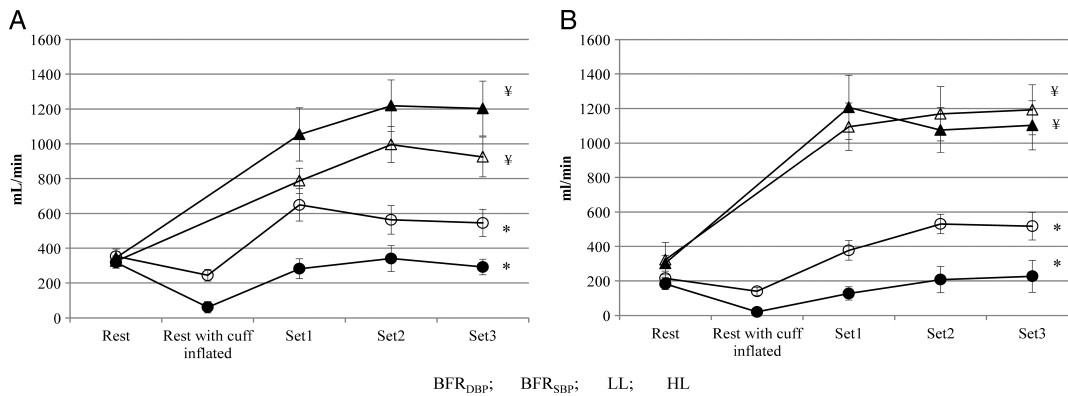


FIGURE 3—Femoral and popliteal artery blood flow. Data are mean \pm SE. **A, Femoral artery blood flow at rest and after each exercise set. B, Popliteal artery blood flow at rest and after each exercise set.** Blood flow increased ($P < 0.05$) from rest during leg press and heel raise exercise in all conditions except BFR_{SBP}. *Mean exercise blood flow is different from all other conditions, $P < 0.05$. †Mean exercise blood flow is different from BFR conditions, $P < 0.05$.

predictor of blood flow ($P = 0.011$); however, exercise load and thigh circumference did not significantly contribute to the model ($P = 0.064$ and $P = 0.399$, respectively). Cuff pressure had a positive regression weight, indicating that blood flow and cuff pressure were inversely related, after controlling for the other variables in the model. Exercise load and thigh circumference had positive regression weights, indicating that blood flow was greater in stronger individuals and in those with larger legs.

Echocardiographic and hemodynamic data. The repeated-measures ANOVA detected a significant time–condition interaction for SV ($P = 0.04$), HR ($P = 0.010$), \dot{Q} ($P < 0.001$), SBP ($P = 0.027$), and DBP ($P = 0.006$). SV increased from rest immediately after HL exercise ($P < 0.05$) and decreased after BFR_{SBP} ($P = 0.066$). \dot{Q} significantly increased during exercise (calculated from data measured within 15 s of exercise cessation) in all conditions except BFR_{SBP}. All conditions resulted in an increase in HR and SBP from baseline rest ($P < 0.05$), and DBP increased in all conditions except HL (Table 2).

DISCUSSION

The main goal of this study was to characterize local artery blood flow and StO₂, and the acute cardiovascular response to unilateral BFR, HL, and LL resistance exercise.

The main findings are as follows: (a) the exercise-induced increase in blood flow was reduced by the cuff pressure, most notably in the BFR_{SBP} condition; (b) \dot{Q} did not increase during exercise in the BFR_{SBP} condition; and (c) SBP and DBP were elevated above baseline during the rest intervals in BFR exercise conditions. The reduced blood flow and heightened BP responses to the BFR conditions agree with our original hypothesis, demonstrating that HL and BFR exercise affect the cardiovascular system differently. The cuff pressure clearly affected blood flow and the ability to perform work in subsequent exercise sets. In our study, subjects experienced ischemia at the exercising muscle for ~ 6 min and ~ 9 min in the BFR_{SBP} and BFR_{DBP} conditions, respectively. No ischemia-related effects were observed other than localized tingling or numbness, which subsided immediately upon cuff release. Previous investigations have shown that significant and irreversible limb skeletal muscle injury did not occur until approximately 3 h of ischemia in rats (1).

During leg press, the rate of fatigue (decrease in repetitions performed) from the first to second set of exercise was greater in the BFR conditions (BFR_{DBP} = 65% and BFR_{SBP} = 82%) compared with the LL and HL conditions (LL = 46% and HL = 36%). During heel raise, cuff pressure in the BFR_{SBP} condition also resulted in a high rate of fatigue (82%). The rate of fatigue was approximately 10%–15%

TABLE 2. Echocardiographic and hemodynamic variables.

	SV (mL)		HR (bpm)		\dot{Q} (L·min ⁻¹)		SBP (mm Hg)		DBP (mm Hg)	
	Baseline	Exercise	Baseline	Exercise	Baseline	Exercise	Baseline	Exercise	Baseline	Exercise
BFR _{DBP}	66.2 \pm 4.8	67.0 \pm 4.5 ^a	72 \pm 5	99 \pm 4 ^{b-d}	4.8 \pm 0.6	5.6 \pm 0.5 ^{b,e}	114 \pm 5	140 \pm 6 ^{a,b,d}	52 \pm 4	67 \pm 4 ^{b,e}
BFR _{SBP}	67.1 \pm 5.1	60.7 \pm 4.1 ^e	75 \pm 6	100 \pm 4 ^{b-d}	4.6 \pm 0.6	5.1 \pm 0.5 ^e	118 \pm 5	156 \pm 7 ^{b,e}	54 \pm 5	80 \pm 4 ^{b,e}
LL	69.3 \pm 5.5	70.8 \pm 4.6 ^a	75 \pm 6	113 \pm 5 ^{a,b,f}	4.5 \pm 0.6	6.7 \pm 0.6 ^{a,b,f}	111 \pm 5	127 \pm 4 ^{b,e}	48 \pm 4	57 \pm 3 ^{a,b,f}
HL	62.1 \pm 4.3	70.1 \pm 4.5 ^{a,b}	69 \pm 7	113 \pm 5 ^{a,b,f}	4.0 \pm 0.6	6.7 \pm 0.6 ^{a,b,f}	115 \pm 4	134 \pm 4 ^{a,b,d}	53 \pm 3	58 \pm 3 ^{a,f}

Data are mean \pm SE.

^aDifferent from LBFR_{SBP}, $P < 0.05$.

^bDifferent from baseline, $P < 0.05$.

^cDifferent from HL, $P < 0.05$.

^dDifferent from LL, $P < 0.05$.

^eDifferent from all other condition, $P < 0.05$.

^fDifferent from LBFR_{DBP}, $P < 0.05$.

BFR_{DBP}, low-load blood flow–restricted exercise with cuff pressure set at 1.3 times resting diastolic BP; BFR_{SBP}, low-load blood flow–restricted exercise with cuff pressure set at 1.3 times resting systolic BP; LL, low-load resistance exercise; HL, high-load resistance exercise.

lower for BFR_{DBP}, HL, and LL conditions for heel raise compared with leg press exercise. Although we did not design the study to compare differences between the leg press and heel raise exercises, it is possible that the metabolic profile or fiber type distribution in the active calf muscles resulted in an increased capacity to work under ischemic conditions (11). These results suggest that the required minimal cuff pressure may be different between muscle groups and may also depend on the muscle fiber type.

Our “exercise” measurements were obtained within 15 s of exercise cessation. Acquiring ultrasound images immediately after exercise allowed for better image quality and more precise and repeatable location of the measurements; however, we do recognize that blood flow obtained during the dynamic resistance exercise would likely be different, particularly in the HL and LL conditions. Specifically, the 15-s postexercise measurements may have been higher than blood flow during exercise in the HL and LL conditions because of the presence of postexercise reactive hyperemia. Alternatively, the weight lifted in the LL condition was fairly light relative to the subjects’ 1RM, and it may not have been sufficient to cause significant arterial or venous constriction. Blood flow measurements obtained within 15 s of exercise completion in the BFR conditions were likely similar during exercise because very little mechanical work was performed and the cuff pressure was maintained during the rest period. The BP measurements reported in this study were obtained during the rest intervals and are likely lower than the BP during exercise because the muscle pump stops and sympathetic activity changes upon exercise cessation (3). In the BFR conditions, BP may be similar during the rest intervals and during exercise because of the maintained cuff pressure and activation of the mechanosensors.

Recent studies have shown that artery blood flow is highly correlated with perfusion, indicating that changes in blood flow can be used to estimate relative change in muscle oxygen availability (2,13). Our NIRS data support the notion that measurements of blood flow under the different exercise conditions likely reflect changes in muscle perfusion and oxygen availability, suggesting that oxygen availability is one of the limiting factors in the ability to perform multiple sets of BFR exercise. The NIRS data collected throughout the leg press exercise suggest that the muscle was depleted of oxygen during the first set of exercise and rest in the BFR conditions, so that the start of each exercise set occurred in a condition of low oxygen availability. In contrast, in the HL and LL conditions, StO₂ was low during exercise and returned to or near baseline before the start of the next exercise set. Because of drop outs in the BP data collected during exercise, we were not able to calculate changes in vascular conductance (calculated as blood flow/MAP) from rest to exercise to further support the NIRS data. However, on the basis of baseline and immediate post-exercise blood flow and BP (collected during the 90-s post-exercise rest period), conductance during exercise in the BFR_{DBP} and BFR_{SBP} conditions would be similar or less

than baseline, respectively, whereas in the LL and HL conditions, conductance during exercise would be nearly double baseline values. Although the NIRS data have been shown to correlate well with muscle perfusion under normal conditions, it is possible that the cuff affects perfusion kinetics via externally applied pressure on the microvasculature, which could ultimately affect the ability to perform work. This particular NIRS system is reliable and well validated (7), but it is possible that changes in blood volume due to the cuff pressure and muscle contraction during exercise could have affected the accuracy of the StO₂ measurements. However, they should still be reliable because such movement should be consistent within a subject.

In this study, immediate postexercise blood flow and total work (sum of the entire exercise session) were higher after the HL and LL conditions than after the BFR conditions, and the reduction in work from the first to third set of exercise for each condition (leg press: BFR_{DBP} ~80%, BFR_{SBP} ~96%, LL ~60%, HL ~55%) was inversely related to postexercise blood flow. Because perfusion was also likely lower in the BFR conditions than that in the HL and LL conditions, our results suggest that the cuff pressure reduces oxygen supply to an extent that limits the ability to perform work and increases the rate of fatigue in the BFR conditions, and to a greater extent in the BFR_{SBP} than that in the BFR_{DBP} condition. Importantly, because LL exercise alone and ischemia alone do not provide a potent hypertrophic stimulus, the balance between the amount of work performed and the level of ischemia necessary to induce muscle hypertrophy needs to be more clearly defined.

The resting DBP in this study was notably low in all subjects. These results may be due to the supine exercise position and the healthy cohort of subjects. SBP and DBP were higher during the BFR sessions than the LL and HL sessions. HR was highest in the LL and HL conditions and was elevated from rest in all conditions. Exercise (with or without ischemia) excites group III and group IV mechanosensitive afferent nerves, which provide feedback to cardiovascular areas and lead to an increase in sympathetic (5,17) activity. Activation of the sympathetic nervous system causes a reflex increase in arterial pressure (i.e., muscle metaboreflex). During postexercise ischemia, the exercise-induced BP response is maintained due the sustained sympathetic activity, whereas HR returns to near resting levels because of parasympathetic reactivation (9,37). The maintained sympathetic activation observed in our study during postexercise ischemia is likely due to a combination of reduced blood flow and oxygen availability, as well as pressure on the muscle from the cuff (27). Although the BFR condition elicited a heightened pressor response, the reported SBP and DBP for all conditions were well within the values prescribed for cardiac rehabilitation.

The isometric and slow dynamic components of high-load resistance exercise cause vasoconstriction and rapid spikes in SBP and DBP, which places a pressure load on the myocardium. In contrast, mounting evidence suggests that dynamic

resistance training does not cause myocardial ischemia or threatening arrhythmias in patients with normal left ventricular function, possibly because elevated DBP and decreased venous return are associated with a pattern of blood flow distribution that favors coronary circulation (10,20,32). With these varying outcomes, there is a need to evaluate the cardiovascular responses that are specific to BFR exercise in clinical populations because the cardiovascular responses to the resistance exercise conditions may be different in a less healthy population. For example, hypertensive individuals are known to have an exaggerated BP response to resistance exercise and ischemia, likely because of enhanced activation of the metaboreceptors (4,18,31,34). Muller et al. (26) demonstrated that the augmented BP response to muscle contraction in peripheral artery disease patients was mitigated by 50% when an ascorbic acid supplement was provided before exercise. Pairing antioxidant supplements with BFR exercise may provide a unique approach means to control the BP response to BFR exercise in hypertensives and those with vascular dysfunction.

We showed that SV, HR, and \dot{Q} increased more during the HL and LL conditions than that in the BFR conditions. The blunted exercise-induced rise in SV observed in the BFR conditions may be caused by increased vascular resistance (i.e., increased cardiac afterload) and/or reduced venous return (i.e., decreased cardiac preload) associated with the cuff pressure (20). Renzi et al. (33) measured HR and estimated \dot{Q} and SV from finger BP waveforms during walking with and without blood flow restriction. HR was higher and SV was lower during walking with blood flow restriction than normal walking, and \dot{Q} was not different between conditions. Although the cardiovascular requirements of resistance and aerobic exercise are inherently different, the occlusion cuff does seem to mitigate the rise in SV during exercise. The measurements of vein CSA showed that the cuff pressure caused significant venodilation distal to the cuff, indicating that cardiac return from the femoral and popliteal arteries was reduced by the cuff pressure, which could affect cardiac preload and, consequently, SV. However, it is likely that muscle metaboreflex activation caused an increase in ventricular contractility (6) as well as central blood volume mobilization (36), which allowed for SV and \dot{Q} to be maintained at or above baseline levels in the BFR conditions. We were not able to acquire measures of left ventricular end-diastolic volume because of the complexity of the data collection protocol; however, future studies should include measurements of ventricular function.

BP and HR responses to HL, LL, and BFR resistance exercise have been measured in one other study (8); however, it should be noted that the measurements were taken 15 and 45 min after exercise. In that study, HR was elevated

after exercise in all conditions and to a greater extent in the HL condition at both 15 and 45 min postexercise. At 15 min postexercise, SBP and DBP were not different from baseline (8). It is likely that arterial resistance imparted by the BP cuff recovered before the 15-min measurement in the data presented by Fahs et al. (8), whereas the increases in BP reported in our study reflect the acute effect of exercise and the cuff pressure. Assessment of BP and HR variability via frequency analysis during the postexercise time (i.e., during 45 min of recovery) may provide important information about autonomic nervous system activity during resistance training that we were not able to detect in the immediate postexercise data.

Our results provide information about the relations between blood flow, total work, and StO₂ during and immediately post-HL, LL, and BFR resistance exercise; however, further work is necessary to improve the comfort of and most effectively prescribe BFR exercise. We demonstrated that cuff pressure does blunt the exercise-induced increase in blood flow to muscle, and the maintained cuff pressure limits recovery and the ability to perform further work. Because little to no work was performed in the BFR_{SBP} condition after the first set of exercise, it is possible that the training adaptations to BFR exercise could be achieved in one set of exercise rather than three. Alternatively, it may be possible to increase the effectiveness and mitigate the discomfort of BFR exercise by using a lower cuff pressure, such as that used in the BFR_{DBP} condition. This configuration would favor more work under a less severe ischemic environment. A future study should measure blood flow using a variety of cuff pressures that are evenly spaced between the low and high pressures in order to accomplish this goal and to establish a method to individualize cuff pressure. We also provided a comprehensive examination of the acute cardiovascular responses to each exercise condition and showed that BFR and HL resistance exercises stress the cardiovascular system differently. Our results suggest that BFR is safe for healthy individuals; however, further evaluations are warranted before prescribing LBFR exercise to individuals with compromised cardiac function.

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