

Restricted Blood Flow Exercise in Sedentary, Overweight African-American Females May Increase Muscle Strength and Decrease Endothelial Function and Vascular Autoregulation

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Key Words

Kaatsu, quadriceps femoris, resistance training, skeletal muscle

Abstract

Objectives: Exercise with partially restricted blood flow is a low-load, low-intensity resistance training regimen which may have the potential to increase muscle strength in the obese, elderly and frail who are unable to do high-load training. Restricted blood flow exercise has also been shown to affect blood vessel function variably and can, therefore, contribute to blood vessel dysfunction. This pilot study tests the hypothesis that unilateral resistance training of the leg extensors with partially restricted blood flow increases muscle strength and decreases vascular autoregulation.

Methods: The subjects were nine normotensive, overweight, young adult African-Americans with low cardi-

orespiratory fitness who underwent unilateral training of the quadriceps' femoris muscles with partially restricted blood flow at 30% of the 1-repetition maximum (1-RM) load for 3 weeks. The 1-RM load and post-occlusion blood flow to the lower leg (calf) were measured during reactive hyperemia.

Results: The 1-RM load increased in the trained legs from 77 ± 3 to 84 ± 4 kg ($P < 0.05$) in the absence of a significant effect on the 1-RM load in the contralateral untrained legs ($P > 0.1$). Post-occlusion blood flow decreased significantly in the trained legs from 19 ± 2 to 13 ± 2 mL·min⁻¹·dL⁻¹ ($P < 0.05$) and marginally in the contralateral untrained legs from 18 ± 2 to 16 ± 1 mL·min⁻¹·dL⁻¹ ($P = 0.09$). Changes in post-occlusion blood flow to the skin overlying the trained and the contralateral untrained muscles were not significant.

Conclusion: These results demonstrate that restricted blood flow exercise, which results in significant gains in muscle strength, may produce decrements in endothelial dysfunction and vascular autoregulation. Future studies should determine whether pharmacopuncture plays a role in treatments for such blood vessel dysfunction.

Received: Oct 09, 2016 Reviewed: Nov 16, 2016 Accepted: Jan 16, 2017

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1. Introduction

Previous studies have shown that low-load, low-intensity, restricted blood flow, resistance (Kaatsu) exercises increase muscle strength and induce muscle hypertrophy at relatively small, 20% - 30% of the 1-repetition maximum (1-RM), loads in subjects in healthy sedentary subjects and athletes, as well as in those undergoing musculoskeletal and cardiac rehabilitation [1-9]. Although Kaatsu exercise is reported to increase the blood flows in the calves of both young and elderly subjects [10, 11], little is known about the hemodynamic effects of such exercise in African-Americans, a population that appears to possess a predilection for endothelial dysfunction [12]. Obese individuals are known to be susceptible to endothelial dysfunction [13], and decrements in the capacity for vasodilation have been demonstrated after Kaatsu exercise [14], perhaps indicating that the mechanism underlying the acute decrease in muscle endurance is associated with such training [15]. This study tests the hypothesis that unilateral Kaatsu exercise of the leg extensors in overweight individuals increases muscle strength and decreases vascular reactivity in both the trained and the untrained legs. Such a finding would suggest an impairment of vascular autoregulation that could exacerbate the endothelial dysfunction that commonly occurs in overweight subjects.

2. Materials and Methods

Nine young-adult African-Americans (7 women, 2 men) with a mean age of 21.4 ± 0.5 years volunteered as participants in this pilot study, but one other subject failed to complete the protocols. The nine study subjects were normotensive, did not smoke, were free of overt disease (assessed by using a medical history questionnaire), were not taking medication, and were physically inactive. The subjects had not been involved in regular strength training during the eight months before the study. The subjects were fully informed of the study's purpose and risk and of the discomfort associated with the experiment before providing written, informed consent. The study was reviewed and approved by the Human Participants Institutional Review Board of Howard University.

At the onset of the study, participants were familiarized with the study protocol, and measurements of body composition and peak oxygen uptake were done to determine the physiological characteristics and capacity for exercise training of the study population. The experiments were performed at the same time of day, 7:00 - 9:00 am, after self-reported overnight fasting. The subjects were instructed not to perform any exercise before reporting to the laboratory. An anthropometric measurement of body fat was performed using the Lunar DPX-L dual-energy X-ray absorptiometer (Lunar Corp., Madison, WI). Pulmonary gas exchange and minute ventilation, functional capacity measures of peak oxygen uptake, were assessed during a standardized cycle ergometer progressive exercise test by using an automated open-circuit Max II metabolic measurement system (Physio-Dyne Instruments Corp., Quogue, NY). Intervention with partially-restricted, low-intensity, leg-extension exercise for 3 weeks consisted of the following measures of interest: (1) leg (calf) blood flow, (2) skin

(thigh) blood flow and (3) leg extensor motor strength.

We measured the blood flow to the skin of the thigh overlying the vastus lateralis muscle, an area exposed to the same conditions as the muscles subjected to the restricted blood flow training. A noninvasive Vasamedics Model BPM-2 Laser Doppler (Vasamedics, Eden Prairie, MN) device was used. An optical fiber of 0.5 mm in diameter delivered light to a probe head attached to the skin's surface with an adhesive ring. The probe was positioned approximately 2 cm below the pressure cuff on the thigh, and the blood flow to the skin was expressed in units of mL/min/100 g. The baseline resting blood flow to the skin was recorded prior to the measurement of the baseline resting blood flow to the leg, and the post-occlusion blood flow to the skin was recorded at the same time as the measurement of the blood flow to the leg during reactive hyperemia.

Blood flow to the calf was measured with the subject in a supine position by using the method of venous occlusion strain-gauge plethysmography. An elastic mercury-in-rubber strain gauge 2 cm smaller than the widest circumference of the calf was placed around the calf and connected to an EC-6 plethysmograph recorder (Hokanson, Bellevue, WA). Inflation cuffs were positioned 6 - 8 cm above the knee and around the ankle. The online analog signals of the EC-6 plethysmograph blood flow traces were processed in real time. To facilitate venous drainage, we placed a 15-cm-thick foam block under the ankle to position the limb above the level of the heart. The thigh cuff was connected to a rapid inflation pneumatic air sources (E20 Rapid Cuff Inflator and AG101 Cuff Inflator Air Source, Hokanson, WA) for venous and arterial occlusions, respectively. Measurements of the blood flow to the leg were made for both limbs. Resting and reactive hyperemic blood flows were calculated by using the slope of the volume change over the first cardiac cycle and NIVP3 version 5.29C software (Hokanson, Bellevue, WA), and the results were expressed in mL/min/100 mL of tissue. Peak changes in blood flow were analyzed [16-19].

Participants were instrumented with the Hokanson plethysmography system, after which they rested for 15 minutes in the supine position. One minute prior to measuring the resting blood flow, the arterial blood flow to the foot was occluded by inflating the ankle cuff to 250-mm Hg. The measurement of the resting blood flow was performed by inflating the thigh cuff to a venous occlusion pressure of 50-mm Hg for 4 seconds, after which the cuff was deflated. This process was repeated three times with 15 seconds between each measurement, and the average was used for data analysis. Vital signs of heart rate and blood pressure were measured using a Dinamap PRO 300 monitor (DRE, Inc., Louisville, KY).

Following the resting blood-flow measurement, reactive hyperemia was produced by inflating the thigh blood-pressure cuff to 250-mm Hg for 5 minutes to induce arterial occlusion. After 4 minutes of arterial occlusion, the ankle cuff was inflated to 250-mm Hg. Before release of the occlusion, the pressure of the thigh cuff was set at a venous occlusion pressure of 50-mm Hg. Blood flow measurements were obtained every five seconds for one minute. The peak value obtained after occlusion was reported as the measurement of the blood flow in the leg during reactive hyperemia.

The strength of the quadriceps' extensor muscle was measured in both limbs during the knee extension exercise with

the 1-RM load, which is defined as the maximum amount of weight that a subject is able to lift once by using a seated leg extension machine with pneumatic resistance (Keiser Sport, Fresno, CA). The test was started by positioning the knee flexion at 90°. The subjects were instructed on and then practiced the proper execution of the seated leg extension exercise. After this familiarization, subjects completed a generalized warm-up of five-min treadmill exercise plus stretching of the quadriceps, hamstrings, and lower back. After this warm-up, subjects were positioned on the leg extension machine, and position measurements were recorded for subsequent testing. The initial load was set at 60% of the subject's estimated 1-RM by using reference values established for this exercise in our laboratory. Subjects were instructed to perform 1 repetition at this load, after which the load was increased by 20 kg until the 1-RM load was identified as the greatest amount of weight lifted through the complete range of motion.

The 3-week training regimen consisted of three sessions per week of supervised resistance training. One leg was randomly selected for training at 30% 1-RM with restricted blood flow. Training consisted of a unilateral knee extension exercise using 30% 1-RM. Following a warm-up, the subjects performed a single leg-knee extension in a sitting position by using the same device employed for the 1-RM strength test. For training, the limb with the restricted blood flow was used to complete three sets of the leg extension exercise with 12 repetitions per set at a cadence of 1.5-s lifting and 1.5-s lowering the limb, with a 30-s rest interval between sets. A vascular occlusion cuff on the thigh was maintained at an occlusion pressure of 2/3 the systolic blood pressure. This pressure was maintained for the entire time of the three sets, including rest periods. The untrained limb with unrestricted blood flow served as the control.

The main dependent cardiovascular response variables of interest were identified as the extensor muscle's strength and the calf's blood flow both in the control, untrained leg and in the experimental, trained leg with a partial blood-flow restriction. The statistical significance of the differences between each of the dependent variables was evaluated across the independent categorical variables, which were designated as pre-training and post-training. The assumption of normality in the distribution of least-squares residuals was met by virtue of the skewness and the kurtosis values being between -1.0 and +1.0, and the statistical significance of the intergroup differences was determined using the SigmaStat (version 3.1.1, Richmond, CA) statistical program.

To examine the influence of three weeks of partially restricted blood flow, low intensity exercise, we used the one-tailed paired *t*-test to compare pre- and post-training conditions. All data are presented as means \pm standard errors (SEs). Differences were considered significant at $P < 0.05$. Adequacy of the sample size was guaranteed by estimating the statistical power ($1 - \beta$) from a one-sided *t*-test statistical power computation [20].

3. Results

The characteristics of the study population showed that the subjects were normotensive, overweight young adults with low cardiorespiratory fitness (Table 1). Measurements were

made of the blood flow to the skin of the thigh exposed to the same partially-restricted blood flow as the trained leg. No significant pre- versus post-training differences were observed in the measurements of the cutaneous blood flow to the skin of the thigh (Table 2). In addition, 1-RM load measurements of the strength of the leg's extensor muscle were made. Resistance training of the quadriceps' muscles with partial blood-flow restriction increased the muscle strength in the trained leg ($P < 0.05$) without a significant change in the strength of the contralateral muscles in the untrained leg ($P > 0.1$) (Table 3). Measurements of the blood flow to the calf during post-occlusion reactive hyperemia showed that the training regimen resulted in a significant decrement in post-occlusion blood flow to the calf of the trained leg ($P < 0.05$) and a marginal decrement in the untrained leg, but this difference did not reach significance ($P = 0.09$) (Fig. 1). The statistical power of these results was 0.81.

4. Discussion

This study showed that three weeks of low-load resistance training of the leg's extensor muscles with partial blood-flow restriction increased the strength of the leg's extensor muscle and decreased post-occlusion blood flow to the calf muscles of the trained legs and marginally decreased that in the untrained legs. These changes occurred in the absence of changes in post-occlusion blood flow to the skin overlying the leg extensors. The present study was performed with arterial restriction.

Peak post-occlusive blood flow has been shown to be a reliable measure of impaired blood-vessel reactivity in normal subjects, in stroke patients, and in patients with peripheral artery disease [16-19]. Thus, we believe the post-training decrements in peak post-occlusive blood flows measured in this study are indicative of physiologically significant decrements in blood-vessel autoregulation associated with four weeks of resistance training with partially restricted blood flow. The decrements in post-occlusion blood flow and in flow-mediated dilation are indicators of the potential for blood-vessel dysfunction and injury [21], as well as for impaired neurovascular responsiveness [22]. In a previous study done by our laboratory on an all-male group of African-American subjects with normal weights, the blood flows to the calf used to compute vascular resistance were about the same as those in the overweight, mostly female group of the present study [23]. In another comparison, the post-occlusion blood flows measured in this study were 10% - 20% lower than the pre-training control measurements and similar to the control values in a group of white students with parental histories of hypertension [23]. The post-occlusion blood-flow measurements were normalized similarly in both studies. Thus, the pre- vs. post-training decrement in post-occlusion blood flows reported in this study likely represents a physiologically significant change in blood-vessel function. Restricted blood-flow training has been reported to impair flow-mediated dilation [14].

A study comparing low-load resistance training of the leg's extensor muscles with restricted blood flow to high-load resistance training without restricted blood flow purports to show that both regimens may increase motor strength without altering nerve or vascular function [24]. However, no phys-

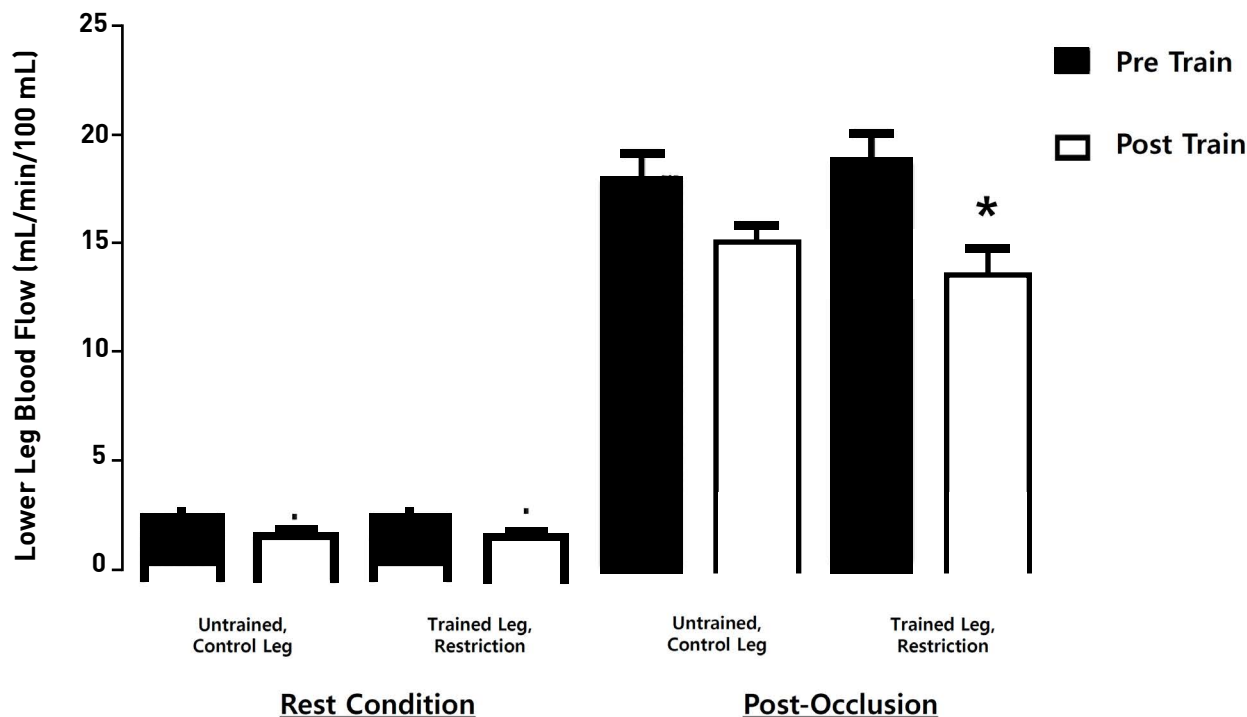


Figure 1 Blood flows measured during baseline (rest) and after 5 minutes of arterial occlusion to the leg muscles associated with reactive hyperemia in the untrained control and in the trained legs before (pre-training) and after (post-training) three weeks of low-intensity resistance training at 30% of the 1-repetition maximum load with partially restricted blood flow.

*The difference in the values of the post-occlusion blood flows before and after training was significant at $P < 0.05$.

Table 1 Characteristics of the study subjects (n = 9)

Variable	Mean \pm SE
Age (year)	21.4 \pm 0.5
Height (cm)	169.6 \pm 3.1
Weight (kg)	75.8 \pm 2.4
Body fat (%)	33.7 \pm 3.3
SBP _{rest} (mm Hg)	119.6 \pm 3.1
DBP _{rest} (mm Hg)	76.6 \pm 1.3
HR _{rest} (b.min ⁻¹)	76.3 \pm 4.0
V.O _{2peak} (mL.kg ⁻¹ .min ⁻¹)	30.6 \pm 2.4
HR _{peak} (b.min ⁻¹)	185.5 \pm 2.8

SE, standard error; SBP_{rest}, systolic blood pressure at rest; DBP_{rest}, diastolic blood pressure at rest; V.O_{2peak}, peak oxygen uptake; HR_{peak}, peak heart rate.

iologically significant measure of the capacity for vasodilation was found, and the measures of vascular function were based mainly on the concentrations of mediators of inflammation and coagulation. That study did demonstrate a positive effect on fibrinolytic activity in the absence of changes in the levels of the mediators of inflammation and coagulation, which may prove beneficial to patients at risk for thrombosis and related cardiovascular diseases. Low-load aerobic exercise (walking) with restricted arterial blood flow has been reported to be associated with higher cardiac work and lower capacity for flow-mediated dilation [25]. In the present study, the reduction in the post-occlusion hyperemic blood flow after three weeks of resistance training with restricted blood flow may be indicative of a predilection for endothelial dysfunction such as that demonstrated in 8- to 18-year-old African-American adolescents [12] at high risk for developing insulin resistance and cardiovascular disease in the future. In light of a recent report that meloxicam pharmacopuncture can decrease endothelial dysfunction [26], future research should determine whether pharmacopuncture with nonsteroidal anti-inflammatory agents can protect blood vessels from decrements in blood-vessel autoregulation associated with insulin resistance, cardiovascular disease, and restricted blood-flow exercise. A major limitation of this pilot study is the small sample size.

5. Conclusion

Table 2 Control measurements of cutaneous blood flows after 5 minutes of occluding blood flow to the skin of the thigh overlying the vastus lateralis muscles

Training	Control, untrained		Trained, restricted blood flow	
	Baseline	Post-occlusion	Baseline	Post-occlusion
Pre-training blood flow (mL/min/100 mL)	2.5 ± 0.2	4.2 ± 0.4*	2.5 ± 0.2	4.8 ± 0.6
Post-training blood flow (mL/min/100 mL)	2.9 ± 0.28*	4.6 ± 0.4*	2.8 ± 0.2*	4.9 ± 0.5*

*The difference from the pre-training value was not significant ($P > 0.1$).

Table 3 Values for the 1-repetition maximum load in the untrained control and in the trained legs before (pre-training period) and after (post-training period) three weeks of low-intensity resistance training at 30% of the 1-repetition maximum load with restricted blood flow

	Untrained leg		Trained leg, restricted blood flow	
	Pre-training	Post-training	Pre-training	Post-training
1-Repetition maximum (kg)	75.0 ± 6.1	78.5 ± 6.2	76.5 ± 3.3	84.0 ± 4.0*

*The difference between the values before and after training was significant at $P < 0.05$.

The present study demonstrates that resistance training using low loads with partially restricted arterial blood flow increases motor strength and decreases post-occlusion blood flow in a group of overweight, young adults. Limitations of post-occlusion blood flow are described in the scientific literature with structural adaptations. Therefore, the limitations described in this study on the mechanisms of skeletal-muscle blood-vessel autoregulation produced by restricted blood flow training regimens may put overweight individuals at risk for blood-vessel dysfunction and remodeling, which are known risk factors for cardiovascular disease. Future studies should determine whether this limitation of post-occlusion blood flow is unique to this population of sedentary, overweight, young-adult African-Americans, which might be a reflection of their predilection for endothelial dysfunction, a condition that can be reversed by using pharmacopuncture.

Acknowledgement

This work was supported in part by grant 2G12 RR003048 from the Research Centers in Minority Institutions (RCMI) Program, Division of Research Infrastructure, National Center for Research Resources, National Institutes of Health, USA.

Conflict of interest

The authors declare that there are no conflicts of interest.

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