Published in final edited form as:
Clin Physiol Funct Imaging. 2008 September ; 28(5): 318–325. doi:10.1111/j.1475-097X.2008.00812.x.

Role of retrograde flow in the shear stimulus associated with exercise blood flow

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Summary

To test the hypothesis that retrograde flow influences the shear stimulus of exercise blood flow, eight healthy men [25.6 ± 3.1 y (SD)] performed 20 min of single-leg knee extension exercise at two contraction velocities: fast (FR, 1.5 $m \cdot s^{-1}$) and slow (SR, 0.4 $m \cdot s^{-1}$). Contraction frequency (30 cpm) and workload (5 kg) were kept constant resulting in a work rate of 15.25 W for both contraction velocities. Common femoral artery diameter and blood velocity were measured at rest and during exercise using ultrasound Doppler. Mean blood flow was not different between contraction velocities while antegrade (2012.4 ± 379.9 vs. 1745.6 ± 601.5 $ml \cdot min^{-1}$, $P = 0.05$) and retrograde (121.7 ± 43.0 vs. 11.2 ± 6.6 $ml \cdot min^{-1}$, $P < 0.001$) flow were higher during FR than SR contractions, respectively. Despite the similar mean blood flow response, vascular resistance was lower during FR than SR contractions (0.06 ± 0.01 vs. 0.08 ± 0.03 U, $P = 0.03$) and was closely related to shear rate (pooled data: $r = -0.77$, $P < 0.01$). Retrograde flow was associated with a lower vascular resistance during exercise (pooled data, $r = -0.48$, $P \leq 0.05$). In addition, calculated oscillatory flow indices were higher during FR than SR contractions and were significantly correlated to retrograde flow, shear rate, and vascular resistance. These results indicate that retrograde blood flow influences the shear stimulus of exercise blood flow by enhancing the oscillatory behavior of flow.

Keywords

ultrasound Doppler; knee extension; shear stress; flow pulsatility; retrograde blood flow

Introduction

The mechanical force that flowing blood exerts on the vessel wall (i.e. wall shear stress) is recognized as a key regulator of endothelial cell function (Davies, 1995). The characteristics of wall shear stress are an important consideration since low arterial shear stress (~ 4 dyne/cm^2) is associated with a pro-thrombotic state of the vascular endothelium which significantly contributes to the development of vascular-related diseases (Malek *et al*., 1999). In contrast, pulsatile shear stress within a physiological range (>15 $dyn \cdot cm^2$) stimulates the vascular endothelium to synthesize and release substances including nitric oxide, prostacyclin, and tissue-type plasminogen activator that act to regulate vascular tone and maintain a healthy vessel wall. Based on the causal relationship between vascular wall shear stress and endothelial function, the observation that chronic physical activity leads to improved endothelial cell function (Clarkson *et al*., 1999; Hambrecht *et al*., 2003; Katz *et al*., 1997; Kingwell *et al*.,

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1997) has led to the hypothesis that exercise-induced blood flow patterns are involved in the vascular modification (Niebauer & Cooke, 1996).

In vivo examination of the blood flow patterns generated during physical activity in humans has mainly been observed in the large conduit arteries using ultrasound Doppler which measures instantaneous changes in blood velocity and vessel diameter (i.e. blood flow) with high temporal resolution (Rådegran, 1997). It has long been appreciated that exercise generates a highly oscillatory (i.e. change in direction) flow pattern characterized by large increases in forward (antegrade) flow as well as reverse (retrograde) flow (Anrep *et al*., 1934; Walloe & Wesche, 1988). The generation of retrograde flow as measured in the blood flow response to contracting muscle is attributed to mechanical impedance of blood flow caused by the restriction of the large vessels at the fascial level as they enter and leave the muscle (Gray *et al*., 1967) and/or by the local compression of intramuscular vessels during the muscle contraction (Barcroft & Dornhorst, 1949; Sadamoto *et al*., 1983). As a result, retrograde flow is found to increase with muscle tension development (Green *et al*., 2005; Lutjemeier *et al*., 2005) and can be equivalent to 15% of the mean blood flow response to exercise (Hoelting *et al*., 2001).

During the rise of muscle blood flow to meet the metabolic requirements set by contracting muscle, the vascular endothelium is exposed to elevated wall shear stress that stimulates the release of vasoactive substances resulting in smooth muscle relaxation and a decreased vascular resistance to flow. Recently, the influence of exercise-induced blood flow patterns on the endothelial-derived release of nitric oxide was examined during lower and upper limb exercise (Green *et al*., 2005). During forearm exercise, brachial artery blood flow was largely comprised of antegrade flow with only negligible contributions of retrograde flow resulting in relatively little oscillations in muscle blood flow. Consequently, the inhibition of nitric oxide during forearm exercise had little effect on exercise blood flow. In contrast, cycling exercise produced significantly higher retrograde flow in the brachial artery than forearm exercise resulting in large oscillations in blood flow (Green *et al*., 2005). In this case, inhibition of nitric oxide during cycling exercise led to a reduction in brachial artery blood flow (Green *et al*., 2005). These findings are consistent with the view that significantly large shifts in antegrade and retrograde flow may be a potent shear stimulus for the release of endothelial-derived nitric oxide (Green *et al*., 2004). However, to date, little attention has been given to the effect of different exercise-induced flow patterns on shear stress-mediated stimulation of the vascular endothelium *in vivo*. Therefore, the purpose of this study was to test the hypothesis that retrograde flow influences the shear stimulus associated with exercise blood flow as observed by changes in vascular resistance.

Methods

Subjects

Eight male subjects with an average age of 25.6 ± 3.1 (SD) y participated in this study. Subjects reported to be either sedentary or recreationally active, and were void of metabolic and cardiovascular disease as assessed through a standard medical history questionnaire. The study was approved by the Human Subjects Research Committee at The University of Toledo and is in accordance with guidelines set forth by the Declaration of Helsinki. All subjects provided written informed consent after being explained all experimental procedures, the exercise protocol, and possible risks associated with participation in the study.

Experimental protocol

Subjects participated in three study visits separated by no less than 48 hrs. During the first visit, anthropometric measurements were obtained including subject height, weight, and maximal

knee extensor strength. The highest workload the subject could lift during one full knee extension (i.e. 1 repetition maximum) was considered their maximal knee extensor strength. In addition, subjects practiced the contraction velocities that would be performed during the subsequent visits until they were proficient with each protocol. During the second and third visits, subjects were seated in a reclined chair (~60°) with the right thigh secured to the chair with a strap placed approximately 10 cm above the knee in order to minimize any extraneous movement. The right foot was secured in a boot that was attached to a custom-built leg ergometer using a pulley and cable system, which allowed for 0.6 m of distance traveled with each knee extension. The left arm was positioned at the level of the heart for the measurement of blood pressure at rest and during exercise. After the subjects were positioned and secured to the ergometer they were allowed to rest for approximately 15 min prior to the measurement of femoral artery diameter, blood velocity and blood pressure. Each subject performed single-leg knee extension exercise at one of two contraction velocities: fast (FR, 1.5 m/s, 0.2 duty cycle) and slow (SR, 0.4 m/s, 0.6 duty cycle). The order of the contraction velocities was randomized between subjects during visit two and three. To prevent muscle fatigue from occurring, the exercise session was divided into four bouts of exercise each lasting 5 min (total exercise duration = 20 min) with 1 to 2 min rest periods allowed between each bout of exercise (see Figure 1). Following at least 60 min of recovery, the exercise task was repeated so that femoral artery diameter and blood velocity could be measured separately. The order of femoral artery diameter and blood velocity measurements was randomized between subjects. Contraction frequency (30 cpm), workload (5 kg) and distance traveled (0.6 m) were kept constant during exercise resulting in a work rate of 15.2 Watts for both the fast and slow contraction velocities according to the equation: work rate (W) = [contraction rate (contractions)/60 s] * [distance of a knee extensor revolution (m)] * [load weight (kg) * 9.8 (m/s^2)] (Osada & Rådegran, 2002).

Measurements

Instantaneous blood velocity ($cm \cdot s^{-1}$) was recorded continuously at rest and during exercise using a Doppler ultrasound velocimetry system (model 500-M, Multigon Industries, NY) operating in pulsed mode. The pulsed-wave Doppler transducer, with an operating frequency of 4 MHz and fixed transducer crystal and sound beam angle of 45° relative to the skin, was placed flat on the thigh 2-3 cm below the inguinal ligament, above and parallel to the common femoral artery. This position was selected to minimize turbulent flow arising from the bifurcation of the common femoral artery into the superficial and profundus branches. The gate was set at full width to ensure complete insonation of the femoral artery. Blood velocity was measured in all subjects by one researcher exhibiting a between-day and test-retest coefficient of variation of 10.4% and 6.4%, respectively. Electrocardiography (ECG) was obtained using a modified 3-lead placement. The continuous cardiovascular (blood velocity, ECG) data were digitized , sampled at 200 Hz (ADInstruments, PowerLab 16SP, Grand Junction, CO) and stored for offline analysis. Femoral artery diameter was measured at rest and during the steady-state phase of each exercise bout using an ultrasound imaging system (Logiq 400, GE Medical Systems, WI) equipped with a linear array transducer operating at an imaging frequency of 7.5 MHz. Images were recorded for 30 s and stored for offline analysis. Femoral artery diameter was measured in all subjects by one researcher exhibiting a between-day and test-retest coefficient of variation of 2.2% and 1.1%, respectively. Blood pressure was measured manually from the left arm by auscultation at rest and during the steady-state of exercise.

Data processing

Femoral artery blood velocity was averaged over each cardiac cycle between R-R wave intervals using software described in a previous study (Hoelting *et al.*, 2001). The mean blood velocity, which is calculated as the integrated area under the average velocity profile, is also reported in terms of antegrade and retrograde velocities. Analysis based on the contraction-

relaxation phases was not performed in the present study since the results of previous studies have shown that mean blood flow (Lutjemeier *et al*., 2005; Rådegran, 1997) as well as maximum and minimum blood flow values are similar regardless of the ECG-or contraction-averaged analysis approach is used, at least at low work loads (< 30 W) (Osada & Rådegran, 2006). Common femoral artery diameter was determined from longitudinal views of the vessel from 10 measurements randomly made where the vessel walls could be most clearly visualized using commercially available tracking software (MaxTRAQ, Innovision Systems Inc., Columbiaville, MI). The mean vessel diameter was used to calculate an average cross-sectional area (CSA = πr^2) of the artery, which in turn was multiplied by the appropriate blood velocity to obtain the corresponding femoral blood flow (mean blood flow = blood velocity * CSA * 60). In addition to mean blood flow, antegrade and retrograde blood flows were also determined for each cardiac cycle. Resting diameter for each subject was used to calculate resting blood flow while an average exercise diameter (mean of the diameter measurements obtained during each bout of exercise) was used to calculate blood flow during exercise. For each subject, blood flow was reduced from cardiac cycle-by-cycle values into 20 s averages for statistical analysis. In addition, blood flow values during the last minute of each exercise bout were averaged together for each subject to determine the average blood flow response to exercise for each contraction velocity. Using mean blood flow and mean arterial pressure, femoral vascular resistance and conductance was calculated using standard equations. Shear rate was calculated using Poiseuille's equation: shear rate = (4*mean blood flow)/πr^3 (Silber *et al*., 2005). Pulsatility index [PI = (maximal-minimal velocity)/mean velocity] was calculated from 10 s averages measured at rest and at 30 s during each recovery phase between the exercise bouts to avoid the influence of muscle contractions on the blood velocity waveform (see Figure 1).

To determine the effect of contraction-induced vascular compressions on cardiac-driven flow, spectral analysis was performed on blood velocity and ECG waveforms using the discrete fast-fourier transform (1024 data points, cosine window, 50% overlap) to calculate the frequency amplitude of blood velocity and ECG waveforms (band-passed filtered 10-0.05 Hz). The spectra were then cross-correlated in the time domain to quantify the degree of blood velocity variation from cardiac activity that was caused by mechanical impedance to flow induced by muscle contractions. The cross-correlation peak amplitude is related to the amount of concordance of the two signals considered with a tight coupling resulting in a cross-correlation coefficient of 1.0 (Nichols & O'Rourke, 1998). Thus, fluctuations in one signal but not the other would decrease the peak cross-correlation coefficient.

Calculated oscillatory flow indices

Several hemodynamic parameters were calculated to relate the influence of contraction-induced flow patterns on shear rate and vascular resistance. The degree of flow oscillation in the shear direction was calculated according to the formula: oscillatory shear index (OSI) = | Retrograde Flow| / |Antegrade Flow| + |Retrograde Flow| (Moore *et al*., 1994). Maximum and minimum shear stresses were calculated from antegrade and retrograde blood flow, respectively, and added together to give an index of pulse shear rate. As an index of the frequency of flow pulsations, Womersley frequency (W_f) number was calculated according to the formula: W_f = 0.5d*SQRT(2πHR/ν), where d = artery diameter (m), SQRT = square root, HR = heart rate, ν = kinematic viscosity (assumed to be $3.8 \cdot 10^{-6}$ $m^2 s^{-1}$). Lastly, analysis of the blood flow velocity waveform was performed on a 10 s segment of the steady-state blood velocity achieved during the last bout of exercise for FR and SR exercise. As an index of the amplitude of flow oscillations, the peak-to-minimum amplitude of the blood velocity waveform was measured using commercially available software (Chart v5.0, ADInstruments).

Statistical analysis

Since steady-state exercise was achieved during each bout of FR and SR exercise, measurements obtained during each bout of exercise for each subject were averaged together so that each subject contributed one average exercise value to be used in the statistical comparisons. Paired t-tests were used to test for differences between rest and exercise values as well as testing for differences between the fast and slow contraction velocities. Linear regression was used to identify correlations between variables. Statistical significance was set *a priori* at $P \leq 0.05$. Values are expressed as mean ± SD unless stated otherwise.

Results

On average subjects weighed 78.8 ± 14.4 kg, were 176.5 ± 6.5 cm tall, and had a body mass index of 25.5 ± 3.0 $kg \cdot m^2$. The group mean maximal knee extensor strength was 564.3 ± 151.5 N. Based on this value the workload used during exercise was 9.1 ± 2.7 % of maximal knee extensor strength. Femoral artery diameter was similar between FR and SR conditions at rest (FR: 9.2 ± 0.5 mm vs. SR: 9.3 ± 0.8 mm, $P = 0.26$) and did not change significantly from rest to exercise during FR (9.3 ± 0.5 mm, $P = 0.09$) or SR (9.4 ± 0.7 mm, $P = 0.07$).

Table 1 shows a comparison of the average resting and exercise values for cardiovascular data between contraction velocities. At rest, no significant difference was present in any of the cardiovascular variables measured. During exercise, heart rate ($P = 0.02$) and vascular resistance ($P = 0.02$) were higher during SR than FR contractions. In the recovery phase following the exercise bouts, pulsatility index was higher following FR than SR exercise ($P = 0.01$). All other variables including mean blood flow ($P = 0.33$) and mean arterial pressure ($P = 0.10$) were not different between contraction velocities during exercise. Vascular resistance was found to have a linear inverse relationship with shear rate during SR ($r = -0.89$, $P < 0.001$) but not FR ($r = -0.38$, $P = 0.34$) contractions. When the data were pooled together, a significant curvilinear relationship ($r = -0.77$, $P < 0.01$) was found between vascular resistance and shear rate during exercise (Figure 2). This finding is in agreement with the shear stimulus being applied to the vascular endothelium by exercise blood flow resulting in a change in vascular resistance.

The muscular contractions associated with FR and SR exercise produced significantly different blood flow patterns (Figure 1). Cross-correlation between blood velocity and cardiac drive was reduced during FR (rest: 0.77 ± 0.05 vs. exercise: 0.60 ± 0.04, $P = 0.0002$) and SR (rest: 0.77 ± 0.05 vs. exercise: 0.71 ± 0.08, $P = 0.01$) exercise with muscle contractions affecting this relationship to a greater extent during FR exercise. At rest, no difference was present in antegrade (FR: 288.9 ± 121.6 vs. SR: 386.4 ± 257.4 $ml \cdot min^{-1}$, $P = 0.29$) or retrograde (FR: 66.8 ± 63.8 vs. SR: 64.4 ± 62.0 $ml \cdot min^{-1}$, $P = 0.90$) blood flow. However, antegrade flow was higher during FR as compared to SR exercise (2012.4 ± 379.9 vs. 1745.6 ± 601.5 $ml \cdot min^{-1}$, $P \leq 0.05$). The major difference between contraction velocities was retrograde flow which reached 121.7 ± 43.0 $ml \cdot min^{-1}$ during FR exercise but only 11.2 ± 6.6 $ml \cdot min^{-1}$ during SR exercise ($P < 0.001$) (Figure 3). Retrograde flow correlated positively with antegrade flow during FR exercise ($r = 0.66$, $P < 0.001$) such that increased retrograde flow was associated with a greater augmented antegrade flow. In contrast, retrograde flow was not significantly correlated to antegrade flow during SR exercise ($r = -0.32$, $P = 0.42$). Lastly, retrograde flow was negatively correlated with vascular resistance during FR ($r = -0.78$, $P = 0.02$) but not SR ($r = -0.44$, $P = 0.26$) contractions. When the data were pooled together, retrograde flow was significantly correlated ($r = -0.48$, $P \leq 0.05$) with vascular resistance during exercise.

The contribution of retrograde flow to the contraction-induced blood flow patterns was evident in the comparisons of oscillatory flow indices between contraction velocities. Table 2 shows that the OSI, shear pulse, and peak-to-minimum velocity amplitude were all significantly

higher during FR as compared to SR exercise. In contrast, W_f was higher during SR than FR exercise likely due to the higher HR reached during SR exercise. Retrograde flow was positively correlated with OSI, shear pulse and peak-to-minimum amplitude (Table 3). Among the calculated oscillatory flow indices, shear pulse and peak-to-minimum velocity amplitude were closely related to antegrade and retrograde flow along with the elevated shear rate and reduced vascular resistance during exercise (Figure 4). These results suggest that the degree of oscillations in blood flow influence the shear stimulus associated with contraction-induced flow patterns.

Discussion

The purpose of the present study was to test the hypothesis that the presence of retrograde flow in the contraction-induced flow pattern would influence the shear stimulus associated with exercise blood flow. Femoral artery blood flow was measured during single-leg knee extension exercise using ultrasound Doppler, a tool that allows instantaneous measurement of bi-directional flow with high temporal resolution (Rådegran, 1997). The common femoral artery was studied because it is the main artery supplying the muscles of the thigh with blood flow during knee extension exercise, and is therefore, the site of elevated shear stress during exercise. The main findings of the present study were as follows. *1)*Contraction velocity influences the generation of retrograde blood flow such that fast contractions produce more retrograde blood flow than slow contractions in spite of performing the same amount of contractile work. *2)* Shear rate was strongly related to changes in vascular resistance which was lower during FR than SR exercise despite a similar mean blood flow response between contraction velocities. *3)*Retrograde flow was significantly related to changes in vascular resistance such that higher retrograde flow was associated with a lower vascular resistance. *4)*The magnitude of flow oscillations were higher during FR than SR exercise and were strongly correlated with retrograde flow, shear rate, and vascular resistance. Collectively, these results indicate that retrograde blood flow influences the shear stimulus of exercise blood flow by enhancing the oscillatory behavior of flow. Further study examining the characteristics of blood flow during exercise is warranted since shear stress waveform influences the expression of proinflammatory and procoagulatory transcripts (Malek *et al*., 1999) along with endothelial cell gene expression and phenotype (Laughlin *et al*., 2007).

Previous studies have shown retrograde blood flow to be a function of both work rate (Green *et al*., 2005; Lutjemeier *et al*., 2005) and contraction frequency (Hoelting *et al*., 2001). In the present study, these variables were kept constant between FR and SR exercise, thereby isolating the effect of contraction velocity on net antegrade and retrograde blood flow. Since force is proportional to acceleration (Hamill & Knutzen, 2003), we suspect that FR exercise produced a greater force and intramuscular pressure than SR exercise. Indeed, previous studies have found muscle activity, as measured using surface electromyography, to be highest at the onset of a fast ballistic contraction as compared to a slow contraction (Ricard *et al*., 2005) and to increase in proportion to shortening velocity (Sjogaard *et al*., 2004). Peak intramuscular pressures in the soleus and tibialis anterior muscles have also been shown to increase in magnitude with contraction velocity during locomotion (Ballard *et al*., 1998; Kirby *et al*., 1988). Therefore, the two-fold increase in retrograde flow during FR as compared to SR exercise in the present study may be due to differences in muscle activity and tissue pressure acting on local vasculature. Evidence for mechanical hindrance to flow in the present study was found in the decreased concordance of blood velocity and ECG signals (i.e. reduced cross-correlation) indicating that FR contractions were successful in disrupting the pulsed rhythm of flow as driven by cardiac activity.

Based on the positive relationship between retrograde and antegrade flow during FR exercise, we suspect that the redirected volume of blood during muscular contractions amplified

antegrade flow during the subsequent relaxation phase. This is consistent with the higher antegrade flow and larger amplitude of blood velocity oscillations (peak-to-minimum) produced by FR as compared to SR exercise. These shifts in blood velocity may increase flow pulsatility and provide the vascular endothelium with greater wall shear stress as flow rapidly changes direction across the endothelial cell surface during exercise. Indeed, *in vitro* studies demonstrate that the amplitude and frequency of pulsatile blood flow increases the synthesis and release of endothelial-derived nitric oxide and prostaglandins (Hendrickson *et al*., 1999; Hutcheson & Griffith, 1991; Nakano *et al*., 2000). In the present study, both the frequency (W_f) and amplitude (peak-to-minimum velocity amplitude) of exercise blood flow were related to a lower vascular resistance in agreement with a shear-mediated stimulation of endothelial cells. Green *et al.* (2005) suggest that the large oscillatory antegrade and retrograde flow pattern generated in the brachial artery during cycling exercise stimulates nitric oxide release from the vascular endothelium since the administration of a nitric oxide antagonist diminished the blood flow response. These studies indicate that the vascular endothelium is sensitive to pulsatile flow which is not appreciated in the shear stress calculations based on mean velocity or blood flow.

Exercise work rate was similar between contraction velocities, and therefore, mean blood flow was not different between FR and SR exercise in agreement with previous studies that show a close coupling between work rate and muscle blood flow during knee extension exercise (Osada & Rådegran, 2002; Rådegran, 1997). The longer concentric and eccentric phases associated with SR exercise may have relied on a higher arterial pressure to drive muscle perfusion. Although not significant, mean arterial pressure may have been elevated sufficiently during SR exercise thereby contributing to the higher vascular resistance found during this contraction velocity. As a consequence, pulsatility index showed a slower recovery following SR than FR exercise. This indicates a greater vasodilation and lower vascular resistance during the recovery period following SR than FR exercise which is likely due to differences in the exercise-induced ischemic state of the muscle (Osada, 2004).

A limitation of the present study is the absence of a direct comparison between the effects of vascular compression (strain) versus blood flow (shear stress) on stimulating endothelial cells during exercise. Clifford *et al.* (2006) has demonstrated that pulse pressure eliciting mechanical deformation of isolated rat soleus feed arteries can significantly increase vasodilation which was partly mediated by the vascular endothelium. Thus, it is uncertain in the present study whether the fast contraction velocity stimulated a greater release of vasoactive substances than the slow contraction velocity through the mechanical strain of the vessel wall associated with muscle contractions (Sun *et al*., 2004) or by the hemodynamic shear stress produced by rhythmic exercise. However, the inverse relationship between vascular resistance and shear rate found in the present study supports the latter mechanism.

In conclusion, the results of the present study indicate that dynamic muscle contractions performed at a fast velocity produce more retrograde blood flow than contractions performed at a slow velocity during knee extensor exercise set at a constant work rate. The incorporation of retrograde flow in the exercise blood flow pattern increased the amplitude of flow pulsatility, which was strongly related to shear stress and the reduction of vascular resistance during exercise. These results suggest that the pattern of blood flow influences the shear-mediated stimulation of endothelial cells during exercise. Further study is needed to determine if retrograde flow plays a role in the vascular modifications often found in endothelial function following chronic physical activity.

Acknowledgments

J.U. Gonzales was supported by a fellowship from the National Heart, Lung, and Blood Institute (F31 HL077996-02).

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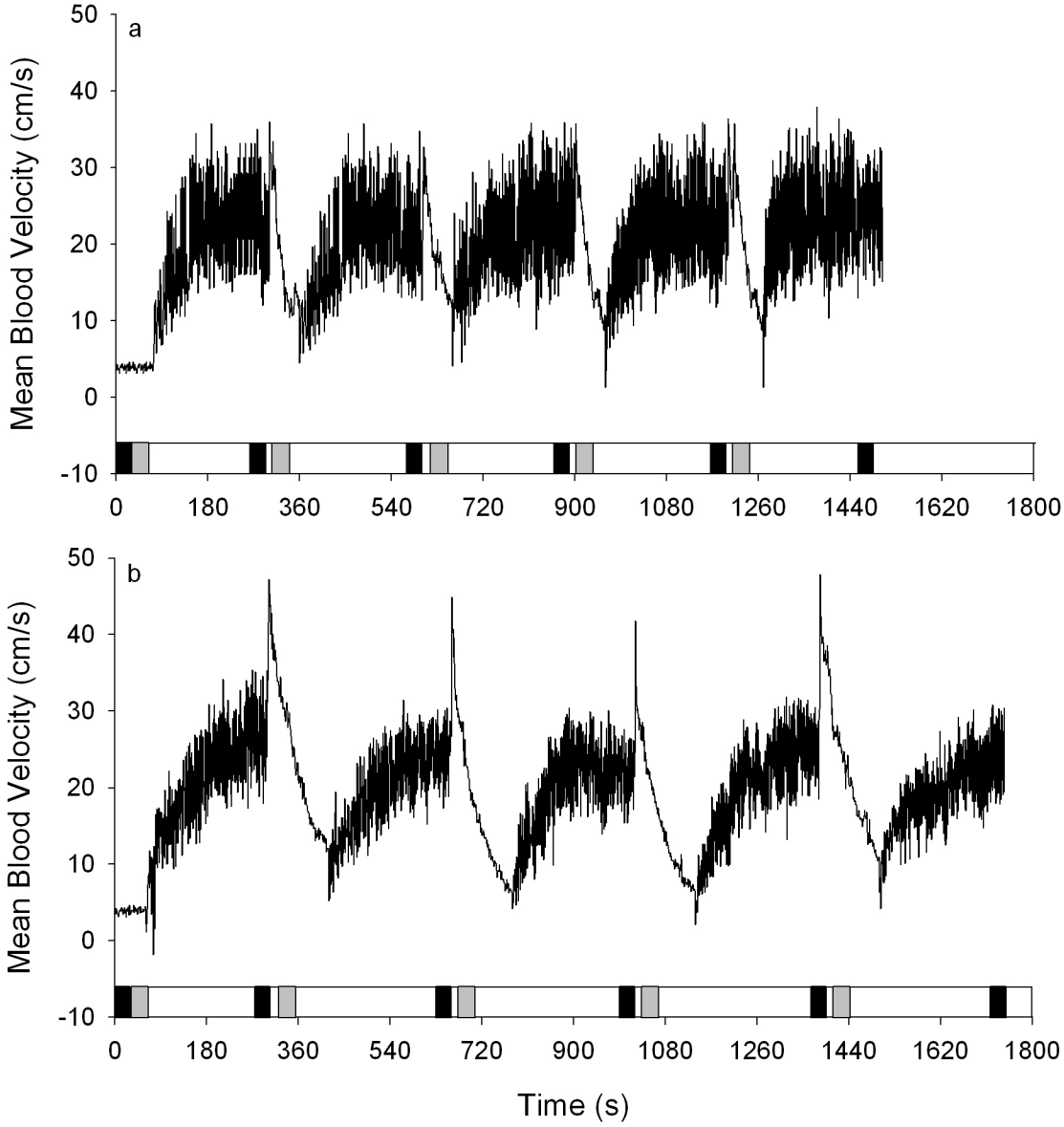

Figure 1.
Mean blood velocity data measured during knee extension exercise from a representative subject. Note the large difference in the blood velocity oscillations during exercise at the fast (a) and slow (b) contraction velocities. Blood flow and diameter were averaged during steady-state exercise (shown on time line with black boxes) and pulsatility index was measured 30 s into recovery (gray boxes).

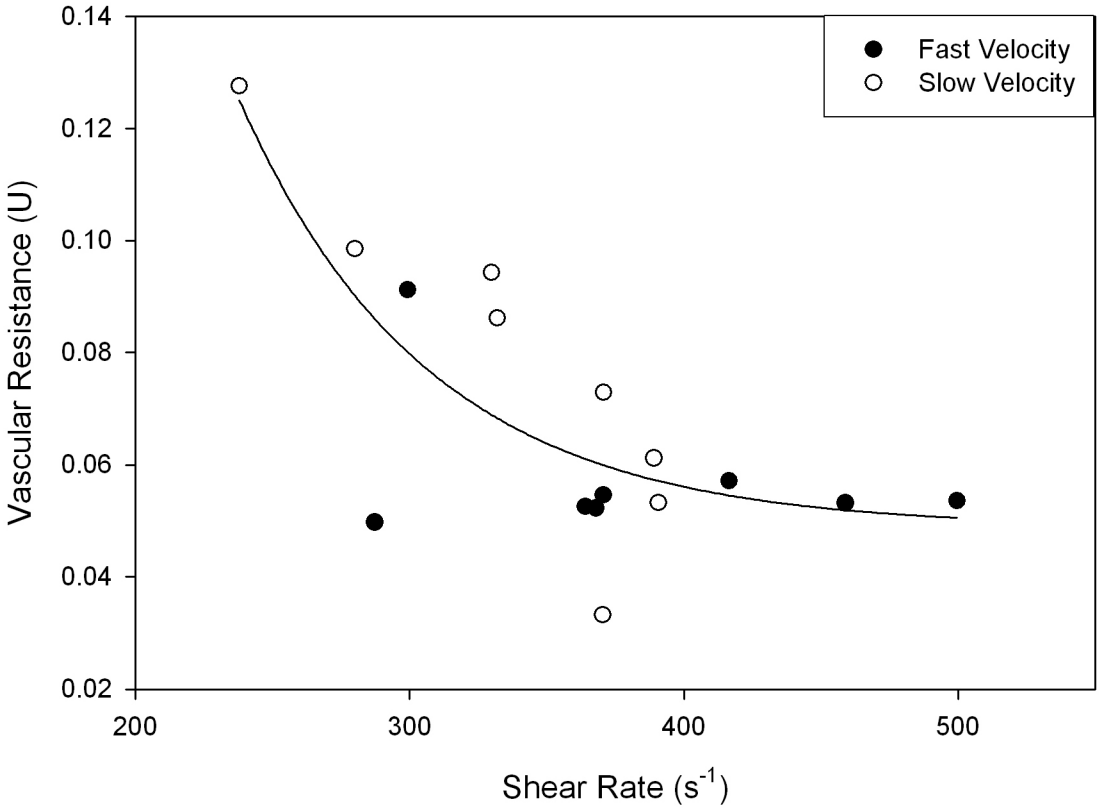

Figure 2.
Curvilinear relationship ($y = 2E\text{-}06x^2 - 0.0015x + 0.3739$, $r^2 = -0.60$) between shear rate (force applied to the vessel wall) and vascular resistance during rhythmic knee extension exercise.

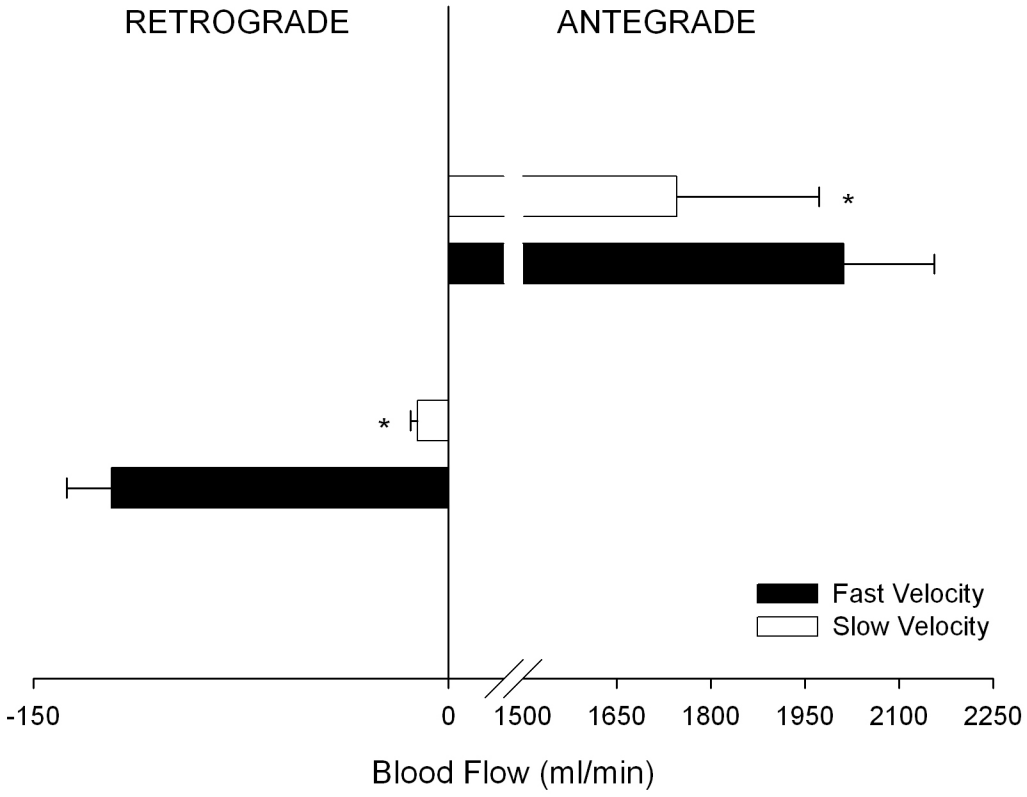

Figure 3.
Comparison of the exercise-induced antegrade and retrograde blood flow generated during knee extension exercise at different contraction velocities. *, statistically significant difference between contraction velocities ($P \leq 0.05$).

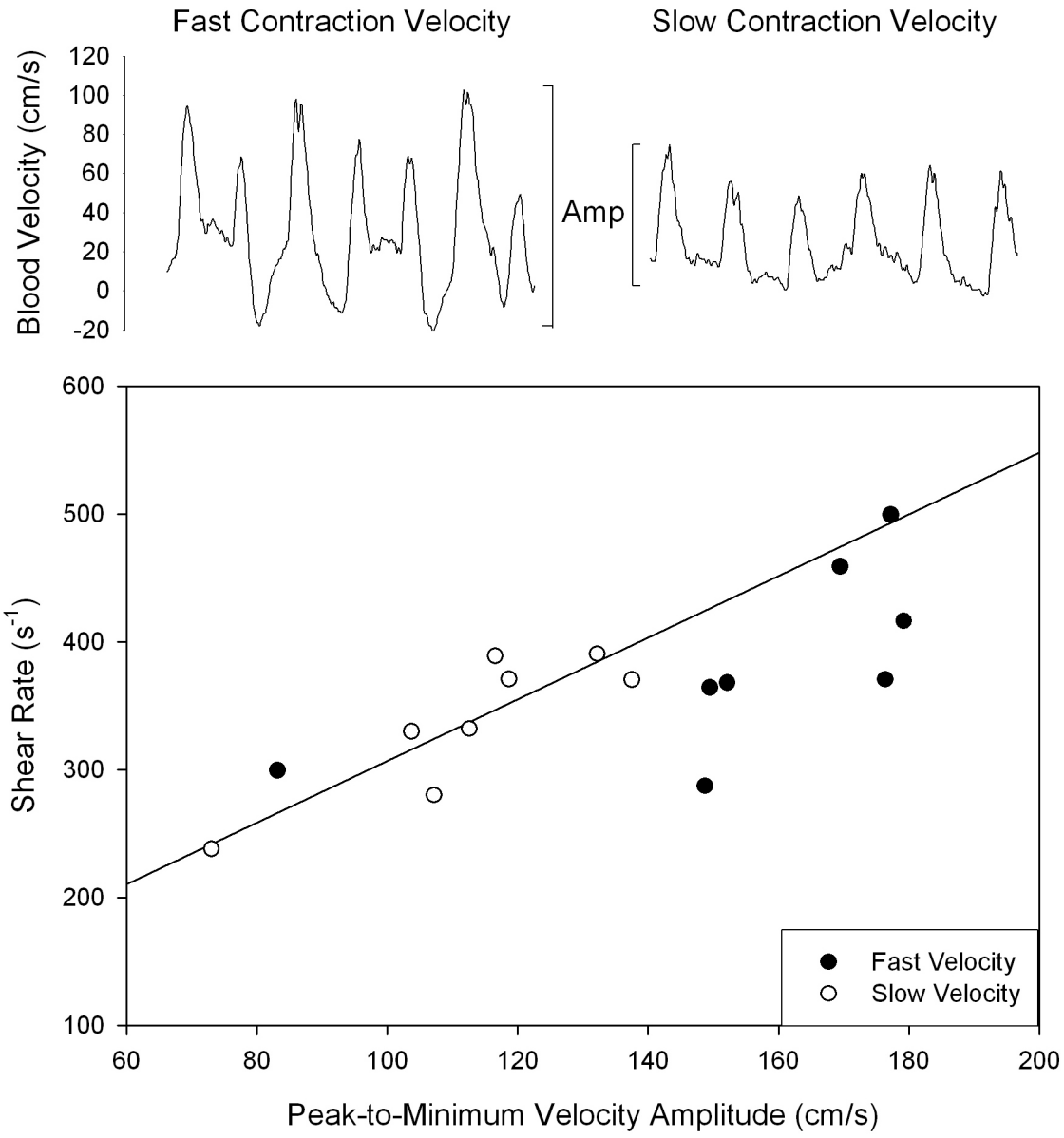

Figure 4.
The oscillatory flow index, peak-to-minimum velocity amplitude (example of measurement shown above), was strongly related to shear rate during rhythmic knee extension exercise ($y = 2.41x + 65.76$, $r^2 = 0.75$).

Table 1

Comparison of cardiovascular variables between fast and slow contraction velocities

	Fast Contraction Velocity		Slow Contraction Velocity	
	Rest	*Exercise*	*Rest*	*Exercise*
Heart Rate (bpm)	70.8 ± 7.3	88.0 ± 9.9	72.5 ± 12.3	95.5 ± 12.3*
Mean Arterial Pressure (mmHg)	92.0 ± 6.0	103.9 ± 7.1	91.4 ± 8.0	115.6 ± 21.2
Mean Blood Flow ($ml \cdot min)^{-1}$	222.0 ± 120.9	1890.7 ± 353.2	322.0 ± 222.4	1734.4 ± 603.7
Vascular Resistance (U)	0.48 ± 0.16	0.06 ± 0.01	0.42 ± 0.30	0.08 ± 0.03*
Shear Rate (s^-1)	46.4 ± 27.6	383.1 ± 147.7	62.0 ± 37.6	337.6 ± 127.3
	Rest	*Recovery*	*Rest*	*Recovery*
Pulsatility Index	14.6 ± 9.3	3.7 ± 1.4	13.0 ± 5.1	2.4 ± 0.5*

Values are mean ± SD.

* significant difference between contraction velocities ($P < 0.05$).

Table 2

Comparison of oscillatory flow indices between fast and slow contraction velocities

	Fast Contraction Velocity		Slow Contraction Velocity	
	Rest	*Exercise*	*Rest*	*Exercise*
OSI (units)	0.17 ± 0.11	0.06 ± 0.02	0.13 ± 0.09	0.01 ± 0.01*
Shear Pulse (s^{-1})	71.2 ± 30.7	431.3 ± 79.9	85.9 ± 46.6	342.3 ± 52.2*
Peak-to-Minimum Amplitude ($cm \cdot s^{-1}$)	55.6 ± 15.3	154.5 ± 31.6	58.4 ± 22.5	112.7 ± 19.7*
Womersley's Frequency (units)	5.1 ± 0.4	5.7 ± 0.3	5.1 ± 0.5	5.9 ± 0.4*

Values are mean ± SD.

* significant difference between contraction velocities ($P < 0.05$).

Table 3

Correlation coefficients for the relationships between oscillatory shear indices and hemodynamic variables (pooled data)

	ANT	RET	Shear Rate	VR
OSI (units)	0.19	0.97†	0.15	-0.32
Shear Pulse (s^{-1})	0.62†	0.53†	0.95†	-0.70†
Peak-to-Minimum Amplitude ($cm \cdot s^{-1}$)	0.70†	0.75†	0.75†	-0.80†
Womersley's Frequency (units)	0.52†	-0.14	0.03	-0.30†

ANT = antegrade flow, RET = retrograde flow, VR = vascular resistance.

† significant relationship ($P < 0.05$).