Muscle blood flow response to contraction: influence of venous pressure

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pressure. *J Appl Physiol* 98: 72–76, 2005. First published September
17, 2004; doi:10.1152/japplphysiol.00151.2004.—The skeletal mus-
cle pump is thought to be at least partially responsible for the
immediate muscle hyperemia seen with exercise. We hypothesized
that increases in venous pressure within the muscle would enhance the
effectiveness of the muscle pump and yield greater postcontraction
hyperemia. In nine anesthetized beagle dogs, arterial inflow and
venous outflow of a single hindlimb were measured with ultrasonic
transit-time flow probes in response to 1-s tetanic contractions evoked
by electrical stimulation of the sciatic nerve. Venous pressure in the
hindlimb was manipulated by tilting the upright dogs to a 30° angle in
the head-up or head-down positions. The volume of venous blood
expelled during contractions was 2.2 ± 0.2, 1.6 ± 0.2, and 1.4 ± 0.2
ml with the head-up, horizontal, and head-down positions, respec-
tively. Although altering hindlimb venous pressure influenced venous
expulsion during contraction, the increase in arterial inflow was
similar regardless of position. Moreover, the volume of blood ex-
pelled was a small fraction of the cumulative arterial volume after the
contraction. These results suggest that the muscle pump is not a major
contributor to the hyperemic response to skeletal muscle contraction.

exercise; hyperemia; muscle pump; vasodilation; dog

IT IS WELL KNOWN THAT, DURING EXERCISE, there is an elevation
in blood flow to exercising skeletal muscle. The muscle pump
is hypothesized to elevate skeletal muscle blood flow by
mechanical factors (16). As the muscle contracts, it compresses
the veins within the muscle and expels the venous contents
toward the heart. On relaxation, it is hypothesized that the
muscle fibers that are tethered to the walls of the veins open the
lumen of the compliant vessels and create low pressure (7, 9).
Because the venous circulation contains one-way valves, one-
way flow is ensured, and the enhanced arteriovenous pressure
gradient results in an increase in arterial inflow to skeletal
muscle (7).

Studies employing both human and animal models have
shown that skeletal muscle blood flow is significantly elevated
within 1 s after the release of a brief tetanic contraction (1, 15,
19). Despite this rapid blood flow response in vivo, direct
observations of arteriolar diameter reveal that dilation of the
skeletal muscle arterioles occurs more slowly (4, 6, 21). Be-
cause activation of the muscle pump is temporally compatible
with the immediate increase in blood flow seen at the onset of
exercise, this observation has been used as prima facie evi-
dence that the muscle pump must be responsible for the rapid
increase in skeletal muscle blood flow with the initiation of
exercise (16).

Fundamental to the muscle pump theory of blood flow
control is that muscular contraction lowers venous pressure
within the active muscle, thus widening the arteriovenous
pressure gradient. However, the relationship between venous
pressure within the muscle before contraction and the ability of
the muscle pump to produce skeletal muscle hyperemia is a
question open for investigation (8). In the present study,
baseline venous pressure in the canine hindlimb was manipu-
lated by postural changes. As arterial pressure remained con-
stant with postural changes and venous pressure was elevated
in the head-up position, we reasoned that maximal contraction
of the hindlimb muscles should produce larger decreases in
venous pressure in the head-up position compared with the
head-down position. Thus we hypothesized that muscle con-
traction would elicit larger increases in skeletal muscle blood
flow in the head-up position.

METHODS

All experimental procedures were conducted in accordance with
the American Physiological Society's Guiding Principles in the Care
and Use of Animals and were approved by the Institutional Animal
Care and Use Committees of the Veterans Affairs Medical Center and
the Medical College of Wisconsin. Nine purpose-bred beagle dogs
(13 ± 0.5 kg, mean ± SE) were used in this study. Anesthesia was
induced with bolus intravenous infusion of 100 mg/kg α-chloralose
and 500 mg/kg urethane into the antecubital vein and was maintained
with continuous intravenous infusion of 20 mg·kg^{-1}·h^{-1} α-chlora-
lose and 100 mg·kg^{-1}·h^{-1} urethane. The animals were intubated and
ventilated with room air by a mechanical ventilator (Harvard Appa-
ratus, Dover, MA). Respiratory tidal volume was set to 15 ml/kg and
end-tidal P_{CO_2}, measured with an infrared analyzer (Ohmeda, Miami,
FL), was kept in a range between 35 and 40 Torr by adjusting
respiratory frequency. Arterial blood samples were regularly taken for
measurement of arterial P_{O_2}, P_{CO_2}, and pH (model ABL-30, Radiom-
eter, Copenhagen, Denmark). If necessary, metabolic acidosis was
corrected with slow intravenous infusion of sodium bicarbonate. Body
temperature of the dogs was maintained via a heating pad (Gaymar,
Orchard Park, NY).

Initial surgical procedures were performed with dogs in the supine
position. The carotid artery was dissected, and an intravascular cath-
eter (18 gauge) was inserted retrogradely into the lumen and attached
to a solid-state pressure transducer (Ohmeda) placed at the level of the
dog's heart for measurement of systemic arterial blood pressure.
Through an abdomino-inguinal incision, an external iliac artery and
vein were exposed and transit-time ultrasound flow probes (Transonic
Systems, Ithaca, NY) placed around them for measurement of arterial
inflow and venous outflow of the hindlimb. An acoustic couplant
(model 1181, Nalco) was used to displace air within the probe's
measurement window. To reduce hindlimb collateral blood flow, the
internal iliac artery and vein, as well as all visible side branches within
the femoral triangle, were ligated. The dog's head was then positioned

in a stereotaxic apparatus (Stoelting, Wood Dale, IL) secured on an aluminum platform, and the torso was extended by caudal tension applied via a hip-pin clamp to place the dog in a normal upright posture (horizontal position). To alter hindlimb venous pressure, the platform was tilted at a 30° angle to situate the dog head up (hindlimb below the heart) or head down (hindlimb above the heart). This resulted in a difference of ~25 mmHg in hindlimb venous pressure between the head-down and head-up position.

Contraction of the hindlimb muscles was evoked by electrical stimulation of the distal end of the sciatic nerve, which had been previously dissected and cut to avoid centrally conducted impulses along afferent nerve fibers. Two stimulating electrodes consisting of 0.20-mm-diameter Teflon-coated stainless steel wires (A-M Systems, Everett, WA) were inserted into the nerve and then wrapped tightly around it to provide constant stimulation in all positions. To prevent movement on hindlimb contraction that could potentially move the position of the ultrasound flow probe, the leg was secured at the ankle to the platform, ensuring that all muscle contractions were isometric in nature. The minimal current required to elicit an observable contraction was defined as the motor threshold, and all contractions were performed at 10 times this intensity (10 × motor threshold). The order (head up, horizontal, or head down) in which the influence of venous loading was examined was randomly assigned for each dog, and duplicate contractions were performed in each of the three experimental postures. The mean of the two responses for each dog was used for statistical analysis.

Data analysis. Systemic arterial blood pressure and blood flow signals were continuously recorded and stored on microcomputer (Apple G3 Power PC) using a MacLab data-acquisition system (AD Instruments, Castle Hill, Australia) sampling at 100 Hz. Baseline was calculated offline as the 10-s period before commencement of contraction. Peak arterial and venous blood flows in response to contraction were recorded. In addition, because the effects of the muscle pump should be evident in the first cardiac cycle after contraction (18), we analyzed the arterial blood flow in the first beat after release of contraction. The volume of venous blood expelled from the muscle during contraction was calculated by integrating the area under the venous flow curve from the beginning of contraction to the point where venous flow returned to baseline. Cumulative arterial blood volume passing through the limb in response to the contraction was calculated as the integral of the area under the arterial flow curve starting at the beginning of contraction and ending at the point where arterial blood flow returned to baseline.

Statistical analysis. To examine the hemodynamic response to contraction, a two-way (time × position) repeated-measures analysis of variance was used to examine the effect of contraction on difference in postcontraction hyperemia, heart rate, and blood pressure. One-way repeated-measures analysis of variance was employed to examine the effect of contraction on volume of blood expelled from the venous system. Where significant F ratios were found, a Tukey's post hoc test was performed. Data are expressed as means ± SE. The level of statistical significance was set at $P < 0.05$.

RESULTS

Figure 1 contains original tracings from an individual dog showing blood pressure and hindlimb arterial and venous blood flow in response to a 1-s tetanic contraction with the three different body positions. Figure 2 shows in more detail that there was an immediate, rapid expulsion of blood from the veins with muscle contraction. Blood flow returned to baseline (and went below baseline) within the duration of the contraction. In contrast, in every condition, the arterial hyperemic response started immediately on the release of contraction, peaked within 3–5 s, and lasted for ~20 s.

Data regarding blood pressure and heart rate during the experiment are presented in Table 1. There was not a significant ($P > 0.05$) effect of position nor was there a significant ($P > 0.05$) effect of contraction on arterial pressure. In contrast, heart rate increased significantly ($P < 0.05$) as posture of the dog changed from head down to head up. A 1-s tetanic contraction did not affect ($P > 0.05$) heart rate at any position.

Figure 3 summarizes changes in venous outflow from the hindlimb at each position. There were no significant ($P > 0.05$) differences in baseline venous flow among the three positions. However, changes in posture significantly influenced the peak venous blood flow measurement during the 1-s contraction, with the highest in the head-up position. Figure 4 depicts the total blood volume expelled from the veins during the contraction under each condition. The blood volume expelled during the contraction was greatest ($P < 0.05$) for the head-up position.

Figure 5 shows the arterial blood flow response to the 1-s tetanic contraction in the three different postures. Baseline arterial blood flows were not significantly ($P > 0.05$) different among the positions. Muscle contraction produced significant ($P < 0.05$) increases in blood flow during the first cardiac cycle after the release of contraction that were not significantly ($P > 0.05$) different among the positions. The peak blood flow response was also not significantly ($P > 0.05$) different among the positions. In addition, there was no significant ($P > 0.05$) difference in the cumulative volume of arterial inflow in response to muscle contraction with the three different postural positions (Fig. 6).

DISCUSSION

There are two new important findings in the present study. First, the magnitude of the increase in arterial blood flow to canine skeletal muscle with a brief tetanic contraction, whether examined over the first cardiac cycle or at peak, was independent of the venous pressure in the muscle over the range of pressures studied. Second, the volume of blood expelled by a single contraction was a small fraction of the total increase in blood flow accumulated. These results suggest that the muscle pump is not a major contributor to skeletal muscle hyperemia in response to a single contraction.

Although there is an immediate increase in blood flow to active skeletal muscle with the onset of exercise (1, 10, 11, 15, 17, 19, 20), the mechanism(s) by which this rapid increase in blood flow occurs has remained elusive. The muscle pump theory has been proposed as a rapid, local mechanism by which blood flow to active skeletal muscle can be regulated. The premise behind the muscle pump theory is that muscle contractions empty the venous circulation, resulting in lower venous pressure during the relaxation phase. The reduction in venous pressure increases the pressure gradient across the muscle vascular bed and enhances muscle perfusion. Ideally, to support this hypothesis, one need only measure the fluctuations in venous pressure within the muscle. Unfortunately, because of the presence of venous valves and the probability of damaging valves by inserting a catheter, it has been technically impossible to measure pressure in the venules of skeletal muscle, so investigators have been forced to make inferences about the muscle pump from indirect data.
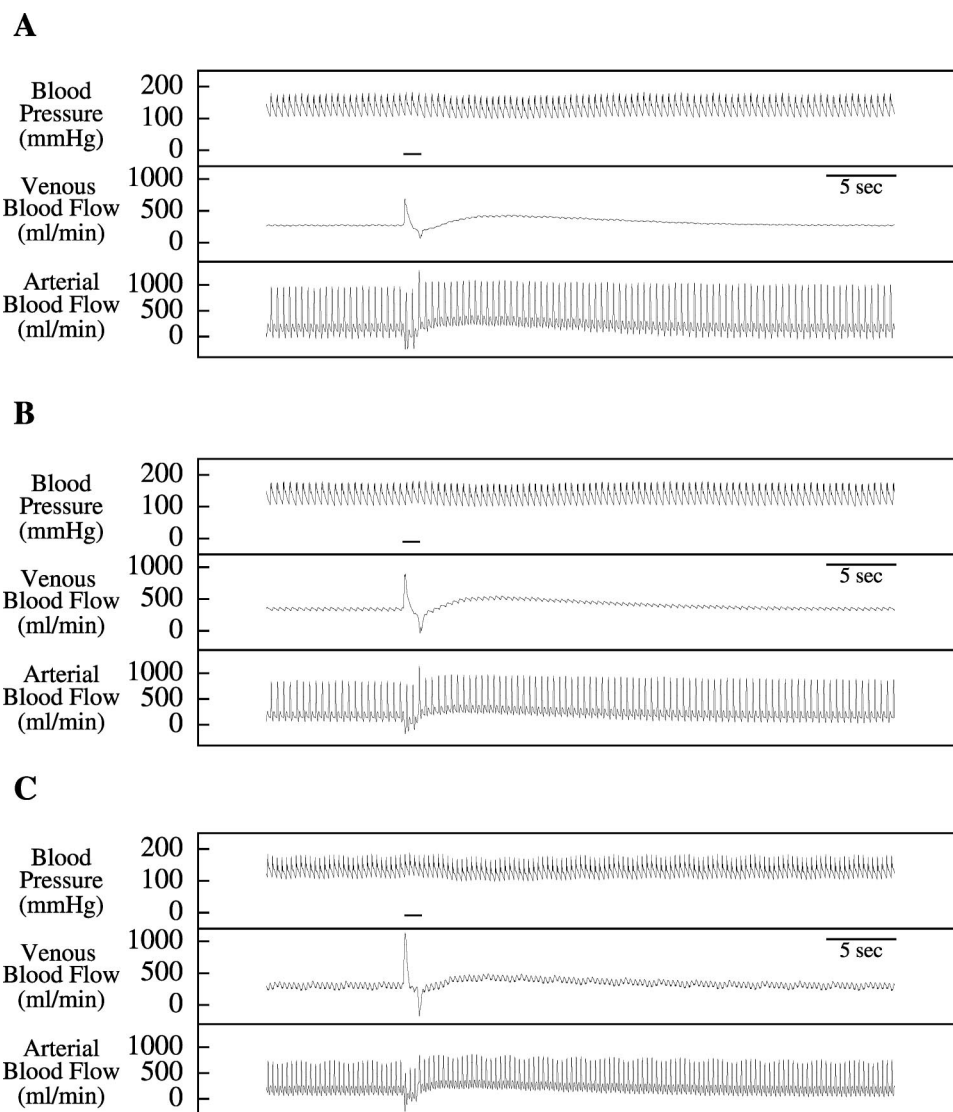
A

B

Fig. 1. Original tracings from an individual dog showing blood pressure and external iliac arterial and venous blood flow in the 3 experimental postures. One-second tetanic contractions were elicited by electrical stimulation of cut sciatic nerve in head-down (*A*), horizontal (*B*), and head-up (*C*) positions. The horizontal bar shows the 1-s contraction. Note the increased response in venous expulsion as the dog was transferred from head-down to head-up position.

C

In accordance with the muscle pump theory, we expected that the elevated venous pressure in the muscles of the hindlimb with the dog in the head-up position would permit a greater contraction-induced reduction in venous pressure, which would translate to a higher blood flow response in the head-up compared with head-down position. The results indi-cate that changes in position altered venous pressure and influenced the amount of blood stored in the veins of hindlimb. Muscle contraction expelled significantly more blood from the venous circulation in the head-up position compared with the head-down position (2.15 ± 0.23 vs. 1.37 ± 0.17 ml) but did not affect the magnitude of muscle hyperemia after contraction whether measured over the first cardiac cycle or at the peak. As shown in Fig. 5, the contraction-induced increase in arterial inflow was similar regardless of position. Thus, contrary to our
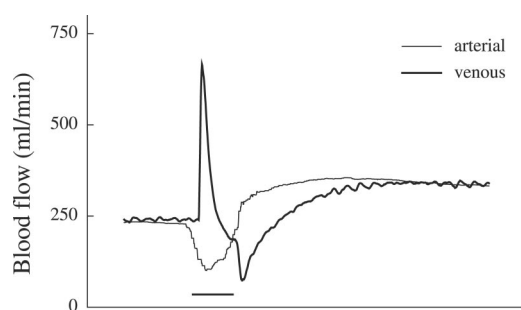

Fig. 2. Overlapping tracings of arterial and venous mean blood flow during a 1-s tetanic contraction (identified by horizontal bar) in a single dog. Note the rapid ejection of blood from the veins concurrent with the mechanical obstruction to arterial inflow.

Table 1. *Blood pressure and heart rate responses to tetanic contractions under 3 different postures*

	Blood Pressure, mmHg		Heart Rate, beats/min	
	Baseline	Peak	Baseline	Peak
Head down	134 ± 3	134 ± 3	113 ± 13*	116 ± 13*
Horizontal	132 ± 4	130 ± 4	126 ± 14	130 ± 13
Head up	134 ± 5	132 ± 4	165 ± 13*	160 ± 13*

Values are means $\pm$ SE. *Significantly different from horizontal position, $P < 0.05$.
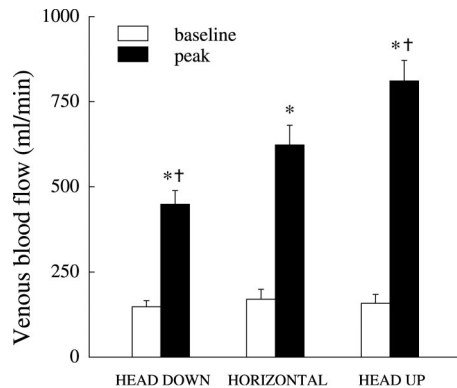
Fig. 3. Venous blood flow response to muscle contraction. Baseline blood flow was similar in the 3 postural positions, but peak blood flow was significantly increased as the dogs were transferred from head-down to head-up position. *Significantly different from baseline ($P < 0.05$). †Significantly different from horizontal position ($P < 0.05$).

Fig. 5. Arterial blood flow response to muscle contraction. Shown are the significant increases from baseline to first beat and peak blood flow in all 3 experimental postures. There were no significant differences in baseline, first beat, or peak flows achieved among the 3 conditions. *Significantly different from baseline ($P < 0.05$).

hypothesis, enhanced muscle pump effectiveness was dissociated from subsequent arterial hyperemia, which is inconsistent with the concept that the muscle pump plays a predominant role in the blood-flow response to a single contraction. These results add to the accumulating evidence that there is limited influence of the muscle pump on the contraction-induced increases in blood flow (2, 5, 9, 12, 14, 15).

By definition, the muscle pump can only influence blood flow for as long as venous pressure is reduced. Once arterial inflow replaces the volume of blood expelled during contraction, venous pressure is restored, and there can be no further effect of the muscle pump on blood flow. Therefore, the proportion of skeletal muscle hyperemia attributable to the muscle pump should be directly related to the volume of blood needed to replace the blood that was expelled from the veins by the contraction. In the present study, comparing the venous blood volume ($\sim$2 ml) expelled by the muscle contraction with the cumulative arterial blood volume response ($>$30 ml) after contraction reveals that the venous volume is a relatively small proportion of the cumulative arterial volume. The amount of blood flow for which the muscle pump can be responsible is a small percentage ($\sim$6%) of the total. Furthermore, at the prevailing venous blood flows, this volume would have been

refilled in $<$1 s, whereas the peak blood flows were observed at $\sim$4 s. This temporal dissociation of the peak muscle pump effect from the peak blood flow effect argues against a predominant role of the muscle pump in contraction-induced hyperemia. In the aggregate, the above findings suggest that another mechanism (vasodilation) produces the majority of skeletal muscle hyperemia associated with a single contraction.

In contrast to our findings, other laboratories have provided evidence that the manipulation of venous pressure within the muscle enhances the effectiveness of the muscle pump. Like the present study, these studies investigated the blood flow response to contraction after venous pressure manipulations by positioning the contracting limb above or below the heart (3, 10, 17, 19). An augmented blood flow response to a single contraction (19) or rhythmic contractions (3, 10, 17) with the limb positioned below the heart was attributed to the muscle pump by these authors. It is possible that these conflicting results indicate a greater role for the muscle pump in skeletal muscle hyperemia associated with voluntary contractions compared with electrically stimulated contractions. One might speculate that, for the muscle pump to be fully effective, natural patterns of muscle fiber recruitment are necessary. Nevertheless, electrically stimulated muscle contractions elicit
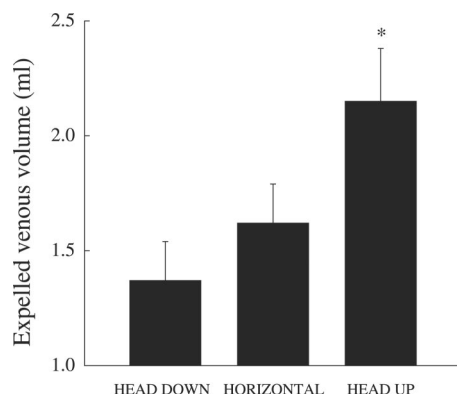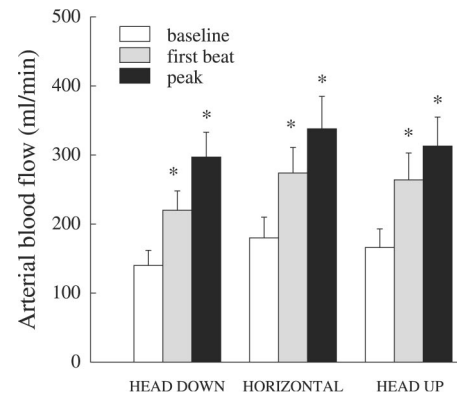

Fig. 4. Total muscle venous blood volume expelled during a 1-s tetanic muscular contraction. There was a significant increase in the volume expelled from the veins of the hindlimb in the head-up position compared with head-down and horizontal postures. *Significantly different from horizontal position ($P < 0.05$).
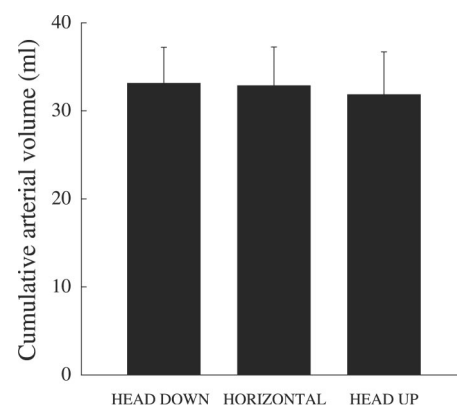

Fig. 6. Total increase in hindlimb arterial blood volume in response to a 1-s tetanic muscular contraction. There was not a significant difference in the increase in the arterial blood volume in response to the muscle contraction between the 3 conditions ($P > 0.05$).

large increases in skeletal muscle arterial blood flow, indicating substantial skeletal muscle hyperemia that appears to be independent of the actions of the muscle pump.

Some of the support for a role for the muscle pump in the immediate increase in skeletal muscle blood flow at the onset of exercise has been spawned by the perception that skeletal muscle vasodilation occurs slowly and cannot be responsible for the immediate hyperemia. The evidence for delayed vasodilation comes from in situ and in vitro preparations in which vessels were directly visualized. Results from the cremaster muscle (4) and hamster retractor muscle (6) show a latency for vasodilation of 5–20 s, with the delay related to vessel size. Wunsch et al. (21) investigated the response of first-order arterioles to various agents (adenosine, acetylcholine, NO, K^+) and found a latency of at least 4 s between exposure of the arterioles to these compounds and the beginning of vasodilation. On the other hand, Marshall and Tandon (13) showed that 1-s tetanic contractions of rat spinotrapezius muscle evoked dilation of terminal arterioles in <2 s. A recent publication from Tschakovsky et al. (18) argued that vasodilation, not an increase in muscle pump effectiveness, explains the contraction intensity-related increases in blood flow in the first cardiac cycle after release of contraction. This argument is strongest for contractions performed with the arm above heart level since it seems unlikely that the muscle pump would be capable of substantial reductions in venous pressure with the arm in this position. In view of the disagreement on this topic, it is obvious that further investigation is warranted to establish the time course of vasodilation at the onset of exercise.

In conclusion, although altering hindlimb venous pressure influenced venous expulsion during contraction, the increase in arterial inflow was similar regardless of position. Moreover, the volume of blood expelled was a small fraction of the cumulative arterial volume after the contraction. These results suggest that the muscle pump is not a major contributor to the hyperemic response to skeletal muscle contraction.

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