Effect of rhythmic tetanic skeletal muscle contractions on peak muscle perfusion

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Dobson, John L., and L. Bruce Gladden. Effect of rhythmic tetanic skeletal muscle contractions on peak muscle perfusion. J Appl Physiol 94: 11–19, 2003. First published August 16, 2002; 10.1152/japplphysiol.00339.2002.—The purpose of this investigation was to examine the effects of rhythmic tetanic skeletal muscle contractions on peak muscle perfusion by using spontaneously perfused canine gastrocnemius in situ. Simultaneous pulsatile blood pressures were measured by means of transducers placed in the popliteal artery and vein, and pulsatile flow was measured with a flow-through-type transit-time ultrasound probe placed in the venous return line. Two series of experiments were performed. In series 1, maximal vasodilation of the muscles' vascular beds was elicited by infusing a normal saline solution containing adenosine (29.3 mg/min) and sodium nitroprusside (180 μg/min) for 15 s and then simultaneously clamping both the popliteal artery and vein for 5 min. The release of occlusion initiated a maximal hyperemic response, during which time four tetanic contractions were induced with supramaximal voltage (6–8 V, 0.2-ms stimuli for 200-ms duration at 50 Hz, 1/s). In series 2, the muscles were stimulated for 3 min before the muscle contractions were stopped for a period of 3 s; stimulation was then resumed. The results of series 1 indicate that, although contractions lowered venous pressure, muscle blood flow was significantly reduced from 2,056 ± 246 to 1,738 ± 225 ml·kg⁻¹·min⁻¹ when contractions were initiated and then increased significantly to 1,925 ± 225 ml·kg⁻¹·min⁻¹ during the first 5 s after contractions were stopped. In series 2, blood flow after 3 min of contractions averaged 1,454 ± 149 ml·kg⁻¹·min⁻¹. Stopping the contractions for 3 s caused blood flow to increase significantly to 1,874 ± 172 ml·kg⁻¹·min⁻¹; blood flow declined significantly to 1,458 ± 139 ml·kg⁻¹·min⁻¹ when contractions were resumed. We conclude that the mechanical action of rhythmic, synchronous, maximal isometric tetanic skeletal muscle contractions inhibits peak muscle perfusion during maximal and near-maximal vasodilation of the muscle's vascular bed. This argues against a primary role for the muscle pump in achieving peak skeletal muscle blood flow.

Although it is currently held that vascular conductance in skeletal muscles is accomplished primarily by local control mechanisms (25), the relative importance of each form of local control throughout the initiation and maintenance of rhythmic contractions has not been well established (8). Similarly, although it is clear that skeletal muscle blood flow is augmented immediately after the initiation of contractions, controversy exists as to whether local vasodilation begins instantaneously (7, 34, 41, 46) or only after a latency period lasting at least 5 s (5, 16, 19, 30, 39). One pertinent issue that might explain why muscle hyperemia may precede local vasodilation is whether the actual mechanical action of rhythmic skeletal muscle contraction acts as an additional form of local blood flow control during exercise. This form of local control, termed the skeletal muscle pump, has been implicated not just as the factor responsible for the onset of active hyperemia (9, 10, 38, 39, 46) but also as an essential component needed for the development of peak muscle blood flow (3, 4, 23, 24, 28).

The compressive force of muscle contraction generates intramuscular pressures in the range of 200–1,700 mmHg (1, 21, 22, 36), imparting enough kinetic energy to squeeze blood into the veins, thereby facilitating venous return (2, 29, 44). Furthermore, Pollack and Wood (37) demonstrated that properly spaced rhythmic contractions can decrease the extent of venous refilling during muscular relaxation enough to reduce and maintain lower venous pressures. Subsequently, Folkow et al. (9) introduced the modern concept of the muscle pump by proposing that this gain in the pressure gradient across a skeletal muscle is sufficient to elevate blood flow during rhythmic contractions. According to Ohm’s law, blood flow through a tissue is determined by the product of the arterial-venous pressure difference and the conductance of the tissue’s vascular bed. Therefore, if this principle is applicable to skeletal muscles during rhythmic contractions, then the kinetic energy imparted to the blood during contraction, combined with the potentially negative pressures in the venules and small veins during relaxation (23), may also provide independent facilitation of muscle hyperemia during exercise.

Support for the muscle pump theory has been provided by numerous investigations (10, 28, 38, 40, 41). The muscle pump has been implicated as the explanation for the significantly higher peak blood flows typi-
cally reported for muscles in vivo vs. the peak flows reported for isolated muscles (3, 4, 23, 24, 28). Nevertheless, only Sheriff et al. (39) have provided specific data to indicate that local muscle hyperemia may occur independently of vasodilation. In contrast, others (27, 41, 45) have provided evidence that the reduction in venous pressure that occurs during rhythmic contractions is not sufficient to account for independent facilitation of hyperemia during exercise. The most compelling argument against the effect of the muscle pump, however, is provided by the proponents of a vascular waterfall theory.

The primary concept of the vascular waterfall theory is that flow through a collapsible tube is described by a different expression of Ohm’s law, wherein the operable pressure gradient is determined by the difference between the arterial and critical closing pressures of the tube (35). Accordingly, the presence of a vascular waterfall, or Starling resistance, at the arterioles would prevent any increase in flow through a muscle due solely to a decrease in pressure on the venous side (6, 18). Evidence in support of the vascular waterfall, and against the muscle pump effect, has been provided by three well-controlled investigations (29, 33, 42), which demonstrated that reductions in venous pressure did not have an effect on arterial inflow.

Despite the evidence against a muscle pump effect, including that from their own investigation, Laughlin and Schrage (26) concluded that the muscle pump most likely exists and could possibly be demonstrated by a study in which instrumentation of the arterial supply and venous outflow of an isolated muscle is minimal. Similarly, recent work in our laboratory suggests both that there is a measurable muscle pump activity during the onset of contractions in the isolated dog gastrocnemius muscle (14) and that cannulation of the arterial inflow to muscles in situ inhibits the maximal rate of blood flow (unpublished results). Each of the investigations that provided evidence that the vascular waterfall prevents a muscle pump effect (29, 33, 42) was performed with the use of isolated canine gastrocnemius muscles with cannulation of the arterial supply. Furthermore, although two (Refs. 33 and 42) of these muscle pump investigations were performed on muscles with maximally vasodilated vascular beds, the peak blood flows reported were less than one-half as great as those measured in our laboratory with a similar muscle preparation (20).

Although it has been postulated that the muscle pump is necessary to achieve maximal muscle perfusion (23, 24), this idea remains controversial (26). Therefore, the purpose of the present study was to determine the effect of rhythmic muscle contractions on peak skeletal muscle perfusion by using a spontaneously perfused canine gastrocnemius preparation in situ with no direct cannulation of the muscle’s arterial supply.

MATERIALS AND METHODS

Animals, housing, and care. For this study, seven mongrel dogs (14.1–27.3 kg), of either sex, were acquired from the Auburn University Laboratory Animal Health Facility at the College of Veterinary Medicine. All procedures were reviewed and approved by the Auburn University Institutional Animal Care and Use Committee (protocol 0308-R-2312).

Animals were obtained after they were fasted overnight. The animals were anesthetized with pentobarbital sodium (30 mg/kg iv) and intubated with an endotracheal tube. The animals were mechanically ventilated (model 613, Harvard Apparatus) to maintain normal blood-gas values, and supplemental oxygen was supplied when necessary. Rectal temperature was monitored and maintained at 37°C with a heating pad placed under the animal and adjusted as needed. Additional doses of pentobarbital sodium were given as needed to maintain a deep surgical plane of anesthesia. The animals were euthanized while still under anesthesia at the end of the experiments.

Surgical procedure. The left gastrocnemius-plantaris musculature group (GP) was surgically isolated as previously described (11–13, 15, 43). Briefly, a medial incision was made through the skin of the left hindlimb from midthigh to the ankle. The insertion tendons of the sartorius, gracilis, semitendinosus, and semimembranosus muscles were transected to allow these muscles to be folded back to expose the GP. All branches of the popliteal vasculature that did not feed directly into or out of the GP were ligated. Sutures also were tied around the heads of the muscle groups to occlude any blood flow through the tissue of the muscle’s origins. Consequently, all inflow into the GP was isolated to the popliteal artery, and all outflow from the GP was isolated to the popliteal vein. Complete arterial isolation was verified by occluding the popliteal artery and observing venous flow. The popliteal vein was cannulated, and the venous outflow was directed through a flow-through-type transit-time ultrasound flow probe (6NBR440, Transonic Systems) before being returned to the animal via a reservoir in the jugular vein. The flow probe was connected to a flowmeter (T206, Transonic Systems), set on the “high flow” setting and calibrated with a graduated cylinder and stopwatch before and during each experiment. The popliteal vein cannula was also attached to two stopcocks, one for the collection of venous blood samples and the other to connect to a pressure transducer (model RP-1500, Narco Biosystems). To avoid interfering with a muscle pump effect by directly cannulating GP inflow, a branch of the popliteal artery that was upstream from the GP, but did not supply the muscle, was cannulated. This arterial cannula was connected via a y-connector to a pressure transducer (model RP-1500, Narco Biosystems) and to an infusion pump. This allowed monitoring of muscle perfusion pressure and introduction of pharmacological agents (vasodilators) with minimal intrusion on the integrity of the popliteal artery itself.

A portion of the calcaneus, with the two tendons of the GP attached, was cut away for connection to an isometric myograph. The two tendons were clamped around a short metal rod and connected via a short section of aluminum pipe (29 mm diameter) and a universal joint coupler to the myograph load cell (Interface SM-250, Narco Biosystems). The universal joint coupler was used to ensure that the muscle always pulled directly in line with the load cell, thus alleviating the application of torque to the load cell. The load cell was calibrated with known weights before each experiment. The proximal end of the GP was connected via a rubber tube to the base of the myograph via bone nails and connecting rods. A turnbuckle strut was placed parallel to the muscle between the tibial bone nail and the arm of the
myograph to minimize flexing of the myograph. The sciatic nerve was exposed, isolated, and ligated near the GP. The distal 1.5- to 3.0-cm stump of the nerve was pulled through an epoxi electrode containing two wire loops for stimulation. Muscle contractions were elicited by stimulating the sciatic nerve with supramaximal (6–8 V) square-wave pulses (Grass S48 stimulator). Before each experiment, the GP was set to optimal length by progressively lengthening the muscle as it was stimulated at a rate of 0.2 Hz, until a peak in developed twitch tension (total minus resting tension) was observed.

**Experimental protocols.** Once surgical isolation of the GP was complete, all cannulas and equipment were in place, and optimal length was determined, the muscle was allowed to rest for 10 min while arterial blood gases and pH and blood flow were measured. After confirmation that these values were within normal limits for this experimental model, the GP was stimulated to contract for 3 min to determine peak contractile values for muscle blood flow and oxygen uptake. Isometric tetanic contractions were evoked by stimulation with trains of stimuli (200-ms duration, 50-Hz frequency) at a rate of one contraction per second; each stimulus pulse was of sufficient intensity to stimulate the infusion while simultaneously occluding both the popliteal artery and vein for 10 min. The hyperemia was maintained long enough for reliable measurements and then immediately restarted. The purpose of this series of experiments was to compare the muscle’s blood flow 1) during rhythmic contractions, 2) immediately after contractions were stopped, and 3) immediately after contractions were resumed. If the blood flow were to decrease immediately after contractions were stopped and then immediately increase as they were restarted, such evidence would again indicate that there was a muscle pump effect.

**Measurements.** Outputs from the flowmeter, pressure transducers, and load cell were recorded on a strip-chart recorder (Narcotrace 40, Narco Biosystems) for monitoring and analysis. Outputs from the load cell, pressure transducers, and flowmeter were also fed into a computerized data-acquisition system (PowerComputing Powerbase 240 Macintosh clone; GW Instruments, Superscope II, InstruNet model 100B A/D converter). The data-acquisition system sampled all variables at 100 data points per second. Heart rate was monitored periodically with the arterial pressure tracing. Arterial and venous blood samples were collected anaerobically in 3-ml plastic syringes both before any experimental perturbations and after 3 min of rhythmic contractions (see above stimulation protocol). The blood was analyzed for PO2, PCO2, and pH with a blood-gas, pH analyzer (Instrumentation Laboratory 1304). The samples were also analyzed for hemoglobin concentration and percent saturation of hemoglobin with a calibrated CO-oximeter (Instrumentation Laboratory 282) set for dog blood. Oxygen uptake by the GP was calculated from the blood flows and corresponding arteriovenous oxygen concentration differences. After each experiment, the muscle was removed from the animal, dissected free of connective tissue, and weighed. The muscle was then dried in an oven at 80°C to determine its percentage of water.

**Data analysis.** The data collected from the experiments of series 1 were divided into three distinct periods for analysis: hyperemia, contraction, and postcontraction. The hyperemia period (mean = 2.0 s) began the moment peak blood flow was achieved, following the release of the occlusion of the popliteal vasculature, and ended immediately before the first contraction began. The contraction period (mean = 4.0 s) began the moment contractions started and ended 1 s after the last contraction began. The first 5 s after the contraction period ended was considered the postcontraction period. The data collected from the experiments of series 2 were also divided into three distinct periods for data analysis: contraction, stop, and resume contraction. The contraction period (mean = 5.0 s) began the moment the fifth-to-the-last contraction began and ended 1 s after the last contraction began. The stop period (mean = 3.3 ± 0.7 s) began the moment the contraction period ended and lasted until the moment before contractions were resumed. The first five contractions after the stop period ended were considered the resume contraction period (mean = 5.0 s).

**Statistics.** Differences among the variables measured in this study were assessed by using a one-way repeated-measures ANOVA. Appropriate post hoc contrasts were used when necessary to determine where significance occurred.
Table 1. Resting and peak steady-state values during muscle contraction

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Contraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous outflow, ml·kg⁻¹·min⁻¹</td>
<td>197 ± 26</td>
<td>1,374 ± 132</td>
</tr>
<tr>
<td>Arterial pressure, mmHg</td>
<td>130 ± 7</td>
<td>133 ± 6</td>
</tr>
<tr>
<td>Venous pressure, mmHg</td>
<td>4.6 ± 0.9</td>
<td>8.1 ± 1.9</td>
</tr>
<tr>
<td>Conductance, ml·min⁻¹·mmHg⁻¹</td>
<td>0.12 ± 0.03</td>
<td>0.92 ± 0.15</td>
</tr>
<tr>
<td>PaO₂, Torr</td>
<td>93 ± 2</td>
<td>93 ± 2</td>
</tr>
<tr>
<td>CaO₂, vol%</td>
<td>19.1 ± 0.8</td>
<td>19.1 ± 0.8</td>
</tr>
<tr>
<td>VO₂, ml·kg⁻¹·min⁻¹</td>
<td>3.7 ± 0.5</td>
<td>189.1 ± 10.8</td>
</tr>
<tr>
<td>Pco₂, Torr</td>
<td>35.1 ± 2.2</td>
<td>35.1 ± 2.2</td>
</tr>
<tr>
<td>pH</td>
<td>7.43 ± 0.01</td>
<td>7.43 ± 0.01</td>
</tr>
<tr>
<td>[HCO₃⁻], mM</td>
<td>22.6 ± 0.3</td>
<td>22.6 ± 0.3</td>
</tr>
<tr>
<td>Peak force, kN/kg wet muscle</td>
<td>4.6 ± 0.46</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 7 dogs. The conductance data from the contraction period actually represent virtual venous outflow muscle conductances. PaO₂, arterial P O₂; CaO₂, arterial O₂ concentration; VO₂, O₂ uptake; [HCO₃⁻], HCO₃⁻ concentration.

The level of statistical significance was set at 0.05. Data are reported as means ± SE.

RESULTS

Table 1 shows mean control values for major variables that were measured during rest and the peak steady state of contractions. Some of the results of series 1 are shown in Table 2. The purpose of the experiments of series 1 was to compare GP blood flow and pressures before, during, and after rhythmic contractions were stimulated throughout a period of maximal muscle vasodilation. In series 1, mean GP blood flow increased to more than 10 times the resting level within an average of 2.6 ± 0.4 s after the release of the popliteal occlusion (Table 2, hyperemia period). Stimulation of rhythmic contractions then caused an immediate 15 and 18% decrease in GP blood flow and conductance (Table 2, contraction period), respectively, followed by a return of both to precontraction levels immediately after the contractions ended (Table 2, postcontraction period). It is important to note that the contractile-induced conductances reported herein actually represent virtual muscle conductances because extravascular compression during muscle contractions affects both intravascular pressure and resistance.

During the postcontraction period of series 1, the cessation of compression of the compliant vasculature, along with the increase in mean muscle outflow, caused sufficient blood to accumulate in the popliteal vein to significantly increase the venous pressure. Figure 1 illustrates responses during each individual contraction as well as the mean response across the entire period of four contractions. Within each distinct muscle contraction, GP outflow, venous pressure, and virtual venous outflow conductance rapidly increased to peak levels along with the force of contraction; during muscle relaxation, GP outflow, venous pressure, and virtual venous outflow conductance values first plummeted to their nadir and then gradually began to rise toward their initial, precontraction levels. Although the highest outflow, venous pressure, and conductance values observed in series 1 occurred at the time of peak force during the contraction of the muscle, the averages of these variables across the entire cycle of four contractions (contraction period) were lower than the corresponding averages during the hyperemia and postcontraction periods (see Fig. 1).

As is shown in Table 3, the results of series 2 are similar to those of series 1. Rhythmic contractions significantly reduced GP blood flow and virtual venous outflow conductance by 22 and 23%, respectively. There were no significant differences in the blood flows of either the hyperemia or postcontraction periods of series 1 vs. the stop period of series 2, indicating that the degree of muscle vasodilation was similar between the two series of experiments. GP outflow, venous pressure, and virtual venous outflow conductance were elevated throughout the period when contractions were stopped, and then these values quickly returned to lower steady-state levels as contractions were resumed. The mean duration of contraction stoppage during the experiments of series 2 was 3.3 ± 0.7 s (Fig. 2). Figure 2 also illustrates that the relationship between GP force production and virtual venous outflow conductance in series 2 was similar to that observed in series 1. Although peak muscle virtual venous outflow conductance was achieved at the peak of muscle force development during the resume contraction period, the highest mean conductance observed in series 2 occurred during the stop contraction period.

A comparison of blood flow values during each contraction within the two series of experiments (Table 4) reveals that there was a significant reduction in the venous outflow after the initial contraction. Additionally, there was an 18% reduction in GP virtual venous

Table 2. Series 1: effect of rhythmic skeletal muscle contractions on hyperemia during maximal muscle vasodilation

<table>
<thead>
<tr>
<th></th>
<th>Hyperemia</th>
<th>Contraction</th>
<th>Postcontraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous outflow, ml·kg⁻¹·min⁻¹</td>
<td>2,056 ± 246</td>
<td>1,738 ± 225*</td>
<td>1,925 ± 225†</td>
</tr>
<tr>
<td>Arterial pressure, mmHg</td>
<td>122 ± 8</td>
<td>122 ± 8</td>
<td>119 ± 8</td>
</tr>
<tr>
<td>Venous pressure, mmHg</td>
<td>9.6 ± 1.4</td>
<td>8.7 ± 1.2</td>
<td>11.0 ± 1.7†</td>
</tr>
<tr>
<td>Conductance, ml·min⁻¹·mmHg⁻¹</td>
<td>1.58 ± 0.27</td>
<td>1.30 ± 0.21*</td>
<td>1.51 ± 0.24†</td>
</tr>
</tbody>
</table>

Values are ± SE; n = 7 dogs. The conductance data from the contraction period actually represent virtual venous outflow muscle conductances. *Significant difference between the hyperemia and contraction periods, P < 0.05. †Significant difference between the contraction and postcontraction periods, P < 0.05. There were no significant differences between the hyperemia and postcontraction periods.
outflow conductance between the first and final three contractions in series 2, along with small but statistically insignificant decreases during the first three contractions of series 1. There were no significant changes in venous pressure from one contraction to the next in either series.

The average weight of the muscles was 87.7 ± 7.7 g. The percentage of muscle tissue that was water at the end of the experiments averaged 76.0 ± 0.5%, which is similar to that found in previous studies in this preparation (11–13).

**DISCUSSION**

Skeletal muscle contractions generate high intramuscular pressures that impede the flow of blood into the arteriolar vasculature, while at the same time expelling blood from the venous vasculature. According to the muscle pump hypothesis, the net effect of these two events is an overall increase in the perfusion of the muscle. It has been proposed that the muscle pump mechanism is necessary to achieve maximal muscle blood flow during high-intensity rhythmic contractions (23, 24, 26). The results of the present investigation, by contrast, indicate that the overall effect of rhythmic contractions is to actually reduce mean muscle blood flow in a maximally vasodilated muscle. To our knowledge, this is the first investigation to demonstrate that the mechanical action of rhythmic tetanic skeletal contractions, on average, reduces peak muscle perfusion.

Our interest in performing this investigation was initiated by the recent review by Laughlin and Schrage (26), in which the authors concluded that the muscle pump effect most likely exists and may be demonstrated in situ using a preparation that does not interfere with the muscle’s vascular mechanics. Recent work in our laboratory also had indicated that cannulation of the arterial inflow to muscles in situ inhibits the maximal rate of blood flow (unpublished results). Consequently, venous outflow was assessed in this investigation using a large-bore flow-through-type flow probe, and the arterial pressure was sampled without direct cannulation of the muscle’s inflow. As a result, our peak contractile flows were in the upper range of those typically reported (23, 26).

To ensure that any potential increases in muscle blood flow during the contractions of series 1 were not due to an increase in muscle metabolism, it was nec-

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**Table 3.** Series 2: effect of suddenly stopping and then restarting rhythmic skeletal muscle contractions

<table>
<thead>
<tr>
<th></th>
<th>Contraction</th>
<th>Stop</th>
<th>Resume Contraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous outflow, ml·kg⁻¹·min⁻¹</td>
<td>1.454 ± 149</td>
<td>1.874 ± 172*</td>
<td>1.458 ± 139†</td>
</tr>
<tr>
<td>Arterial pressure, mmHg</td>
<td>132 ± 9</td>
<td>132 ± 8</td>
<td>134 ± 9</td>
</tr>
<tr>
<td>Venous pressure, mmHg</td>
<td>8.3 ± 2.2</td>
<td>10.5 ± 2.3*</td>
<td>9.4 ± 2.3</td>
</tr>
<tr>
<td>Conductance, ml·min⁻¹·mmHg⁻¹</td>
<td>1.03 ± 0.17</td>
<td>1.34 ± 0.21*</td>
<td>1.02 ± 0.15†</td>
</tr>
<tr>
<td>Force, kN/kg wet muscle</td>
<td>3.97 ± 0.4</td>
<td></td>
<td>4.05 ± 0.4</td>
</tr>
</tbody>
</table>

Values are ± SE; n = 6 dogs. The conductance data from the contraction and resume contraction periods actually represent virtual venous outflow muscle conductances. *Significant difference between stop and contraction periods, P < 0.05. †Significant difference between the stop and resume contraction periods, P < 0.05. There were no significant differences between the contraction and resume contraction periods.
Fig. 2. Effect of rhythmic skeletal muscle contractions on virtual venous outflow conductance during peak contractile-induced perfusion of the muscle (n = 6 dogs). The recordings are illustrations of data averaged from the experiments of series 2. According to the timeline provided, the initial contraction period ended at second 1.0, the stop contraction period ended at second 4.3, and the resume contraction period ended at second 9.3. The numbers above the schematic are the means ± SE of the conductances from each period of data collection.

Table 4. Contraction comparison data

<table>
<thead>
<tr>
<th></th>
<th>1st Contraction</th>
<th>2nd Contraction</th>
<th>3rd Contraction</th>
<th>4th Contraction</th>
<th>5th Contraction</th>
</tr>
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<tbody>
<tr>
<td><strong>Series 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous outflow, ml·kg⁻¹·min⁻¹</td>
<td>1,958 ± 279</td>
<td>1,723 ± 220†</td>
<td>1,617 ± 190†</td>
<td>1,627 ± 176*</td>
<td></td>
</tr>
<tr>
<td>Conductance, ml·min⁻¹·mmHg⁻¹</td>
<td>1.39 ± 0.31</td>
<td>1.25 ± 0.29</td>
<td>1.07 ± 0.18</td>
<td>1.13 ± 0.19</td>
<td></td>
</tr>
<tr>
<td><strong>Series 2 (resume contraction)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous outflow, ml·kg⁻¹·min⁻¹</td>
<td>1663 ± 182‡</td>
<td>1486 ± 164†</td>
<td>1353 ± 123†</td>
<td>1363 ± 116†</td>
<td>1412 ± 134†</td>
</tr>
<tr>
<td>Conductance, ml·min⁻¹·mmHg⁻¹</td>
<td>1.10 ± 0.21</td>
<td>1.02 ± 0.21</td>
<td>0.91 ± 0.19†</td>
<td>0.90 ± 0.15†</td>
<td>0.90 ± 0.16†</td>
</tr>
</tbody>
</table>

*Significant difference from the 1st contraction of series 1, P < 0.05. †Significant difference from the 1st contraction of series 2, P < 0.05. ‡Significant difference between the 1st contraction and the stop period (1,791 ± 185) of series 2, P < 0.05.
observed during high-intensity rhythmic contractions without the mechanical compression of the vasculature, we would expect the perfusion, and perhaps the peak performance, of the muscle to increase.

Although it was beyond the scope of our investigation to determine whether a Starling resistor at the level of the arterioles prevented a muscle pump effect, our results do support previous findings that reductions in venous pressure do not enhance blood flow through skeletal muscle tissue (29, 33, 42). It is interesting, however, in light of the similarities between our experimental preparations, that the results obtained by Naamani et al. (33) did not demonstrate that rhythmic contractions reduce muscle perfusion during vasodilation. Because the duty cycle they (33) used was slightly greater than ours, the contractile-induced reduction in muscle blood flow observed in the present investigation was most likely not due to duration of contraction. It is possible that the higher absolute forces generated in the present investigation occluded the intramuscular vasculature more completely and thus inhibited blood flow to a greater extent. It is important to mention that the data we used for the comparison of peak forces produced were taken from the original thesis written by Naamani (32) because we believe there was an error in the forces published in the journal article (33).

When the blood flows during each contraction within a series of experiments are compared, we see that the venous outflow during the first contraction is greater than the outflow of each subsequent contraction. This indicates that either the contractile-induced inhibition of muscle perfusion was additive throughout the first two contractile cycles or that the volume of blood contained within the muscle’s compliant vasculature was greatest before the first contraction. When the venous outflow values were converted into volumes of blood flowing from the muscle, the change between the first and subsequent contractions was only ~0.4 ml per contraction. On the basis of this evidence, it seems likely that the perfusion of the muscle was inhibited as completely by the first contraction as it was by each contraction thereafter, yet the venous outflow during the first contraction was greater due to compression of the compliant region (see Table 4). More specifically, the muscle’s compliant vasculature had swelled with blood during the hyperemia and stop periods of series 1 and 2, respectively, and then this blood was rapidly expelled when contractions were initiated. During the second, third, fourth, and so forth contractions, the rhythmic compression of the vasculature prevented the compliant region from fully refilling.

In terms of limitations to the present investigation, we measured muscle venous outflow and therefore our results do not provide specific data to indicate how the flow of blood into the muscle is affected by rhythmic contractions. According to the muscle pump theory, intense rhythmic contractions enhance venous outflow by emptying the muscle’s compliant region, and so the net flow of blood out of the muscle should be at least as great as the net inflow. Because we observed decreases in net venous outflow during rhythmic contractions, we conclude that the net inflow of blood must also have been reduced during rhythmic contractions. Furthermore, we reason that if the inflow of blood had increased during the second, third, fourth, and so forth contractions within a series, then the venous outflow should have also increased with each subsequent contraction. Nevertheless, because we do not know how the inflow varied with each contraction, we must use caution when interpreting these results, particularly as to the effect of the initial contraction on arterial inflow.

Care must also be taken when interpreting the results of series 1 because the extent of GP vasodilation observed may have exceeded the greatest dilation that could be achieved in response to high-intensity rhythmic contractions. It is also possible that the insertion of a relatively noncompliant catheter into the venous drainage of the muscle may have inhibited the muscle pump effect. Still, we anticipated this problem and, therefore, made attempts to alleviate any possible vascular interference by using a catheter with a bore size greater than that of the lumen of the popliteal vein. Consequently, the use of isometric tetanic muscle contractions was probably the most significant limitation to this investigation.

Much of the support for the muscle pump effect has developed from the observation that peak blood flows typically reported for muscles in vivo are significantly higher than the peak flows reported for isolated muscles (3, 4, 23, 24, 28). Because locomotion involves both sequential muscle fiber recruitment and muscle shortening, whereas synchronous isometric contractions do not, Laughlin and Schrage (26) hypothesized that the disparity in peak blood flows typically reported in vivo vs. in situ is due to the possibility that the muscle pump is less efficient in isolated muscle preparations. Although it seems likely that the muscle pump effect would be optimized by contractions that progressed in a wavelike manner from arterial to venous sites within the muscle, we are not aware of any specific data indicating that this actually occurs during locomotion. Although we cannot be sure how blood flow through the muscle was specifically affected by the use of synchronous tetanic contractions, it is clear that we were able to use contractions to decrease the blood volume in the muscle’s compliant region enough to reduce venous pressures proximal to the muscle. Because the muscle pump is thought to operate by simple mechanical augmentation of the muscle’s perfusion gradient, and given that we were able to produce this effect using the animal’s own muscles and vasculature, we conclude that our results should be indicative of muscle blood flow during peak perfusion in vivo. Laughlin and Schrage also concluded that, if the muscle pump effect does exist, then it should be possible to demonstrate it with an isolated muscle preparation. We found no muscle pump effect despite the fact that we obtained muscle flows that were within the highest range reported for dogs in vivo (31) and were also well within the range of the those others reported in vivo that were
used as indirect evidence for a muscle pump effect (3, 4, 23, 24, 28). Despite these arguments, we cannot be absolutely certain that our results preclude operation of the muscle pump under muscle contraction patterns in vivo. However, it is important to note that data from the companion manuscript (17) provide evidence that the muscle pump also does not elevate hindlimb blood flow during the spontaneous contractions of rhythmic locomotor exercise in intact, awake dogs.

In conclusion, given the limitations discussed above, the results of the present investigation suggest that the mechanical action of rhythmic, synchronous, maximal tetanic skeletal muscle contractions reduces peak muscle perfusion. Therefore, maximal skeletal muscle vascular conductance under such conditions is accomplished exclusively via dilation of the muscle's vascular bed, most likely in response to endothelial-derived nitric oxide and/or a combination of accumulated metabolites (25). The hemodynamic benefit of rhythmic contractions during maximal muscle vasodilation may be to compress the compliant region, thereby facilitating venous return and possibly reducing tissue edema by decreasing capillary filtration pressures (29, 33).

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