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# Venous blood gas and metabolite response to low-intensity muscle contractions with external limb compression

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**Abstract**

The effect of low-intensity resistance exercise with external limb compression (100 [EC100] and 160 [EC160] mm Hg) on limb blood flow and venous blood gas-metabolite response was investigated and compared with that of high-intensity resistance exercise (no external compression). Unilateral elbow flexion muscle contractions were performed at 20% (75 repetitions, 4 sets, 30-second rest intervals) and 70% of 1-repetition maximum (1-RM; 3 sets, each set was until failure, 3-minute rest intervals). Precontraction brachial arterial blood flow (Doppler ultrasound) was reduced with EC100 or EC160 (56% and 39% of baseline value, respectively) compared with no external compression (control). At 20% 1-RM, brachial arterial blood flow increased after contractions performed with EC160 (190%), but not with the others. Decreases in venous oxygen partial pressure ($P_vO_2$) and venous oxygen saturation ($S_vO_2$) were greater during EC100 and EC160 than control (mean [SE]: $P_vO_2$, 28 [3] vs 26 [2] vs 33 [2] mm Hg; $S_vO_2$, 41% [5%] vs 34% [4%] vs 52% [5%], respectively). Changes in venous pH ($pH_v$), venous carbon dioxide partial pressure ($P_vCO_2$), and venous lactate concentration ($[L^-]_v$) were greater with EC160 than EC100 and/or control ($pH_v$, 7.19 [0.01] vs 7.25 [0.01] vs 7.27 [0.02]; $P_vCO_2$, 72 [3] vs 64 [2] vs 60 [3] mm Hg; $[L^-]_v$, 5.4 [0.6] vs 3.7 [0.4] vs 3.0 [0.4] mmol/L, respectively). Seventy percent 1-RM contractions resulted in greater changes in $pH_v$ (7.14 [0.02]), $P_vCO_2$ (91 [5] mm Hg), and $[L^-]_v$ (7.0 [0.5] mmol/L) than EC100 and EC160, but $P_vO_2$ (30 [4] mm Hg) and $S_vO_2$ (40% [3%]) were similar. In conclusion, changes in $pH_v$, $P_vCO_2$, and $[L^-]_v$, but not in $P_vO_2$ and $S_vO_2$, are sensitive to changes in relative, "internal" intensity of low-intensity muscle contractions caused by reduced blood flow (EC160) or high-intensity muscle contractions. Given the magnitude of the changes in $pH_v$, $P_vCO_2$, and $[L^-]_v$, it appears plausible that they may be involved in stimulating the observed increase in muscle activation via group III and IV afferents.


## 1. Introduction

Resistance exercise is a potent stimulus for muscle hypertrophy and muscular strength gain, although training at low intensities (<65% of 1-repetition maximum [1-RM]) rarely produces significant gains [1]. In recent years, a number of publications have shown that low-intensity (20%-50% 1-RM) resistance exercise training combined with an appropriate level of external limb compression leads to adaptations comparable to those observed during high-intensity resistance exercise training [2-7]. Vessel compression and occluded blood flow appear to be a prominent feature of muscular adaptation (muscle hypertrophy and muscular strength) associated with high-intensity exercise [1,8]; hence, the method of applying external limb compression that leads to a combination of vessel compression, venous pooling, and reduced arterial blood flow (termed collectively hereafter as *reduced blood flow*) appears to be the primary stimulus for the potentiated adaptive response after low-intensity training.

Previous studies have suggested that the mechanism by which low-intensity training with reduced blood flow leads to significant muscular adaptation may be increased muscle activation at a given load [9-14]. Recently, work from our laboratory indeed demonstrated increased muscle activation (increased integrated electromyographic activity [iEMG])

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during low-load (20% 1-RM) muscle contractions with external compression and reduced blood flow such that there was a greater internal activation intensity of the muscle relative to external load [13,14]. The increment in muscle activation was dependent upon the level of external compression, up to 160 mm Hg external compression [13], and beyond which resulted in premature fatigue and muscular failure due to complete occlusion of blood flow [14]. Importantly, the incremented muscle activation during low-load muscle contractions was comparable to that observed during 50% to 60% 1-RM muscle contractions with an unperturbed, spontaneous blood flow response [13]; this likely explains the comparable muscular adaptive responses [2-7]. What remains to be ascertained is the mechanism by which the external limb compression and reduced blood flow signal increased muscle activation.

The observed increased muscle activation is most likely associated with changes in the energy demand-supply relationship. The greater activation may be a compensation for deficit in muscle force development after changes in energy supply [15,16]. Furthermore, muscle contractile output during low-intensity contractions (20% of maximal voluntary contraction [MVC]) with complete occlusion of blood flow was maintained by greater neural activation [14,17]. Complete occlusion of blood flow leads to reduced reflex inhibition of α-motoneurons, increased mean power frequency, and increased motor unit recruitment [18]. However, with reduced blood flow, we observed a reduction in mean power frequency with increasing iEMG such that the increase in motor unit recruitment appears to be related to reductions in motor unit discharge rates to maintain force by protecting against conduction failure [19,20]. Thus, the basis for the increased activation appears to be impairment of sensory function that disturbs central nervous system regulation of muscle force generation secondary to the external compression and/or blood flow perturbation.

Given the metabolic changes secondary to reduced blood flow and/or venous occlusion, the focus of the present study is the possible role of altered group III and IV afferent feedback due to production of a stimulatory intramuscular environment [5,11,21]. Group III and IV afferents fibers respond to reduced tissue $O_2$ and an accumulation of $CO_2$, $H^+$, and metabolites (eg, lactate) with peripheral venous distension or vasodilatory action [22-24] and could potentially stimulate muscle activation directly or through altered sensory feedback. With high levels of external compression and complete occlusion of blood flow, the acidic and/or hypoxic intramuscular environment has been suggested to increase muscle activation [17,18].

Thus, the purpose of the present study was to investigate the effect of low-intensity resistance exercise with external compression and reduced limb blood flow on venous blood gases and metabolite levels and to compare these changes with that of high-intensity resistance exercise. It is hypothesized that the changes in the intramuscular environment (indicated by venous blood) during low-intensity muscle contractions would (*a*) show a dose dependency with increasing levels of blood flow restriction (external compression), (*b*) ultimately produce changes in the intracellular milieu comparable to that observed during high-intensity muscle contractions (70% 1-RM) with spontaneous blood flow response, and (*c*) would be of sufficient magnitude to stimulate group III and IV afferents.

## 2. Methods

### 2.1. Experimental approach to the problem

Intramuscular venous pH ($pH_v$), venous oxygen partial pressure ($P_vO_2$), venous carbon dioxide partial pressure ($P_vCO_2$), venous lactate concentration ($[L^-]_v$), and venous glucose concentration $[G]_v$ are highly reflected by venous blood levels and would effectively indicate the direction and magnitude of change in the muscle [25-29]. Therefore, muscle venous blood was analyzed as an index of the muscle environment to show if changes in $H^+$, blood gases, and metabolites after low-intensity (20% 1-RM) muscle contractions with and without external compression and reduced blood flow (*a*) changed with increasing external compression (100 and 160 mm Hg), (*b*) were similar in magnitude to that observed during high-intensity muscle (70% 1-RM), and (*c*) were of sufficient magnitude to impact group III and IV afferents.

### 2.2. Subjects

Sixteen healthy men between the ages of 21 to 36 years (mean ± SE, 25.9 ± 4.8 years) volunteered for the study. The subjects in this study were classified as "recreationally active"; 7 of 16 participated in regular aerobic-type exercise (walking, jogging, or cycling; 2-3 times per week for approximately 30 minutes in duration). None of the subjects had participated in strength/resistance-type training for a minimum of 6 months before the start of the study. All subjects were nonsmokers, normotensive (blood pressure <135/85 mm Hg), nonobese (body mass index <30 kg/m$^2$), not on any medication, and free of overt chronic diseases as assessed by medical history. All subjects received a verbal and written description of the study and provided written informed consent before participating in the experiments. The study was approved by the Ethics Committee for Human Experiments of the University of Tokyo, Japan.

### 2.3. Experimental protocol

Two experiments were performed to evaluate the impact of muscle contractions on brachial artery blood flow (experiment 1) and venous blood gases and metabolites (experiment 2). Each experimental protocol is summarized in Fig. 1. For both experiments, all contraction bouts were completed on separate days, with individual contraction bouts presented in random order and with 3 to 4 days of rest between each contraction bout. Experiments were completed

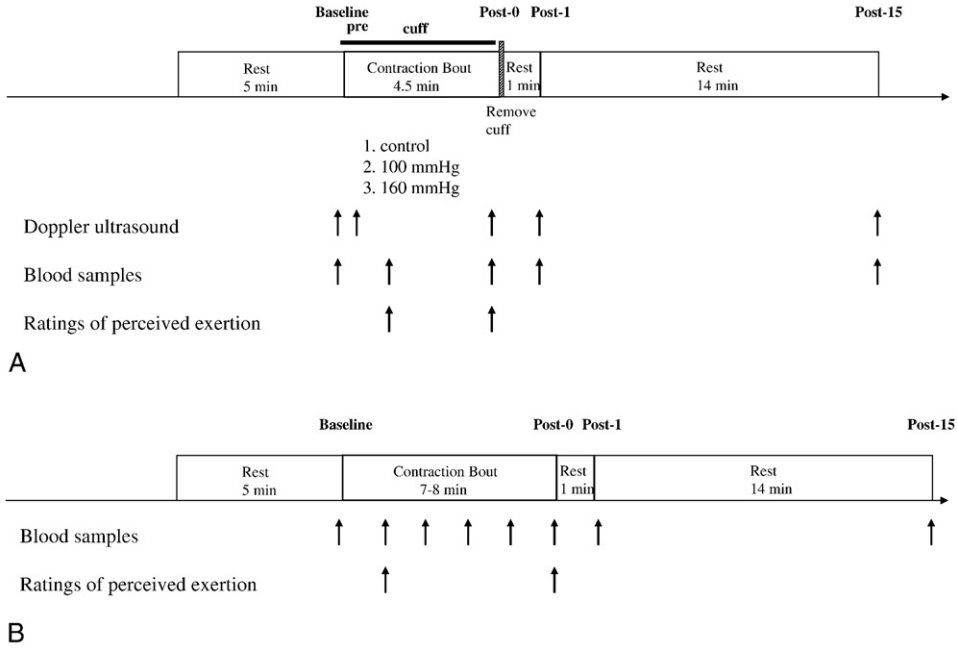


Fig. 1. Experimental timeline. Basic format for low-intensity (20% 1-RM; A) and high-intensity muscle contractions (70% 1-RM; B). Doppler ultrasound intervals are baseline, pre is a rest interval with no external compression (control) or external compression at 100 and 160 mm Hg, post 0 is immediately after the contraction bout with no external compression (control) or external compression at 100 and 160 mm Hg, post 1 is 1 minute after removal of the pressure cuff, and post 15 is 15 minutes after the contraction bout (A). Blood samples intervals are baseline, after the 30 repetitive contractions, post 0, post 1, and post 15 for 20% 1-RM (A) and baseline, immediately after each set, at 1.5 minutes of each rest interval, and post 15 for 70% 1-RM (B). Ratings of perceived exertion were measured at the end of each set.

in the laboratory with controlled temperature (25.1°C ± 0.5°C) and relative humidity (43.7% ± 4.0%) between January 25 and March 28 for experiment 1 and between September 10 and October 31 for experiment 2. All contraction bouts were carried out in the same arm of a particular subject, but use of dominant or nondominant arm was randomized between subjects.

One week before experiments, all subjects completed an orientation session to familiarize them with the equipment and external compression cuff and performed a 1-RM biceps curl test. During this orientation, the subjects sat in the experimental chair with testing arm placed on a table at heart level; and blood pressure was measured 3 times after a 5-minute rest. The systolic and diastolic blood pressures were determined by the mean of the 3 measurements.

The 1-RM biceps curl test was conducted as described previously [13,14]. Subjects performed 5 to 6 biceps curls with a moderate load as a warm-up and to familiarize subjects with the biceps curl exercise. After warming up, the load was set at approximately 80% of the predicted 1-RM. After each successful lift, the load was increased by approximately 5% until the subject failed to lift the load through the entire range of motion. A test was considered valid if the subject used proper form and completed the entire lift in a controlled manner without assistance. On average, 5 trials were required to complete a 1-RM test. Approximately 2 to 3 minutes of rest was allotted between each attempt to ensure recovery.

### 2.4. Experiment 1—brachial artery blood flow

Subjects (n = 8; mean ± SE: age, 25.3 ± 1.4 years; height, 172.1 ± 1.5 cm; body mass, 66.1 ± 1.7 kg) performed 3 trials of unilateral elbow flexion (biceps curls) contractions at 20% 1-RM (Fig. 1A): control (spontaneous blood flow response) or with EC100 or EC160. Subjects were comfortably seated on a chair, and the testing arm was maintained in the horizontal plane at heart level for Doppler measurements. Brachial arterial blood flow was recorded at 5 intervals (rest [baseline], with or without external compression before the start of contractions [pre], immediately after the contraction bout [post 0], 1 minute after removal of cuff [post 1], and 15 minutes after the end of the contraction bout [post 15]). With EC100 and EC160, pre and post 1 were measured with external compression in place and/or before removing the cuff.

### 2.5. Experiment 2—venous blood gases and metabolites

Subjects (n = 8; mean ± SE: age, 26.5 ± 2.0 years; height, 171.9 ± 3.0 cm; body mass, 66.8 ± 3.5 kg) performed 4 trials of unilateral elbow flexion (biceps curls) contractions at 20% (3 trials) or 70% 1-RM (1 trial) as depicted in Fig. 1B. The 20% 1-RM contraction bout and external compression trials (control, EC100, and EC160) were conducted exactly as in experiment 1. Subjects were comfortably seated on a chair, and the testing arm was maintained in the horizontal plane at heart level for venous blood sampling. Cephalic vein blood

samples were obtained from the catheter at 5 intervals for the 20% 1-RM contractions: rest (baseline), after the 30 repetitive contractions (C30), immediately after the contraction bout (post 0), 1 minute after removal of cuff (post 1), and 15 minutes after the end of the contraction bout (post 15). For the 70% 1-RM contraction bout, cephalic blood was sampled at 8 intervals: baseline, immediately after each set (1 set, 2 sets, and post 0), at 1.5 minutes of each rest interval (rest 1 and rest 2), 1 minute after the last set of contractions (post 1), and 15 minutes after the last set of contractions (post 15).

### 2.6. Contraction bout

All bouts consisted of unilateral elbow flexion (biceps curls) contractions as previously described [13,14]. During each experiment, subjects sat on the arm curl bench, with the arm positioned in front of the body supporting the shoulder at 45° flexion. Elbow joint range of motion during exercise was completed from full extension to full flexion. The 20% 1-RM contraction bout consisted of 30 repetitive contractions followed by 3 sets of 15 contractions separated by 30 seconds of rest. Contraction duration was 2.4 seconds with a 1.2:1.2-second shortening-lengthening contraction duty cycle controlled by a metronome (50 beats per minutes). The 70% 1-RM contraction bout consisted of 3 sets of contractions with each set conducted to volitional failure, and each set was separated by 3-minute rest period. The contraction duration was performed at a moderate contraction velocity with approximately 1.5 to 2.5:1.5 to 2.5-second shortening-lengthening contraction duty cycle.

### 2.7. External compression

The method for applying external compression to the limb and reducing blood flow has been previously described [13,14]. A specially designed elastic cuff belt (30 mm wide for the arm; Kaatsu Master, Sato Sports Plaza, Tokyo, Japan) was used. The cuff is placed around the most proximal portion of the test arm and inflated to the desired experimental pressure: EC100 or EC160.

### 2.8. Brachial arterial blood flow

Blood flow of superficial brachial artery was calculated from the cross-sectional area (CSA) of the artery and mean blood velocity (MBV) using Doppler ultrasound (ViVid 7, GE Healthcare, Tokyo, Japan). First, the superficial brachial artery was identified in the 2-dimensional mode at a distance of 70% to 80% of the upper-arm limb length (close to the elbow); and CSA was measured at the period of the T wave of the cardiac cycle. Afterward, in the pulse-Doppler method, MBV, calculated as the integral area under the velocity curve, was measured. Adjustment of the angle for the measurement was within 60°. Brachial arterial blood flow per minute ($Q_{ba}$) was obtained by multiplying CSA by MBV. The $Q_{ba}$ was measured twice at each time interval, and the mean value was selected as each point. Coefficients of variation for $Q_{ba}$ measurements at baseline were approximately 0.08.

### 2.9. Venous blood gases and metabolites

Venous blood was sampled from an indwelling heparin-lock catheter inserted into the cephalic vein at distance of 50% to 60% upper-arm length (approximately the midpoint between the shoulder and elbow). Venous $PO_2$, $P_vCO_2$, $S_vO_2$, $pH_v$, venous hematocrit, $[G]_v$, and $[L^-]_v$ of blood were measured in duplicate using a blood gas analyzer (GEM Premier 3000, IL-Japan, Tokyo, Japan). All blood samples were collected into 1-mL plastic syringes (G1470J, Smiths Medical ASD, Weston, MA) preheparinized with 23.15 IU electrolyte-balanced heparin. All blood samples were analyzed within 15 minutes of collection. The test variability of venous blood samples was assessed with the 8 subjects on 2 separate days. Coefficients of variation at baseline were approximately 0.10 for $P_vO_2$, 0.09 for $P_vCO_2$, 0.08 for $S_vO_2$, 0.002 for $pH_v$, 0.06 for hematocrit, 0.05 for $[G]_v$, and 0.11 for $[L^-]_v$.

### 2.10. Ratings of perceived exertion

Ratings of perceived exertion were measured using the Borg scale [30] after the final repetition of first and last set of contractions in each experiment (Fig. 1).

### 2.11. Statistics

Results are expressed as means ± SE for all variables. Statistical analyses were performed by 2-way analysis of variance with repeated measures in 1 domain: compression level (control, EC100, EC160) × time. Significant F values were evaluated by Tukey post hoc test where appropriate. A priori $\alpha$ levels were set at .05 and corrected for multiple comparisons using the Bonferroni technique when appropriate. The sample size (n = 8) was estimated from a priori power analysis [31] to detect differences ($\alpha$ = .05) in blood flow (Doppler ultrasound) or blood gas-metabolite measures for the interventions planned. Statistical power ranged from 0.80 to 1.00 for all comparisons reported.

## 3. Results

There were no significant differences between subjects in experiments 1 and 2 in age, height, body mass, and resting systolic (116 ± 3 and 121 ± 4 mm Hg, respectively) or diastolic blood pressure (67 ± 2 and 66 ± 4 mm Hg, respectively). None of the subjects (n = 16) had high systolic (>135 mm Hg) or diastolic (>85 mm Hg) pressure.

### 3.1. Experiment 1—brachial arterial blood flow

During the 20% 1-RM contractions, all subjects maintained the desired duty cycle and completed all prescribed contractions. Blood flow data are summarized in Fig. 2. Baseline $Q_{ba}$ was not different among control, EC100, and

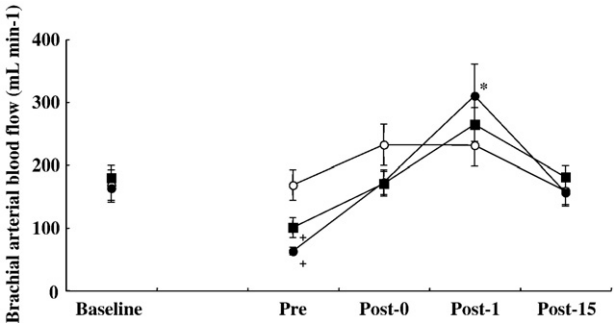


Fig. 2. Effects of low-intensity (20% 1-RM) muscle contractions with external compression on superficial brachial artery blood flow. n = 8. Data are mean ± SE. Brachial blood flow determinations and blood sampling intervals are as defined in Fig. 1. ○, no external compression (control); ■, external compression at 100 mm Hg; ●, external compression at 160 mm Hg. *Different from baseline, $P < .05$. $^{+}$Different from control, $P < .05$.

EC160. Upon application of external compression (pre), $Q_{ba}$ decreased in EC100 and EC160 (56% and 39% of baseline, respectively). In controls, $Q_{ba}$ increased 38% immediately after the contractions (post 0) to a level greater than pre. The increase in $Q_{ba}$ after contractions (post 0) with EC100 (70%) and EC160 (175%) were similar to pre values but tended to be lower than control ($P = .12$). The $Q_{ba}$ continued to increase in EC100 and EC160 (164% and 392% of pre, respectively) at post 1 to levels that were greater than control; which were not different from post 1. At post 15, $Q_{ba}$ had returned to pre levels in all trials.

### 3.2. Experiment 2—venous blood gases and metabolites

#### 3.2.1. 20% 1-RM contraction bout

During the 20% 1-RM contractions, all subjects maintained the desired duty cycle and completed all prescribed contractions. Blood gas data are summarized in Fig. 3. Baseline $P_vO_2$ (49 ± 15 mm Hg), $P_vCO_2$ (41 ± 6 mm Hg), $S_vO_2$ (79% ± 13%), $pH_v$ (7.40 ± 0.02), hematocrit (41% ± 3%), $[G]_v$ (83 ± 13 mg $dL^{-1}$), and $[L^-]_v$ (0.6 ± 0.2 mmol $L^{-1}$) were not significantly different across all trials (control, EC100, and EC160). The decrease in $P_vO_2$ with contractions (C30) and after contractions (post 0) was significantly greater in EC100 and EC160 than in controls (Fig. 3A). The decrease in $S_vO_2$ with contractions (C30) and after contractions (post 0) was significantly ($P < .05$) greater with EC160 than EC100, which was greater than control (Fig. 3C). $P_vCO_2$ increased with contractions in all trials and was greater in EC100 and EC160 than control (Fig. 3B). $pH_v$ was decreased with contractions (C30) and after contractions (post 0 and post 1) in all trials, and the changes were greater with EC160 than EC100 and control (Fig. 3E).

Hematocrit and $[G]_v$ did not significantly change during contractions in all trials and remained similar to baseline values (40%~45% and 80~90 mg $dL^{-1}$, respectively). The increase in $[L^-]_v$ with contractions (C30) and after contractions (post 0) was greater in EC160 than with EC100 or control, which were similar (Fig. 3D).

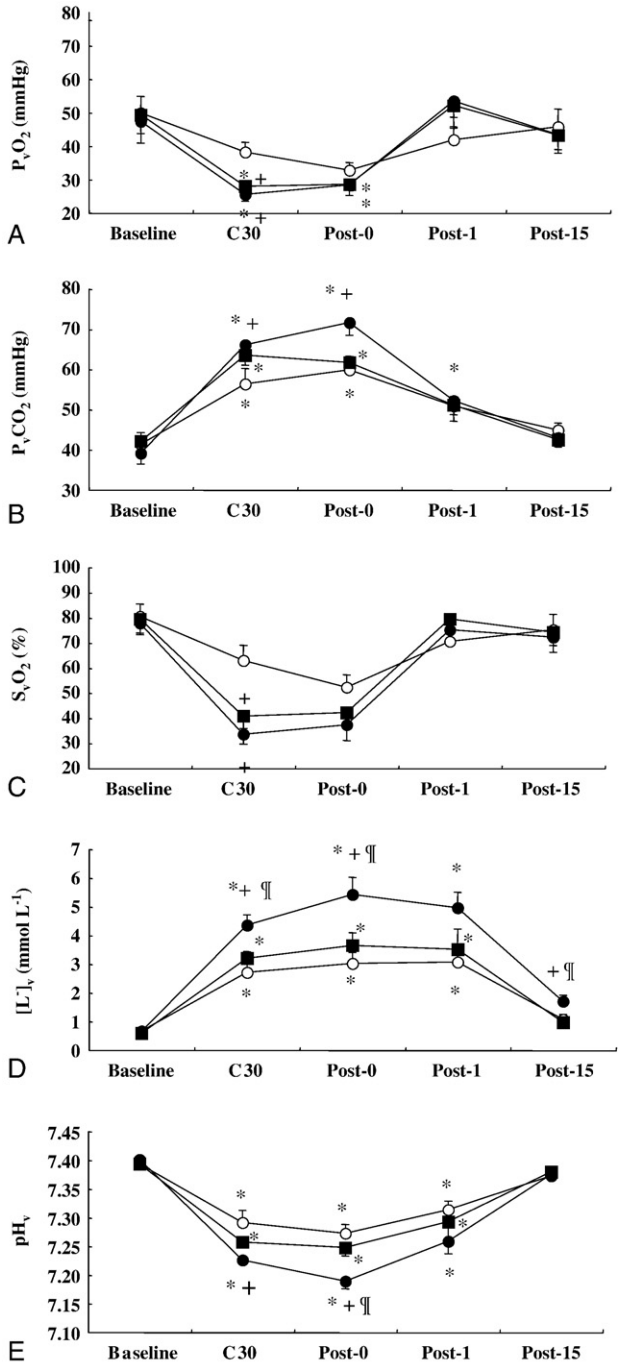


Fig. 3. Effects of low-intensity (20% 1-RM) muscle contractions with external compression on venous blood gases and metabolites. n = 8. Data are mean ± SE. Blood sampling intervals are as defined in Fig. 1—baseline, post 0, post 1 and post 15. C30 is after the 30 repetitive contractions. ○, no external compression (control); ■, external compression at 100 mm Hg; ●, external compression at 160 mm Hg. *Different from baseline, $P < .05$. $^{+}$Different from control, $P < .05$. ¶Different from 100 mm Hg external compression, $P < .05$.

#### 3.2.2. 70% 1-RM contraction bout

Subjects competed 3 sets of muscle contraction consisting of 11.8 ± 0.8, 10.0 ± 0.7, and 9.0 ± 0.6 repetitions, respectively. During each set, the mean contraction times for

shortening and lengthening were approximately 3.2 ± 0.2, 3.9 ± 0.4, and 4.0 ± 0.5 seconds, respectively. Baseline $P_vO_2$ (45 ± 3 mm Hg), $P_vCO_2$ (40 ± 6 mm Hg), $S_vO_2$ (70% ± 8%), $pH_v$ (7.36 ± 0.01), hematocrit (40% ± 2%), $[G]_v$ (83 ± 6 mg $dL^{-1}$), and $[L^-]_v$ (1.0 ± 0.2 mmol $L^{-1}$) were not different from the 20% 1-RM trials. $P_vO_2$ and $S_vO_2$ decreased and $P_vCO_2$ increased immediately after each set of contractions, but recovered rapidly during each rest period (Fig. 4). The change in $S_vO_2$ and $P_vO_2$ with 70% 1-RM contractions was similar to that observed with both EC100 and EC160 20% 1-

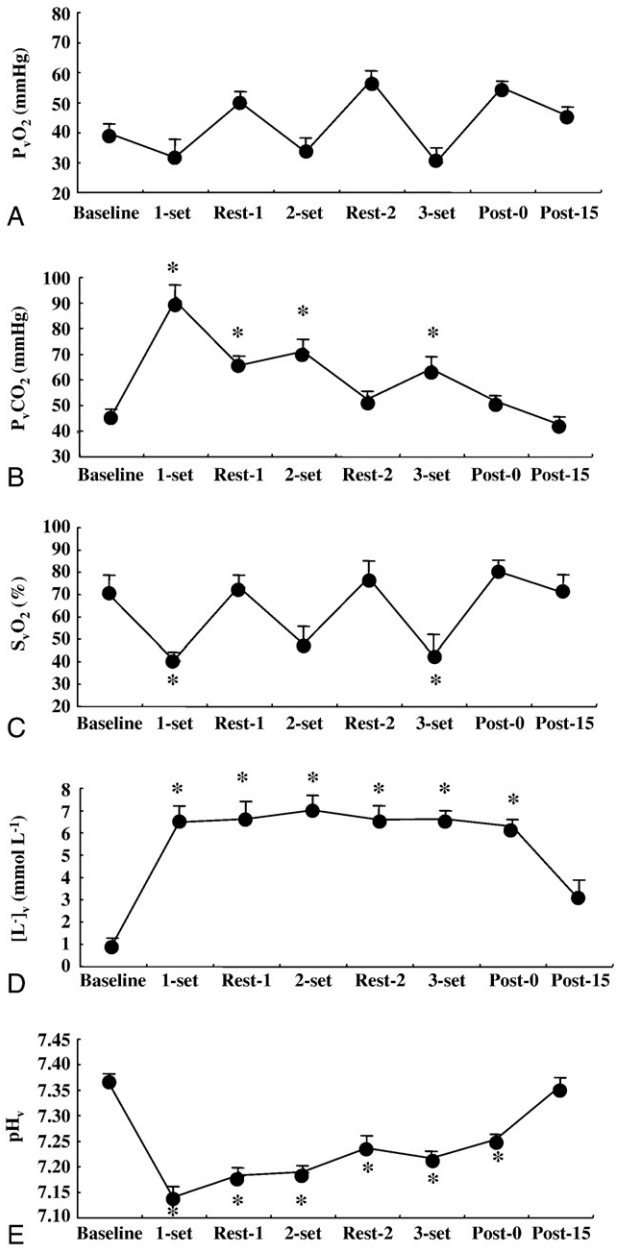


Fig. 4. Effects of high-intensity (70% 1-RM) muscle contractions on $P_vO_2$, $P_vCO_2$, $S_vO_2$, $[L^-]_v$, and $pH_v$. n = 8. Data are mean ± SE. Blood sampling intervals are immediately after each set (1, 2, and 3 sets), 1.5 minutes into each rest period (rest 1 and rest 2). Baseline, post 0, and post 15 are as defined in Fig. 1. *Different from baseline, $P < .05$.

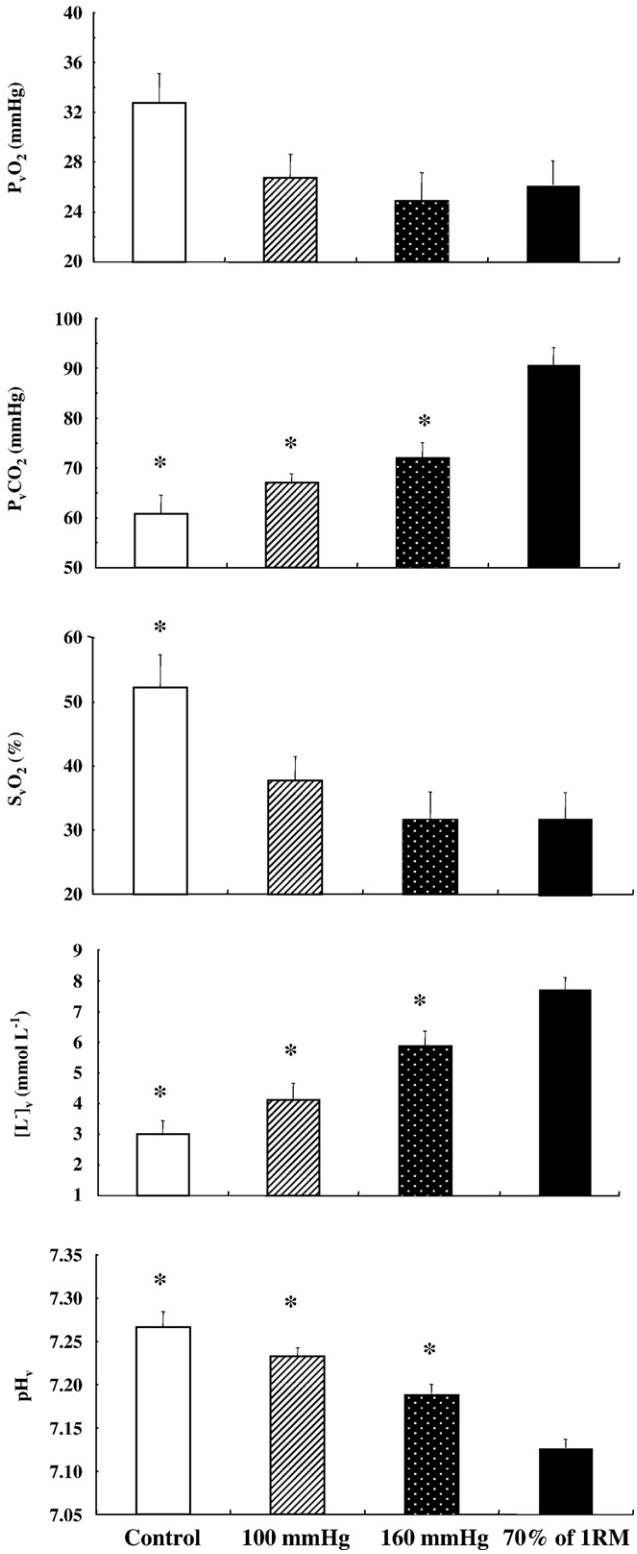


Fig. 5. Minimum value of $P_vO_2$, $S_vO_2$, and $pH_v$ or maximum value of $P_vCO_2$ and $[L^-]_v$ after the contraction bout in 20% 1-RM with no external compression (control), 20% 1-RM with external compression at 100 mm Hg, 20% 1-RM with external compression at 160 mm Hg, and 70% 1-RM. n = 8. Data are mean ± SE. *Different from 70% 1-RM trial, $P < .05$. When compared with the resting level, all types of conditions caused significant changes ($P < .05$).

Table 1
Ratings of perceived exertion during experiments 1 and 2, contraction bout of biceps curls performed at 20% or 70% of 1-RM

| | 1st set | Last set |
|---|---|---|
| Rating of perceived exertion | | |
| Experiment 1 | | |
| Control | 11.1 (0.6) | 12.3 (0.8) |
| EC100 | 12.5 (0.5) | 14.6 (0.7) |
| EC160 | 13.1 (0.4)* | 15.3 (1.2)* |
| Experiment 2 | | |
| Control | 11.0 (0.8) | 12.1 (0.9) |
| EC100 | 12.0 (0.6) | 14.0 (0.6) |
| EC160 | 13.1 (0.5)* | 14.9 (0.4)* |
| 70% of 1-RM trial | 16.0 (0.9)*,†,‡ | 18.7 (0.3)*,†,‡ |

Values are mean ± SE. n = 8. At 20% of 1-RM, first set = 30th contraction, last set = 15th repetition of the third set. At 70% of 1-RM, first and last set = conduction to volitional failure, respectively. Control = no external compression at 20% of 1-RM; EC100 = external compression at 100 mm Hg with 20% of 1-RM; EC160 = external compression at 160 mm Hg with 20% of 1-RM.

* Different from control, $P < .05$.

† Different from 100 mm Hg, $P < .05$.

‡ Different from 160 mm Hg external compression, $P < .05$.

RM contractions (Fig. 5). The change in $P_vCO_2$ with 70% 1-RM contractions was greater than that observed in any of the 20% 1-RM trials (Fig. 5). There was no change in hematocrit or $[G]_v$ with 70% 1-RM contractions (41%∼44% and 82∼88 mg $dL^{-1}$, respectively); and thus, they remained similar to 20% 1-RM trials. $[L^-]_v$ increased significantly and $pH_v$ decreased significantly immediately after the first set of contractions and remained at that level throughout the remainder of the bout (Fig. 4). These changes were significantly greater than those observed during any of the 20% 1-RM trials (Fig. 5).

### 3.3. Ratings of perceived exertion

In experiment 1, the ratings of perceived exertion were significantly greater during EC160 than EC100 or control, which were similar (Table 1). In experiment 2, the ratings of perceived exertion were significantly greater in 70% 1-RM contractions compared with any of the 20% 1-RM contraction bouts. As with experiment 1, the ratings of perceived exertion were greater in EC160 than EC100 or control, which were similar.

## 4. Discussion

Previous studies [13,14] have shown that low-intensity muscle contractions with an appropriate level of external compression leads to increased muscle activation theoretically due to altered central nervous system control of muscle contractile function. The findings of the present study demonstrate that dose-dependent alterations in blood gases and metabolites during low-intensity muscle contraction with 2 levels of external compression (EC100 and EC160) are limited to blood flow, blood $pH_v$, $P_vCO_2$, and $[L^-]_v$. Likewise, it is only these variables that responded differently to intensity of muscle contractions, the response being lesser in the low-intensity contractions with reduced blood flow. Furthermore, only these variables appear to change in a magnitude that could alter neural function and impact muscle activation through group III and IV stimulation.

Hyperemia is indicative of an imbalance between blood supply and its demand by muscle tissue after occlusion of blood flow (reactive) or increased blood flow during muscle contractions (active). Furthermore, the level of hyperemia indicates the level of imbalance such that the hyperemia is greater with increasing levels of blood flow reduction or exercise intensity [32,33]. In the present study, $Q_{ba}$ was reduced at rest (compared with control) and resulted in significant hyperemia after removal of the external compression after muscle contractions. Furthermore, it appears that the impairment of venous outflow and arterial inflow was increased incrementally with external compression, as the level of hyperemia was significantly greater after EC160 than with EC100 (Fig. 2). These levels suggest that $Q_{ba}$ was reduced by approximately 45% (EC100) and approximately 60% (EC160) compared with control (pre and post 0; Fig. 2). Thus, the $Q_{ba}$ reduction with EC100 and EC160 appears quantitatively similar to that of Takarada et al [5] and significantly greater than the Sundberg [10] study. Thus, in agreement with our hypothesis, it is concluded that $Q_{ba}$ was significantly and incrementally reduced with increasing external compression.

Initial venous blood gases and metabolite levels were similar to previous studies [27,29,34]. Strandell and Shepherd [35] reported that the reduced blood supply is compensated by increased oxygen extraction to maintain the oxygen uptake. This appears to be the case here, as $P_vO_2$ and $S_vO_2$ were significantly lower during EC100 and EC160 muscle contractions than during control (Fig. 3). $P_vO_2$ decreased to 26 mm Hg at C30 and post 1 and was essentially unchanged despite the increased external compression and greater reduction in $Q_{ba}$ (Fig. 3). These minimum values are consistent with previous studies (21 mm Hg for forearm vein [27], 15-25 mm Hg for femoral vein [36]). Furthermore, Soller et al [27] reported that $P_vO_2$ was decreased and leveled off at 15% MVC, whereas intramuscular $P_vO_2$ continued to decrease near zero levels at 30% and 45% MVC, an intensity of muscle contraction significantly greater than that used here. Taken together, the present results demonstrate that $P_vO_2$ was approaching a minimum achievable level for the conditions of these experiments and that intramuscular oxygen level was low, but may not be minimal or even approaching zero. When blood flow is reduced and oxygen extraction is not changing (as concluded from similar $P_vO_2$ and $S_vO_2$ above), energy supply is augmented by increased utilization of creatine phosphate and increased energy flux through glycolysis (increased lactate production) [37,38]. These changes are typically associated with increased $[H^+]$

[26,37,38]. Hence $[L^-]_v$ and $pH_v$ were significantly greater in EC160, where $Q_{ba}$ was the least (Fig. 3), suggesting that lactate production and glycolytic flux were increased relative to EC100 or control. This is in agreement with previous studies [5,10,34] that reported that lactate was elevated with increasing levels of external compression; similar to compression levels used here.

In conclusion, muscle activation (iEMG activity) increases during low-intensity muscle contractions, with external compression, EC160 being greater than EC100 [13,14] due to greater, but "appropriate," level of blood flow reduction (present data). The term *appropriate* is used here, as the reductions in blood flow did not result in premature muscle fatigue or muscular failure as observed with complete blood flow occlusion [14]. Accordingly, it is suggested that the increased muscle activation results in a greater energy demand as indicated by an increased reliance on oxygen-independent energy supply supported by incremental changes in $pH_v$, $P_vCO_2$, and $[L^-]_v$ at the same external load, as hypothesized. On the other hand, oxygen levels were reduced during low-intensity contractions with reduced blood flow (compared with controls); but contrary to our hypothesis, the reduction was independent of the level of external compression and blood flow reduction.

Similar conclusions can be drawn when comparing low-intensity and high-intensity contractions. $P_vO_2$ and $S_vO_2$ were not significantly different between the 20% 1-RM (EC100 or EC160) and 70% 1-RM contractions. However, $pH_v$, $P_vCO_2$, and $[L^-]_v$ were significantly greater with 70% 1-RM than EC160, which were greater than EC100 (Fig. 3-5). Accordingly, based on tissue oxygenation levels as discussed above, it seems likely that there was not much difference in intramuscular oxygenation level among 3 conditions; but 70% 1-RM requires greater dependence on oxygen-independent metabolism than muscle contractions performed at 20% 1-RM with EC160 or EC100. Again, as above, this would seem to suggest that muscle contractions performed at 70% 1-RM require greater muscle activation and present a greater energetic demand than contractions performed at 20% 1-RM with EC160. Given these differences, it is concluded that blood gas/metabolite perturbations do not support a similarity in exercise intensity as was hypothesized. However, the muscle activation pattern is similar to muscle contractions performed at 50% to 60% 1-RM without external blood flow impairments [13] and would still appear to support the conclusion that performing low-intensity muscle contractions (20% 1-RM) with EC160 yields an apparent high-intensity training stimulus. The apparent high-intensity nature of the 20% 1-RM contractions would be of sufficient magnitude to induce muscle enlargement and muscular strength gains that have been observed after training with the low-intensity, reduced blood flow contractions [2-7].

Previous studies indicated that increased muscle activation during low-intensity muscle contractions with blood flow restriction may be caused by the inhibition of α-motoneuron activity due to increased input from group III and IV afferents [17,18]. The observed magnitude of changes in $pH_v$, $P_vCO_2$, and $[L^-]_v$ agrees favorably with previous work [27,29,34] and appears to be of the magnitude necessary to stimulate group III and IV afferents. Furthermore, the level of $P_vCO_2$ appears to be of the magnitude necessary to alter sensory function [18,39]. However, the decrements in $P_vO_2$ or $S_vO_2$, although greater than observed in controls and similar to those observed during 70% 1-RM contractions, do not appear to be of sufficient stimulatory magnitude and thus would seem to have a limited role, if any, in signaling muscle activation. As discussed above, the oxygen levels observed suggest that oxygen extraction is maximized under these conditions, but clearly are not minimally low or zero. The lack of large decrements in oxygen levels may be related to the fact that blood flow is only partially reduced and thus would be expectedly different from complete blood flow occlusion studies. Still, the lack of difference in oxygen levels across compression levels and contraction intensity is curious given the apparent increased energy demand associated with EC160 especially because oxygen uptake has been reported to be higher during walking with EC160 [40]. Thus, it would seem that oxygen uptake is not limited in this setting. Given this, other potential signals for the increased activation observed during low-intensity muscle contractions with reduced blood flow may be related to changes in perfusion pressure and/or muscle blood flow distribution after the application of external compression, reduction in blood flow, and venous occlusion [41-43]. Clearly, additional work is needed to fully understand the role of blood flow distribution, oxygen delivery, and oxygen uptake kinetics in meeting the increased energy demands of low-intensity muscle contractions with reduced blood flow.

Another potential mechanism for neural derangement could be direct effects of external compression on nerve/neural function [13,14]. The physical compression of the nerve exerted by the external compression cuff could alter impulse traffic [44,45]. Alterations in the α-motoneuron excitability were observed with external compression independent of any other experimental perturbation [46]. Although the compressive forces used to create reduced blood flow are significantly less than required for complete occlusion, the role of the compressive effect on nerve function cannot be ignored; unfortunately, this effect is very difficult to study independently in intact humans.

In conclusion, it appears that the increment in muscle activation observed with increasing levels of external compression is related to reduced blood flow to the muscle. Changes in $pH_v$, $P_vCO_2$, and $[L^-]_v$, but not in $P_vO_2$ and $S_vO_2$, are sensitive to changes in relative, "internal" intensity of low-intensity muscle contractions caused by reduced blood flow (EC160) or high-intensity muscle contractions. The muscle venous blood gas and metabolite changes indicate a different intramuscular environment and do not

reflect equivalence between low-intensity and high-intensity muscle contractions. Given the magnitude of the changes in $pH_v$, $P_vCO_2$, and $[L^-]_v$, it appears plausible that they may be involved in stimulating the observed increase in muscle activation via group III and IV afferents.

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