Effects of augmented respiratory muscle pressure production on locomotor limb venous return during calf contraction exercise

Miller, Jordan D., David F. Pegelow, Anthony J. Jacques, and Jerome A. Dempsey. Effects of augmented respiratory muscle pressure production on locomotor limb venous return during calf contraction exercise. J Appl Physiol 99: 1802–1815, 2005. First published July 28, 2005; doi:10.1152/japplphysiol.00278.2005.—We determined effects of augmented inspiratory and expiratory intrathoracic pressure or abdominal pressure (Pab) excursions on within-breath changes in steady-state femoral venous blood flow (Qfv) and net Qfv during tightly controlled (total breath time = 4 s, duty cycle = 0.5) accessory muscle “rib cage” (ΔPab < 2 cmH2O) or diaphragmatic (ΔPab > 5 cmH2O) breathing. Selectively augmenting inspiratory intrathoracic pressure excursion during rib cage breathing augmented inspiratory facilitation of Qfv from the resting limb (69% and 89% of all flow occurred during nonloaded and loaded inspiration, respectively); however, net Qfv in the steady state was not altered because of slight reductions in femoral venous return during the ensuing expiratory phase of the breath. Selectively augmenting inspiratory esophageal pressure excursion during a predominantly diaphragmatic breath at rest did not alter within-breath changes in Qfv relative to nonloaded conditions (net retrograde flow = −9 ± 12% and −4 ± 9% during nonloaded and loaded inspiration, respectively), supporting the notion that the inferior vena cava is completely collapsed by relatively small increases in gastric pressure. Addition of inspiratory + expiratory loading to diaphragmatic breathing at rest resulted in reversal of within-breath changes in Qfv, such that >90% of all anterograde Qfv occurred during inspiration. Inspiratory + expiratory loading also reduced steady-state Qfv during mild- and moderate-intensity calf contractions compared with inspiratory loading alone. We conclude that 1) exaggerated inspiratory pressure excursions may augment within-breath changes in femoral venous return but do not increase net Qfv in the steady state and 2) active expiration during diaphragmatic breathing reduces the steady-state hyperemic response to dynamic exercise by mechanically impeding venous return from the locomotor limb, which may contribute to exercise limitation in health and disease.

blood flow; breathing mechanics; expiratory flow limitation; Starling resistor

DURING MODERATE-INTENSITY locomotor exercise, ventilatory mechanics are changed in three major ways: 1) the magnitude of the inspiratory and expiratory intrathoracic pressure (ITP) excursions is increased, resulting in increases in airflow and tidal volume (VTr), 2) transverse intercostal muscle contraction facilitates expansion of the rib cage during inspiration, which spares diaphragmatic shortening and minimizes inspiratory increases in abdominal pressure (Pab) and diaphragmatic work (3), and 3) expiration becomes active, which forces end-expiratory lung volume below functional residual capacity and serves to keep the diaphragm near its optimum length (10). In patients with obstructive lung disease (1) or chronic heart failure (4), inspiratory and expiratory pressures may be exaggerated even at rest and may become more pronounced during even mild-intensity exercise (19, 20).

Although there is a large body of literature examining the effects of changes in production of respiratory muscle pressure on cardiovascular function in resting and/or anesthetized animals, our understanding of the cardiovascular consequences of these changes in breathing mechanics during exercise, when the skeletal muscle pumps are rhythmically forcing blood centrally, remains unclear. More specifically, previous studies measuring femoral venous blood velocity have suggested that more-negative inspiratory ITP excursions are significant, independent contributors to increases in locomotor limb venous return during exercise in humans (11, 21). However, previous work from our laboratory showed that changes in breathing pattern do not appear to contribute significantly to the increases in locomotor limb venous blood flow during calf contraction exercise in the semirecumbent human, although they exert a significant within-breath modulatory effect on femoral venous return (15). However, we did not alter the magnitude of the inspiratory ITP excursion above resting eupneic levels, and passive expiration was maintained.

Other studies that have attempted to address the role of the “respiratory pump” in the cardiovascular response to dynamic exercise in healthy subjects used voluntary hyperventilation, transient augmented VT, or inspiratory loading to augment the inspiratory and/or expiratory ITP and Pab excursions. However, indirect estimates of pulmonary blood flow (2, 5), estimates of locomotor limb venous blood flow that did not adequately control for changes in venous vessel cross-sectional area (11, 21), confounding effects of changes in arterial CO2 on local arteriolar tone (6, 13), and loosely controlled breathing mechanics have precluded determination of the effects of the augmented inspiratory and expiratory ITP excursions on the return of blood from the locomotor limb to the heart. Also, because in many investigations the subjects were supine (11, 21), application of the results to the upright, exercising human is difficult at best (see DISCUSSION).

In contrast to healthy subjects, the ventilatory responses to exercise in patients with obstructive pulmonary disease have been hypothesized to impede venous return at rest and during exercise (25). However, the experimental data to support this postulation are sparse and are primarily derived from observations in healthy humans and animals subjected to high levels of positive-pressure ventilation (>10 cmH2O) (9, 17). Although cardiac output and stroke volume are depressed with positive-
In a separate trial, arterial blood velocity was measured in the superficial femoral artery using the same Doppler ultrasound system. Arterial blood velocity and vessel diameter (d) were acquired during the same trial, and arterial cross-sectional area was calculated from the longitudinal arterial vessel image at the point of peak arterial blood flow at 1-min intervals as follows: \( \pi(d/2)^2 \).

Instantaneous arterial and venous blood flow were calculated as the product of blood velocity and the interpolated value for vessel cross-sectional area at 100 equally spaced points over the course of a breath. Arterial limb vascular conductance was calculated as \( Q_a / MAP \).

**Breathing Pattern**

During rib cage breathing, subjects were instructed to inspire using predominantly their accessory inspiratory muscles, such that the inspiratory change in gastric pressure (Pga) during inspiration was \(<3\) cmH\(_2\)O. During diaphragmatic breathing, subjects were instructed to inspire such that the diaphragm descended and forced an outward excursion of the abdominal wall during inspiration and a concomitant inspiratory increase in Pga of \( \geq 5\) cmH\(_2\)O. Breathing frequency was set at 15 breaths/min with a duty cycle of 0.50. Pga and esophageal pressure (Pes) changes over the course of a breath were monitored closely throughout the study to ensure that the pressure waveform was uniform across breaths, the ITP excursions were comparable between rib cage and diaphragm breathing, and the breath timing and breathing patterns conformed to the instructions given to the subjects at the beginning of the study. Although VT was not controlled specifically, the subjects were encouraged to maintain similar VT and end-expiratory lung volume across rib cage and diaphragm breathing.

**Exaggeration of the Inspiratory Pes Excursion**

To examine the effects of an increased inspiratory Pes excursion alone, the magnitude of the inspiratory Pes excursion was increased by application of a fixed inspiratory resistance (\(-12\) cmH\(_2\)O·L\(^{-1}\)·s\(^{-1}\)) during rib cage or diaphragm breathing \((n = 5\) subjects; Fig. 1, A and B; see supplemental information at http://jap.physiology.org/cgi/content/full/00278.2005/DC1 for a schematic of the order of testing). Subjects were instructed to exhale passively and maintain similar VT and operating lung volumes (relative to nonloaded breathing conditions) during the inspiratory loaded portions of the trials.

**Exaggeration of Inspiratory and Expiratory Pes and Pga Excursions**

During diaphragmatic breathing, a fixed inspiratory resistance was again used to increase the magnitude of the inspiratory Pes excursion. The expiratory Pes and Pga excursions were increased by addition of an expiratory threshold valve set to open at 10 cmH\(_2\)O. Subjects \((n = 4\) were instructed to exhale actively against the expiratory load and maintain similar VT and operating lung volumes (relative to nonloaded breathing conditions) during the combined inspiratory and expiratory loaded portions of the trials (see supplemental information for a schematic of the order of testing). Despite verbal encouragement to do otherwise, one subject persistently responded to the expiratory loading with pronounced hyperinflation, making the Pga waveform qualitatively similar to that observed during diaphragmatic breathing alone, and was excluded from further analysis.

**Calf Contraction**

The subjects were placed in a semirecumbent \((\sim 45^\circ)\) position, with knees extended and parallel to the floor. They performed plantar flexion exercise, with the range of motion limited by two adjustable metal bars. The subjects were instructed to lightly touch the distal bar during plantar flexion and maintain a consistent level of force production with each contraction. The force generated by the subject during calf contraction could be altered by addition or removal of elastic bands \((7 \text{ or } 11 \text{ kg of peak force})\). The calf was contracted at a
frequency of 30 min\(^{-1}\) with a duty cycle of 0.50, which allowed for synchronization of contraction with the onset of inspiration and expiration (i.e., 1 contraction cycle occurred during inspiration and 1 during expiration).

**Data Analysis**

Composite waveforms were generated over the course of each breath for each variable by sampling each variable at 100 equally spaced points over the course of a breath and averaging these values for each 5-min condition. A repeated-measures ANOVA with Tukey's post hoc test was used to detect differences in the mean values of each variable during inspiration and expiration between rib cage and diaphragm breathing with and without inspiratory and expiratory loading and across different levels of calf contraction.

**RESULTS**

*Effects of Exaggerated Inspiratory ITP Excursions on Q\(_{fa}\) and Femoral Arterial Vascular Conductance at Rest and During Mild and Moderate Calf Contraction*

Across all resting and calf contraction conditions, augmentation of the inspiratory ITP excursion did not elicit significant within-breath changes in Q\(_{fa}\) or femoral arterial vascular con-
ductance, nor did it affect these variables in the steady state (Figs. 2–5).

**Effects of an Exaggerated Inspiratory ITP Excursion on $Q_{fv}$ During Rib Cage Breathing at Rest and During Calf Contraction**

The signal-averaged, quantitative data for all subjects at rest and during moderate calf contraction are shown in Figs. 2 and 3, respectively; results during mild calf contraction are reported in Table 1. The subjects were able to significantly increase the magnitude of their inspiratory Pes excursion ($P < 0.05$) during rib cage breathing with inspiratory loading, whereas $P_{ab}$ was relatively unchanged. The addition of mild- or moderate-intensity calf contraction elicited significant increases in mean $Q_{fv}$ over resting conditions ($P < 0.05$; Table 1).

During nonloaded rib cage breathing at rest and at both levels of calf contraction, $Q_{fv}$ tended to be slightly higher during early inspiration than during expiration, although this effect was not sustained throughout inspiration and was not sufficient to elicit a significant difference between mean inspiratory and mean expiratory $Q_{fv}$ (Figs. 2 and 3). When the inspiratory ITP excursion was augmented, however, mean inspiratory $Q_{fv}$ became significantly higher than mean $Q_{fv}$

![Fig. 2. Effects of augmenting inspiratory intrathoracic pressure (ITP) excursion during rib cage breathing on femoral arterial flow ($Q_{fa}$), mean arterial pressure (MAP), and $Q_{fv}$ over the course of a breath at rest ($n = 5$, 60 breaths per subject per condition). Increasing the magnitude of the inspiratory Pes excursion significantly increased mean inspiratory $Q_{fv}$ but did not change $Q_{fa}$. Nonloaded rib cage breathing; • inspiratory loaded rib cage breathing. *$P < 0.05$, nonloaded rib cage breathing vs. inspiratory loaded rib cage breathing.](http://jap.physiology.org/)
during the ensuing expiratory phase of the breath at rest and during both levels of calf contraction. However, the extent to which further reductions in ITP during inspiration could facilitate anterograde $Q_{fv}$ was only modestly augmented by addition of an inspiratory load [within-breath changes in $Q_{fc}$ were significant only during inspiratory loaded conditions ($P < 0.05$) for mean inspiratory $Q_{fc}$ vs. mean expiratory $Q_{fc}$].

Effects of Exaggerated Inspiratory ITP Excursions on $Q_{fv}$

The signal-averaged, quantitative data for all subjects at rest and during moderate calf contraction are shown in Figs. 4 and 5, respectively; results during moderate calf contraction are reported in Table 1. The subjects were able to significantly increase the magnitude of their inspiratory Pes excursion during diaphragmatic breathing with inspiratory loading ($P < 0.05$), whereas the magnitude of the Pga excursion was relatively unchanged. The addition of mild or moderate calf
contraction elicited significant increases in $\dot{Q}_{fv}$ over resting conditions ($P < 0.01$; Table 1).

$\dot{Q}_{fv}$ showed significant within-breath variation during non-loaded diaphragmatic breathing at rest (Fig. 4) and during mild (Table 1) and moderate (Fig. 5) calf contraction, such that mean $\dot{Q}_{fv}$ was significantly lower during inspiration than during the ensuing expiratory phase of a nonloaded diaphragmatic breath ($P < 0.05$ for all). However, more than doubling the magnitude of the inspiratory Pes excursion (while leaving the inspiratory $\Delta P_{ga}$ unchanged) did not affect the magnitude or qualitative characteristics of the within-breath changes in $\dot{Q}_{fv}$ during diaphragmatic breathing at rest (Fig. 4) or during mild (Table 1) or moderate (Fig. 5) calf contraction. Furthermore, neither level of calf contraction significantly increased mean $\dot{Q}_{fv}$ during a nonloaded diaphragmatic inspiration over that observed at rest ($P = $ not significant; Table 1), and mean inspiratory $\dot{Q}_{fv}$ remained significantly lower than that observed during rib cage breathing at the same intensity of calf contraction ($P < 0.01$).

**Effects of Augmented Inspiratory and Expiratory ITP Excursions on $\dot{Q}_{fv}$ During Predominantly Diaphragmatic Breathing at Rest and During Calf Contraction**

The signal-averaged, quantitative data for all subjects at rest and during moderate calf contraction are shown in Figs. 6 and 7, respectively; results during moderate calf contraction are

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![Graph](image.png)

**Fig. 4.** Effects of augmenting inspiratory ITP excursion during diaphragmatic breathing on $\dot{Q}_{tv}$, MAP, and $\dot{Q}_{tv}$ over the course of a breath at rest ($n = 5$, 60 breaths per subject per condition). Selectively augmenting the Pes excursion did not affect inspiratory reductions in $\dot{Q}_{tv}$ or expiratory resurgence of $\dot{Q}_{tv}$ during nonloaded diaphragmatic breathing ($P < 0.05$, mean inspiratory $\dot{Q}_{tv}$ vs. mean expiratory $\dot{Q}_{tv}$ during nonloaded and inspiratory loaded conditions). ○, Nonloaded diaphragm breathing; ●, inspiratory loaded diaphragm breathing. *$P < 0.05$, nonloaded diaphragm breathing vs. inspiratory loaded diaphragm breathing.
reported in Table 2. The addition of combined inspiratory and expiratory loading to diaphragmatic breathing in the remaining subjects significantly lowered the mean inspiratory Pes ($P < 0.05$), while the mean expiratory Pga was unchanged; during expiration, we observed significant increases in mean expiratory Pes and mean expiratory Pga ($P < 0.05$; Figs. 6 and 7). In contrast to diaphragmatic breathing during passive expiration, expiratory loading during diaphragmatic breathing significantly lowered mean expiratory Qfv at rest (Fig. 6) and during mild (Table 1) and moderate (Fig. 7) calf contraction ($P < 0.05$ vs. mean expiratory Qfv when expiration was passive for all). Additionally, mean inspiratory Qfv was significantly higher during expiratory loaded diaphragm breathing than during passive expiration at rest and during both levels of calf contraction ($P < 0.05$, expiratory load vs. no expiratory load for all; Figs. 6 and 7, Table 1). Consequently, the within-breath modulation of Qfv was directionally opposite during nonloaded and expiratory loaded diaphragmatic breathing, such that the majority of anterograde flow occurred during inspiration when expiration was active (Figs. 6 and 7; Qfv,I/Qfv,T in Table 2).

In the steady state (i.e., over the course of >50 complete respiratory cycles), Qfv at rest tended to be slightly lower during expiratory loading but was not significantly different
from nonloaded diaphragmatic breathing at rest (Table 2). In
contrast, addition of an expiratory load to diaphragmatic
breathing significantly blunted the increase in steady-state
blood flow in response to mild and moderate calf contraction
\((P < 0.05 \text{ vs. inspiratory loading alone; Fig. 8). Steady-state}
\(Q_{fv}\) was reduced at both intensities of calf contraction, despite
the presence of a small but nonsignificant pressor response
with the addition of an expiratory load \((P = \text{not significant vs.}
inspiratory loading alone). Accordingly, the blunted hyperemic
response to calf contraction exercise was mediated by signifi-
cant reductions in vascular conductance \((P < 0.05 \text{ vs. inspira-
tory loading alone; Table 2, Fig. 8).}

**DISCUSSION**

The main findings of this study can be summarized as
follows: 1) More-negative inspiratory ITP excursions increased
the inspiratory facilitation of \(Q_{fv}\) during rib cage, but not
diaphragm, breathing patterns. 2) More-negative inspiratory
ITP excursions were unable to significantly increase steady-
state \(Q_{fv}\) during rib cage breathing because of reductions in \(Q_{fv}\)
during the ensuing expiratory phase of the breath. 3) Addition
of an expiratory load reversed the within-breath modulation of
\(Q_{fv}\) during diaphragm breathing, such that the majority of
femoral venous return occurred during the initial portion of a
diaphragmatic inspiration. 4) Addition of an expiratory load to
diaphragm breathing significantly reduced steady-state \(Q_{fv}\)
during mild and moderate calf contraction.

**Respiratory Influences on Locomotor Limb Inflow and Outflow: A Model Based on Resistors and Capacitors in Series**

The model is based on the principles governing the current
flow through an electrical capacitor. Our approach relies on a
physiological analog to the constitutive relation equations for
flow through an electrical capacitor, which states that the
change in blood flow through any capacitance vessel bed will
be proportional to the rate of change of the driving pressure
across it and its capacitance. The general structure of our
model is depicted in Fig. 9.

To interpret our present findings in the context of the model
outlined in Fig. 9, we make the following two simplifying
assumptions: 1) right atrial pressure \(P_{ra}\) is always reduced
during inspiration (resulting from a more-negative right atrial
transmural pressure as a result of reductions in ITP), and 2)
splanchnic venous return is always reduced during inspiration
because of compression of the hepatic sinusoids resulting from
diaphragmatic contraction \((16). Because the nonloaded condi-
tions have been discussed in the context of this model else-
where \((15), we focus more on the findings from the exagger-
ated respiratory muscle pressure production.

**Within-Breath Modulation of \(Q_{fv}\) During Inspiratory
Loading: Regulation of \(Q_{fv}\) by Passive Venous Properties
and “Starling” Resistors**

**Rib cage breathing.** In this study, augmenting the inspiratory
ITP excursion elicited a greater inspiratory facilitation of \(Q_{fv}\)
during loaded than during nonloaded rib cage breathing, such
that mean \(Q_{fv}\) during inspiration was significantly greater than
mean \(Q_{fv}\) during expiration in inspiratory-loaded conditions.
Inasmuch as \(P_{ab}\) was relatively unchanged during inspiratory-
loaded rib cage breathing, this initial inspiratory facilitation is
the result of a lower \(P_{ab}\) secondary to the more-negative
inspiratory ITP excursion.

However, during the latter portion of a rib cage inspiration,
the magnitude of the inspiratory facilitation of \(Q_{fv}\) became
dissociated from the change in ITP, as \(Q_{fv}\) progressively fell in
the face of a more-negative ITP \((\text{Figs. 2 and 3). There are two}
possible explanations for this progressive decrement in antero-
grade \(Q_{fv}: 1) a decrease in the effective driving pressure for
venous return and/or 2) an increase in the resistance for venous
return.

First, a loss of peripheral venous recoil due to a central
translocation of blood volume from the upper thigh early

### Table 1. Group mean \(Q_{fv}\) responses to diaphragm and rib-cage breathing at rest and during calf exercise

<table>
<thead>
<tr>
<th></th>
<th>(Q_{fv}, \mu\text{L/min})</th>
<th>MAP, \text{mmHg}</th>
<th>(Q_{fv}/Q_{fb}, %)</th>
<th>CSAfV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\mu\text{L/min/m²})</td>
<td>(\mu\text{L/min/m²})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rib cage</td>
<td>0.89±0.15</td>
<td>84±3</td>
<td>69±6</td>
<td>1.23±0.10</td>
</tr>
<tr>
<td>Rib cage + IL</td>
<td>1.19±0.29</td>
<td>84±3</td>
<td>89±12</td>
<td>1.21±0.09</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>0.83±0.15</td>
<td>86±2</td>
<td>−9±12</td>
<td>1.31±0.08</td>
</tr>
<tr>
<td>Diaphragm + IL</td>
<td>0.95±0.21</td>
<td>84±2</td>
<td>−4±9</td>
<td>1.24±0.09</td>
</tr>
<tr>
<td>Mild calf contraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rib cage</td>
<td>1.29±0.17</td>
<td>84±3</td>
<td>59±5</td>
<td>1.21±0.08</td>
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<tr>
<td>Rib cage + IL</td>
<td>1.33±0.22</td>
<td>84±3</td>
<td>72±10</td>
<td>1.21±0.09</td>
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<tr>
<td>Diaphragm</td>
<td>1.20±0.15</td>
<td>92±3</td>
<td>12±8</td>
<td>1.42±0.10</td>
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<tr>
<td>Diaphragm + IL</td>
<td>1.37±0.16</td>
<td>89±3</td>
<td>14±5</td>
<td>1.44±0.08</td>
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<tr>
<td>Moderate calf contraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rib cage</td>
<td>1.74±0.29</td>
<td>86±4</td>
<td>64±8</td>
<td>1.31±0.14</td>
</tr>
<tr>
<td>Rib cage + IL</td>
<td>1.67±0.38</td>
<td>84±4</td>
<td>74±7</td>
<td>1.25±0.13</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>1.64±0.18</td>
<td>84±3</td>
<td>18±7</td>
<td>1.35±0.08</td>
</tr>
<tr>
<td>Diaphragm + IL</td>
<td>1.75±0.18</td>
<td>82±4</td>
<td>16±6</td>
<td>1.39±0.08</td>
</tr>
</tbody>
</table>

Values are means ± SE; \(n = 5); IL, inspiratory load; EE and EI, end expiration and end inspiration; \(Q_{fv}\), steady-state femoral venous blood flow over >50
breathing cycles; MAP, steady-state mean arterial blood pressure over >50 breathing cycles; \(Q_{fv}/Q_{fb}\) mean inspiratory \(Q_{fv}\) divided by total \(Q_{fb}\) over the course
of a breath; CSAfV, femoral venous cross-sectional area. *Significantly different from rest during the same breathing pattern \((P < 0.05). †Significantly different from EE during the same breathing pattern \((P < 0.05).}
during inspiration would reduce the effective upstream driving pressure for venous return from the locomotor limb (15, 22), a phenomenon reflected in our reductions in femoral venous cross-sectional area over the course of a rib cage inspiration (Table 1). However, this is not likely to be the sole contributor to the progressive decrements in Q_˙_{fv} during the latter portion of a rib cage inspiration, because end-inspiratory femoral venous cross-sectional area was not further reduced by augmentation of the inspiratory ITP excursion.

Thus we postulate that increases in resistance to outflow (R_IVC in Fig. 9) are most likely to contribute to the reductions in Q_˙_{fv} during the latter portions of a loaded rib cage inspiration. The partial collapse of the suprahepatic abdominal inferior vena cava (IVC) and/or intrathoracic IVC, which is consistently found when the magnitude of the inspiratory ITP excursion is augmented (7, 18), would limit the transmission of reductions in Pra to the infrahepatic IVC (i.e., because infrahepatic IVC pressure can be considered a more immediate downstream pressure for locomotor limb venous return; Fig. 9) and ultimately limit the increase in effective driving pressure for locomotor limb venous return under these breathing conditions. Increases in abdominal IVC resistance due solely to reductions in ITP (and, subsequently, Pra and intravascular pressure) also are consistent with our observation that the effectiveness of the skeletal muscle pump is unaffected under these conditions, inasmuch as, by definition, flow through a patent Starling resistor will be proportional to the change in upstream driving pressure (P_IVC in Fig. 9).

Fig. 6. Effects of combined inspiratory and expiratory loading (EL) during diaphragmatic breathing on Q_˙_{fv} over the course of a breath at rest (n = 4, ≥60 breaths per subject per condition). Addition of combined inspiratory and expiratory loading to diaphragmatic breathing reversed within-breath changes in Q_˙_{fv}, such that the majority of anterograde blood flow occurred during the inspiratory phase of the breath (*P < 0.05, mean inspiratory Q_˙_{fv} vs. mean expiratory Q_˙_{fv} during combined inspiratory and expiratory loaded diaphragm breathing). ○, Nonloaded diaphragm breathing; ●, combined inspiratory and expiratory loaded diaphragm breathing. *P < 0.05, nonloaded diaphragm breathing vs. combined inspiratory and expiratory loaded rib cage breathing.

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Diaphragm breathing. The finding that a more-negative inspiratory ITP excursion during diaphragm breathing did not further alter the magnitude of the within-breath changes in $Q_v$ at rest or during calf contraction (Figs. 4 and 5) provides strong evidence that modest increases in Pab exceed the critical closing pressure of the abdominal IVC and that the abdominal IVC is fully collapsed during a diaphragmatic inspiration (15, 27, 29). Furthermore, our observation that the increases in mean inspiratory $Q_v$ elicited by moderate calf contraction were not affected by the magnitude of the inspiratory ITP excursion during diaphragmatic breathing suggests that a more-negative inspiratory ITP excursion (in the presence of an identical Pab excursion) does not affect the critical femoral venous driving pressure required to open the abdominal IVC (Fig. 9).

Our finding that net $Q_v$ in the steady state was not altered by the magnitude of the inspiratory ITP excursion is inconsistent with the findings of Kwon et al. (11), who concluded that “deep” diaphragmatic breathing increases steady-state venous return from the locomotor limb. However, these investigators failed to control for changes in venous vessel cross-sectional area and, thus, relied solely on velocimetric estimates of blood flow (11). Our data clearly show that femoral venous cross-sectional area changes significantly over the course of a breath (often changing >20%) and must be taken into account to accurately measure venous blood flow. Hence, we would not agree with the recommendation of Kwon et al. that a combination of deep breathing and calf muscle contraction would be the most effective method for preventing venous stasis in patients subjected to prolonged bed rest (11), inasmuch as our
Diaphragmatic Breathing Reduces Steady-State Locomotor Venous Return During Calf Contraction

With the addition of an expiratory load to inspiratory-loaded diaphragmatic breathing, we observed a reversal of the within-breath modulation of Qfv from the resting limb, such that mean Qfv during inspiration was now significantly higher than during expiration. Even our highest level of calf contraction was not able to elicit a significant increase in mean expiratory Qfv over resting levels. Thus it would appear that, under conditions of active expiration, the impedance to outflow from the locomotor limb far exceeds the recoil pressure generated by distension of the calf and thigh veins, even when the veins are considerably distended by the presence of a hydrostatic column.

During the majority of the expiratory phase of an expiratory loaded breath, Pga and Pes change in parallel (Figs. 6 and 7). Thus we cannot state with certainty whether the near abolition of anterograde Qfv during expiration is the result of an elevated resistance to locomotor limb outflow in the abdomen (i.e., compression of the abdominal IVC by an elevated Pga) or an elevated backpressure to venous return in the thorax (i.e., an increase Pra due to an elevated ITP). However, the fact that anterograde Qfv remains virtually absent (and even slightly retrograde) during the transition from inspiration to expiration, where Pga is already elevated and Pes is still rising, provides evidence that the elevated Pab (and thus, IVC resistance in Fig. 9) is likely to be the dominant factor impeding Qfv.

Augmented Expiratory Pressure Production During Diaphragmatic Breathing Reduces Steady-State Locomotor Limb Venous Return During Calf Contraction

In contrast to our observation that steady-state Qfv was unaffected by the magnitude of the inspiratory ITP excursions during diaphragmatic breathing, the addition of combined inspiratory and expiratory loading during diaphragmatic breathing resulted in significant reductions in net, steady-state Qfv and vascular conductance at both levels of calf contraction (Fig. 8). In essence, the decreased Qfv during an inspiratory-loaded diaphragmatic inspiration remained low during the ensuing active, loaded expiratory effort (Figs. 6 and 7). Although some may ascribe the reductions in steady-state blood flow and vascular conductance with expiratory loading to reflex vasoconstriction (23, 24), our observation that femoral venous return was abolished over the last three-quarters of a breath strongly suggests a direct mechanical component to this observation. More specifically, because our subjects’ limb veins were relatively distended because of their semirecumbent body position, the blocking of venous outflow by addition of an expiratory load to diaphragmatic breathing would ultimately narrow the effective driving pressure across the capillary bed by increasing effective downstream pressure (i.e., postcapillary/venular pressure) in the steady state. This effect has frequently been referred to as a change in “virtual conductance”1 (12), because it is not possible to measure the effective downstream pressure for the arterial circulation at rest and during calf contraction.

Implications for Femoral Venous Return During Whole Body Exercise

Our finding that steady-state Qfv is not increased with augmented inspiratory muscle pressure excursions differs from several previous investigations that have suggested that augmented inspiratory ITP excursions could independently contribute to increases in steady-state venous return in the resting human (2, 5). Our data show that any increases in venous

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**Table 2. Group mean Qfv responses to combined inspiratory and expiratory loading during diaphragmatic breathing at rest and during calf exercise**

<table>
<thead>
<tr>
<th>Group</th>
<th>Qfv, l/min</th>
<th>MAP, mmHg</th>
<th>Qfv, %IL</th>
<th>Qfv, ΔQfv, %</th>
<th>CA, cmHg</th>
<th>LVC, l/mmHg</th>
<th>ΔLVC, l/mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>0.83±0.22</td>
<td>84±3</td>
<td>-11±8ad</td>
<td>1.49±0.18</td>
<td>1.66±0.34</td>
<td>0.17±0.02</td>
<td>10±3</td>
</tr>
<tr>
<td>Diaphragm + IL</td>
<td>0.56±0.09</td>
<td>94±3</td>
<td>89±34</td>
<td>1.94±0.17</td>
<td>1.57±0.42</td>
<td>-0.37±0.08</td>
<td>6±1</td>
</tr>
<tr>
<td>Mild calf contraction</td>
<td>1.42±0.19</td>
<td>91±3</td>
<td>13±6ad</td>
<td>1.52±0.19</td>
<td>1.69±0.33</td>
<td>0.17±0.03</td>
<td>13±2</td>
</tr>
<tr>
<td>Diaphragm + IL</td>
<td>0.96±0.24</td>
<td>98±4</td>
<td>65±9</td>
<td>1.96±0.14</td>
<td>1.65±0.43</td>
<td>-0.31±0.09</td>
<td>10±2</td>
</tr>
<tr>
<td>Moderate calf contraction</td>
<td>1.75±0.23</td>
<td>83±3</td>
<td>11±2ad</td>
<td>1.52±0.13</td>
<td>1.77±0.31</td>
<td>0.25±0.05</td>
<td>18±2</td>
</tr>
<tr>
<td>Diaphragm + IL</td>
<td>0.16±0.01</td>
<td>87±3</td>
<td>60±3</td>
<td>2.09±0.15</td>
<td>1.75±0.44</td>
<td>-0.34±0.09</td>
<td>13±2</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 4. EL, expiratory load; LVC, steady-state venous return conductance over >50 breathing cycles; see Table 1 footnote for other abbreviations. aSignificantly different from resting conditions during the same breathing pattern (P < 0.05). bSignificantly different from mild calf contraction during the same breathing pattern (P < 0.05). cSignificantly different from flow during inspiration and expiration (P < 0.01). dSignificantly different from EE during the same breathing pattern (P < 0.05).

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1 The concept of a virtual vascular conductance was first proposed by Laughlin (12) in an attempt to explain the observation that the maximum pharmacologically induced vascular conductance is far less than that observed during high-intensity exercise. In particular, they postulated that, during the relaxation phase of dynamic exercise, the skeletal muscle pump significantly lowers postcapillary pressures by pulling outward on the venous vasculature, which would in turn widen the effective driving pressure for arterial inflow. Such a phenomenon would lead one to the incorrect conclusion that arteriolar diameter had increased and falsely elevated maximum vascular conductance during exercise.
return (and, presumably, in turn, cardiac output) with augmented inspiratory ITP excursions are not originating from the locomotor limb. These findings are consistent with our working model, suggesting that augmented inspiratory ITP excursions cannot increase steady-state blood flow without additional changes in the physical properties of the vasculature, such as concomitant reductions in venous compliance and/or regional vascular time constants (15).

In contrast, our findings are consistent with a growing body of data supporting the notion that excessive expiratory muscle pressure production limits whole body venous return and cardiac output during stationary cycling (14, 26). The possibility that these reductions in cardiac output resulting from augmented expiratory muscle pressure production may be the result of an impeded locomotor limb blood flow is supported by the observation that the limb blood flow response to incremental exercise is often significantly blunted in patients with chronic obstructive pulmonary disease (25). In such patients, expiratory flow limitation and dynamic hyperinflation result in more-positive Pab during inspiration and expiration (1), breathing mechanics that are very similar to those produced by combined inspiratory and expiratory loaded resting conditions. *Significantly different from inspiratory resistance at the same level of calf contraction ($P < 0.05$).

†Significantly different from nonloaded breathing at the same level of calf contraction ($P < 0.05$). †Significantly different from rest under the same breathing conditions ($P < 0.05$).

![Graph](Fig. 8. Effects of nonloaded, inspiratory loaded, and combined inspiratory and expiratory loaded diaphragm breathing on steady-state $Q_{\text{fv}}$ and locomotor limb vascular conductance at rest and during mild and moderate calf contraction. Addition of combined inspiratory and expiratory loading during diaphragmatic breathing significantly reduced $Q_{\text{fv}}$ and locomotor limb vascular conductance compared with inspiratory loading alone during both levels of calf contraction. During inspiratory and expiratory loading, only moderate levels of calf contraction significantly increased limb blood flow over the combined inspiratory and expiratory loaded resting conditions. *Significantly different from inspiratory resistance at the same level of calf contraction ($P < 0.05$).

†Significantly different from nonloaded breathing at the same level of calf contraction ($P < 0.05$). †Significantly different from rest under the same breathing conditions ($P < 0.05$).
Limitations in Application of Our Findings to Whole Body Exercise

Perhaps the greatest limitation in applying the present findings to whole body exercise is that our subjects performed only calf contraction exercise, whereas whole body exercise typically involves rhythmic contraction of the muscles of the upper thigh. Thus one may expect to see a smaller within-breath variation in $Q_{fv}$ during all the breathing conditions described here, inasmuch as quadriceps contraction would result in sig-
sificant decreases in thigh venous compliance (Fig. 9) and increases in femoral venous driving pressure (Fig. 9). Additionally, locomotor and respiratory muscle contraction is frequently asynchronous during whole body exercise; however, the effects of muscle contraction at different points throughout the breathing cycle can be predicted by applying a time component to the equations in Fig. 9.

Despite these limitations, data from Wexler et al. (28) demonstrated respiratory modulation of IVC blood velocity during supine cycling with spontaneous breathing in normal, healthy humans. Thus the within-breath and steady-state effects of augmented ITP and Pab excursions during inspiration and expiration on Qv, in the present investigation may no longer be allowed because of the case during maximal exercise, where peak inspiratory and expiratory pressures are larger than those produced in the present investigation (ITP excursions of $\pm 30 \text{ cmH}_2\text{O}$ and Pga excursions from $-10 \text{ cmH}_2\text{O}$ during inspiration to $+30 \text{ cmH}_2\text{O}$ during expiration), filling time for the skeletal muscle pump is greatly reduced, and increases in arterial inflow (and thus venous filling rate) may no longer be allowed because of active sympathetic vasoconstriction in the locomotor limbs.

REFERENCES

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