Heart failure alters the strength and mechanisms of arterial baroreflex pressor responses during dynamic exercise

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Heart failure alters the strength and mechanisms of arterial baroreflex pressor responses during dynamic exercise. Am J Physiol Heart Circ Physiol 287: H1682–H1688, 2004. First published June 17, 2004; 10.1152/ajpheart.00358.2004.—Arterial baroreflex function is well preserved during dynamic exercise in normal subjects. In subjects with heart failure (HF), arterial baroreflex ability to regulate blood pressure is impaired at rest. However, whether exercise modifies the strength and mechanisms of baroreflex responses in HF is unknown. Therefore, we investigated the relative roles of cardiac output and peripheral vasoconstriction in eliciting the pressor response to bilateral carotid occlusion (BCO) in conscious, chronically instrumented dogs at rest and during treadmill exercise ranging from mild to heavy workloads. Experiments were performed in the same animals before and after rapid ventricular pacing-induced HF. At rest, the pressor response to BCO was significantly attenuated in HF (33.3 ± 1.2 vs. 18.7 ± 2.7 mmHg), and this difference persisted during exercise in part due to lower cardiac output responses in HF. However, both before and after the induction of HF, the contribution of vasoconstriction in active skeletal muscle toward the pressor response became progressively greater as workload increased. We conclude that, although there is an impaired ability of the baroreflex to regulate arterial pressure at rest and during exercise in HF, vasoconstriction in active skeletal muscle becomes progressively more important in mediating the baroreflex pressor response as workload increases with a pattern similar to that observed in normal subjects.

**HVC** during carotid sinus hypotension increased with increasing workloads. Furthermore, Collins et al. (1) quantified that as the workload increased, vasoconstriction within skeletal muscle contributed a progressively greater fraction of the pressor response to BCO. Together, the findings from these studies suggest that the relative role of vasoconstriction within skeletal muscle to the carotid baroreflex-mediated change in arterial pressure progressively increases from rest throughout mild to heavy exercise (1, 6, 12).

Many investigators have documented a depression in arterial baroreflex function at rest in subjects with heart failure (HF) (17, 24, 25, 26). Whang et al. (24) found that during carotid sinus hypotension, mean arterial pressure (MAP) did not increase to the same extent in the HF group compared with the normal dogs due to the depressed baroreceptor sensitivity. Wilson et al. (26) and White (25) reported that the arterial baroreflex control of both HR and arterial blood pressure were impaired in heart failure. Olivier and Stephenson (17) also demonstrated that arterial baroreflex responses to carotid hypotension were significantly depressed in chronically instrumented dogs with HF at rest. However, no studies have investigated the mechanisms contributing to baroreflex-mediated pressor responses during dynamic exercise in subjects with HF.

Therefore, the purpose of this study was to determine the relative roles of CO and peripheral vasoconstriction in eliciting the pressor response to BCO in conscious dogs with pacing-induced HF. We tested the hypothesis that at rest and during dynamic exercise, the magnitude of the pressor response mediated by the arterial baroreflex will be smaller after the induction of HF compared with the control. In addition, we hypothesized that the mechanisms eliciting the pressor response will rely more on the component of peripheral vasoconstriction at rest and during dynamic exercise in HF compared with the control. Furthermore, CO will make a smaller contribution to the carotid baroreflex-mediated pressor re-
spontaneous at rest and during dynamic exercise in HF, because our laboratory has previously identified depressed reflex control of CO during mild to moderate exercise in HF (4).

**MATERIALS AND METHODS**

All experiments were performed on six conscious dogs (20–25 kg) of either gender selected for their willingness to run on a motor-driven treadmill. Each dog was studied in the normal state and after the induction of HF. After several control experiments at rest and across workloads, the studies were repeated at rest and identical exercise workloads in HF. The protocols employed in the present study were reviewed and approved by the Wayne State University Animal Investigation Committee.

**Surgical preparation.** All animals were surgically instrumented in the same manner, allowing the same animal to be used for multiple studies. The surgical procedures were performed in a series of three sterile surgical sessions with at least 1 wk between surgeries and between the last surgery and the first experiment. Before all instrumentation, all animals were accustomed to human handling and trained to run freely on a treadmill. For all surgical procedures, the animals were anesthetized with intravenous pentothal sodium (Duraqetic, Jansen Pharmaceuticals), which delivered at a dose of 125–150 μg/kg for 3 days for analgesia. Immediately before and after each surgery, Cefazolin (500 mg iv) was given and then Cephalixin (30 mg/kg by mouth, 2 times/day) was given to avoid postoperative infection. During recovery from surgery, buprenorphine (0.015 mg/kg iv) and acepromazine (0.1 mg/kg im) were administered for pain control and sedation whenever deemed necessary.

In the first surgical session, a left thoracotomy was performed at the fourth intercostal space. The pericardium was opened, and a blood flow transducer (20 mm, Transonic Systems) was placed around the ascending aorta to monitor CO. For studies unrelated to the present investigation, a second blood flow transducer (3 mm) was placed around the left circumflex coronary artery, and two sonomicrometry crystals were implanted in the myocardium of the left ventricle. Three stainless steel ventricular pacing electrodes were sutured to the apex of the left ventricle for subsequent ventricular pacing. The pericardium was reaproximated loosely over the heart, and the chest was closed in layers.

In the second surgical session, through a midventral abdominal approach, blood flow probes (Transonic Systems) were placed on the terminal aorta (10 mm probe) and left renal artery (3 mm) to measure hindlimb blood flow (HLBF) and renal blood flow (RBF), respectively. A pneumatic vascular occluder (In Vivo Metrics) was placed on the terminal aorta just distal to the flow probe for separate studies. All side branches between the iliac arteries and the HLBF probe were ligated and severed. A catheter was placed in a side branch of the aorta proximal to the HLBF probe and occluder to measure systemic arterial pressure.

In the final surgical session, a catheter was introduced into the jugular vein and advanced to the arterial-caval junction to measure central venous pressure (CVP). Additionally, a pneumatic vascular occluder was placed around each common carotid artery to perform BCO. All cables, wires, occluder tubing, and catheters were tunneled subcutaneously and exteriorized between the scapula.

**HF induction.** HF was induced by rapid left ventricular pacing at 225–250 beats/min for ~30 days using a fixed rate pacemaker built in our laboratory. Threshold values for pacing voltage and pulse width that were necessary for ventricular capture were determined by means of a pacing system analyzer (model 5311b, Medtronic). The pacemakers were adjusted to 1.5 times the threshold values. The presence of HF was determined from hemodynamic values, such as the increase in CVP, tachycardia, and decrease in MAP and CO.

**Experimental design.** All experiments were performed after the animals had fully recovered from the last surgery and were active, afbrile, and of good appetite. The arterial baroreflex was activated during rest, mild (3.2 km/h, 0% grade), moderate (6.4 km/h, 10% grade), and heavy (8 km/h, 15% grade) exercise via rapid 2-min occlusions of both common carotid arteries. Each dog finished several control experiments and at least one experiment after left ventricular pacing-induced HF across the workloads.

**Data collection.** The blood flow transducers were connected to the flowmeters (Transonic System). The MAP and CVP catheters were connected to pressure transducers (TVP4, Abbott Laboratories). All flow and pressure transducers were coupled to both a Gould recording system (model RS3800) and a Sonometrics recording system. HR was monitored via a cardiotachometer triggered by the CO signal. A laboratory computer sampled all data at 1,000 Hz, and average values for each cardiac cycle were saved on hard disk for subsequent data analysis.

**Experimental procedures.** Each animal was transported to the laboratory, allowed to roam freely for 15–30 min, and then taken to the treadmill. All flow probes and catheters were connected. Baseline hemodynamic variables were collected at standing rest. Subsequently, both common carotid arteries were rapidly occluded by inflation of the hydraulic occluders for 2 min and rapidly deflated. For exercise experiments, the treadmill was accelerated to the selected speed and grade. After all data reached steady state (~5 min), the BCO was performed as at rest. The order of each experiment was selected randomly.

**Data analysis.** One-minute averages of all variables were taken during steady state immediately before BCO and the last 30-s averages of the hemodynamic responses during BCO. All data of each animal were averaged to produce mean responses at rest and at each exercise intensity. These mean values were again averaged across animals to yield mean responses for the experimental group. Each animal served as its own control and contributed only once to the mean response for all animals.

The average values of MAP, HR, CO, CVP, HLBF, HVC (i.e., HVC = HLBF/(MAP – CVP)), RBF, and renal vascular conductance [RVC = RBF/(MAP – CVP)] were collected before and in response to BCO. RBV and RVC values were doubled to account for the hemodynamic responses in both kidneys. Total vascular conductance (TVC) was calculated as CO/(MAP − CVP). The percent contribution of regional vasconstriction and CO in mediating the pressor response to the baroreflex was calculated as described by Collins and coworkers (1). Briefly, the predicted change in MAP during BCO was calculated if only the individual changes in CO, HVC, or RVC occurred and all other variables remained at control levels, indicating the cardiac or regional peripheral vasconstriction components of the pressor response. The following equations were used:

Predicted change in MAP_{CO} = [(CO_{obs}/TVC_{avg control}) + CVP_{avg control}] − MAP_{avg control} \tag{1}

where MAP_{CO} is the MAP response to BCO due to CO alone, CO_{obs} is the CO observed during BCO, and TVC_{avg control} and MAP_{avg control} are 1-min averaged baseline control values before BCO. The predicted change of MAP_{HVC} was as follows:

Predicted change in MAP_{HVC} = [(CO_{avg control}/HVC_{obs control}) + RVC_{avg control} + EVC_{avg control}] + CVP_{avg control} − MAP_{avg control} \tag{2}

where EVC = TVC − (HVC + RVC) and indicates vascular conductance elsewhere in the body besides the hindlimbs and kidneys. The predicted change of MAP_{RVC} was as follows:

Predicted change in MAP_{RVC} = [(CO_{avg control}/HVC_{avg control}) + RVC_{obs control} + EVC_{avg control}] + CVP_{avg control} − MAP_{avg control} \tag{3}
BAROREFLEX FUNCTION DURING EXERCISE IN SUBJECTS WITH HEART FAILURE

Table 1. The number of animals observed in each setting for each major cardiovascular parameter

<table>
<thead>
<tr>
<th></th>
<th>MAP</th>
<th>CO</th>
<th>HR</th>
<th>SV</th>
<th>CVP</th>
<th>RBF</th>
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<tbody>
<tr>
<td>Rest</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td>6</td>
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<td>6</td>
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<td>3.2 km/h</td>
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<td>HF</td>
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<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>6.4 km/h, 10%</td>
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<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
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<td>5</td>
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<td>HF</td>
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<td>6</td>
<td>6</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>8.0 km/h, 15%</td>
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<tr>
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<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>2</td>
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</tbody>
</table>

MAP, mean arterial pressure; CO, cardiac output; HR, heart rate; SV, stroke volume; CVP, central venous pressure; RBF, renal blood flow; HF, heart failure.

Table 2. Average baseline hemodynamic data collected at standing rest for the control and HF states

<table>
<thead>
<tr>
<th>Condition</th>
<th>MAP, mmHg</th>
<th>CO, l/min</th>
<th>HR, beats/min</th>
<th>SV, ml</th>
<th>CVP, mmHg</th>
<th>HVC, ml/min/mmHg</th>
<th>TVC, ml/min/mmHg</th>
<th>RBC, ml/min</th>
<th>RVC, ml/min/mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>98.5±3.7</td>
<td>5.08±0.57</td>
<td>102.3±5.9</td>
<td>4.0±0.6</td>
<td>0.90±0.08</td>
<td>9.48±0.78</td>
<td>53.55±5.16</td>
<td>199.0±22.7</td>
<td>2.06±0.22</td>
</tr>
<tr>
<td>HF</td>
<td>84.1±3.4*</td>
<td>3.95±0.32*</td>
<td>127.1±6.1*</td>
<td>9.5±0.5*</td>
<td>0.68±0.07*</td>
<td>9.02±0.53</td>
<td>53.85±5.9</td>
<td>127.5±25.8*</td>
<td>1.64±0.3*</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE. HBF, hindlimb blood flow; HVC, hindlimb vascular conductance; TVC, total vascular conductance; RVC, renal vascular conductance. *Significantly different from control, P < 0.05.

Statistical analysis. Data are expressed as means ± SE. With the use of the averaged responses for each animal, further statistical analyses were performed on the data with Systat software (Systat 8.0). An α-level of P < 0.05 was set to determine statistical significance. For hemodynamic data obtained at rest and during exercise before and during BCO, two-way repeated-measures ANOVA was used for comparison with respect to cardiac condition and workload. If significant interaction was found, a test for simple effects post hoc analysis was performed to determine significant group mean differences. A linear regression analysis was used to establish the relationship between the percent contribution of HVC, RVC, and CO to the pressor response mediated by BCO as workload and baseline HLBF increased (14, 15). Because of technical limitations, not all parameters could be measured in all animals in all conditions. Table 1 shows the number of animals we observed in each setting for each major cardiovascular parameter. In addition, after the induction of HF, two animals would not perform the highest workload for a sufficient amount of time to obtain steady-state and BCO data (7 min total).

RESULTS

Baseline hemodynamics in control and HF states. Table 2 presents the average baseline hemodynamic data collected at standing rest for the control and HF states. HR and CVP were significantly higher in the HF state, whereas CO, MAP, and RBF, signifi
cantly different from zero in both settings (P = 0 < 0.001, P = 0.021, respectively). These findings (Fig. 3 and Table 3) indicate that decreases in HVC gradually become more important in mediating the pressor response during BCO as exercise intensity increases. Compared with the control, the carotid baroreflex-induced pressor response relies there was significant reduction in CO in HF compared with control values when exercise intensity increased from standing rest to the heavy exercise, whereas significant increases in HR (only rest and 3.2 km/h) and CVP occurred. Furthermore, although no interaction was observed, significant workload and cardiac condition effects in MAP and stroke volume (SV) occurred. As workloads increased in control runs, MAP and SV significantly increased in both conditions, but these variables were significantly depressed in HF compared with the control. These results indicate that in HF, although MAP and CO were progressively increased as workload increased, they were depressed significantly compared with the control.

Hemodynamic responses to baroreflex activation at rest and during dynamic exercise. Figure 2 shows the absolute changes in MAP, CO, HR, and HVC in response to BCO at rest and during exercise in both control and HF conditions. A workload effect and a cardiac condition effect were observed for the changes in CO and HVC during BCO. Only a workload effect was seen for the reflex increases in HR. A cardiac condition effect was observed for the changes in SV and MAP, although the workload effect for MAP approached statistical significance (P = 0.08). In the control condition, at rest and during exercise, MAP rose significantly during BCO; however, the increase in MAP with baroreflex activation was reduced in HF. There was a significant difference in the CO response between the control and HF in response to arterial baroreflex activation. During BCO in the HF state, CO significantly decreased compared with a small increase or no change in normal dogs. In addition, with carotid sinus hypotension, a significant workload effect and cardiac condition effect on the decrease in HVC were observed. These results indicate that in both conditions a greater vasoconstrictor response in the hindlimb vascular bed occurred from rest throughout the heavy exercise. However, BCO resulted in greater reduction in HVC in HF.

Percent contributions of the various components to BCO-mediated pressor response. Figure 3 shows the relationship between the percent contributions of HVC, RVC, and CO to the pressor response during BCO and baseline HLBF in both control and HF states. Average values in each setting are shown in Table 3. Baseline HLBF was used because it was reported that HLBF values are closely related to exercise intensity (2, 10). Linear regression analysis showed that there was a positive correlation between the percent contribution of HVC to the pressor response and baseline HLBF in both control and HF states (r = 0.75, r = 0.50, respectively), and the slope was significantly different from zero in both settings (P = 0 < 0.001, P = 0.021, respectively). These findings (Fig. 3 and Table 3) indicate that decreases in HVC gradually become more important in mediating the pressor response during BCO as exercise intensity increases. Compared with the control, the carotid baroreflex-induced pressor response relies...
more on the reduction on HVC across increasing workloads in 
HF. In contrast, a negative correlation was observed between 
the percent contribution of RVC to the pressor response and 
baseline HLBF in both conditions ($r = 0.54, r = 0.51$,
respectively), and the slope was significantly different from 
zero in both settings ($P = 0.02, P = 0.039$, respectively).
These findings imply that reductions in RVC become less 
important in mediating the pressor response during BCO as 
exercise intensity increases. There was also negative correla-
tion between the percent contribution of CO and baseline 
HLBF ($r = 0.57$) in the control state, and the slope was
significantly different from zero ($P = 0.007$). The percent contribution of CO to the pressor response did not change with exercise intensity in HF. At rest and across all workloads, CO tended to decrease with BCO.

**DISCUSSION**

To our knowledge, this is the first study to investigate the relative contributions of CO and peripheral vasoconstriction in mediating the pressor response to BCO both at rest and during dynamic exercise in subjects before and after the induction of HF. Our new findings are that in conscious dogs with moderate HF, despite the inability to increase CO, the arterial baroreflex activation via BCO still produced a significant pressor response at rest and throughout mild to heavy exercise; however, these pressor responses were depressed compared with those observed in control experiments. Thus HF decreases the ability of the arterial baroreflex to increase systemic arterial blood pressure at rest and during exercise.

As in control experiments, in HF, despite little difference in the pressor response to BCO across workloads, vasoconstriction in the hindlimbs contributed to a progressively greater extent to the increase in pressure as exercise intensity in-

**Table 3. Percent contribution of HVC, RVC, and CO to the pressor response during BCO at rest and during exercise in both control and HF states**

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>3.2 km/h</th>
<th>6.4 km/h</th>
<th>8 km/h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>HF</td>
<td>Control</td>
<td>HF</td>
</tr>
<tr>
<td>HVC</td>
<td>3.7±4.4</td>
<td>18.1±7.2</td>
<td>14.8±4.9</td>
<td>21.9±4.8</td>
</tr>
<tr>
<td>RVC</td>
<td>3.1±0.8</td>
<td>2.4±0.8</td>
<td>5.0±1.9</td>
<td>2.4±0.6</td>
</tr>
<tr>
<td>CO</td>
<td>30.6±12.1</td>
<td>−15.8±17.9</td>
<td>11.1±12.1</td>
<td>−29±18.7</td>
</tr>
</tbody>
</table>

Values are means ± SE (in %). BCO, bilateral carotid occlusion.
increased. Indeed, the baroreflex induced reductions in HVC were significantly greater in HF, although this greater reduction in HVC caused a smaller increase in MAP due to the concomitant decrease in CO. Thus the primary mechanism mediating the pressor response during carotid sinus hypotension at rest and across workloads was peripheral vasoconstriction. The present study extends our previous observations (1) by quantifying the relative role of CO and peripheral vasoconstriction in mediating the pressor response to the arterial baroreflex activation in subjects with HF.

Arterial baroreflex-mediated pressor responses with HF. Previous studies found that the depressed pressor response to arterial baroreflex activation in chronic HF may be due to a decrease in baroreceptor discharge sensitivity, an altered central processing of baroreceptor activity, and/or poor end-organ responses (24, 25, 26). Thus our data observed at rest are in agreement with previous reports of attenuation in the pressor response mediated by the arterial baroreflex activation in HF (17, 25). The attenuated pressor response to BCO stems mainly from the decrease in CO, which is likely due to an increase in ventricular afterload sensitivity. Similar effects of HF were observed by Olivier and Stephenson (17) in conscious dogs at rest. They demonstrated that arterial baroreflex regulation of blood pressure was impaired in subjects with HF at rest compared with control and concluded that abnormal reflex regulation of blood pressure was due to a depression in cardiac responses, not the peripheral vasoconstriction component. The present study extends this previous observation by determining the pressor response mediated by the arterial baroreflex activation at rest and during exercise.

CO versus systemic vascular conductance. Similar to what was observed in our laboratory previously (1), the modulation in peripheral vasoconstriction plays the major role in mediating BCO-induced changes in arterial blood pressure at rest and during exercise in the HF state. During BCO in control experiments, we demonstrated that as exercise intensity increased, the significant contribution of CO observed at rest to the pressor response gradually decreased with the end result being no contribution of CO during heavy exercise, whereas the contribution of HVC becomes greater. Thus this study is in agreement with previous studies (1, 6, 12) demonstrating that the sympathetic control of vascular conductance plays an important role in regulation of blood pressure mediated by the arterial baroreflex activation at rest and during exercise, with little CO contribution. In contrast, CO response to arterial baroreflex activation was significantly reduced in HF at rest and across workloads. In this setting, CO does not contribute to the pressor response during carotid sinus hypotension but rather the pressor response due to peripheral vasoconstriction is partially offset by a fall in CO. This indicates differential baroreflex control of the heart versus peripheral vasculature as workload increases. Previous studies have shown that carotid sinus hypotension causes little change in HR and CO at rest and during exercise in normal subjects (1, 12, 22). The modest tachycardia observed at rest was virtually abolished at the highest workload (change of 2–5 beats/min from baseline values of >210 beats/min). Furthermore, other investigators reported that pacing-induced HF produced ventricular impairment (8). Taken together, these findings may explain that in HF, the CO response initiated by the arterial baroreflex activation would be depressed due to a fall in SV and little change in HR.

After the induction of HF, vasoconstriction in active skeletal muscle becomes progressively more important in mediating the baroreflex pressor response as workload increases with a pattern similar to that observed in normal subjects. Previously, O’Leary (13) reported that whether a given change in regional vascular conductance effectively contributes to blood pressure regulation depends on the magnitude of the change relative to the level of TVC. In other words, if a given regional vascular conductance constitutes a large fraction of TVC, then vasoconstriction within this regional vascular bed has a greater potential to increase systemic blood pressure. Because in the present investigation we simultaneously measured CO and regional blood flows, we were able to determine the relative contribution of HVC and RVC to the pressor response mediated by arterial baroreflex activation. We found that in HF, reductions in HVC during carotid sinus hypotension gradually provided a larger contribution to the pressor response with increasing workloads, indicating that active skeletal muscle is an increasingly important site for baroreflex-induced vasoconstriction. Thus our data observed at rest are in agreement with previous reports of attenuation in the pressor response mediated by arterial baroreflex activation in HF (17, 25). The attenuated pressor response to BCO stems mainly from the decrease in CO, which is likely due to an increase in ventricular afterload sensitivity. Similar effects of HF were observed by Olivier and Stephenson (17) in conscious dogs at rest. They demonstrated that arterial baroreflex regulation of blood pressure was impaired in subjects with HF at rest compared with control and concluded that abnormal reflex regulation of blood pressure was due to a depression in cardiac responses, not the peripheral vasoconstriction component. The present study extends this previous observation by determining the pressor response mediated by the arterial baroreflex activation at rest and during exercise.

The term “functional sympatholysis” (20) is that the accumulation of metabolites produced by the active skeletal muscle during exercise inhibits the vasoconstriction mediated by an increase in the sympathetic tone. There have been many arguments about whether or not an augmented sympathetic outflow overrides the metabolic vasodilation in active skeletal muscle during exercise. Several investigators have suggested that sympathetic vasoconstriction during exercise opposes local metabolic vasodilation in the active skeletal muscle (15, 16, 23). In contrast, other studies have reported that contraction-induced metabolic vasodilation reduces vasoconstriction response to sympathetic stimulation (5, 7). This controversy regarding vasomotor response may be due to differences in methods used to analyze muscle perfusion. O’Leary et al. (13) indicated that with different baseline state in blood flow, resistance, and conductance, opposite conclusions can be drawn depending on which index (resistance vs. conductance) is used in quantifying the magnitude of the vasoconstrictor response. For example, during a high flow state, the magnitude of vasoconstrictor response is small when the response is analyzed in terms of resistance and is much greater in terms of conductance. Our data showed that in HF experiments, the contribution of reductions in HVC to the pressor response during carotid sinus hypotension increased as exercise intensity increased to a greater extent compared with the control. These conclusions are independent of whether resistance or conductance is used in the equations (although the equations are...
simpler using conductance). Limitations inherent in this study include that we do not know whether BCO elicits a greater increase in sympathetic activity to active muscle as workload increases or whether this changes with HF. Furthermore, we compared the responses at the same absolute exercise intensities before and after the induction of HF, which likely reflects different relative workloads in the two settings (e.g., percent maximal exercise intensity).

In summary, our results indicate that in subjects with HF, the pressor response during BCO is significantly depressed at rest and during exercise and modulations of CO do not contribute to the carotid baroreflex-mediated increases in MAP. In this setting, the contribution of reduction in HVC had a progressively larger impact on MAP during BCO from rest through heavy exercise but that of RVC decreased. Although there is an abnormality in baroreflex function to regulate MAP at rest and during exercise in HF, our study strongly suggests that vasocostriction in active skeletal muscle plays an important role in the pressor response to carotid baroreflex activation as workload increases with a pattern similar to that observed in normal subjects.

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