Overshoot in Mixed Venous Oxygen Saturation During Recovery From Supine Bicycle Exercise in Patients With Recent Myocardial Infarction*

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During recovery from dynamic exercise, systemic oxygen extraction rapidly decreases below the resting level in patients with heart failure, which leads to a subsequent increase in mixed venous oxygen saturation (SvO2) above its resting value (postexercise SvO2 overshoot). To evaluate the pathophysiological basis of this phenomenon, postexercise SvO2 overshoot was evaluated in relation to hemodynamic, metabolic, and neurohumoral responses during recovery from maximal supine bicycle exercise in 23 patients with recent myocardial infarction. Postexercise SvO2 overshoot closely correlated with increased systemic vascular resistance (r = 0.79, p < 0.001) and reduced cardiac output (r = -0.74, p < 0.001), suggesting that SvO2 overshoot is primarily due to increased peripheral arteriovenous shunting caused by an enhanced peripheral vasoconstriction in the setting of reduced cardiac output. Postexercise SvO2 overshoot and systemic vascular resistance were significantly higher and cardiac output was significantly lower in New York Heart Association functional class 3 and 4 (8 patients) compared with class 1 and 2 (14 patients), whereas systemic arterial blood pressure was maintained at normal levels in both groups. Thus, postexercise SvO2 overshoot and, hence, decreased systemic oxygen extraction during recovery represent a compensatory response of an enhanced peripheral vascular tone that maintains systemic arterial blood pressure in the setting of reduced cardiac output by linking central and peripheral blood flow.

(Chest 1993; 103:514-20)

So2 = oxygen saturation; SvO2 = mixed venous oxygen saturation

In patients with heart failure, blood flow to skeletal muscle is frequently reduced both at rest and during exertion. A number of studies have demonstrated that the reduced perfusion of skeletal muscle during exertion is the major factor limiting the exercise performance in stable ambulatory patients with this disorder. When blood flow is reduced, the primary compensation for maintaining oxygen consumption is an increased oxygen extraction of peripheral tissues. At rest, an increase in oxygen extraction fully compensates for the reduced blood flow and maintains oxygen consumption at normal levels even in severely impaired patients with this disorder. During exercise, however, blood flow to skeletal muscle in such patients fails to rise normally and the compensatory increase in oxygen extraction is not sufficient to maintain normal oxygen consumption, which leads to early skeletal muscle anaerobic metabolism causing exertional fatigue. Although profound fatigue is often reported to continue after exercise in patients with heart failure, a rapid decrease in oxygen extraction below resting level accompanied with excessive blood flow have been reported in the early recovery period following both static and dynamic exercise. In patients with recent myocardial infarction, we have also observed that arteriovenous oxygen difference rapidly decreased below resting level during recovery from supine bicycle exercise when cardiac output and systemic oxygen consumption remained elevated. Since arterial oxygenation is not disturbed throughout exercise and recovery, this decreased arteriovenous oxygen difference during recovery is mainly responsible for a rapid increase in mixed venous oxygen saturation (SvO2) above its resting value (postexercise SvO2 overshoot). However, the pathophysiological basis of this phenomenon has been unclear. Accordingly, this study was undertaken to examine the postexercise SvO2 overshoot in relation to hemodynamic, metabolic, and neurohumoral responses after maximal supine bicycle exercise, and to further characterize systemic oxygen extraction during recovery in patients with heart failure.

METHOD

Study Patients

We studied 22 patients with clinically stable heart failure. There were 18 men and 4 women aged 38 to 68 years (mean, 58±9 years). Of the 22 patients studied, 2 had New York Heart Association functional class 1, 12 had functional class 2, 6 had functional class 3, and 2 had functional class 4 heart failure. The resting left ventricular ejection fractions ranged from 15 percent to 48 percent (mean, 32±9 percent). All patients included in this study had had their first acute myocardial infarction 6 to 8 weeks before the study, and none of the patients had postinfarction angina, critical arrhythmia, or uncontrolled heart failure at least for 2 weeks prior to the

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Oxygen Saturation after Exercise in Patients with Recent MI (Sumimoto et al)
study. Myocardial infarction was documented by a typical clinical history, characteristic Q waves and ST segment changes in the ECG, and a significant increase in the serum creatine kinase-MB isoenzyme level. Before entry into the study, each patient underwent a complete physical examination, and the patients were excluded from the study if they had physical or radiographic signs of obstructive lung disease and had angina pectoris or intermittent claudication that limited their exercise capacity. Treatment with all medication was discontinued for at least 24 h before the study. None of the patients was receiving β-blockers. The risks of the study were explained fully and informed consent was obtained from all patients before the study.

**Exercise Protocol**

Patients were studied in the supine position at rest, during bicycle ergometric exercise, and during recovery. Two or three days before the study, supine bicycle exercise was performed to familiarize the patients with a bicycle ergometer (Monark 881E ergometer, Sweden). On the day of the study, a Swan-Ganz catheter was inserted through the internal jugular vein and advanced to the pulmonary artery, and an arterial catheter was inserted in the radial artery. After 30 min of supine rest, bicycle exercise testing was performed with an ECG monitoring and expired gas analysis. Exercise began at a work load of 25 W with the pedal speed maintained at 60 rpm and increased by 25 W every 3 min until a symptom-limited maximum.

**Expired Gas Analysis**

Expired gases were analyzed (Oxycon-4, Mijnhardt Company, Holland). Instruments were calibrated at the beginning of each study. From these data, systemic oxygen consumption was measured at supine rest on the bicycle and continuously during exercise and for the first 5 min of recovery. Averaged measurements during the last 30 s of each exercise stage and during 30 s before 2 and 5 min of recovery were used for analysis.

**Hemodynamic and Metabolic Measurements**

Right atrial, pulmonary arterial, and systemic arterial pressures were recorded continuously, and pulmonary capillary wedge pressure was recorded intermittently at rest, at each exercise stage, and at 2 min and 5 min of recovery (DS-3300 system, Fukuda Denshi, Japan). Blood samples were drawn simultaneously from the radial and pulmonary artery at rest, within the last 30 s of each exercise stage, and within 30 s before 2 and 5 min of recovery. The blood samples were used for the immediate measurements of pH, PaO₂, PCO₂ (Radiometer Company ABL2) as well as oxygen saturation (SO₂) and hemoglobin concentration (Radiometer Company OSM2). Lactate concentration, plasma catecholamine levels, and erythrocytic 2,3-diphosphoglycerate concentration corrected for hemoglobin concentration were determined in arterial blood samples.

**Derived Variables**

Cardiac output was determined by the Fick principle with use of systemic arteriovenous oxygen difference and directly measured systemic oxygen consumption. Systemic vascular resistance was calculated using standard formula and is expressed as mm Hg/L/min. Systemic oxygen extraction was calculated as the ratio of systemic arteriovenous oxygen difference to arterial oxygen content × 100. Postexercise SVO₂ overshoot was calculated as follows: SVO₂ at 2 or 5 min of recovery − SVO₂ at rest.

**Statistical Analysis**

All data are presented as mean ± SD. Student’s t test for unpaired data and paired t test for paired data were used for statistical analysis. The least-squares regression was used to assess the relationship between the two variables. Probability values of <0.05 were considered to be significant.

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Table 1 — Hemodynamic Response to Supine Bicycle Exercise*

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Peak Exercise</th>
<th>2 min</th>
<th>5 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>68 ± 13</td>
<td>138 ± 16†</td>
<td>98 ± 16†</td>
<td>89 ± 14†</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>3.5 ± 1.1</td>
<td>9.0 ± 4.4†</td>
<td>8.0 ± 3.8†</td>
<td>4.9 ± 1.8†</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>96 ± 17</td>
<td>129 ± 23†</td>
<td>106 ± 17†</td>
<td>97 ± 16</td>
</tr>
<tr>
<td>SVR, mm Hg/L/min</td>
<td>25.9 ± 5.5</td>
<td>15.4 ± 6.1†</td>
<td>14.8 ± 6.9†</td>
<td>21.5 ± 9.0†</td>
</tr>
<tr>
<td>RA pressure, mm Hg</td>
<td>5 ± 4</td>
<td>12 ± 5†</td>
<td>7 ± 4†</td>
<td>5 ± 4</td>
</tr>
<tr>
<td>PCW pressure, mm Hg</td>
<td>10 ± 6</td>
<td>30 ± 12†</td>
<td>13 ± 7†</td>
<td>10 ± 6</td>
</tr>
</tbody>
</table>

*PCW = pulmonary capillary wedge; RA = right atrial; SVR = systemic vascular resistance.

†p<0.01; all p values indicate differences from resting values.

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Table 2 — Metabolic Response to Supine Bicycle Exercise*

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Peak Exercise</th>
<th>2 min</th>
<th>5 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>92 ± 11</td>
<td>95 ± 13</td>
<td>118 ± 6†</td>
<td>113 ± 9†</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>99.0 ± 1.2</td>
<td>99.0 ± 1.2</td>
<td>99.7 ± 0.7†</td>
<td>99.7 ± 0.5†</td>
</tr>
<tr>
<td>PVO₂ (mm Hg)</td>
<td>36 ± 5</td>
<td>24 ± 3†</td>
<td>43 ± 5†</td>
<td>44 ± 5†</td>
</tr>
<tr>
<td>SVO₂ (%)</td>
<td>68.3 ± 11.3</td>
<td>34.8 ± 7.6†</td>
<td>72.2 ± 8.9†</td>
<td>74.2 ± 8.8†</td>
</tr>
<tr>
<td>Oxygen extraction, %</td>
<td>31.5 ± 11.3</td>
<td>65.0 ± 7.7†</td>
<td>28.6 ± 8.6†</td>
<td>26.3 ± 8.8†</td>
</tr>
<tr>
<td>Oxygen consumption, ml/min</td>
<td>198 ± 52</td>
<td>1167 ± 553†</td>
<td>447 ± 330†</td>
<td>269 ± 117†</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.42 ± 0.03</td>
<td>7.36 ± 0.05†</td>
<td>7.33 ± 0.04†</td>
<td>7.33 ± 0.04†</td>
</tr>
<tr>
<td>Mixed venous pH</td>
<td>7.39 ± 0.03</td>
<td>7.24 ± 0.05†</td>
<td>7.26 ± 0.05†</td>
<td>7.28 ± 0.05†</td>
</tr>
</tbody>
</table>

*PaO₂ = arterial oxygen tension; PVO₂ = mixed venous oxygen tension; SaO₂ = arterial oxygen saturation; SVO₂ = mixed venous oxygen saturation.

†p<0.01; all p values indicate differences from resting values.
RESULTS
In all 22 patients, the bicycle exercise was limited by exercising muscle fatigue, and not by dyspnea. No
patient developed angina or ischemic ST segment changes during exercise and recovery. The maximal
work load ranged from 25 W to 100 W (mean, 65 ± 20 W), which was comparable with patients' functional
class. The hemodynamic, metabolic, and neurohumoral responses to peak supine bicycle exercise and
recovery are given in Tables 1 through 3.

$SvO_2$, Systemic Oxygen Extraction, and Systemic Oxygen Consumption (Fig 1)
The relative changes in $SvO_2$, systemic oxygen extraction, and systemic oxygen consumption during
exercise and recovery are shown in Figure 1. $SvO_2$ decreased progressively with increasing work load and
reached the lowest value at peak exercise. During recovery, however, $SvO_2$ increased rapidly above the

### Table 3—Neurohumoral Response to Supine Bicycle Exercise

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Peak Exercise</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 min</td>
</tr>
<tr>
<td>Lactate, mmol/L</td>
<td>0.9 ± 0.3</td>
<td>5.8 ± 2.1*</td>
<td>6.9 ± 2.3*</td>
</tr>
<tr>
<td>Norepinephrine, pg/ml</td>
<td>267 ± 199</td>
<td>1,608 ± 1,072*</td>
<td>1,044 ± 680*</td>
</tr>
<tr>
<td>Epinephrine, pg/ml</td>
<td>97 ± 59</td>
<td>542 ± 438*</td>
<td>207 ± 144*</td>
</tr>
<tr>
<td>2,3-DPG, μmol/gHb</td>
<td>16.3 ± 2.4</td>
<td>16.3 ± 1.1</td>
<td>16.6 ± 2.6</td>
</tr>
</tbody>
</table>

*p<0.01; all p values indicate differences from resting values.
†DPG = diphosphoglycerate.

Figure 1. Relative changes in $SvO_2$ (top, A), systemic oxygen extraction (center, B), and systemic oxygen consumption (bottom, C) at peak supine bicycle exercise and during recovery. Note that $SvO_2$ rapidly increased above the resting level and systemic oxygen extraction rapidly decreased below the resting level in the early recovery period, whereas systemic oxygen consumption remained elevated during recovery. Each point represents the mean ± SD. Asterisk = p<0.01; all p values indicate differences from resting values. $SvO_2$ = mixed venous oxygen saturation.

Figure 2. Changes in postexercise $SvO_2$ overshoot. Open circles represent the points at 2 min of recovery and closed circles represent the points at 5 min of recovery. $SvO_2$ = mixed venous oxygen saturation.
resting level within 2 min of recovery and increased further at 5 min (Fig 1A). These changes in SVo₂ were accompanied by reciprocal changes in systemic oxygen extraction so that systemic oxygen extraction increased to the maximal value at peak exercise and decreased rapidly below its resting level in the early recovery period (Fig 1B). In contrast, systemic oxygen consumption remained elevated during recovery (Fig 1C).

Postexercise SVo₂ Overshoot (Figs 2 and 3)

Of the 22 patients, 21 patients had increased SVo₂ above their resting values at 2 min of recovery. However, at 5 min of recovery, SVo₂ increased above their resting values in all patients. The mean postexercise SVo₂ overshoot at 2 min of recovery was 4.6 ± 3.3 percent (range, -1.6 to 14.3 percent), which increased significantly to 6.4 ± 3.3 percent (range, 1.5 to 15.9 percent) at 5 min of recovery (Fig 2). Postexercise SVo₂ overshoot was positively correlated with systemic vascular resistance at 5 min of recovery (Fig 3A). Although weak but significant positive correlations were observed between SVo₂ and cardiac output at rest and during exercise and recovery (all r > 0.42, p < 0.05), postexercise SVo₂ overshoot was inversely related to cardiac output at 5 min of recovery (Fig 3B). In addition, modest inverse relation was found between postexercise SVo₂ overshoot and systemic oxygen consumption at 5 min of recovery (Fig 3C). Similar correlations were also observed between postexercise SVo₂ overshoot and the above variables at 2 min of recovery. However, no significant relationships were seen between postexercise SVo₂ overshoot and arterial P0₂ and S0₂, right atrial pressure, pulmonary capillary wedge pressure, mean systemic arterial pressure, lactate concentration, plasma catecholamines (both epinephrine and norepinephrine), 2,3-diphosphoglycerate concentration, and arterial and mixed venous pH.

Postexercise SVo₂ Overshoot and Clinical Functional Class (Table 4)

Postexercise SVo₂ overshoot at 5 min of recovery were 1.6 ± 0.1 in class 1, 5.3 ± 1.7 in class 2, 8.4 ± 1.9 in class 3, and 12.5 ± 4.9 in class 4 patients. To further characterize postexercise SVo₂ overshoot in heart failure, patients were subdivided into two groups: mildly impaired (functional class 1 and 2) and severely impaired (functional class 3 and 4) patients. Postexercise SVo₂ overshoot at 5 min of recovery was significantly higher in class 3 and 4 patients than that in class 1 and 2 patients. Cardiac output was significantly lower and systemic vascular resistance was significantly higher in class 3 and 4 patients than those in class 1 and 2 patients. However, mean systemic arterial pressure and plasma catecholamine levels were not significantly different between the two groups.

Discussion

In stable patients with recent myocardial infarction, a rapid decrease in systemic oxygen extraction and a subsequent increase in SVo₂ above its resting value (postexercise SVo₂ overshoot) were observed in the early recovery period following supine bicycle exercise when systemic oxygen consumption remained elevated (Fig 1). This is consistent with previous reports that oxygen utilization during recovery is further dependent on excessive blood flow rather than oxygen.
4.8±2.1
98
Cardiac output, L/min
16.5±3.7
30.1±9.2†
Mean arterial pressure, mm Hg
96±16
98±16
Norepinephrine, pg/ml
587±312
630±505
Epinephrine, pg/ml
121±86
104±86
*SVo2 = mixed venous oxygen saturation; SVR = systemic vascular resistance.
†p<0.01; all p values indicate differences between class 1, 2 patients and class 3, 4 patients.

The physiologic mechanisms that control peripheral perfusion during recovery following dynamic exercise in patients with heart failure have not been well understood. Although several investigators have emphasized the importance of arterial blood pressure in determining peripheral perfusion, although our findings are consistent with previous reports demonstrating that peripheral function is important in regulating arterial blood pressure during exercise.6,10-12,23 Zelis and Flaim6 have suggested that the limited capacity for vasodilation in skeletal muscle may play an important role in maintaining systemic arterial blood pressure during exercise in patients with heart failure. Sullivan et al18 have demonstrated that in patients with chronic heart failure, increased skeletal muscle vascular resistance and reduced leg blood flow during upright bicycle exercise have a function to maintain systemic arterial blood pressure and therefore prevent hypoperfusion in important nonexercising regions. Although we did not measure peripheral blood flow directly in exercising skeletal muscle, adequate arterial blood pressure accompanied by increased systemic vascular resistance and reduced cardiac output during recovery in our patients was also likely to preferentially maintain blood flow to vital nonexercising organs at the expense of hypoperfusion in less vital regions, including exercising skeletal muscle. This may give an insight into the mechanism responsible for profound or sustained fatigue during recovery following maximal exercise in stable patients with heart failure.

Although several considerable contributions such as sympathetic activity, humoral factors (angiotensin II, vasopressin), neurogenic vasomotor tone, or vascular stiffness to peripheral vasoconstriction in response to exercise have been reported in patients with heart failure, the present study does not define the primary factor causing an enhanced systemic vascular resistance during recovery and thereby postexercise SVo2 overshoot. However, our results that plasma catecholamines were unrelated to postexercise SVo2 overshoot, and were not significantly different between mildly impaired (functional class 1 and 2) and severely impaired (functional class 3 and 4) patients indicate that increased sympathetic activity may play a minimal role in regulating peripheral vasoconstriction during recovery from dynamic exercise. This is consistent with previous reports demonstrating that α-adrenergic blockades failed to improve the maximal
exercise capacity or increase blood flow to the exercising muscle in patients with heart failure. Although it remains to be seen whether other contributors are in any way related to the peripheral vasoconstriction during recovery, a close regulation of arterial blood pressure in our patients suggests that an enhanced systemic vascular resistance during recovery is mediated, in part, by the alterations in neurogenic vasomotor tone.

Three limitations of our study should be addressed. First, as there was no control group in this study, we cannot document whether postexercise $\text{SVO}_2$ overshoot phenomenon observed in our patients is characteristic in heart failure. However, our finding that postexercise $\text{SVO}_2$ overshoot, caused by enhanced peripheral vasoconstriction to maintain systemic arterial blood pressure, was significantly higher in severely impaired patients than in mildly impaired patients may support the fact that this phenomenon is characteristic in heart failure. Second, all patients included in this study had recent myocardial infarction and none of the patients had different causes of heart failure. However, our results may not have been different if patients were studied later in their course or if patients with different causes of heart failure were included because postexercise $\text{SVO}_2$ overshoot was associated with the severity of heart failure but not with the duration or the cause of heart failure. Third, we have chosen supine bicycle exercise to evaluate postexercise $\text{SVO}_2$ overshoot phenomenon in this study because maximal and invasive exercise can be done more safely. It remains to be seen whether other types of exercise can in any way affect our results.

In conclusion, during recovery from maximal supine bicycle exercise in patients with recent myocardial infarction, we observed a rapid decrease in systemic oxygen extraction below resting level and a subsequent increase in $\text{SVO}_2$ above its resting value (postexercise $\text{SVO}_2$ overshoot) when systemic oxygen consumption remained elevated. In addition to decreased metabolic oxygen demand during recovery, postexercise $\text{SVO}_2$ overshoot was caused by increased peripheral arteriovenous shunting due to an enhanced peripheral vasoconstriction. Furthermore, this phenomenon may represent a compensatory response of peripheral vasoconstriction to maintain systemic arterial blood pressure in the setting of reduced cardiac output by linking central and peripheral blood flow during recovery from maximal supine bicycle exercise in patients with recent myocardial infarction.

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Oxygen Saturation after Exercise in Patients with Recent MI (Sumimoto et al)