Short-Term Physical Training Improves Ventilatory Response to Exercise After Coronary Arterial Bypass Surgery

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The issue of whether exercise training improves exercise hyperpnea in patients after coronary arterial bypass graft (CABG) surgery has not been fully explored. Effects of short-term physical training on ventilatory response and cardiac output during exercise in patients following coronary arterial bypass grafting surgery is studied. Thirty-four patients underwent exercise training for 2 weeks after the second postoperative week (Ex group); 23 stayed sedentary (Sed group). Ventilatory and cardiac output response during the cardiopulmonary exercise test was measured before and after the training period. The minute ventilation–carbon dioxide output (VE–VCO₂) slope decreased from 38.9±8.1 to 35.1±6.7 (p<0.05) in the Ex group, but failed to decrease in the Sed group (39.7±11.1 to 41.5±11.4). Cardiac output during exercise at 20 W and at peak exercise, and peak oxygen pulse (VO₂/HR) increased significantly only in the Ex group after training. There was a correlation between improvement of the VE–VCO₂ slope and peak cardiac output during the training interval (r=–0.47) in the Ex group. Short-term physical training after CABG improves ventilatory response to exercise and increases cardiac output during exercise. Improvement of cardiac output is correlated with a decreased value of the VE–VCO₂ slope. (Jpn Circ J 2001; 65: 419–423)

Key Words: Coronary arterial bypass grafting; Exercise training; VE–VCO₂ slope

Cardiac rehabilitation after coronary arterial bypass grafting (CABG) surgery is known to have several favorable effects. In these patients, training enhances exercise tolerance,1 activity of daily living, and quality of life.2 Additionally, shortness of breath during exercise is often noted to have diminished after physical training.

Shortness of breath is a major complaint when ventilation is accelerated during exercise. This exercise-induced hyperpnea can be assessed using cardiopulmonary exercise (CPX) testing, in which the slope of the relationship between minute ventilation and carbon dioxide output (VE–VCO₂ slope) has been proposed as a parameter for evaluating ventilatory response to exercise.3–5 The VE–VCO₂ slope increases when breathing is rapid and shallow,5 reflecting the increased dead space accompanying this respiratory pattern. The VE–VCO₂ slope also steepens when the physiologic dead space increases as a result of greater ventilation–perfusion mismatch.8,9 Cardiac output during exercise has been reported to be related inversely to the ratio of total dead space to tidal volume (VD/VT)10 when cardiac output fails to increase sufficiently during exercise, the physiologic increase of pulmonary blood flow is attenuated and, consequently, ventilation–perfusion mismatch increases. By this mechanism the VE–VCO₂ slope becomes steeper when cardiac function during exercise is compromised. Accordingly, the VE–VCO₂ slope is steeper in patients with chronic heart failure (CHF) than in normal subjects.

Although exercise training is known to attenuate shortness of breath during exercise, the issue of whether exercise training improves exercise hyperpnea in patients after coronary arterial bypass grafting (CABG) has not been fully explored. Because patients after CABG show exercise hyperpnea and a steep VE–VCO₂ slope as seen in patients with CHF, it is assumed that the mechanism inducing the exercise hyperpnea in patients after CABG is similar to that of CHF patients. Therefore, in the present study, we first sought to assess the effect of exercise training on ventilatory response during exercise in post-CABG patients. Exercise hyperpnea was evaluated using the VE–VCO₂ slope with CPX testing. Our second aim was to determine whether a slope improvement was related to a training-related improvement of cardiac output during exercise in these patients.

Methods

Patients

We enrolled 57 patients (Table 1) whose underlying diseases were old myocardial infarction and/or angina pectoris, assigning them to either physical training (34 patients, Ex group) or sedentary convalescence (23 patients, Sed group) randomly according to the ward to which they were admitted. Patients with peripheral vascular obstructive disease, obstructive pulmonary disease, anemia, a history of recent heart failure and those aged over 75 years old were excluded. No difference in left ventricular ejection fraction, which was evaluated using left ventriculography, was evident between the 2 groups (59±13% in Ex group,
63±7% in Sed group). Coronary arterial bypass grafting was performed successfully and no major perioperative events such as reoperation or cerebral vascular disease occurred. The number of grafts did not differ between groups (2.6±1.0 in Ex group, 2.4±1.1 in Sed group). All patients received aspirin, dipyridamole, and nitrates; these medications were not altered throughout the period of the study. No patients were taking β-blocking agents. The study was approved by the hospital ethics committee. Informed consent was obtained from all subjects.

**Exercise Testing**

Two weeks after surgery, all patients underwent a symptom-limited CPX test in an upright position on a calibrated cycle ergometer (CPE2000, MedGraphics, St Paul, MN, USA). Cadiopulmonary exercise was administered 2–4 h after a light meal. This test began with 4 min of rest and 4 min of warm-up at 20 W followed by a continuous increase of the work rate by 1 W every 6 s until the test was terminated by complaints of exhaustion. A second CPX test was performed 2 weeks after the first in the same manner.

**Gas Exchange Measurements**

Oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), and minute ventilation (VE) were measured on a breath-by-breath basis using a gas analyzer (MINATO 280S, Minato Science, Osaka, Japan).

The slope of the VE–$\dot{V}CO_2$ relationship was calculated by linear regression analysis using the values of VE and $\dot{V}CO_2$. Because the relationship between VE and $\dot{V}CO_2$ during incremental exercise changes above the respiratory compensation point, the VE–$\dot{V}CO_2$ slope was calculated below the respiratory compensation point.

The dead space was likely to be the same for the first and second CPX study as the same type and size of face mask was used for both sessions.

**Exercise Training**

For the Ex group, exercise training using the treadmill or cycle ergometer was performed twice a day at an intensity level of 22–25% of the first CPX test for 30–40 min. The total work done on the cycle ergometer was 324±35 kJ.

### Table 1 Patients Profiles

<table>
<thead>
<tr>
<th></th>
<th>Ex group</th>
<th>Sed group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>34</td>
<td>23</td>
</tr>
<tr>
<td>Male/female</td>
<td>28/6</td>
<td>18/5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61±8</td>
<td>63±8</td>
</tr>
<tr>
<td>Basal disease (AP/OMI)</td>
<td>21/13</td>
<td>14/9</td>
</tr>
<tr>
<td>Graft number</td>
<td>2.6±1.0</td>
<td>2.4±1.1</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>59±7</td>
<td>63±7</td>
</tr>
</tbody>
</table>

Values are mean±SD. Ex, exercise; Sed, sedentary; AP, angina pectoris; OMI, old myocardial infarction.

### Table 2 Aerobic Capacity and Ventilatory Variables in Physical Training Group (Ex Group)

<table>
<thead>
<tr>
<th></th>
<th>Entry</th>
<th>After training</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilatory anaerobic threshold (ml·min⁻¹·kg⁻¹)</td>
<td>11.3±2.1</td>
<td>12.4±2.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peak oxygen uptake (ml·min⁻¹·kg⁻¹)</td>
<td>14.3±2.7</td>
<td>20.3±5.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Respiratory rate (l/min)</td>
<td>Rest: 19.5±5.0</td>
<td>17.3±5.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Warm-up: 26.2±6.5</td>
<td>24.3±6.5</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Tidal volume (ml)</td>
<td>Rest: 728.1±204.6</td>
<td>766.2±320.2</td>
<td>NS</td>
</tr>
<tr>
<td>Warm-up: 1,080.6±377.7</td>
<td>1,064.2±277.8</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Minute ventilation (l/min)</td>
<td>Rest: 13.5±1.7</td>
<td>13.2±5.6</td>
<td>NS</td>
</tr>
<tr>
<td>Warm-up: 24.7±6.0</td>
<td>22.2±6.0</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Minimum VE/\dot{V}CO₂</td>
<td>42.3±6.4</td>
<td>38.3±6.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peak HR</td>
<td>156±25</td>
<td>162±19</td>
<td>NS</td>
</tr>
<tr>
<td>Peak SBP</td>
<td>189±23</td>
<td>196±24</td>
<td>NS</td>
</tr>
<tr>
<td>Peak respiratory equivalent (R)</td>
<td>1.16±0.13</td>
<td>1.19±0.31</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD. VE/\dot{V}CO₂, minute ventilation/carbon dioxide production; HR, heart rate; SBP, systolic blood pressure.

### Table 3 Aerobic Capacity and Ventilatory Variables in Sedentary Group

<table>
<thead>
<tr>
<th></th>
<th>Entry</th>
<th>After training</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilatory anaerobic threshold (ml·min⁻¹·kg⁻¹)</td>
<td>11.9±1.7</td>
<td>11.4±1.6</td>
<td>NS</td>
</tr>
<tr>
<td>Peak oxygen uptake (ml·min⁻¹·kg⁻¹)</td>
<td>13.7±2.5</td>
<td>14.3±2.3</td>
<td>NS</td>
</tr>
<tr>
<td>Respiratory rate (l/min)</td>
<td>Rest: 20.6±5.8</td>
<td>19.0±4.8</td>
<td>NS</td>
</tr>
<tr>
<td>Warm-up: 30.7±7.0</td>
<td>28.0±6.8</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Tidal volume (ml)</td>
<td>Rest: 637.4±155.4</td>
<td>621.3±151.1</td>
<td>NS</td>
</tr>
<tr>
<td>Warm-up: 921.0±229.6</td>
<td>975.0±264.3</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Minute ventilation (l/min)</td>
<td>Rest: 12.5±2.4</td>
<td>11.0±0.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Warm-up: 25.2±6.0</td>
<td>23.2±4.7</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Minimum VE/\dot{V}CO₂</td>
<td>41.2±10.5</td>
<td>45.3±7.2</td>
<td>NS</td>
</tr>
<tr>
<td>Peak HR</td>
<td>151±30</td>
<td>154±23</td>
<td>NS</td>
</tr>
<tr>
<td>Peak SBP</td>
<td>188±26</td>
<td>183±19</td>
<td>NS</td>
</tr>
<tr>
<td>Peak respiratory equivalent (R)</td>
<td>1.20±0.16</td>
<td>1.17±0.23</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD. VE/\dot{V}CO₂, minute ventilation/carbon dioxide production; HR, heart rate; SBP, systolic blood pressure.
equivalent to each patient’s ventilatory anaerobic threshold, as determined from the V-slope method for 2 weeks. The duration of a single bout of exercise training was 30 min.

**Cardiac Output**

Cardiac output during exercise at 20 W and at peak exercise was measured in 23 patients. A 19-gauge catheter was inserted into a vein in the upper arm, and cardiac output was determined by a dye-dilution method using an ear piece. To detect cardiac output at the peak of exercise, indocyanine green was injected when patients claimed to be exhausted. They kept pedalling for a further 20 s until the measurement was completed.

**Data Analysis**

All data are expressed as the mean±SD. Differences between the Ex and Sed groups were assessed by an unpaired t-test, and differences between CPX before and after training by a paired t-test. The slope of VE vs VCO₂ was assessed by analyzing the linear regression of the breath-by-breath plot from the point of warm-up to the point of respiratory compensation. The relationship between cardiac output and the VE–VCO₂ slope was calculated using linear regression analysis. A value of p<0.05 was considered significant.

**Results**

All patients completed the protocol. No major difficulties or complications occurred during the training period in the Ex group.

**Aerobic Capacities**

No differences in exercise capacities were present at the beginning of the protocol between groups. Oxygen consumption (VO₂) at the ventilatory anaerobic threshold (VAT) and at peak exercise showed no differences between the 2 groups.

As shown in Tables 2 and 3, the ventilatory anaerobic threshold increased significantly (p<0.01) after exercise training in the Ex group, whereas it failed to increase in the Sed group. Peak oxygen uptake also increased only in the Ex group (p<0.05).

**Ventilation Pattern During Exercise (Tables 2, 3)**

The respiratory rate at rest and during warm-up in the Ex group decreased significantly (p<0.01) after exercise training. It also significantly decreased in the Sed group during warm-up. Tidal volume during warm-up exercise showed no increase in either the Ex or Sed groups.

**VE–VCO₂ Slope**

The VE–VCO₂ slope decreased 9.8±1.2% after exercise training in the Ex group (from 38.9±8.1 to 35.1±6.7; p<0.05). The minimum value of VE/VCO₂ during ramp exercise (minimum VE/VCO₂) also decreased significantly (9.5±0.9%) in the Ex group after physical training (from 42.3±6.4 to 38.3±6.1; p<0.01). In contrast, in the Sed group, the VE–VCO₂ slope and minimum VE/VCO₂ failed to decrease over the 2-week period (VE–VCO₂ slope, from 39.7±11.1 to 41.5±11.4, NS; minimum VE/VCO₂, from 41.2±10.5 to 45.3±7.2, NS). These results are shown in Fig 1 and in Tables 2 and 3.

**Peak VO₂/Heart Rate**

As shown in Fig 2, peak VO₂/heart rate (VO₂/HR) at peak exercise represents a peak stroke volume. Peak VO₂/HR increased only in the exercise group after the training period. VO₂/HR, oxygen output/heart rate; Ex, exercise group; Sed, sedentary group.

**Fig 1.** Effect of exercise training on the VE–VCO₂ slope. The VE–VCO₂ slope decreased only in the exercise group after the training period. VE–VCO₂, minute ventilation−carbon dioxide output; Ex, exercise group; Sed, sedentary group.

**Fig 2.** Effect of exercise training on peak VO₂/HR. VO₂/HR at peak exercise represents a peak stroke volume. Peak VO₂/HR increased only in the exercise group after the training period. VO₂/HR, oxygen output/heart rate; Ex, exercise group; Sed, sedentary group.

**Fig 3.** Effect of exercise training on CO during exercise at 20 W. CO at the given work rate increased only in patients undergoing physical training. CO, cardiac output; Ex, exercise group; Sed, sedentary group.

**Fig 4.** Effect of exercise training on CO at peak exercise. Peak CO increased only in the Ex group. CO, cardiac output; Ex, exercise group; Sed, sedentary group.
exercise hyperpnea. Therefore, we investigated whether exercise training after CABG also improves exercise hyperpnea.

A rapid, shallow breathing pattern might be regulated by pulmonary capillary pressure. Whether the pulmonary capillary pressure changed with physical training in the study is unclear, but regulation of interstitial pressure appears not to have played a major role in improving exercise hyperpnea because the breathing pattern altered in the same manner in both groups after the training period; the respiratory rate with exercise at 20 W decreased in both groups. As seen in Tables 2 and 3, in the Ex group respiratory rate decreased 7.3% from 26.2/ min before training to 24.3/ min after training. In the Sed group, respiratory rate decreased 8.8% from 30.7/ min to 28.0/ min. The degree of decrease in respiratory rate was similar. As for tidal volume, it showed no change in either group, with no significant difference in degree of alteration evident between groups. Thus, improvement of breathing pattern was not the main mechanism ameliorating exercise hyperpnea in the present study.

Thoracic pain associated with deep breathing also is believed to influence breathing patterns in patients after CABG because the sternum and several ribs are cut or displaced during surgery. Surgical trauma to the thorax would lead to severe thoracic pain during exercise and limit depth of inspiration. Therefore, after open heart surgery, the ventilation pattern shifts toward rapid, shallow breathing. However, as chest wall pain gradually attenuates with time, breathing patterns become slower and deeper, with less ventilation– perfusion mismatch resulting during exercise. The VE– V̇CO₂ slope would become shallower. Thus, the reduction of the VE– V̇CO₂ slope seen in the present study partly reflects spontaneous normalization of patients’ postoperative rapid, shallow breathing pattern. However, because the VE– V̇CO₂ slope decreased more in the Ex group than in the Sed group, physical training is believed to have favorable effects in reducing ventilation– perfusion mismatch during exercise.

In the present study, peak oxygen uptake increased extremely after the training period in the Ex group. The reason for this extreme improvement is unclear. Training effect at the second test, attenuated wound pain, and spontaneous recovery after surgery might explain the improvement in the peak oxygen uptake. However, in the Sed group, peak oxygen uptake showed no statistical change after the training period. Therefore, exercise training also plays an important role in increasing peak oxygen uptake.

Cardiac output was shown to increase after exercise training (Fig 4); peak cardiac output increased only in the Ex group, and cardiac output at peak exercise was higher in the Ex group than in the Sed group. Hence, cardiac output was shown to improve at the second test, attenuated wound pain, and spontaneous recovery after surgery might explain the improvement in the peak oxygen uptake. However, in the Sed group, peak oxygen uptake showed no statistical change after the training period. Therefore, exercise training also plays an important role in increasing peak oxygen uptake.

Cardiac output was shown to increase after exercise training (Fig 4); peak cardiac output increased only in the Ex group, and cardiac output at peak exercise was higher in the Ex group than in the Sed group. The same difference applied for peak VO₂/HR, which is known to indicate stroke volume at peak exercise. Peak VO₂/HR was significantly higher in the Ex group after physical training than before (Fig 2), and physical training improved cardiac output during exercise at 20 W, which did not increase in the Sed group. Hence, cardiac output was shown to improve at a given work rate. This change is assumed to be the main reason for the improvement of hyperventilation during exercise in the present study.

Cardiac output is related closely to patency of blood vessels; with decreased cardiac output blood vessels tend to constrict and vice versa. Vascular tone is regulated by the sympathetic nervous systems as well as by other vasoac-
tive substances such as endothelial cell-derived compounds including nitric oxide, endothelin-1 and prostacyclin. It has been reported that nitric oxide production during exercise is attenuated in heart failure patients compared to normal subjects and that it recovers with exercise training. That is, after exercise training, the peripheral vessel is likely to dilate. Also, β-adrenoceptor activity can be improved by exercise training, although it deteriorates in heart disease via catecholamine injury. The same thing is reported to occur in peripheral vessels. Through the improvement of catecholamine sensitivity after exercise training, the peripheral vessel is assumed to restore its ability to dilate.

In the present study, cardiac output during exercise is believed to have improved via such mechanisms.

The present study also showed that the ΔVE–VCO2 slope with training was significantly related to Δcardiac output with training, showing a similar correlation coefficient to that reported previously in heart failure patients. Because the VE–VCO2 slope is related to physiologic dead space, ventilation–perfusion mismatch, and pulmonary blood flow, a result that shows that the VE–VCO2 slope correlates with cardiac output during exercise is reasonable. Therefore, an improvement of cardiac output is able to be assessed by measuring the VE–VCO2 slope in CPX. Of course, as was discussed earlier, there are several mechanisms that affect the VE–VCO2 slope. This might be the reason why the correlation was not as strong.

Patients participating in the study had an almost normal ejection fraction and thus, the results of the present study cannot be adopted to those CABG patients with deteriorated cardiac function. However, patients with a lowered ejection fraction are regarded as patients with CHF, and there is much evidence that exercise training has favorable effects on exercise hyperpnea. Therefore, the results obtained here might be applied to those CABG patients with a deteriorated ejection fraction. However, further studies are necessary to prove this.

In summary, the present study found that physical training for 2 weeks after CABG improves abnormal ventilation during exercise and attenuated cardiac output during exercise. Also, the VE–VCO2 slope can be used as an index of cardiac output during exercise.

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References