Beneficial Effect of Short-term Endurance Training on Glucose Metabolism During Rehabilitation After Coronary Bypass Surgery*

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Aims: Our study was aimed at determining whether beneficial modification of carbohydrate metabolism can be obtained after a short-term training program and whether it is associated with an increase in binding and degradation of $^{125}$I-insulin by erythrocyte receptors that suggests a decrease in insulin resistance.

Methods: The study was conducted in a group of 20 patients aged 56 ± 1.9 years (mean ± SEM), within 1 to 6 months after coronary bypass surgery. All patients completed 15 training sessions based on 30 min of cycling with a constant load. Before and after a 3-week training program, glucose, insulin, and C-peptide blood levels, as well as binding and degradation of $^{125}$I-insulin by erythrocyte receptors, were determined.

Results: A statistically significant decrease was found in the blood glucose level, from 111.2 ± 4.2 to 97.8 ± 3.5 mg/dL (p < 0.01); this decrease was not accompanied by significant insulin concentration changes. There was also a significant increase in insulin binding, from 0.535 ± 0.059 to 0.668 ± 0.042 pg $^{125}$I/10$^{11}$ RBCs (p < 0.01), and degradation from 7.64 ± 0.54 to 9.49 ± 0.58 pg $^{125}$I/10$^{11}$ RBCs (p < 0.05).

Conclusion: The results indicated that even short-term endurance training in patients rehabilitated after coronary bypass surgery induced favorable modification of glucose metabolism, presumably caused by a decrease in insulin resistance. (CHEST 2000; 117:47–51)

Key words: coronary bypass surgery; endurance training; insulin resistance

Abbreviations: BMI = body mass index

Coronary artery bypass surgery does not eliminate the risk factors for coronary heart disease, which promote further progression of atherosclerosis in coronary arteries and may also contribute to coronary artery bypass graft atherosclerosis and graft occlusions.1–3 Insulin resistance and hyperinsulinemia are considered independent risk factors for cardiovascular disease.4,5 In 1989, Foster6 described insulin resistance as a “secret killer.” Barnard et al7 studied the influence of physical training and diet on the insulin resistance phenomenon in patients with an impaired glucose tolerance test and provided evidence that physical training reduces insulin resistance. Investigations conducted in patients after myocardial infarction showed that physical training, continued for 1 year, decreased insulin blood level.8 However, a short-term (3-week) endurance training program conducted in patients after myocardial infarction decreased insulin blood level only in subjects with hyperinsulinemia.9 In patients rehabilitated after coronary bypass surgery, no significant changes in insulin blood level have been found in response to physical training, while the glucose blood level has been seen to substantially decrease compared with patients who have not exercised.10 The authors of the latter publication did not investigate insulin resistance indicators and suggested only that the observed decrease in glucose blood level after exercise training is related to a decrease in insulin
resistance. The results in patients who have undergone coronary bypass surgery need to be verified by more detailed research with respect to the above-mentioned metabolic risk factors. This is necessary because in recent years, in general only patients with severe pathology and multivessel disease are referred for coronary bypass surgery. Therefore, we have undertaken studies to establish whether improvement of glucose metabolism in patients rehabilitated after coronary bypass surgery depends on lowering of insulin resistance in response to physical training. Also, we were interested in determining whether such an effect can already be detected after a short-term rehabilitation course, and if it is associated with improvement in physical performance and in blood lipid profile.

Materials and Methods

The study was conducted in a group of 20 men between 33 and 68 years of age, with a body mass index (BMI) of 26.49 ± 0.81 kg/m², 1 to 6 months after coronary bypass surgery (mean, 3.8 months). This investigation was performed after receiving the approval of patients and the Regional Ethics Board of the Committee for Science and Research.

Patients with an ejection fraction of < 35% who did not reach at least 75 W in a preselction symptom-limited exercise test (test 1) were eligible to participate in the study. Patients who demonstrated signs of angina pectoris or severe arrhythmia or had diabetes mellitus were excluded from our study. Forty percent of studied individuals were hypertensive, with BP well controlled by drugs.

After the preliminary examination, the second symptom-limited exercise test (test 2) was carried out on the following day to establish the individual load applied in the training program. It was accompanied by the analysis of oxygen consumption and CO2 output using a CardiO2 analyzer with a CPX-D computer system (Medical Graphics Corp; St. Paul, MN). The exercise test started with a load of 25 W and increased by 25 W every 3 min. The ventilatory threshold was determined by the computerized V-slope method described by Beaver et al.11 with software supplied by Medical Graphics. Before the test and 3 min after its completion, capillary blood from the pulp of the finger and venous blood from the basilic vein were taken.

The following parameters in the capillary blood samples were measured: acid-base balance on the AVL 995 Hb analyzer (AVL Scientific Corp; Rosewell, GA); lactate level by the Boehringer Mannheim test (Boehringer Mannheim Corp; Indianapolis, IN); and glucose level by the Cormay Company test (Cormay Company; Lublin, Poland). The samples of venous blood plasma were analyzed for insulin level by radioimmunoassay with double antibodies using radioimmunoassay insulin sets, and for C-peptide level using the Biodat-Serono test (Biodat-Serono; Serono, Italy). The erythrocytes were isolated from heparinized blood, and 125I-insulin binding and degradation by erythrocyte receptors were determined according to the method described by Gambhir and Nerurkar.12 After the initial investigation, the whole group of patients underwent training for 3 weeks. Each patient received identical dietary instructions according to European Atherosclerosis Society recommendations.13

The first stage of the training sessions was continuous endurance training on a bicycle ergometer. The training started not earlier than 2 h after a meal and was preceded by a medical examination every day. The training load was applied for 3 weeks, 5 times a week (15 training units altogether). The duration of each training unit was 30 min and included 5 min of warming up (riding a bicycle without the load); 20 min of riding with the load; and 5 min of active rest (riding a bicycle without the load). Training was performed with the load at 10% below the load obtained at the ventilatory threshold during the cardiopulmonary exercise test carried out after the preliminary examination. BP and pulse were systematically recorded during each training unit. Three to 5 days after the beginning of the training program, lactic acid levels were measured following the termination of the training session in order to evaluate whether the training exertion was performed under aerobic conditions. In no case did the lactic acid levels determined exceed the threshold values. In addition, patients participated in overall conditioning exercises for 30 min daily, along with 30 to 60 min of walking.

After 3 weeks, the analyzed parameters were reexamined according to the protocol. The third exercise test (test 3), involving gas exchange analysis, was stopped at the same workload as in the second test. One day before discharge from the hospital, the fourth consecutive exercise test (test 4), of the symptom-limited type, was performed. This was introduced to assess the differences in the amount of work before and after the training course.

During the study period, patients continued the same drug treatment they used before admission to the hospital.

Statistical Analysis

Results are expressed as mean value ± SEM. To compare the data within the same group before and after the training program, the Wilcoxon test was used. To compare the data between the groups, the Mann-Whitney test was applied. A value of p < 0.05 was considered significant.

Results

Physiologic parameters measured at rest and at the end of the cardiopulmonary exercise test (test 2 and test 3), before and after a 3-week rehabilitation course, are listed in Table 1. No major variations were recorded in either the resting or exercise heart rate before and after the training program. However, a significant decrease was found in the resting and exercise systolic BP, from 143.20 ± 4.97 mm Hg to 129.10 ± 5.63 mm Hg (p < 0.05) and from 193.60 ± 6.07 mm Hg to 168.20 ± 4.64 mm Hg (p < 0.01), respectively. Similarly, resting diastolic BP was noticeably reduced, from 94.50 ± 2.65 mm Hg to 85.50 ± 3.40 mm Hg (p < 0.05). The marked decrease in rate-pressure product (from 24,344 ± 1,361 to 19,910 ± 1,449; p < 0.001) was accompanied by a significant reduction in the lactic acid blood level in the final exercise test (from 3.34 ± 0.26 mmol/L to 2.93 ± 0.17 mmol/L; p < 0.05). Mean BMI was 26.49 ± 0.81 kg/m² before the training program and 26.69 ± 0.84 kg/m² at the final examination.

During the 3-week physical training period (15 training sessions), a significant improvement was observed in physical performance, as expressed by a...
substantial increase in the amount of work achieved in the symptom-limited exercise test. The average amount of work was 23.7 ± 1.8 kJ in the preliminary examination (test 2) and 33.0 ± 2.4 kJ (p < 0.001) at the end of training program (test 4; Table 2). Also the maximal physical performance and duration of the exercise symptom-limited test after the rehabilitation course increased significantly, from 91.2 ± 4.3 W to 112.0 ± 5.2 W and from 7.3 ± 0.3 min to 9.1 ± 0.4 min, respectively (Table 2). Table 3 demonstrates the average fasting plasma concentrations of carbohydrate metabolism parameters and indicators of insulin resistance measured at rest. Short-term physical training markedly decreased the glucose concentration, from 111.2 ± 4.2 mg/dL to 97.8 ± 3.5 mg/dL (p < 0.01). Generally, the insulin serum level did not change substantially, and the simultaneously measured C-peptide blood level increased significantly from 2.38 ± 0.25 ng/mL to 3.1 ± 0.45 ng/mL (p < 0.05). Both the binding and degradation of 125I-insulin by erythrocyte receptors in examined patients increased during exercise training, from 0.535 ± 0.059 to 0.668 ± 0.042 pg 125I/1011 RBCs for binding (p < 0.01), and from 7.64 ± 0.54 to 9.49 ± 0.58 pg 125I/1011 RBCs for degradation (p < 0.05).

The changes in carbohydrate parameter values were accompanied by a statistically significant decrease in the total cholesterol blood level, from 213.5 ± 12.6 mg/dL to 199.7 ± 10.3 mg/dL (p < 0.05; Table 4). There were no substantial correlations between the changes in parameters of carbohydrate metabolism and lipid metabolism during the rehabilitation course. The change in high-density lipoprotein cholesterol blood level was correlated with a change in the amount of tolerated exercise load (r = 0.62; p < 0.01). Otherwise, no other correlations between improvement of metabolic parameters and increase in physical performance were recorded.

**Discussion**

Our study revealed that even a short-term period of physical training in patients rehabilitated after coronary bypass surgery, besides resulting in an improvement in exercise tolerance, leads to beneficial modification of glucose metabolism and the advantageous alteration of lipid metabolism parameters. This corresponds with the study undertaken by Ågren and coworkers,10 who also observed a beneficial metabolic modification, as expressed by a decrease in blood glucose level detected only in patients engaged in the exercise program. They did not observe the same tendency in a group of untrained patients. Our data confirm the hypothesis of Ågren et al10 that favorable carbohydrate metabolic modification is probably associated not with a decrease in insulin secretion, but rather, mainly with an increase in receptor affinity to insulin. Such a suggestion can be put forward on the grounds of the observation that after training, the C-peptide level increases commensurate with the increase in insulin secretion. If the insulin level has not been significantly elevated in spite of the increase in insulin secretion, it could not be put forward on the grounds of the observation that after training, the C-peptide level increases commensurate with the increase in insulin secretion. If the insulin level has not been significantly elevated in spite of the increase in insulin secretion, it could not be put forward on the grounds of the observation that after training, the C-peptide level increases commensurate with the increase in insulin secretion.

**Table 1—Physiologic Parameters**

<table>
<thead>
<tr>
<th>Measures</th>
<th>Rest Before Rehabilitation</th>
<th>Rest After Rehabilitation</th>
<th>p Value</th>
<th>Exercise Before Rehabilitation</th>
<th>Exercise After Rehabilitation</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beat/min</td>
<td>78.60 ± 3.21</td>
<td>75.40 ± 3.32</td>
<td>NS</td>
<td>125.20 ± 4.44</td>
<td>117.50 ± 6.08</td>
<td>NS</td>
</tr>
<tr>
<td>BPS, mm Hg</td>
<td>143.20 ± 4.97</td>
<td>129.10 ± 5.63</td>
<td>&lt; 0.05</td>
<td>193.60 ± 6.07</td>
<td>168.20 ± 4.64</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>BPD, mm Hg</td>
<td>94.50 ± 2.65</td>
<td>85.50 ± 3.40</td>
<td>&lt; 0.05</td>
<td>105.90 ± 3.56</td>
<td>95.60 ± 3.02</td>
<td>NS</td>
</tr>
<tr>
<td>RPP</td>
<td>11.29 ± 664</td>
<td>9.702 ± 539</td>
<td>NS</td>
<td>24,344 ± 1,361</td>
<td>19,910 ± 1,449</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LA, mmol/L</td>
<td>1.37 ± 0.078</td>
<td>1.37 ± 0.078</td>
<td>NS</td>
<td>3.34 ± 0.26</td>
<td>2.93 ± 0.17</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

*Data are means ± SEM. HR = heart rate; BPS = systolic blood pressure; BPD = diastolic blood pressure; RPP = rate-pressure product; LA = lactic acid; NS = not significant.

**Table 2—Results of Symptom-Limited Exercise Test**

<table>
<thead>
<tr>
<th>Test</th>
<th>Before Rehabilitation</th>
<th>After Rehabilitation</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount of work, kJ</td>
<td>23.7 ± 1.8</td>
<td>33.0 ± 2.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Maximum physical performance, W</td>
<td>91.2 ± 4.3</td>
<td>112.0 ± 5.2</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Duration of exercise test, min</td>
<td>7.3 ± 0.3</td>
<td>9.1 ± 0.4</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

*Data are means ± SEM.
mean that insulin binding to receptors may have been increased; this may be an indicator of reduction of insulin resistance. This suggestion has been confirmed by the present study, which showed an increase in binding and degradation of $^{125}$I-insulin by erythrocyte receptors. We used the model of Gambhir et al, a relatively simple clinical test that is easier to use in the assessment of rehabilitation than the glucose clamp applied in the evaluation of insulin sensitivity.12,14 It is important to note that RBCs are not a typical site for the action of insulin because the main target areas are skeletal muscles and adipose tissue. The insulin-binding characteristics of insulin receptors on erythrocytes are comparable to those on myocytes and adipocytes, and it has been corroborated that defects in insulin binding correlate with insulin sensitivity.15,16

Because the training started an average of 3.8 months after surgery in our study, it can be implied that favorable results in exercise capacity and also in glucose and lipid metabolism were not dependent on convalescence time but, rather, that they were mainly the effect of physical training. Such a conclusion can be drawn from the work of Dubach et al, who reported that a considerable spontaneous increase in exercise capacity generally occurs up to 2 months after coronary bypass surgery.

It is interesting that the alteration of lipid profile relates better to the improvement in physical performance than changes in glucose metabolism. Previous studies showed that the increase in insulin resistance was related to a rise in triglyceride blood level.18

We consider that, in the case of our patients, physical training alone, and the diet only to a small extent, had an influence on this modification. This is suggested by the lack of change in BMI, which was, in fact, slightly higher at the final investigation. The information obtained from the questionnaire survey also indicates that during the rehabilitation course, the patients only partly adhered to dietary recommendations.

The observation time of 3 weeks is short, and the beneficial effects of physical training may be transient.19,20 The studies carried out by Björntorp et al in patients undergoing rehabilitation for 1 year after myocardial infarction indicated that a reduction in the insulin blood level is permanent. It would appear that this favorable effect of a decrease in resistance to insulin-mediated glucose disposal in patients after coronary bypass surgery can be also sustained throughout the continuation of physical exercise.

It is suggested that insulin resistance can be the underlying cause of other risk factors of coronary heart disease, such as arterial hypertension, obesity, type II diabetes (ie, non-insulin-dependent diabetes mellitus), hypercholesterolemia, and hypertriglyceridemia.5,21 This suggestion has not been accepted indisputably, and confirmation of these associations is needed from further studies.16 However, we cannot rule out the possibility that insulin resistance may intensify the development of atherosclerosis in coronary arteries, leading to ischemic heart disease, even if it does not influence the functioning of grafts. Thus, it seems that the issue of beneficial modification of insulin resistance is one of the arguments suggesting that endurance training on a bicycle ergometer may be useful for the secondary prevention of coronary heart disease in patients who have

### Table 3—Parameters of Carbohydrate Metabolism and Insulin Resistance Before and After the 3-Week Rehabilitation Course*

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Before Rehabilitation</th>
<th>After Rehabilitation</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose, mg/dL</td>
<td>111.2 ± 4.2</td>
<td>97.8 ± 3.5</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Insulin, μIU/mL</td>
<td>9.07 ± 1.03</td>
<td>10.98 ± 2.26</td>
<td>NS</td>
</tr>
<tr>
<td>C-peptide, ng/mL</td>
<td>2.38 ± 0.25</td>
<td>3.10 ± 0.45</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Insulin binding, pg $^{125}$I/10$^{11}$ RBC</td>
<td>0.535 ± 0.039</td>
<td>0.608 ± 0.042</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Insulin degradation, pg $^{125}$I/10$^{11}$ RBC</td>
<td>7.64 ± 0.54</td>
<td>9.49 ± 0.38</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

*Data are means ± SEM. NS = not significant.

### Table 4—Lipid Profile Before and After the 3-Week Rehabilitation Course*

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Before Rehabilitation</th>
<th>After Rehabilitation</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>213.5 ± 12.6</td>
<td>199.7 ± 10.3</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>125.7 ± 11.1</td>
<td>114.7 ± 8.6</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>53.2 ± 2.8</td>
<td>56.4 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Triglyceride, mg/dL</td>
<td>173.5 ± 19.9</td>
<td>165.1 ± 17.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Data are means ± SEM. LDL = low-density lipoprotein; HDL = high-density lipoprotein; NS = not significant.
undergone coronary bypass surgery, especially in patients with substantial pathology of the carbohydrate and lipid metabolism.

References