Effects of residential exercise training on heart rate recovery in coronary artery patients

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Effects of residential exercise training on heart rate recovery in coronary artery patients. Am J Physiol Heart Circ Physiol 292: H510–H515, 2007. First published September 15, 2006; doi:10.1152/ajpheart.00748.2006.—The aims of the present study are twofold: 1) to investigate whether heart rate recovery (HRR) after a cycle ergometry test is affected by exercise training and 2) to test the ability of HRR to replicate baroreflex sensitivity (BRS) changes that occur in response to an exercise training program in coronary artery patients. We randomized 82 coronary artery patients undergoing a residential cardiac rehabilitation program to an exercise training group (TR; n = 43) and an untrained group (UTR; n = 39). All of the patients underwent an exercise test before and after the rehabilitation program. HRR was recorded at the end of the 1st and 2nd min after exercise. BRS was determined at rest before and after treatment. HRR after the 2nd min was significantly improved in TR patients (from 3.2 ± 0.4 ms/mmHg; P < 0.001), whereas no significant change was evident in UTR patients (from 3.5 ± 0.4 ms/mmHg; P = 0.230). Our data show that HRR in the 2nd min after the cessation of a cycle ergometer exercise test increased in coronary artery patients after an exercise training period. This result confirms the positive effect induced by exercise training on HRR and extends the conclusions of previous studies to different modalities of exercise (i.e., cycle ergometry). HRR might provide an additional simple marker of the effectiveness of physical training programs in cardiac patients.

HEART RATE RECOVERY (HRR) after a bout of exercise has been defined as the reduction in rate from the peak exercise level to the rate in the recovery period after the cessation of exercise. Previous studies have clearly indicated that impaired HRR after an exercise test predicts mortality in survivors of an acute myocardial infarction (AMI) (2, 19, 24) and even in healthy subjects (12).

The rise in heart rate during exercise is considered to be due to the combination of parasympathetic withdrawal and sympathetic activation. The fall in heart rate immediately after exercise is considered to be a function of the reactivation of the parasympathetic nervous system (11).

Although the mechanism(s) by which impaired HRR confers an increased risk of death is not completely delineated, a blunted parasympathetic predominance in the recovery phase after exercise is widely considered to play a primary role.

Because exercise training is increasingly utilized for the management of patients after a cardiac event, HRR in these patients has also been a subject of interest (18). Previous studies have shown that treadmill exercise training in patients with cardiac diseases induces a significant increase in HRR (5, 23). However, the retrospective nature of these studies and lack of untrained control groups do not allow definitive conclusions. Moreover, no data exist, at least to our knowledge, on the effect of a cycle ergometry exercise on HRR. This is not a trivial point because 1) different effects among different modalities of exercise are possible and 2) in Europe cycle ergometry is used much more than is treadmill exercise in cardiac rehabilitation programs.

Consequently, in this study, we examined HRR after an incremental bicycle exercise test before and after cycling-based exercise training to address the main following question: Is HRR after a cycle ergometry test affected by exercise training in coronary artery patients?

In addition, it has been recently reported that HRR after treadmill exercise in dogs with experimentally induced myocardial infarction provides a prognostic marker of arrhythmia induction after the acute cardiac event (22). This finding is in line with the widely accepted concept that neural control of the heart, characterized by decreased vagal activity and relative sympathetic predominance, plays a major role in the occurrence of arrhythmic events during myocardial ischemia or infarction (16, 25).

Moreover, a large prospective trial has definitely indicated that reduced baroreflex sensitivity (BRS), which reflects primarily vagally mediated responses to rapid, transient changes in arterial pressure, carries a prognostic value for cardiac mortality and cardiac events after myocardial infarction (15). In accordance with these findings, our group (9) has shown that the baroreflex control of sinus node was significantly improved after exercise training in a group of patients with coronary artery disease.

Consequently, to acknowledge and propose the use of HRR as a useful estimate of autonomic nervous system function and in particular of the parasympathetic modulation of the sinus node, the present study also tested the ability of HRR to replicate BRS changes occurring in response to an exercise training program in coronary artery patients.

METHODS

The study population consisted of patients with coronary artery disease consecutively referred to our cardiac rehabilitation center. Patients had undergone coronary artery bypass grafting (CABG) on the basis of arteriographically documented coronary artery disease. All patients came from the same cardiac surgery division; therefore, the costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

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they shared the same surgical procedures and pre- and postoperative clinical management.

Criteria for eligibility were as follows: male patients and sinus rhythm and left ventricular ejection fraction >50%, as determined at preoperative cardiac catheterization and by echocardiographic examination before hospital discharge and at the rehabilitation center. Exclusion criteria were as follows: age >70 yr, coexisting valvular and/or peripheral vascular diseases, concomitant endoarterectomy, contraindications to exercise stress testing, frequent atrial or ventricular premature beats, conduction defects, insulin-dependent diabetes, arterial blood pressure >160/90 mmHg, pericarditis, peripheral neuropathy, orthopedic or neurological limitations, and perioperative AMI or any other serious postoperative complication.

The patients were admitted to the rehabilitation center during the first postoperative week and after the initial screening. They were randomly assigned to either a supervised, residential, exercise training program (TR) or to an untrained group (UTR).

Eighty-two patients (43 TR and 39 UTR) were enrolled and completed the study. In post-AMI patients, the time elapsed after myocardial infarction ranged from 9 to 2 mo. However, in 66% of patients, myocardial infarction occurred from 2 to 12 mo before the study. Clinical characteristics of the patients are summarized in Table 1. Medications were not altered throughout the study. All patients gave written, informed consent to participate to this study, which was approved by the Scientific and Ethical Committee of the rehabilitation center.

**Experimental protocol.** Fourteen to sixteen days after CABG, all of the patients underwent a functional (symptom-limited) incremental exercise test in an upright position on a bicycle ergometer (Corival 400; Lode) with monitoring of gas exchange (CPX). Exercise started with 1 min of unloaded pedaling at 60–70 rpm and increased by 20 W every 2 min. The recovery phase started with a workload reduction (40 W for the 1st min and 20 W successively). The patients were encouraged to maintain 60 rpm for the first two recovery minutes with a gradual reduction starting from the third recovery minute. A 12-lead ECG and oxygen consumption (Vmax 29 C; SensorMedics) were recorded continuously. At the end of the study, all patients repeated the symptom-limited exercise test with the same characteristics as those described above.

**Heart rate analysis.** Heart rate was monitored during the entire CPX. Midway through each stage of exercise, at the end of the stage, at peak exercise, and 1 and 2 min after the cessation of exercise, data on symptoms, heart rate, and blood pressure (as measured by indirect arm-cuff sphygmomanometry) were collected. HRmax was defined as the maximum heart rate value attained at peak exercise. %HRmaxT was defined as the percentage of the age-predicted HRmax (calculated as 220 – age) reached at peak exercise. The value for HRR was defined as the difference between heart rate at peak exercise and heart rate 1 min (HRR1) and 2 min (HRR2) after cessation of exercise.

**BRS assessment.** BRS assessment was made in the day before CPX at the entry and at the end of the training period. The recordings were performed as previously described (6–9). Briefly, patients were studied while resting supine in a quiet room at ambient temperature; patients were asked to relax and to avoid sleeping and talking. Recordings started after 10–15 min of acclimation and were continued for 10 min. Patients were connected to an analog multichannel signal conditioner and amplifier/filter (Marazza). The ECG signal was recorded from a precordial chest lead. Arterial blood pressure was continuously and noninvasively measured by Finapres (Finapres 2300, Ohmeda). This device has been proven to provide accurate estimates of changes of intra-arterial pressure during laboratory tests, including the BRS testing employed in the present investigation (20). The analog signals were sampled at 300 Hz per channel and stored on a hard disk for subsequent analyses.

BRS was dynamically assessed by the spontaneous baroreflex method (1). Details of this technique have been previously described (6–9). Briefly, the beat-by-beat time series of systolic arterial pressure (SAP) and R-R interval are scanned by a computer to identify sequences of three or more consecutive beats in which SAP and R-R interval change in the same direction (either increasing or decreasing). A linear regression is applied to each individual sequence, similar to the technique employing bolus injections of phenylephrine, and the mean slope of the SAP-R-R interval relationship, obtained by averaging all slopes computed within a given test period, is calculated and taken as a measure of the spontaneous BRS for that period. This method allows a quantification of the baroreceptor-cardiac reflex sensitivity at the current, prevailing levels of arterial pressure and R-R interval and reflects vagally mediated baroreflex responses (1, 17, 21).

Subjects in the control group continued to perform walking and calisthenics with the same daily schedule (2 daily sessions for 6 times/wk for 2 wk) as the TR group. The activity for the control group was not designed to improve cardiovascular performance. All sessions were held under the supervision of a cardiologist.

**Statistical analysis.** Differences in baseline characteristics between TR and UTR groups were evaluated by χ² and unpaired t-tests. Within-group changes in the reported variables were evaluated by paired t-test or Wilcoxon’s signed rank test for nonnormally distributed variables. Between-group comparisons were performed by unpaired t-tests and Mann-Whitney rank sum test. Relations between variables were assessed by a linear regression analysis. Data were expressed as means ± SE, unless otherwise specified. Statistical significance was assumed at P < 0.05.

**RESULTS**

There were no significant differences in the baseline characteristics between TR and UTR groups with respect to all
Table 2. Metabolic and cardiovascular results at baseline and after training

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<th>Trained</th>
<th>Untrained</th>
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<tr>
<td></td>
<td>Before</td>
<td>After</td>
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<tr>
<td>Peak V̇O₂, ml</td>
<td>1.287±0.385</td>
<td>1.468.6±0.478</td>
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<tr>
<td>ml·kg⁻¹·min⁻¹</td>
<td>17.4±0.4</td>
<td>20.0±0.5*</td>
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<tr>
<td>SAP, mmHg</td>
<td>118.8±2.1</td>
<td>124.4±2.8</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td>62.7±1.6</td>
<td>64.3±1.6</td>
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<tr>
<td>HR, beats/min</td>
<td>87.6±2.1</td>
<td>82.4±2.1†</td>
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Values are means ± SE. V̇O₂, oxygen uptake; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; HR, heart rate. *P < 0.001 vs. baseline.

variables, including peak oxygen uptake (V̇O₂), arterial pressure, heart rate (Tables 1 and 2), and BRS (3.2 ± 0.3 ms/mmHg for TR vs. 3.5 ± 0.4 ms/mmHg for UTR; not significant). In addition, the cardiovascular drugs used in our patients did not result in significant differences in the two experimental groups (Table 1), as determined by χ² tests.

Exercise training resulted in a significant increase in peak V̇O₂ (Table 2). A small increase in peak V̇O₂ was also observed in the UTR group, confirming that even a reduced amount of daily physical activity, compared with the TR group, and also in part a normal recovery from surgery might contribute to this functional improvement. However, the magnitude of the V̇O₂ increase was significantly and markedly greater in the TR group (176.9 ± 27.6 vs. 68.7 ± 18.9 ml/min; P = 0.001). In TR patients, resting heart rate was significantly reduced (~6%), whereas no significant changes were observed in UTR patients (Table 2).

Both experimental groups showed a similar pattern of cardiovascular and functional responses to the exercise test both before and after the cardiac rehabilitation program (Table 3). In particular, the workload reached by the two groups was similar at baseline and showed a similar increase after the cardiac rehabilitation program. Also, HRmax, T attained during the exercise test, expressed both as absolute values and in terms of %HRmax,T, was similar at baseline, showing similar increases in the two groups after the rehabilitation program. As expected, heart rate showed significant decreases in the 1st and 2nd min of recovery after the cessation of exercise in both TR and UTR patients (Fig. 1) in baseline conditions and after the rehabilitation program.

In particular, HRR2 after the cessation of exercise was significantly and substantially greater in TR than in UTR patients at the end of the training (Fig. 2, bottom).

BRS increased significantly in TR patients after the training program (from 3.2 ± 0.3 ms/mmHg at baseline to 5.3 ± 0.8 ms/mmHg after the rehabilitation program; P < 0.001), whereas no significant changes were evident in UTR patients (from 3.5 ± 0.4 ms/mmHg at baseline to 4.0 ± 0.4 ms/mmHg after the rehabilitation program; P = 0.230).

We did not show significant correlations between HRR and BRS changes in response to the cardiac rehabilitation program, except for a weak but significant correlation for TR patients between HRR1 and BRS (r = 0.3, P = 0.046).

DISCUSSION

Our data show that in patients with coronary artery disease HRR is significantly greater in TR than in UTR patients after 2 wk of a cardiac rehabilitation program, suggesting that exercise training with a cycle ergometer can improve HRR in this group of patients. The relevance of this finding should be placed in the context of the growing evidence indicating the adverse effect of a reduced HRR. This is the first study, to our knowledge, that suggests a role for HRR as a marker of the effectiveness of cycle ergometer exercise training within a program of cardiac rehabilitation in coronary artery patients.

Two recent reports showed that exercise training within a structured program of cardiac rehabilitation was associated with a significant increase in HRR (5, 23) in patients with coronary artery disease. Klighfield et al. (14) extended the evaluation of heart rate in the recovery phase after exercise in response to bouts of submaximal exercise, confirming that also in these conditions exercise training within structured programs of cardiac rehabilitation produces a significant increase of HRR.

However, some peculiar features of our study compared with these previous reports deserve comments to disentangle its novelty and originality. Whereas the latter was not structured as case-control studies, in our study, the responses of TR patients have been compared with those obtained in a similar group of patients performing no exercise training or alternatively a minimal level of physical activity, the latter thereby functioning as the control group (UTR patients).

Because patients resided at the Cardiac Rehabilitation Division, we were able to control the level of physical activity along with all the clinical characteristics (i.e., drugs, diet, health condition, etc.) of both experimental groups during the whole duration of the study. This aspect is particularly relevant for the therapy. It is well known that various cardiovascular drugs may interfere with the control of sinus node (e.g., β-blockers, calcium antagonists, etc.). For these reasons, we enrolled only patients who did not modify their therapy during

Table 3. Cardiovascular responses to exercise tests at baseline and after rehabilitation program

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<th>Trained</th>
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<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>HRmax, beats/min</td>
<td>129.6±2.0</td>
<td>134.0±2.0†</td>
</tr>
<tr>
<td>HRmax,T, %</td>
<td>80.2±1.1</td>
<td>83.2±1.2†</td>
</tr>
<tr>
<td>Maximum workload, W</td>
<td>82.3±2.8</td>
<td>95.8±3.1†</td>
</tr>
<tr>
<td>Maximum SAP, mmHg</td>
<td>179.2±3.6</td>
<td>187.0±3.3*</td>
</tr>
<tr>
<td>Maximum DAP, mmHg</td>
<td>85.9±1.8</td>
<td>91.2±2.2*</td>
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Values are means ± SE. HRmax,T, percentage of the predicted maximum heart rate reached during the stress test. *P < 0.05; †P < 0.001 vs. baseline; ‡P < 0.05 vs. untrained.
the duration of the study. Furthermore, as shown in Table 1, no significant difference existed between the cardiovascular drugs used by TR and those used by UTR patients.

Our results clearly show that, despite similar clinical characteristics and similar levels of effort attained during the stress tests, as evidenced by similar levels of maximum workload and HR_max (Table 3), TR patients had a greater heart rate reduction during HRR2 than did UTR patients after training (Fig. 2). This finding clearly supports a direct effect on HRR exerted by training.

Thus this is the first randomized, controlled study showing that exercise training results in an improvement of HRR in coronary artery patients. Moreover, this is the only study, to date, to investigate the effectiveness of a stationary cycling training on HRR. This would be relevant inasmuch as in most European countries cycle ergometry is used more than treadmills in exercise-based cardiac rehabilitation programs.

Two considerations led us to compare in our patients the BRS and HRR responses in a period of exercise training within the structured program of cardiac rehabilitation. First, our laboratory (9) previously demonstrated in a similar group of patients that baroreflex control of sinus node is improved after an exercise training program. Second, BRS and HRR share similar pathophysiological mechanisms, reflecting primarily vagally mediated responses to rapid, transient changes in arterial pressure (1, 11, 17, 21). In particular, the sudden restoration of vagal activity ensuing from removal of central command and from restoration back to the level at rest of BRS (8, 10) on cessation of exercise might provide the functional basis for HRR.

Fig. 1. Heart rate recovery (HRR) at the 1st (REC 1) and 2nd (REC 2) min after the cessation of exercise for each individual subject before (top) and after (bottom) the cardiac rehabilitation in coronary artery patients who had undergone (trained; n = 43) and not undergone (untrained; n = 39) the exercise training program. Black stars show the group mean value at peak exercise (PEAK EXE) and at REC 1 and REC 2. *P < 0.05 vs. PEAK EXE; §P < 0.05 vs. REC 1.

Fig. 2. Bars show the reduction in heart rate from the peak exercise level to the recovery period (HRR) in the 1st min (top) and in 2nd min (bottom) after the cessation of exercise in trained (hatched bars) and untrained (black bars) coronary artery patients before (PRE) and after (POST) the cardiac rehabilitation program. Data represent group mean values ± SE. *P < 0.05 vs. untrained coronary artery patients.

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Only a weak correlation was found between BRS and HRR changes after a period of exercise training in our coronary artery patients despite two parameters, when considered separately, showing an increase in response to exercise training (Ref. 9 and present data). Although we do not have direct experimental evidence explaining this lack of correlation, we can try some speculations.

In our experimental design, we compare the BRS calculated during a relatively long time (~10 min for each recording) with HRR calculated in 2 min after the peak of exercise. Because of these different conditions, we could imagine that the two parameters provide parallel but complementary information about the vagal modulation of sinus node, which is widely considered as a physiological marker of the positive effect and of the real effectiveness of an exercise training program in cardiac patients. Whereas the vagally mediated heart rate responses to spontaneous blood pressure fluctuations, as expressed by BRS, likely concern a “homeostatic” vagal modulation of sinus node, the abrupt rise of the parasympathetic discharge to the sinus node, which causes the drastic heart rate reduction in the immediate recovery phase after the peak exercise, should be caused by a “dynamic” modulation of sinus node in response to a cardiovascular challenge. This difference could have weakened in some way the correlation showed in our study. However, the opportunity to easily investigate different aspects of the vagal modulation of sinus node during exercise could be particularly interesting because of the great pathophysiological role of the parasympathetic modulation of sinus node (12, 13, 15).

Moreover, a strong respiratory modulation has been observed in the cardiac vagal outflow (4) in humans. The respiratory activation in the immediate recovery phase after exercise, when we calculated HRR, compared with the basal conditions, when we calculated BRS, might have contributed to the weak correlation, as calculated by linear regression analysis.

Nonetheless, this is the first study that addressed the ability of HRR to parallel a well-known estimate of the autonomic nervous system function, that is, BRS, a widely accepted marker of the vagal control of the sinoatrial node. Our study, by showing significant and parallel increases of BRS and HRR in trained vs. untrained patients, provides evidence, although indirectly, that HRR can also be considered a useful marker of the effect of exercise training on autonomic cardiac modulation in coronary artery patients undergoing exercise-based cardiac rehabilitation programs.

This is important because the introduction of a further simple and noninvasive marker of cardiac neural regulation provides an additional tool to investigate the effect of exercise training on the autonomic cardiac modulation also in consideration of the paramount role exerted by the parasympathetic modulation of sinus node in the prognostic evaluation of coronary artery patients (12, 13, 15).

Some possible limitations of the present investigation deserve comment. The first is the generalization of the reported effects to other patient populations with coronary disease, namely, those who have not undergone CABG. However, we speculate that the benefits of exercise training would extend to patients who have not undergone CABG but are eligible for a formal exercise training program; no data indicate whether CABG per se could affect the HRR in response to an exercise stress test in patients without AMI or in the recovery phase after AMI. Consistent with this assumption is the lack of a significant increase in HRR, at least in the 2nd min of recovery, after the end of the exercise test in the control group. In any event, the patients of the present study were representative of a large population of ischemic patients, for whom cardiac rehabilitation is highly recommended (3) and who could benefit from improved cardiac autonomic function.

Second, we do not know whether the increase in HRR caused by exercise training actually affects the outcome in terms of prognosis of coronary artery patients. However, the present study was not designed for this purpose; rather, it is aimed at addressing the question of whether exercise training is able per se to increase HRR, a marker whose reduction has been shown to carry a poor prognosis in ischemic heart disease (2, 19, 24). The answer to this question is positive. As a matter of fact, the increase in HRR goes in a direction that would be associated with a better outcome in coronary patients (2, 18, 23). However, the potential of HRR enhancement after an exercise training program to improve the risk profile in patients with coronary artery disease remains to be demonstrated. This would require a large, multicenter trial. Nevertheless, among the many beneficial effects of exercise training in secondary prevention of ischemic heart disease, the improvement in HRR should be considered.

Finally, our study was limited to patients with preserved systolic function (ejection fraction >50%); thus we do not know whether these HRR behaviors can also be extrapolated to coronary artery patients with depressed systolic function involved in cardiac rehabilitation programs.

In conclusion, our data show that HRR in the 2nd min after the cessation of a cycle ergometer exercise test increased in coronary artery patients after an exercise training program. This result confirms the positive effect induced by exercise training on HRR and extends the conclusions of previous studies to different modalities of exercise (i.e., cycle ergometer).

The evaluation of HRR after exercise might provide an additional simple marker of the effectiveness of physical training programs in cardiac patients undergoing cardiac rehabilitation. In fact, HRR is a more straightforward and easily obtained measurement than is BRS, heart rate variability, or other indexes of cardiac vagal tone because it requires less time for data collection and no data processing algorithms.

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REFERENCES


EXERCISE TRAINING AND HEART RATE RECOVERY


