Effects of exercise training on heart rate recovery in patients with chronic heart failure

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Background Heart rate recovery (HRR) is a marker of vagal tone that is associated with survival, but little is known about the effects of exercise training on HRR in patients with heart failure (HF).

Methods Twenty-four patients with HF were randomized to a 2-month residential rehabilitation program or to usual care. Symptom-limited exercise testing was performed at baseline and at discharge from the program. Heart rate recovery was expressed as the decline in heart rate from peak exercise through 6 minutes into recovery. In addition, HRR recovery curves were normalized to a range of 1 at peak heart rate and 0 at 6 minutes and adjusted for differences in heart rate reserve, facilitating the comparison of recovery curve shapes between groups.

Results Mean peak oxygen uptake and oxygen uptake at the lactate threshold increased 26% ($P < .05$) and 39% ($P < .001$), respectively, in the exercise group, whereas neither of these responses changed significantly among controls. Heart rate recovery was significantly more rapid in the exercise group after training (main effect 12.6 vs 2.6 beat/min in the trained and control groups, respectively, $P = .005$). The normalized curves showed that the largest improvement in recovery curve shape occurred in the exercise group, but most of the HRR improvement was accounted for by a widening of the difference between peak and resting heart rate.

Conclusion Exercise training results in a faster HRR in patients with HF. Heart rate recovery, as a simple marker of autonomic function, is an easily acquired response that may be useful for evaluating patient outcomes in cardiac rehabilitation. (Am Heart J 2007;153:1056-63.)

Autonomic nervous system (ANS) imbalance is associated with mortality in patients with cardiovascular disease.[1] The heart rate response to, and recovery from, a bout of exercise is mediated by the dynamic interaction between the sympathetic and parasympathetic components of the ANS.[1,2] Specifically, greater sympathetic tone predominates as heart rate increases during exercise, and vagal reactivation mediates the rate at which heart rate recovers after exercise. A growing body of studies in recent years has shown that the rate at which heart rate recovers from exercise (termed *heart rate recovery*, or *HRR*) is associated with all-cause and cardiovascular mortality.[1,3-6]

The better survival associated with a more rapid HRR is thought to reflect higher vagal tone commonly linked to better fitness and cardiovascular health.[1] A particularly large number of recent studies have demonstrated an association between autonomic imbalance and poor outcomes in patients with chronic heart failure (HF).[7,8] In addition to the numerous physiologic benefits of cardiac rehabilitation in patients with HF, exercise training has been associated with higher vagal tone.[9-11] However, the application of HRR as a marker for improved cardiovascular health in the context of cardiac rehabilitation has not been fully explored. Heart rate recovery could potentially represent a simple, noninvasive tool to identify high-risk patients and assess patient outcomes during cardiac rehabilitation.

Previous studies on HRR have generally compared only the heart rate at a given point in recovery (eg, 1 or 2 minutes) before and after training or between patients with favorable versus poor outcomes. Some investigators have theorized that the transition processes from sympathetic control of heart rate at peak exercise to vagally mediated heart rate at rest is reflected in the shape of the HRR curve, providing additional insight into autonomic balance and the degree of risk.[12-14] Previous studies investigating the effects of exercise training on HRR have not incorporated the potentially important information contained in the entire recovery period. In addition, it is well known that training widens the heart

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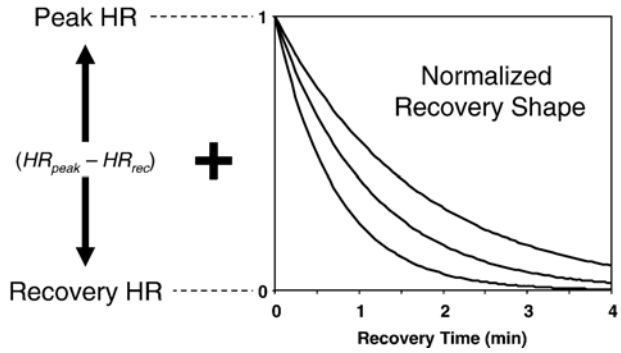
Table I. Baseline characteristics

	Exercise group (n = 12)	Control group (n = 12)
Age (y)	56 ± 5	55 ± 7
Height (cm)	173 ± 7	169 ± 5
Weight (kg)	76.9 ± 7.5	71.5 ± 10.2
Ejection fraction (%)	31.5 ± 6.7	34.6 ± 4.1
Forced vital capacity (% normal)	88.8 ± 11	84.2 ± 20
Medications (n)		
Digoxin	8	6
ACE inhibitor	12	11
Diuretic	6	6
Other	3	5
MI (n)		
Anterior	6	6
Inferior	4	3
Posterior	2	2
Risk factor (n)		
Smoking	11	10
Diabetes mellitus	1	0
Hyperlipidemia	7	4
Hypertension	7	4
Family history of CAD	7	8
Procedure (n)		
PCI	2	1
CABS	9	10

ACE, Angiotensin-converting enzyme; *CAD*, coronary artery disease; *PCI*, percutaneous coronary intervention; *CABS*, coronary artery bypass surgery.

Figure 1



Example of the calculation of the normalized HRR curves.

rate reserve (the difference between peak and resting heart rate), which has been suggested to have a significant effect on HRR and the shape of the HRR curve.[12,15,16] The purpose of the current study was to characterize the effects of a concentrated, high-intensity residential exercise training program on HRR and the shape of the HRR curve in patients with HF.

Methods

Patients

Twelve male patients (mean age 56 ± 5 y) were randomized to an exercise group, and 12 male patients (mean age 55 ± 7 y) were randomized to a control group (Table I). All had sustained a myocardial infarction (MI), and the hospital course in all patients included the diagnosis of HF. The presence of HF was documented by signs, symptoms, and an angiographically determined ejection fraction <40%. All were limited by fatigue or dyspnea on baseline exercise testing, and none had clinical evidence of pulmonary disease. Written informed consent was obtained, and all patients had stable symptoms for at least 1 month before randomization.

Exercise training

After stabilization and initial testing, patients in the exercise group resided in a rehabilitation center in Seewis, Switzerland, for a period of 8 weeks. The center has its own staff of physicians, consisting of a medical director and 3 interns/residents. Program components included education, exercise, and low-fat meals prepared by the center's cook. Two outdoor walking sessions daily for a duration of approximately 1 hour were performed, once in the morning and once in the afternoon. To facilitate monitoring, walking groups were stratified into 4 levels based on clinical status, exercise capacity, and performance on a 500-m walking test (50-m increase in altitude) on a nearby hill. Target exercise heart rates were individualized and monitored for each subject. The patients were accompanied by a physician and exercise leaders during these walking sessions. A van equipped with emergency equipment remained near the group.

In addition to these walking periods, the patients performed four 45-minute periods of monitored stationary cycling per week. The cycling sessions were designed to elicit an intensity of roughly 60% to 80% of the patient's heart rate reserve and were increased progressively as tolerated. Control patients received usual care.

Exercise testing

Before randomization, each patient performed a preliminary exercise test to help ascertain clinical stability and to habituate the patients to the testing procedure and gas exchange apparatus. Maximal exercise testing was performed on an electrically braked cycle ergometer using an individualized ramp protocol. Briefly, this test entailed choosing an individualized ramp rate to yield a test duration of approximately 10 minutes.[17] A 12-lead electrocardiogram was monitored continuously, and blood pressure was measured manually every minute during exercise and throughout the recovery period. The patient's subjective level of exertion was quantified every minute using the Borg 6-20 scale.[18] All tests were continued to volitional fatigue/dyspnea; no patients were limited by angina.

Respiratory gas exchange variables were acquired continuously throughout exercise using the Schiller CS-100 metabolic system (Baar, Switzerland). The gas exchange data were obtained breath-by-breath and expressed as rolling 30-second averages printed every 10 seconds. Blood was sampled each minute using an indwelling arterial catheter, and plasma was separated immediately for analysis. The lactate threshold was determined visually by consensus between 2 experienced reviewers (blinded to group and pre-/posttest identity) using a computerized plot of the oxygen uptake versus lactate relationship.

Table II. Exercise test responses (mean ± SD)

	Exercise group (n = 12)		Control group (n = 12)		
	Baseline	**Post**	**Baseline**	**Post**	***P****
Rest					
Heart rate (beat/min)	84 ± 17	73 ± 16	8 ± 13	79 ± 15	.84
Systolic BP (mm Hg)	128 ± 15	131 ± 13	128 ± 20	124 ± 22	.46
Diastolic BP (mm Hg)	73 ± 12	74 ± 10	74 ± 12	68 ± 10	.28
Lactate threshold					
Heart rate (beat/min)	117 ± 18	113 ± 19	115 ± 16	107 ± 13	.70
Systolic BP (mm Hg)	152 ± 20	161 ± 14	157 ± 25	148 ± 19	.18
Diastolic BP (mm Hg)	85 ± 13	82 ± 18	84 ± 12	79 ± 12	.77
Oxygen uptake ($mL \cdot kg^{-1} \cdot min^{-1}$)	13.6 ± 2.8	18.9 ± 2.3†	13.5 ± 3.1	11.5 ± 1.9	<.001
Oxygen uptake (L/min)	1.063 ± 0.233	1.437 ± 0.199†	0.963 ± 0.243	0.829 ± 0.160	<.001
Minute ventilation (L/min)	31.8 ± 7.0	40.4 ± 6.0‡	28.9 ± 7.9	24.2 ± 3.8	.001
V_{CO_2} (mL/min)	952 ± 237	1329 ± 225‡	956 ± 366	735 ± 157	<.001
RER	0.89 ± 0.09	0.92 ± 0.06	0.97 ± 0.14	0.90 ± 0.07	.11
Workload (watts)	69.7 ± 18	105.1 ± 17†	64.2 ± 28	56.2 ± 15	.001
Perceived exertion	10.5 ± 2.4	9.7 ± 1.6	11.2 ± 2.2	11.3 ± 1.7	.40
Maximal exercise					
Heart rate (beat/min)	144 ± 23	151 ± 24	141 ± 18	139 ± 16	.46
Systolic BP (mm Hg)	170 ± 24	178 ± 24	175 ± 30	174 ± 23	.51
Diastolic BP (mm Hg)	86 ± 14	87 ± 18	89 ± 11	90 ± 17	.99
Oxygen uptake ($mL \cdot kg^{-1} \cdot min^{-1}$)	19.7 ± 3.2	24.8 ± 4.7‡	18.8 ± 4.3	18.8 ± 4.6	.04
Oxygen uptake (L/min)	1.513 ± 0.258	1.873 ± 0.396‡	1.334 ± 0.284	1.323 ± 0.310	.05
Minute ventilation (L/min)	65.1 ± 12.3	78.5 ± 10.8‡	52.1 ± 10.9	49.7 ± 11.7	.02
V_{CO_2} (mL/min)	1792 ± 321	2261 ± 444‡	1644 ± 366	1562 ± 418	.02
RER	1.19 ± 0.13	1.21 ± 0.06	1.23 ± 0.12	1.18 ± 0.12	.23
Workload (watts)	129.0 ± 21	171.9 ± 28†	115.2 ± 28	117.4 ± 32	.01
Perceived exertion	18.7 ± 0.98	18.9 ± 0.90	19.0 ± 0.95	18.7 ± 0.98	.30
Exercise time (min)	9.4 ± 1.7	12.3 ± 1.7†	9.0 ± 2.2	9.1 ± 1.7	<.01

BP, Blood pressure; *RER*, respiratory exchange ratio.
*Represents *P* value from group/test interaction.
†$P < .01$, versus baseline within group.
‡$P < .05$, versus baseline within group.

Heart rate recovery

Heart rate was measured supine, standing, during each minute of exercise, at maximum exercise, and during active recovery (zero load) at minutes 1 through 6. The HRR curves were divided into 2 elements: a normalized recovery curve that characterizes how quickly peak heart rate (HR_{peak}) recovers to a posttest resting rate and an amplitude scaling term defined by the difference between HR_{peak} and the postexercise resting heart rate as described previously.[12] This is illustrated in Figure 1. To compare the shape of the normalized recovery curves, HRR was standardized to a uniform range of 1.0 at HR_{peak} and zero at 6 minutes into recovery (HRR_6). Heart rate recovery at 6 minutes into recovery was subtracted from each HRR value, and the difference was divided by ($HR_{peak} - HRR_6$). This normalization process supports the comparison of the shape of the recovery curve independent of the amplitude scaling factor related to changes in peak and resting heart rates.

Statistics

NCSS (NCSS, Kayesville, UT) was used to perform multivariate analysis of variance (ANOVA) procedures comparing exercise, recovery, and ventilatory gas exchange responses between groups. This procedure considered both inter- and intragroup comparisons and interactions among the factors (group and test) for each dependent variable. Post hoc multiple comparison procedures were performed using the Bonferroni method. Clinical and demographic data were compared using unpaired *t* tests and χ^2 analyses. Normalized HRR curves between exercise and control groups were compared using multivariate ANOVA with group and test as independent factors. Data are expressed as mean ± SD.

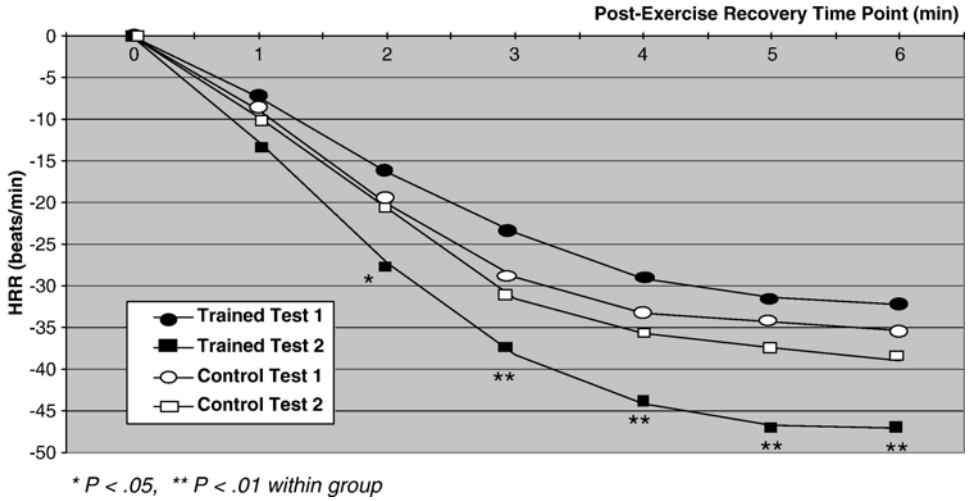
Results

No differences were observed between groups initially in clinical or demographic data, including age, height, weight, resting blood pressure, pulmonary function, ejection fraction, or maximal oxygen uptake (Table I).

Maximal exercise testing

Both groups achieved maximal respiratory exchange ratios of approximately 1.20 and perceived exertion levels of approximately 19 on both tests, suggesting that maximal efforts were generally achieved (Table II). No patient in either group was limited by angina, and none exhibited electrocardiographic evidence of ischemia during baseline exercise testing. The exercise group

Figure 2



The effects of exercise training on HRR in the trained and control groups.

demonstrated a 29% increase in maximal oxygen uptake (19.7 ± 3.2 to 24.8 ± 4.7 mL·kg^{-1}·min $^{-1}$, P = .04 between groups). Concomitant increases in maximal minute ventilation, CO_2 production, exercise time, and watts achieved were observed in the exercise group. No differences between tests were observed among control patients in maximal oxygen uptake, exercise time, or watts achieved.

Oxygen uptake at the lactate threshold increased by 39% in the exercise group, whereas a small decrease was observed among controls (P < .001 between groups). Similar increases in exercise time and watts achieved at the lactate threshold were observed among patients in the exercise group, whereas no differences were observed in these responses in the control group. No differences were observed within or between groups for heart rate, systolic or diastolic blood pressure, respiratory exchange ratio, or perceived exertion at this point.

Heart rate recovery

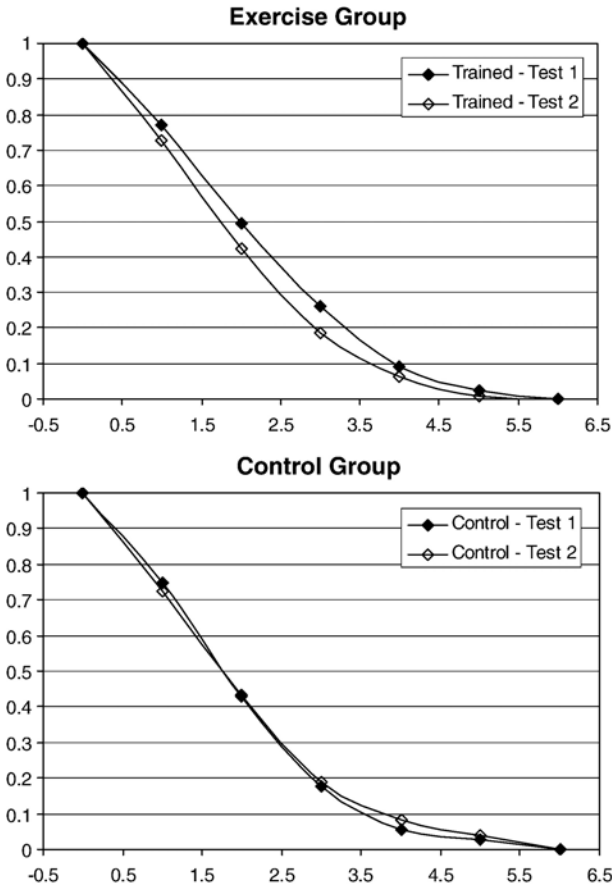
Heart rate recovery was significantly faster in the exercise group for minutes 2 to 6 after training (ANOVA main effect in trained subjects 12.6 beats/min, P < .001; main effect among controls 2.6 beats/min, P = .27; between-group interaction P = .005; pooled variance 15.7 beats/min). Among trained subjects, the faster HRR was more pronounced as the recovery period progressed; heart rate was 5.4, 10.9, 14.6, 15.1, 15.4, and 14.8 beats/min lower at minutes 1 through 6, respectively, after training in the exercise group. Heart rate in the control group did not change significantly at any of the individual minutes in recovery (Figure 2).

The exercise group was characterized by a slight but systematic increase in the slope of the normalized recovery curve (ie, faster recovery) after training, evident at 1 minute and continuing throughout the recovery period (change in overall slope 0.72 to 0.76, not significant) Figure 3). Among control subjects, the curves for the pre- and posttests were closely matched throughout recovery (slopes 0.75 and 0.75 for the pre- and posttests, respectively). At 2 minutes, the normalized curve improved from 0.51 to 0.44 for the exercise group and remained unchanged among controls (0.57 to 0.57). Multiplying the difference in the normalized shapes by the scaling term (HR_{peak} − HRR_6) from test 2 provided an estimate of the contribution to improving HRR from changes in the shape of the recovery curve.[12] Table III summarizes the results for HRR at 2 minutes. Thirty percent of the improvement in HRR for the exercise group was contributed by an improvement in the shape of the recovery curve, whereas there was no contribution to HRR by the change in the shape of the curve among controls. The remaining difference in HRR between the pre- and posttests (70% for the exercise group) was the result of a widening of the heart rate reserve (reduced resting heart rate and higher HR_{peak} between the baseline and 2-month exercise tests).

Discussion

The ability of heart rate to recover after exercise is related to the capacity of the cardiovascular system to reverse ANS (withdrawal of vagal activity) and baroreceptor (detection of changes in blood pressure

Figure 3



Normalized HRR responses in the exercise (top) and control (bottom) groups for minutes 1 to 6 in recovery. The differences in the shapes of the curves did not differ within or between groups.

and inhibition of sympathetic discharge) adaptations that occur during exercise, often termed *vagal reactivation*.[13,19] The association between HRR and cardiovascular health is underscored by the long-established observation that recovery of heart rate is faster in athletes[13] and the fact that autonomic imbalance, principally a deficiency in vagal tone, is associated with mortality.[1,8,11] Presumably because of impaired vagal reactivation, HRR has been widely recognized in recent years as a powerful marker of prognosis in patients with cardiovascular disease.[3-6,20] Because of the strong association between HRR and mortality,[3-6,12,20] and the link between HRR and exercise capacity or physical activity patterns,[1,11,21] HRR has the potential to be an additional marker of training efficacy and risk stratification in patients undergoing cardiac rehabilitation.

In the current study, a sizable training effect was evidenced by 26% and 39% increases in VO_2 at peak exercise and the lactate threshold, respectively, whereas controls showed no changes in exercise capacity. These adaptations were larger than in most previous studies on HF,[22] which is likely explained by the comparatively high training stimulus associated with the residential program. The improvement in exercise capacity was associated with a more rapid HRR after training; the ANOVA main effect from minutes 1 to 6 in recovery was a reduction of 13 beats/min, with HRR $\approx$15 beats/min faster at minutes 3 through 6. This degree of improvement in HRR would have a marked effect on mortality risk based on recent studies.[1,3-6] We recently observed a 3% reduction in all-cause mortality per (faster) beat at 2 minutes in recovery.[23] The present results therefore suggest that training may have a considerable effect on outcomes in patients with HF via altered vagal modulation. The fact that the improvement in HRR among patients randomized to the exercise training group was correlated with the degree of increase in peak VO_2 (r = 0.59 at 2 minutes, P = .04) and the increase in VO_2 at the lactate threshold (r = 0.70, P = .03) further suggests a link between aerobic capacity and HRR.[1,11,21]

Comparison of HRR curves

Previous studies addressing the association between HRR and mortality have generally been limited to a single time point in recovery (eg, 1 or 2 minutes) and have ignored the potentially important information contained in the shape of the HRR curve. To our knowledge, no studies have assessed the effects of *training* on the HRR curve. In theory, a curve fit to HRR data offers the potential to both minimize the error associated with a single estimate and to leverage information that may be contained in the overall shape of the curve. Because it has recently been suggested that recovery heart rate is significantly affected by heart rate reserve (eg, a rapid HRR is associated with a comparatively low resting heart rate higher heart rate achieved),[12,15,16] we were interested in the effect training would have on the relation between heart rate reserve and HRR. We therefore decomposed HRR into 2 elements: a normalized recovery curve that defines how quickly HR_{peak} recovers to a stable posttest resting rate and an amplitude term defined by the difference between peak and resting recovery heart rate ($HR_{peak} - HRR_6$).[12] This decomposition provided a method to uniformly compare HRR curve shapes for patients with significantly different heart rate reserves.

Training increased HR_{peak} by 7 beat/min and decreased supine resting heart rate by 11 beat/min in the exercise group (a widening of 18 beat/min in the heart rate reserve). The comparison changes in the control group were a decrease of 2 beat/min at peak exercise and a decrease of 9 beat/min at rest (a widening of 7 beat/min in the heart rate reserve). Although the normalized HRR curve was slightly more rapid after

Table III. Contributions to HRR at 2 minutes from changes in normalized recovery shape and amplitude scaling associated with a widening range between peak and resting heart rate

	HRR (2 min)			Peak HRR (6 min)		Contributions to increasing HRR (2 min)			
Group	Test 1	Test 2	Increase	Test 1	Test 2	Shape		Scaling	
Exercise	16.3	27.2	10.8	32.2	47.0	3.3	30%	7.5	70%
Control	20.1	22.0	1.9	35.3	38.9	−0.2	−9%	2.1	109%

In the exercise group, recovery curve shape changes accounted for a larger percentage of the contribution to total HRR relative to the control group. The largest contribution to improving HRR for both groups was increasing amplitude scaling.

training in the exercise group, the fact that the curves did not differ between the exercise and control groups (Figure 3) suggests that the improved HRR after training (Figure 2) is largely attributable to the wider heart rate reserve observed in the trained group. By normalizing HRR and using a scaling term throughout the recovery period ($HR_{peak} - HRR_6$),[12] we observed that 70% of the change in HRR was attributable to a greater heart rate reserve after training. This is in accordance with the observations of Desai et al,[15] who reported that abnormal HRR in patients with coronary artery disease was explained almost entirely by an impaired heart rate response *during* exercise. Similarly, Racine et al[16] reported that when HRR was normalized by heart rate reserve, there was virtually no difference between healthy subjects and patients with HF; HR_{peak} achieved appeared to be the primary determinant of HRR. Hadley et al[12] also observed that HRR was strongly correlated with heart rate reserve. In a multivariate model, none of several HRR measurements were significant predictors of either cardiovascular or all-cause mortality; only heart rate reserve was associated with these outcomes.

The comparison of HRR curves in the present study was novel and requires confirmation by larger randomized trials. Our findings suggest that the improvement in HRR after training is attributable at least in part to a widening of the heart rate reserve but do not negate the potential influence of training on autonomic balance. An increase in vagal tone after training is implied by the reduction in resting heart rate, and the higher HR_{peak} suggests enhanced sympathetic drive, lowered vagal influence, or both at peak exertion. These results indicate, however, that heart rate reserve should be considered when applying HRR to assess the effects of training or stratifying risk in patients with cardiovascular disease.

Previous studies on training and HRR

The effects of training on autonomic tone, baroreflex sensitivity, and heart rate variability (HRV) have been widely studied in animal models, and these studies suggest that exercise training provides a nonpharmacologic benefit to cardiac autonomic control.[9,24-26] In conscious dogs, training increases HRV and baroreflex sensitivity and reduces the susceptibility to experimentally-induced ventricular fibrillation.[26,27] Numerous investigators have observed that exercise training in patients with cardiovascular disease increases HRV.[11,28] Baroreflex sensitivity, measured using heart rate and systolic blood pressure variability after phenylephrine infusion or by the spontaneous baroreflex technique, has been shown to increase after programs of cardiac rehabilitation.[29,30] However, no studies to our knowledge have reported changes in HRR along with these indices of autonomic function before and after training.

Although faster HRR has long been associated with higher levels of fitness,[31] few data are available regarding HRR in patients with cardiovascular disease undergoing training. Tiukinhoy et al[32] observed that HRR was 18 beats/min faster 1 minute into recovery after 12 weeks of rehabilitation among patients after a cardiac event. Hao et al[33] reported modest (3-6 beats/min) improvements in HRR 1 minute into recovery (using a walking cool-down protocol) among both elderly and younger patients referred to a 12-week rehabilitation program. Kligfield et al[34] demonstrated that 1-minute-postexercise HRR was more rapid (by 2-4 beats/min) in response to submaximal activity after 12 weeks of rehabilitation. Streuber et al[35] reported that HRR 1 minute postexercise improved by 5 beats/min after 12 weeks, but the improvement was only observed among those with the lowest initial exercise capacity. Similarly, Giallauria et al[36] reported that HRR 1 minute postexercise improved by approximately 6 beats/min after 3 months of training after MI. To our knowledge, the recent study of Dimopoulos et al[37] is the only analysis of training and HRR in patients with HF. Heart rate recovery was compared between subjects randomized to 36 sessions of continuous (n = 14) or interval (n = 10) training. At 1 minute postexercise, HRR improved (by 9 beats/min) only among subjects in the continuous training group, whereas HRR in the interval group did not differ between evaluations. Similar to these previous studies, we observed an improvement of 5.4 beats/min at 1 minute into recovery after training; however, a more dramatic improvement in HRR occurred later into recovery, with training having an overall improvement on HRR of $\approx$13 beats/min

(Figure 1). Differences between these studies may be explained by differences in HRR measurement points, whether patients performed a cool-down walk, and the training stimulus used.

Limitations

Our study sample size was small and included only patients with HF with an ischemic etiology after MI or bypass surgery; the responses may not be applicable to the wider population of patients with HF. In addition, the training program was intensive, and the adaptations we observed in our residential program may not occur in more conventional outpatient programs.

Summary

Heart rate recovers more rapidly after exercise after a concentrated, intensive program of exercise training in patients with HF. Most of the improvement in HRR was associated with a widening of the difference between resting and peak exercise heart rate. Nevertheless, HRR, as a simple marker of autonomic function, is an easily acquired response that may be useful in identifying high-risk patients and for evaluating patient outcomes in cardiac rehabilitation.

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