Impact of Exercise on Heart Rate Recovery

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Background—Abnormal heart rate recovery (HRR) has been shown to predict mortality. Although small studies have found that HRR can be improved with cardiac rehabilitation, it is unknown whether an improvement would affect mortality. The aim of this study was to determine whether HRR could be improved with cardiac rehabilitation and whether it would be predictive of mortality.

Methods and Results—We evaluated 1070 consecutive patients who underwent exercise stress testing before and after completion of a phase 2 cardiac rehabilitation program. Heart rate recovery, defined as the difference between heart rate at peak exercise and exactly 1 minute into the recovery period, and mortality were followed up as the primary end points. Of 544 patients with abnormal baseline HRR, 225 (41%) had normal HRR after rehabilitation. Of the entire cohort, 197 patients (18%) died. Among patients with an abnormal HRR at baseline, failure to normalize after rehabilitation predicted a higher mortality ($P<0.001$). After multivariable adjustment, the presence of an abnormal HRR at exit was predictive of death in all patients (hazard ratio, 2.15; 95% confidence interval 1.43–3.25). Patients with abnormal HRR at baseline who normalized afterward had survival rates similar to those of the group with normal HRR at baseline and after cardiac rehabilitation ($P=0.143$).

Conclusions—Heart rate recovery improved after phase 2 cardiac rehabilitation in the overall cohort. There was a strong association of abnormal HRR at exit with all-cause mortality. Patients with abnormal HRR at baseline who normalized HRR with exercise had a mortality similar to that of individuals with baseline normal HRR. **(*Circulation*. 2011;124: 1520-1526.)**

Key Words: exercise ■ heart rate ■ mortality

Exercise-based phase 2 cardiac rehabilitation (CR) has been well established as a means to positively affect all-cause mortality, cardiac mortality, and various risk factors associated with cardiovascular disease.[1] Many of the salient effects of exercise are thought to work by its effect on the carefully orchestrated interplay between the sympathetic and parasympathetic nervous systems. Specifically, exercise training has been shown to increase resting parasympathetic tone and to decrease sympathetic tone in both humans and animals.[2–7] Heart rate recovery (HRR) is an easily derived variable that has been established as an independent prognostic marker of overall mortality[8,9] and is thought to be reflective of vagal tone.[10,11] Small studies have shown that HRR can be modified by exercise training, but whether such modification might translate into clinically beneficial end points remains unknown.[12–16]

Clinical Perspective on p 1526

The purposes of this retrospective study are to further explore the relationship between CR and improvement of HRR and to determine whether such a relationship might be predictive of all-cause mortality.

Methods

Patient Sample

We identified a total of 1347 consecutive patients who were referred specifically for CR at the Cleveland Clinic over an 18-year period between February 1991 and April 2009. Each patient underwent exercise ECG before and after phase 2 CR during which HRR was prospectively recorded. Patients were excluded if they had a history of pacemakers, atrial arrhythmias, or cardiac transplantation or lacked a valid Social Security number. After all inclusion and exclusion criteria were accounted for, the final study sample consisted of 1070 patients; 245 patients were excluded because of a history of pacemakers, atrial fibrillation, or heart transplantation, and 32 patients were excluded owing to missing HRR both before and after phase 2 CR. The Cleveland Clinic's institutional review board has approved research based on the clinical databases of the exercise stress laboratory.

Cardiac Rehabilitation

All patients met the entry criteria for phase 2 CR. Phase 2 CR consisted of a highly structured, physician-monitored environment in which patients followed a specific exercise prescription according to established protocols from the American Association of Cardiovascular and Pulmonary Rehabilitation.[17] Patients exercised under physician supervision for 12 weeks, typically involving 3 visits per week. Sessions generally consisted of a 10- to 15-minute warm-up

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and stretching period, followed by 30 to 50 minutes of continuous aerobic exercise at an intensity of 50% to 80% of heart rate reserve calculated from the entry exercise treadmill test.[17] Sessions ended with a 15- to 20-minute cool-down period. Depending on patient abilities or physician preference, treadmills, bicycles ergometers, seated step machines, or elliptical trainers were used. In addition to exercise, patients were provided routine management of diet, weight, blood pressure, lipids, diabetes mellitus, and psychosocial counseling. At the time of CR initiation, a comprehensive physical examination and history were obtained, including patient demographics, medical and surgical history, relevant symptoms, current medications, social history, functional status, cardiac risk factors, dietary habits, and laboratory testing. An exercise prescription and educational goals were determined for CR, tailored according to the patient's baseline exercise treadmill test and other patient-specific limitations. Greater than 95% of the study sample underwent CR after cardiac revascularization (percutaneous intervention with angioplasty, stent, or atherectomy) or cardiac surgery (coronary artery bypass grafting, valvular surgery, or myocardial reduction surgery). Baseline entrance stress tests were obtained <3 months before the initiation of CR, and exit stress tests were obtained within 1 month of completion of CR.

Hypertension was defined as systolic/diastolic blood pressure >140/90 mm Hg or the use of antihypertensive treatment.[18] Diabetes mellitus was defined as fasting blood sugar >125 mg/dL or the use of insulin or hypoglycemic medications. Prior coronary artery disease was diagnosed by previous cardiac catheterization, pathological Q waves in 2 contiguous ECG leads, or history of percutaneous or surgical revascularization, myocardial infarction, or unstable angina. Peripheral arterial disease was based on diagnosis in the medical record, prior peripheral angiography, or symptoms of claudication. Tobacco use was documented if the patient admitted to current smoking or use within the past year.

Entrance and Exit Stress Testing

Entrance and exit stress testing was performed according to previously published protocols.[19] Values for clinical and exercise variables were recorded prospectively into a computerized database[19] with the use of defined variables and structured data entry that are used for routine clinical care and documentation at our institution. Personnel were formally trained on computer data entry, stress test protocol, and stress ECG administration.

Patients underwent symptom-limited exercise treadmill testing using 2-minute exercise protocols, primarily the Cornell or Naughton[20–22] protocols, which are standard at our institution for patients enrolling in CR. These ramp protocols were used on the basis of previous studies that have demonstrated that more gradual treadmill protocols allow more accurate and individualized exercise prescription and were performed in a standardized manner.[23] Patients were instructed to exercise until limited by symptoms, and use of handrails was allowed when needed for balance only, not for support. Blood pressure, heart rate, and symptoms were recorded every minute. After achieving peak workload, all patients spent at least 2 minutes in a cool-down recovery period at a speed of 2.4 km/h (1.5 mph) and a grade of 2.5%. Estimated workload, expressed in metabolic equivalents (METs; 1 MET equals 3.5 mL of oxygen uptake per kilogram of body weight per minute), was recorded into the database. To facilitate comparison of functional capacity, patients were required to undergo the same treadmill protocol for entrance and exit stress tests. Maximum predicted heart rate was calculated as 220 minus the patient's age. Patients were encouraged to exercise until symptoms occurred, despite achievement of 85% maximum predicted heart rate. At each stage of exercise and recovery, vital signs, symptoms, ECG changes, and arrhythmias were documented.

Heart Rate Recovery

After peak exercise, the patient was required to undergo a 2-minute cool-down period at 1.5 mph and a 2.5% grade. This cool-down period was selected on the basis of its validation in previous studies.[8,24] Heart rate recovery was defined as the difference between heart rate at peak exercise and exactly 1 minute into the recovery period. A HRR value ≤12 bpm was considered abnormal on the basis of previously published and validated work.[8,24]

End Points

Using a large population, we sought to further characterize whether HRR is modifiable with CR given its widespread use and reproducibility in this patient population. Furthermore, we sought to determine whether improvement in HRR leads to a reduction in all-cause mortality and which clinical and exercise characteristics predicted lack of improvement in HRR after exercise. All-cause mortality, as determined by the Social Security Death Index, was used as an objective and unbiased end point.[25]

Statistical Analysis

Baseline patient characteristics are presented for patients with normal HRR (>12 bmp) versus abnormal HRR (≤12 bpm). Continuous variables are summarized as mean±SD and compared by use of the Student *t* test. Nonnormally distributed continuous data are presented as median with 25th and 75th percentiles (quartiles 1–3). Categorical data are presented as percents of nonmissing values and compared by use of χ^2 tests.

Logistic regression methods were used to calculate single-variable odds ratios and 95% confidence intervals (CIs) of abnormal HRR after rehabilitation in patients who were abnormal at entry. Bootstrapping of stepwise selection methods was used to select significant variables for adjustment in a multivariable model. The variables considered for multivariable adjustment are listed in Table 1. Variables that were statistically significant ($P<0.05$) were kept in the final adjusted model and include age (per 10 years), change in exercise capacity (METs), history of congestive heart failure, and peripheral arterial disease.

Kaplan-Meier methods were used to estimate mortality rates. Cox proportional hazards models were developed to assess the risk of mortality for patients with abnormal HRR versus normal HRR. Single-variable hazard ratios (HRs) and their associated 95% CIs were calculated. Bootstrapping methods and model selection were also used as described above. Variables that remained in the multivariable mortality model were age (per 10 years), sex, history of peripheral vascular disease, change in exercise capacity (METs), and use of statins and nitrates.

All values of $P<0.05$ were considered statistically significant. All analyses were performed with SAS version 9.1 (SAS Inc, Cary, NC).

Results

A total of 1070 patients (age, 61±11 years; 77% men) underwent symptom-limited exercise ECG testing before and after the completion of CR. The medium time between entry and exit stress testing was 108 days (range, 45–212 days). At baseline stress testing, 526 patients (49%) had normal HRR and 544 patients (51%) had an abnormal HRR.

A summary of baseline clinical characteristics, medications, and exercise characteristics is shown in Table 1. Patients with an abnormal baseline HRR before CR were older and more likely to have other comorbidities. These included a history of coronary artery bypass grafting, percutaneous coronary intervention, peripheral arterial disease, hypertension, diabetes mellitus, valve disease, and congestive heart failure.

The subgroup of patients with baseline normal HRR tended to have a higher use of aspirin, nitrates, β-blockers, nondihydropyridine calcium channel blockers, and statins compared with patients with abnormal HRR. On the other hand, patients with an abnormal baseline HRR were more likely to be on other antihypertensive medications, digoxin, and nonstatin medications.

Patients with an abnormal HRR at baseline had lower peak METs, a characteristic that was consistent across both sexes.

Table 1. Baseline Clinical Characteristics, Medications, and Exercise Characteristics According to Baseline Heart Rate Recovery

Characteristics	Normal HRR (n=526)	Abnormal HRR (n=544)	P
Age, mean (SD), y	58.2 (11)	64.1 (11)	<0.001*
Men, n (%)	421 (80)	400 (74)	0.01
BMI, mean (SD), kg/m^2	28.4 (6)	28.9 (6)	0.35*
Prior CABG, n (%)	272 (52)	361 (66)	<0.001
Prior PCI, n (%)	236 (45)	152 (28)	<0.001
Peripheral arterial disease, n (%)	18 (3)	50 (9)	<0.001
Hypertension, n (%)	295 (56)	373 (69)	<0.001
Diabetes mellitus, n (%)	92 (37)	183 (56)	<0.001
Valvular heart disease, n (%)	88 (17)	148 (27)	<0.001
Prior CHF, n (%)	32 (6)	85 (16)	<0.001
Recent tobacco use, n (%)†	79 (15)	96 (18)	0.25
Aspirin, n (%)	456 (87)	448 (82)	0.05
β-blocker, n (%)	327 (62)	332 (61)	0.70
Nitrates, n (%)	106 (20)	101 (19)	0.51
Antihypertensives, n (%)	115 (22)	216 (40)	<0.001
Digitalis, n (%)	29 (6)	62 (11)	0.001
Nondihydropyridine CCB, n (%)	55 (11)	48 (9)	0.37
Nonstatin lipid medication, n (%)	37 (7)	41 (8)	0.75
Statin, n (%)	275 (53)	262 (48)	0.18
Peak METs, men, median (Q1–Q3)	8.5 (7.1–10)	6.5 (5.3–7.8)	<0.001*
Peak METs, women, median (Q1–Q3)	6.5 (5.5–8.1)	5.1 (4.30–6.05)	<0.001
Peak systolic blood pressure, median (Q1–Q3), mm Hg	182 (160–198)	170 (150–190)	<0.001
Peak heart rate, median (Q1–Q3), bpm	145 (129–157)	130 (111–145)	<0.001*
Resting heart rate, median (Q1–Q3), bpm	68 (61–78)	75 (65–87)	<0.001*
1-min HRR, mean (SD), bpm	20.1 (6.2)	6.5 (4.1)	<0.001*

HRR indicates heart rate recovery; BMI, body mass index; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; CHF, congestive heart failure; CCB, calcium channel blocker; METs, metabolic equivalents; Q1, quartile 1; and Q3, quartile 3. Percentages are based on nonmissing data.

*Nonparametric test.

†Defined as current use or use within the past year.

Additionally, these patients had lower peak systolic blood pressures, lower peak heart rate at exercise, and higher resting heart rates.

Heart Rate Recovery at Baseline and After Cardiac Rehabilitation

In the entire cohort, the average value of HRR at baseline stress testing was 13.2±8.6 bpm. After CR, the HRR increased to 16.6±9.4 bpm (1-sample *t* test *P* for change in HRR <0.001; Figure 1).

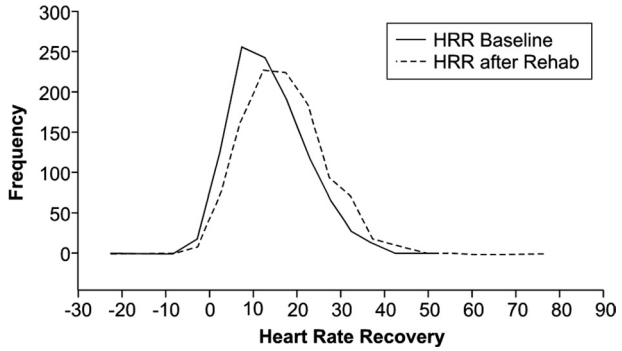


Figure 1. Heart rate recovery (HRR) at baseline and after cardiac rehabilitation in the study sample (n=1070). Median HRR improved from 13.2±8.6 bpm at baseline to 16.6±9.4 bpm after rehabilitation for the entire study sample (*P* for change <0.001). Negative values reflect patients in whom the heart rate at 1 minute into recovery increased.

Of the 526 patients with normal baseline HRR, 470 patients (89%) continued to have normal HRR after CR, and 56 (11%) had an abnormal HRR at exit. Of the 544 patients with abnormal baseline HRR, 225 patients (41%) normalized their HRR after CR, and 319 (59%) maintained an abnormal HRR at exit. Because this observation may merely reflect regression to the mean, we also analyzed the impact on all-cause mortality (see below).

Patients with normal baseline HRR had an improvement from an average of 20.1±6.2 bpm before CR to 21.9±8.9 bpm afterward (1-sample *t* test *P* for the change in HRR <0.001). Those patients with an abnormal baseline HRR had a mean value of 6.5±4.1 bpm, which increased to a mean value of 11.5±6.8 bpm (1-sample *t* test *P* for the change in HRR <0.001).

Abnormal Baseline Heart Rate Recovery and Predictors of Failure to Normalize After Cardiac Rehabilitation

Table 2 summarizes the characteristics of patients with abnormal baseline HRR according to improvement or lack of improvement of HRR after CR. The single-variable predictors that were significantly associated with failure to normalize HRR include older age, failure to increase exercise capacity, diabetes mellitus, prior congestive heart failure, use of nitrates, and peripheral arterial disease. In a multivariable model, independent predictors of failure to improve HRR included older age (per 10-year increase, adjusted odds ratio, 1.47; 95% CI, 1.23–1.75), lack of improvement in exercise capacity (adjusted odds ratio, 0.70; 95% CI, 0.59–0.83), peripheral arterial disease (adjusted odds ratio, 3.02; 95% CI, 1.37–6.68), and prior congestive heart failure (adjusted odds ratio, 1.93; 95% CI, 1.12–3.32; Table 3). Among these patients, failure to normalize after rehabilitation predicted a higher mortality (*P*<0.001). After multivariable adjustment, the presence of an abnormal HRR at exit was predictive of death in these patients (HR, 2.15; 95% CI, 1.43–3.25). Diabetes mellitus was purposefully left out of these models owing to a high number of missing values.

Table 2. Characteristics of Patients With Abnormal Baseline Heart Rate Recovery According to Improvement in Heart Rate Recovery After Cardiac Rehabilitation

Characteristics	Normal HRR (n=225), n (%)	Abnormal HRR (n=319), n (%)	Odds Ratio (95% CI)	*P*
Age				<0.001
Age <65 y	127 (56)	124 (39)	2.04 (1.44–2.88)	
Age ≥65 y	98 (44)	195 (61)		
Sex				0.09
Female	51 (23)	93 (29)	0.71 (0.48–1.06)	
Male	174 (77)	226 (71)		
Recent tobacco use				0.70
No	187 (83)	261 (82)	1.09 (0.70–1.72)	
Yes	38 (17)	58 (18)		
Change in METS ≥1.5 increase				<0.001
No	91 (40)	190 (60)	0.46 (0.33–0.65)	
Yes	134 (60)	129 (40)		
Diabetes mellitus*				0.003
No	62 (56)	84 (39)	2.02 (1.27–3.21)	
Yes	49 (44)	134 (61)		
Prior MI				0.26
No	135 (60)	176 (55)	1.22 (0.86–1.72)	
Yes	90 (40)	143 (45)		
Prior CABG				0.39
No	71 (32)	112 (35)	0.85 (0.59–1.23)	
Yes	154 (68)	207 (65)		
Prior PCI				0.09
No	171 (76)	221 (69)	1.40 (0.95–2.07)	
Yes	54 (24)	98 (31)		
Valvular heart disease				0.16
No	171 (76)	225 (71)	1.32 (0.90–1.95)	
Yes	54 (24)	94 (29)		
Peripheral arterial disease				<0.001
No	217 (96)	277 (87)	4.11 (1.89–8.94)	
Yes	8 (4)	42 (13)		
Prior CHF				0.01
No	201 (89)	258 (81)	1.98 (1.19–3.29)	
Yes	24 (11)	61 (19)		
Nonstatin lipid medication				0.75
No	209 (93)	294 (92)	1.11 (0.58–2.13)	
Yes	16 (7)	25 (8)		
Statins				0.81
No	118 (52)	164 (51)	1.04 (0.74–1.47)	
Yes	107 (48)	155 (49)		
Nitrates				0.03
No	193 (86)	250 (78)	1.67 (1.05–2.64)	
Yes	32 (14)	69 (22)		
ACE inhibitors				0.44
No	149 (66)	201 (63)	1.15 (0.81–1.65)	
Yes	76 (34)	118 (37)		
Aspirin				0.77
No	41 (18)	55 (17)	1.07 (0.69–1.67)	
Yes	184 (82)	264 (83)		
β-blockers				0.76
No	86 (38)	126 (40)	0.95 (0.67–1.35)	
Yes	139 (62)	193 (60)		
Digitalis				
No	206 (92)	276 (87)	1.69 (0.96–2.98)	0.07
Yes	19 (8)	43 (13)		
Nondihydropyridine CCB				0.96
No	205 (91)	291 (91)	0.99 (0.54–1.80)	
Yes	20 (9)	28 (9)		
Completed >70 sessions*	84	133		0.34
No	8 (10)	8 (6)	1.65 (0.59–4.56)	
Yes	76 (90)	125 (94)		

HRR indicates heart rate recovery; CI, confidence interval; METs, metabolic equivalents; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; CCB, calcium channel blocker; and ACE, angiotensin-converting enzyme.

*Patients for whom data were available.

Heart Rate Recovery and Mortality

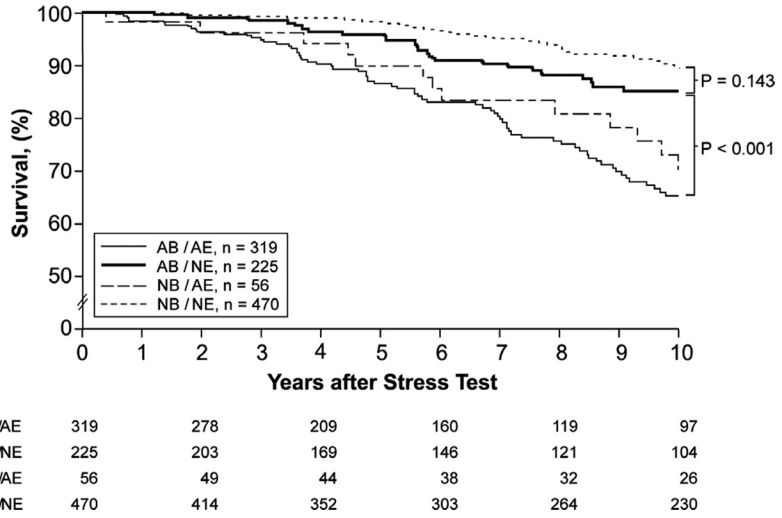
The sample was followed up for a median of 8.1 years. Of 1070 patients identified for the entire cohort, we observed 197 deaths (18.4%). Of the 526 patients with normal HRR, 68 patients (13%) died versus 129 of the 544 patients (24%) with abnormal HRR at baseline (log-rank $P<0.001$).

Unadjusted Kaplan-Meier survival curves for each group are shown in Figure 2. Patients with abnormal HRR at baseline and exit had the lowest survival, whereas patients with normal HRR at baseline and exit had the highest survival. Patients with abnormal HRR at entrance who subsequently normalized after CR had improved survival compared with those who remained abnormal (log-rank $P<0.001$). There was no difference in survival between those

Table 3. Multivariable Predictors of Failure to Normalize Heart Rate Recovery

Characteristics	Odds Ratio (95% CI)	*P*
Age per 10 y	1.47 (1.23–1.75)	<0.001
Peripheral arterial disease	3.02 (1.37–6.28)	0.006
Prior CHF	1.93 (1.12–3.32)	0.02
Change in peak METs	0.70 (0.59–0.83)	<0.001

CI indicates confidence interval; CHF, congestive heart failure; and METs, metabolic equivalents. Variables were retained in at least 50% of 200 bootstrap samples.



AB/AE	319	278	209	160	119	97
AB/NE	225	203	169	146	121	104
NB/AE	56	49	44	38	32	26
NB/NE	470	414	352	303	264	230

Figure 2. Survival according to heart rate recovery (HRR) before and after cardiac rehabilitation. There were 197 deaths in the entire study sample in the median follow-up of 8.1 years. Patients with abnormal HRR that normalized at exit had improved survival compared with those who did not ($P<0.001$) and were no different from the cohort with normal HRR at baseline and exit ($P=0.143$). Data presented are unadjusted. AB indicates abnormal baseline; NB, normal baseline; AE, abnormal exit; and NE, normal exit.

who had normal HRR at entry and exit and those who had abnormal HRR at entrance who normalized (log-rank $P=0.14$).

Both abnormal HRR at baseline and abnormal CR exit HRR were individually predictive of mortality (unadjusted HR, 2.27; 95% CI, 1.69–3.05; and unadjusted HR, 3.34; 95% CI, 2.52–4.44, respectively). After bootstrapping and variable selection, abnormal exit HRR remained statistically significant in addition to age, sex, change in exercise capacity, peripheral arterial disease, and statin and nitrate use. The presence of an abnormal HRR at exit was still strongly predictive of death in all patients (adjusted HR, 2.24; 95% CI, 1.66–3.03; Table 4), whereas entrance abnormal HRR was no longer predictive of mortality. The patient's year of entry into the CR program (by decade) was added into the multivariable model to determine whether changes in standard of care over the duration of the analysis affected the ability of HRR to predict mortality. Year of entry did not affect mortality and did not change HRR and its effect on mortality.

In addition to the analysis of HRR as a dichotomous variable detailed above, we analyzed baseline, exit, and change in HRR as continuous variables in predicting overall mortality. In this analysis, all were individually associated with a decrease in mortality risk as HRR and change in HRR increased (HR=0.94, $P<0.001$ for baseline; HR=0.92, $P<0.001$ for exit [Figure I in the online-only Data Supplement]; HR=0.98, $P=0.035$ for change). Baseline and exit HRR remained statistically significant after adjustment for variables listed in the multivariable model; however, the change in HRR (as a continuous variable) was no longer statistically significant (HR, 0.99; $P=0.12$). A simple linear regression analysis showed that HRR at baseline was significantly associated with HRR at exit (parameter estimate $\beta=0.70$; $P<0.0001$). Additionally, piecewise linear splines were calculated to explore the possibility of a threshold of 12 bpm to predict mortality. Our data showed that a threshold of 14 bpm rendered the lowest −2 log-likelihood of all possible cutoff points. After 14 bpm was used as a cutoff in our multivariable model, the results did not change. Therefore, we chose to report the data using the 12-bpm cutoff because it has been repeatedly established in the literature for this patient population.

Table 4. Multivariable Predictors of Mortality

Characteristics	Hazard Ratio (95% CI)	*P*
Abnormal exit HRR	2.24 (1.66–3.03)	<0.001
Change in peak METs	0.80 (0.70–0.91)	0.001
Age per 10 y	1.67 (1.42–1.96)	<0.001
Peripheral arterial disease	2.31 (1.55–3.45)	<0.001
Male	1.73 (1.18–2.53)	0.005
Use of statins, baseline	0.59 (0.42–0.82)	0.002
Use of nitrates, baseline	1.75 (1.26–2.44)	0.001

CI indicates confidence interval; HRR, heart rate recovery; and METs, metabolic equivalents. Variables were retained in at least 50% of 200 bootstrap samples.

Discussion

Our study sought to further characterize the relationship between exercise, the use of phase 2 CR, and HRR, specifically focusing on whether HRR is a variable that can be modified with the use of CR and whether its modification can affect all-cause mortality. Because of the retrospective nature of this analysis, the present study should be considered hypothesis generating. It is neither designed nor able to detect a causal relationship between exercise and improvement in HRR; rather, it seeks to illuminate an association between the two that might provide a useful framework for further study. In this retrospective cohort of patients undergoing CR, HRR improved in 41% of patients with an abnormal baseline HRR before CR. Predictors of failure to improve HRR included older age, peripheral arterial disease, diabetes mellitus, prior heart failure, and the use of nitrates. Because these observations may merely be due to regression to the mean, we performed a mortality analysis. Not surprisingly, those patients who had an abnormal HRR at baseline had a markedly increased mortality risk overall, a finding consistent with prior studies using HRR to predict mortality.[8,24] However, among those patients who had an abnormal HRR at baseline, those whose HRR normalized after CR had improved survival compared with those who remained abnormal. After

multivariable adjustment, abnormal HRR at exit was strongly predictive of mortality.

The association between structured exercise and improvement in HRR has been suggested on the basis of previously published work limited primarily by small sample sizes.[12,26] To the best of our knowledge, this study encompasses the largest sample population to date to address the relationships between HRR, CR, and survival.[16] Whether HRR improves as a direct result of CR or simply reflects recovery from a debilitating event such as bypass surgery or myocardial infarction has been evaluated in several studies. Tiukinhoy and colleagues[12] compared the effect of CR in a study population (n=34) similar to ours with a control group (n=35) who did not participate in CR but experienced similar index events. They found that CR lowered resting heart rate, increased peak heart rate and total treadmill time, and increased HRR, whereas the control group showed no significant change from baseline. Hao et al[15] explored this concept even further to compare the effect of CR on patients after coronary artery bypass graft with patients with only chronic stable angina to determine whether simple deconditioning was the primary factor driving improved exercise parameters. Both groups significantly lowered their resting heart rate and increased HRR, whereas only the post–coronary artery bypass graft group improved their METs. This implies that HRR and exercise capacity, expressed in METs, change independently. Hai et al[14] compared patients after myocardial infarction who underwent CR and a smaller control group (also after myocardial infarction) who did not participate in CR. In the study group, an improvement in both METs and HRR was observed, whereas in the control group, only METs improved while HRR remained unchanged. Taken together, these studies imply that HRR only consistently improves in association with exercise training but that exercise capacity (METs) can be improved both with or without formal exercise and thus may reflect recovery from a deconditioning event. The impact of β-blockers on the ability of HRR to predict mortality has long been a theoretical concern; however, most studies of a size similar to this one have shown no demonstrable interaction, a finding congruent with ours. Importantly, compared with similar analyses, our cohort has the highest β-blocker use reported to date with an overall incidence of 62%, more than twice that of the next largest study and more reflective of contemporary practices.[27]

An abnormal HRR reflects abnormal vagal tone[10,11] and has been shown to have prognostic value in multiple patient populations.[8,9,24,28] It has also been shown to give additional prognostic information independently of functional capacity, ischemia,[8,24,28] and the results of coronary angiography.[9] Furthermore, exercise training has been shown to improve autonomic tone,[2–7] to enhance endothelial function,[29] and to positively affect all-cause mortality in patients with coronary heart disease.[30] These beneficial autonomic responses have been found in healthy adults[6] and in patients with heart failure[7] and acute myocardial infarction.[31] The beneficial autonomic effects of exercise training, specifically enhanced vagal reactivation,[7] suggest a plausible explanation as to why CR may favorably affect HRR, even independently from other exercise parameters that work through different mechanisms.

This study has several limitations. For one, it is a retrospective analysis with data amassed from a single-center experience. It was left to individual physician discretion as to which patients were enrolled in CR. Although we attempted to control for medication changes, weight reduction, smoking cessation, improvements in lipid profile, and exercise prescription compliance, it is difficult to control for all specific and nonspecific aspects of an exercise-training program. Furthermore, there was not a favorable cohort of patients in our CR database who could serve as a placebo group for this retrospective analysis because exercise treadmill testing is not routinely done as a surveillance test in patients who forgo CR. Heart rate variability, another exercise-derived parameter reflecting autonomic function, was not included because it is not routinely captured during exercise stress testing at our institution. Finally, our inclusion and exclusion criteria, specifically the necessity for obtaining an exercise treadmill test after CR, led to a much higher compliance rate than that observed in typical CR programs. In our entire cohort, >90% of patients completed 70% of all sessions. Although this compliance rate is useful for interpreting the validity of our conclusions on the influence of exercise on HRR, it unfortunately masks our ability to make inferences as to whether a dose-response relationship exists.

Conclusions

Heart rate recovery improved after exercise training in a sample of patients referred for phase 2 CR. There was a strong association between abnormal HRR at exit and all-cause mortality. Patients with abnormal HRR at baseline who subsequently had normalized HRR with CR had a mortality similar to those with baseline normal HRR.

Disclosures

None.

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CLINICAL PERSPECTIVE

An abnormal heart rate recovery has been shown to have prognostic value in multiple patient populations and to give additional prognostic information independently of functional capacity, ischemia, or coronary artery disease. However, whether abnormal heart rate recovery can be reversed is controversial. Because exercise has been shown to improve autonomic tone, it stands to reason that perhaps exercise training can improve abnormal heart rate recovery. To date, studies of cardiac rehabilitation on heart rate recovery have been limited by small sample size. In our study of 1070 consecutive patients who underwent symptom-limited exercise ECG testing before and after completion of phase 2 cardiac rehabilitation, we found that heart rate recovery improved with exercise training. There was a strong association of abnormal heart rate recovery at exit of cardiac rehabilitation with all-cause mortality. Patients who had abnormal heart rate recovery at baseline but had normalized heart rate recovery at exit had survival rates similar to those with normal heart rate recovery. The beneficial autonomic effect of exercise training, specifically enhanced vagal reactivation, suggests a plausible explanation as to why exercise training may favorably improve heart rate recovery.