Influence of the Maximum Heart Rate Attained during Exercise Testing on Subsequent Heart Rate Recovery

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Background: Abnormal heart rate recovery (HRR) following exercise testing has been shown to be a predictor for adverse cardiovascular events. The actual maximum heart rate (MHR) attained during the exercise test does not however have a distinct significance in traditional HRR assessment. The objective of this study was to investigate the role of MHR in HRR.

Methods: This prospective study consisted of 164 patients (62% male, mean age 53.7 ± 11.7 years) who were referred for a symptom-limited standard Bruce Protocol treadmill exercise test, based on clinical indications. The patients were seated immediately at test completion and the heart rate (HR) recorded at one and two minutes postexercise. A normal HRR was defined as a HR drop of 18 beats per minute or more at the end of the first minute of recovery. The HRR profile of patients who reached $\geq 85\%$ of their maximum predicted heart rate (MPHR) during peak exercise were then compared to HRR profile of those who could not.

Results: One hundred twelve patients (Group A) achieved a $MHR \geq 85\%$ of MPHR during peak exercise whereas 52 patients (Group B) did not. Chi-square analysis showed a higher incidence of normal HRR in Group A compared to Group B ($p = 0.029$). Analysis of variance with repeated measures showed that group A had a greater HRR at the first minute $F_{1,162} = 6.98$, $p = <0.01$) but not the second minute ($F_{1,162} = 1.83$, $p = .18$) postexercise.

Conclusion: There is a relation between the peak heart rate attained during exercise and the subsequent HRR. A low peak heart rate increases the likelihood of a less than normal HRR. Assessment of the entire heart-rate response seems warranted for more thorough risk-stratification.

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Heart rate recovery (HRR) is of interest because it is thought, in large part, to be a function of vagal reactivation and it is appreciated that a generalized decrease in vagal tone may be a risk factor for death.^{1–6} Indeed, HRR has been shown to be an independent predictor for adverse cardiac events, including sudden cardiac death.^{7–11}

Given that different patients usually attain different peak heart rates during maximal exercise stress testing, the question arises whether HRR is influenced by the achieved maximal HR. We addressed this question in this prospective study of 164 patients undergoing clinically indicated stress testing. We also investigated whether the HRR data obtained at the end of second minute postexercise were similar to the HRR data obtained at the end of the first minute of exercise.

METHODS

Patients

Patients for this prospective study were 164 non-consecutive adults referred for routine radionuclide stress testing at the UMDNJ-University Hospital Exercise Stress Test Laboratory. The test was clinically indicated and requested by the patient's personal physician in each instance. The exclusion criteria for participation in the study were: presence of atrial fibrillation, overt congestive heart failure, a pacemaker or an implantable defibrillator, as well as the standard clinical exclusion criteria for patients undergoing exercise testing. All testing was performed between the hours of 9AM and noon. The protocol was approved by the

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University Institutional Review Board and informed consent was obtained from all patients.

Protocol

All patients came to the laboratory in fasting state with no beta-blockers taken on the day of testing. All stress tests were performed under the direct supervision of the Exercise Test Laboratory medical staff. Patients were connected to a Quinton QStress TM55 treadmill/monitor system (Cardiac Science, Bothell, WA, USA) and began symptom-limited exercise testing according to the standard Bruce protocol. The heart rate (HR) was continuously monitored and blood pressure (BP) measurements taken at each exercise stage. The maximum predicted heart rate (MPHR) was calculated by the formula: $220 - \text{age}$ and an adequate HR response to exercise was defined as reaching $\geq 85\%$ of the MPHR. Patients were seated immediately after the maximal exercise effort and remained connected to the electrodes for at least 2 minutes during which time continuous HR data were recorded by the treadmill and the HR and BP were also manually recorded at 1 and 2 minutes postexercise. A radionuclide myocardial perfusion study was subsequently performed on almost all of the patients.

Data Analysis

In this study, HRR was defined as the change in HR as measured from that at peak symptom-limited exercise to that at the end of the first minute after exercise was stopped suddenly without a cooling-down period. A normal HRR under these conditions was defined as a HR drop of 18 beats/min or more at the end of the first minute of recovery.⁹

Each patient was then placed in one of two groups according to their MPHR. Those who attained $\geq 85\%$ of their MPHR were placed in group A and those who attained $< 85\%$ of their MPHR were placed in group B. There were a total of 112 patients in group A and 52 in group B. Relevant clinical data were obtained from the routine questionnaire completed by the patients prior to the stress test as well as the stress test itself and, when available, the results of the subsequent radionuclide study.

Chi-square testing was used to determine whether normal HRR was related to the ability to achieve $\geq 85\%$ MPHR for normally distributed continuous variables. Analysis of variance (ANOVA)

using repeated measures was used for comparison among groups. A P value of < 0.05 (or less when using the Bonferroni correction) was taken to be statistically significant.

Additionally, as part of a poststudy subanalysis, the patients were further categorized into "Normal" and "Abnormal" subgroups based solely on observed cardiac function as well as the presence or absence of reversible perfusion defects, fixed perfusion defects, and/or wall motion abnormalities as determined by the radionuclide scan that the patients underwent immediately after the stress test and the HRR data collection period. The "Normal" group was defined to be those patients with a radionuclide scan interpreted as normal: normal left ventricular ejection fraction ($\text{LVEF} \geq 55\%$) with absence of reversible perfusion defects, fixed perfusion defects, as well as absence of wall motion abnormalities. The "Abnormal" group comprised those patients with either decreased LVEF ($< 55\%$) or any of the additional scan abnormalities already described. Eleven patients did not get radionuclide scans following the stress testing so only 153 patients could be categorized: 102 group A patients (46 in the Normal subgroup and 56 in the Abnormal subgroup), and 51 group B patients (16 in the Normal subgroup and 35 in the Abnormal subgroup). These groups were then compared to see whether these additional data provided additional information regarding HRR.

RESULTS

Study Group

A total of 164 patients, of which 62.2% were men, were enrolled in this study. The mean LVEF was $56.9 \pm 10.7\%$ (data available in 157 patients with four of the values obtained from echocardiograms performed close to the study date) and abnormalities in the cardiac radionuclide study were present in 42.5% (data available in 153 patients). Comparison of group A ($n = 102$) with group B ($n = 51$) revealed no significant statistical difference in the incidence of fixed perfusion defects (11.8% vs 15.7%), reversible perfusion defects (27.5% vs 25.5%) or wall motion abnormalities (12.7% vs 15.7%). There were also no statistically significant differences between the two groups with respect to age, gender, LVEF, prior myocardial infarction, prior revascularization, congestive heart failure, hypertension, diabetes

Table 1. Study Group Baseline Characteristics

	Total (n = 164)	Group A (n = 112)	Group B (n = 52)	P-Value
Age (years)	53.7 ± 11.7	54.5 ± 12.2	51.9 ± 10.6	0.18
Males, n (%)	102 (62.2%)	68 (60.7%)	34 (65.4%)	0.57
LVEF, (%) n	56.9 ± 10.7 157	57.5 ± 10.9 106	55.9 ± 10.5 51	0.4
Heart rate sitting, (/min) n	68.8 ± 11.2 159	70.2 ± 11.3 107	65.9 ± 10.3 52	0.024
Normal nuclear myocardial perfusion scan, n (%)	153 (57.5%)	102 (57.8%)	51 (56.8%)	0.91
Prior myocardial infarction, n (%)	13 (7.9%)	7 (6.3%)	6 (11.5%)	0.24
Prior revascularization (coronary intervention or bypass surgery), n (%)	20 (12.2%)	13 (11.6%)	7 (13.5%)	0.74
Prior congestive heart failure, n (%)	7 (4.3%)	5 (4.5%)	2 (3.8%)	0.86
Hypertension, n (%)	95 (57.9%)	61 (54.5%)	34 (65.4%)	1.0
Diabetes mellitus, n (%)	47 (28.7%)	31 (27.7%)	16 (30.7%)	0.68
Beta-blockers held 24 hours prior, n (%)	37 (22.6%)	21 (18.8%)	16 (30.7%)	0.86

LVEF = left ventricular ejection fraction.

mellitus, and use of beta-blockers. Additional data are displayed in Table 1. There was, however, a statistically significant difference in the mean ($\pm$ SD) sitting HR between the two groups. The mean HR was higher in group A (70.2/min $\pm$ 11.3) than in group B patients (65.9/min $\pm$ 10.3). Comparison of the sitting HR after excluding patients on beta-blockers showed no significant difference. The patients had been instructed not to take beta-blockers on the day of the study although the time of the last dose was not determined and a persisting beta-blockade at time of testing cannot be excluded. There was one patient in group A on clonidine with sitting HR of 95/min and two patients in group B on clonidine with sitting HR of 59/min and 54/min, respectively, as well. No patients were being treated with other potential sinus node depressant agents such as diltiazem or verapamil. Presence of diabetes had no effect on the sitting HR difference between the two groups.

HRR—Chi-Square Analysis

A chi-square test of independence was conducted to determine whether normal HRR was related to the ability to achieve $\geq 85\%$ MPHR. Overall, 21 of

164 (12.8%) patients had an abnormal HRR. Data obtained showed that 102 (91%) of group A patients, who attained $\geq 85\%$ MPHR, had a normal HRR at 1 minute versus 41 (79%) of those in group B. This difference in proportions of normal HRR between the two groups within the first minute was statistically significant ($\chi^2_1 = 4.75$, $P = 0.029$). Of note, as shown in Table 1, there were no significant differences present between these same two groups with respect to age, gender, revascularization history, diabetes mellitus, LVEF, or abnormal nuclear cardiac scans.

HRR—Analysis of Variance

ANOVA using repeated measures was performed across the first 2 minutes postexercise to determine whether the decrease in average HR was significantly different for the two groups. The peak HR for group A was 150 $\pm$ 12.9/min. At 1 minute postexercise the HR was 112 $\pm$ 15.4/min and 94 $\pm$ 14.5/min at 2 minutes postexercise. The peak HR for group B was 129 $\pm$ 13.4/min. At 1 minute postexercise the HR was 98 $\pm$ 15.2/min and 82 $\pm$ 13.6/min at 2 minutes postexercise. A significant time effect was found for the first minute

Figure 1. Decline in HR for group A and group B patients as function of the MPHR at 1 and 2 minutes from end of exercise, with no cool-down period, in the sitting position. HR = heart rate; MPHR = maximum predicted heart rate.

postexercise ($F_{1,162} = 804.2$, $P < 0.001$) and the second minute postexercise ($F_{1,162} = 575.7$, $P < 0.001$) indicating that a significant decrease in HR occurs during each of the first 2 minutes of recovery.

However, as displayed in Figure 1, the decrease in average HR during the first minute of recovery appears to be greater than the decrease in HR during the second minute of recovery and the amount of HRR within each of the two groups appears to be the same. Consequently, post hoc analyses with separate ANOVAs were performed on the change from peak HR to 1 minute postexercise and from 1 minute to 2 minutes postexercise using a Bonferroni Correction ($P = 0.05/2 = 0.025$) to test whether HRR is different for each group during the first and second minutes. A significant interaction was found between time and MPHR, ($F_{1,162} = 6.98$, $P < 0.01$) only for the first minute and not the second minute ($F_{1,162} = 1.83$, $P = 0.18$). Thus, the average decrease in HR for the first minute (from peak HR to 1 minute postexercise) was significantly greater for group A than for group B but the average decrease in HR during the second minute (from 1 minute postexercise to 2 minutes postexercise) was not significantly different for the two groups.

Additionally, repeated measures ANOVA was performed to examine whether patients' cardiac status ("Normal" vs "Abnormal"), as defined in this study, influenced HRR. Results of the three-factor, repeated measures ANOVA found, as expected, a significant time effect, ($F_{2,298} = 977.2$, $P < 0.001$) indicating that patients' HR does decrease signifi-

cantly during the 2 minutes postexercise. A significant interaction was also found between time and MPHR, ($F_{2,298} = 5.86$, $P < 0.01$) but not between time and cardiac status of the patients ($F_{2,298} = 0.63$, $P = 0.53$). The interaction of time, MPHR, and cardiac status was also not significant ($F_{2,298} = 0.52$, $P = 0.59$).

To understand the effects of diabetes mellitus, (present in 27.7% of group A and 30.7% of group B, $P = \text{ns}$), the previous statistical analyses were conducted again after removing all diabetic patients ($n = 47$) reducing the sample to 117 nondiabetic patients—among who 10 did not get radionuclide scans. The results were similar to that of the full 164-patient study. A significant time effect was found in the first minute postexercise ($F_{1,115} = 632.7$, $P < 0.001$) and in the second minute postexercise ($F_{1,115} = 421.7$, $P < 0.001$). A significant interaction between time and MPHR was found for the first minute postexercise ($F_{1,115} = 5.2$, $P = 0.024$) but not for the second minute ($F_{1,115} = 0.76$, $P < 0.39$) indicating (as in the full patient study population) that the average HR for nondiabetics decreases significantly greater for group A than group B only in the first minute postexercise. Finally, the results of the three-factor ANOVA for the nondiabetics were also similar to the results of the full patient population study. There was a significant time effect ($F_{2,206} = 708.7$, $P < 0.001$) and a significant interaction between time and MPHR ($F_{2,206} = 5.01$, $P = 0.008$) but not between time and cardiac status ($F_{2,206} = 0.03$, $P = 0.97$) nor between

Figure 2. Relative decreases in HR at 1 and 2 minutes of recovery as a function of the MPHR (group A $\geq 85\%$, group B $< 85\%$) as well as the presence or absence of abnormal cardiac function and/or myocardial perfusion study abnormalities within each group (see text).

time, MPHR, and cardiac status ($F_{2,206} = 0.12$, $P = 0.88$).

Thus, patients recover differently depending on the level of MPHR and are independent of the cardiac and the clinical variables as defined in this study. These results are displayed in Figure 2.

DISCUSSION

Our results indicate that there is a direct correlation between the peak HR obtained during a symptom-limited exercise test and the subsequent HRR measured at 1 minute, as defined and measured in this study. A chi-square test showed that patients in the group who achieved $\geq 85\%$ MPHR had a higher likelihood of a normal HRR. The ANOVA techniques similarly showed that patients in the group who achieved $\geq 85\%$ MPHR had greater HRR in the first minute than the patients in the group who achieved $< 85\%$ MPHR. Our results also show that there is no significant difference in HRR between the two groups when the second minute postexercise HR is compared to peak HR. Furthermore, the usual clinical variables such as history of CAD, LVEF, abnormal radionuclide myocardial perfusion studies were not found to play a role in affecting the HRR outcomes in this study.

Previous studies have shown that chronotropic incompetence (CI), usually defined as an inability to attain 85% of MPHR, is associated with increased risk of mortality and coronary heart disease risk.^{12–14} Jouven et al. demonstrated this finding in another fashion by showing that abnormal heart-

rate profiles in 5713 asymptomatic subjects undergoing bicycle exercise testing could predict sudden death.¹¹ Patients who did not reach 80% of their MPHR as well as patients with known or suspected coronary artery disease were excluded from this study, however. More recently, Myers et al. found that both CI and abnormal HRR (defined as a decrease of < 22 beats/min at 2 minutes in recovery) are independent predictors for cardiovascular mortality with CI being the stronger predictor.¹⁵ Maddox et al. have also described a significant increase in all-cause mortality or nonfatal myocardial infarction in those patients who have both abnormal HRR and CI and less so when either variable was evaluated separately.¹⁶

Our findings are very much in line with the findings of Myers et al. in that there seems to be a relation between the peak HR achieved during exercise testing and the subsequent HRR—despite the presence of procedural differences and the fact that we did not look at clinical outcome. In their study, 91% of the 275 patients with an abnormal HRR had CI versus 23.8% in those with normal HRR. Although the correlation between HRR and stress myocardial perfusion score was the highest, a report by Georgoulas et al. also reported, with a different HRR determination method, that there is a statistically significant relationship between HRR and chronotropic variables.¹⁷ This same study, in contradistinction to our results, found that there were statistically significant differences in clinical variables in those with abnormal HRR compared to normal HRR. The results from the Maddox

study, where an abnormal HRR was defined as ≤ 12 beats/min after a 1 minute cool down, are very different, however. In that study, 11% of the study population had an abnormal HRR and CI versus 19.8% with abnormal HRR only. The reason for this discrepancy is not clear although differences in technique probably play a large role.

We found no correlation between the peak HR and the HRR during the second minute of recovery with the use of the ANOVA technique. It should, however, be noted that Lipinski et al. have proposed that the HR decrease during the second minute of recovery, specifically, may have a clinical predictive value, a factor not assessed in our study.¹⁸

Our third finding, that the routine patient clinical variables did not affect the relation between the attained peak HR and the HRR, is supported to some degree by previous studies that have shown that HRR is an independent predictor for cardiovascular mortality.¹⁹ Blood glucose has been shown to influence HRR in patients without CAD but statistical significance was lost when diabetes itself was considered as a variable; the only independent correlates of an abnormal HRR being decreased exercise capacity and male gender.²⁰ The mean sitting heart rate, the one significant baseline difference between the two groups in our study was due to beta-blocker therapy as demonstrated but this difference has no effect as beta-blocker do not seem to influence the predictive power HRR.^{21,15}

Results of this study suggest that a specific assessment of the attained peak HR during exercise is necessary for a complete evaluation of the HRR postexercise. Additionally, while CI and an abnormal HRR may act as independent clinical predictors they may nevertheless be interrelated at the level of the patient undergoing the stress test by mechanisms yet to be elucidated. Further study and understanding of physiological mechanisms that control and possibly link the processes of MPPHR and HRR are needed.

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