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Heart Rate Recovery from Peak Exercise and Cardiac Autonomic Control in Male Coronary Heart Disease Patients

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ABSTRACT

Kelly JS, Delaney J, Wiggins T. Heart Rate Recovery from Peak Exercise and Cardiac Autonomic Control in Male Coronary Heart Disease Patients. **JEPonline** 2011;14(4):64-74. Heart rate recovery (HRR) from maximal exercise is due in part to changes in autonomic balance in favor of the parasympathetic arm of the autonomic nervous system. Heart rate variability (HRV) analysis allows for a non-invasive measurement of autonomic balance. Both HRR and autonomic function are compromised in patients with coronary heart disease (CHD). The aim of this investigation was to determine HRR from maximal exercise in patients with CHD and to correlate that measure with indices of their autonomic function. Forty-eight male patients with CHD (17 post-coronary artery bypass graft surgery, 31 following a myocardial infarction; 24 of whom were taking beta blockers and 7 who were not) and 8 sedentary controls matched for body mass and age were recruited to the study. Subjects completed a graded exercise treadmill test to volitional exhaustion. Heart rate at 1 min post-cessation of exercise was recorded. On a separate occasion, the subjects' autonomic function was assessed using HRV analysis. Although the results showed no difference in exercise capacity between the two groups, the control group had markedly better HRR and a superior autonomic function. Indices of HRV were correlated with HRR but not exercise capacity.

Key Words: Heart Rate Variability, Heart Rate Recovery, Maximal Exercise

INTRODUCTION

Recently, investigators have shown that an impaired heart rate recovery (HRR) from maximal exercise is associated with an increased risk of death from all causes (6) and from coronary heart disease (CHD) (5). The physiological mechanisms that allow heart rate to recover to resting values following maximal exertion are not fully elucidated (19). However, it is likely that a combination of sympathetic withdrawal and parasympathetic reactivation along with a reduction in blood pressure are responsible for early cardio-deceleration following exercise (4,12,21). Imai et al. (11) demonstrated that early HRR is primarily the result of vagal reactivation. This effect was blunted in heart failure patients, accelerated in athletes, and abolished by the administration of atropine.

The analysis of beat-to-beat heart rate variability (HRV) has been used extensively to investigate autonomic cardiac regulation in many populations (2), and has been shown to be reliable in short-term and long-term measurements (22). The variations in the heart rate interval may be quantified by time domain analysis via the recording of the R-R interval (RRint) or by spectral analysis to give a measure of total spectral power (TSP). Within TSP is a high frequency component (0.15 to 0.4 Hz: HFP), which is believed to reflect the activity of the parasympathetic division of the autonomic nervous system while the low frequency component (0.04 to 0.15 Hz: LFP) is thought to be generated by baroreceptor modulation of sympathetic and parasympathetic tone (18,20).

Given that HFP and to some extent the LFP measures of HRV are mediated by parasympathetic activity, as is HRR, then, HRV and HRR should show an association. The purpose of the present study was to compare autonomic function as assessed by HRR and HRV between CHD patients and a control group (disease free). A secondary purpose was to investigate the relationship between HRR and HRV.

METHODS

Subjects

Following the cardiologists' referral of subjects to a cardiac rehabilitation program, 48 male subjects were recruited to participate in this study prior to commencing the exercise component. Subjects were allocated to groups depending on their primary cardiac diagnosis and history of beta-blocker therapy. An additional 8 subjects were recruited from University staff as a sedentary control group matched for age and body mass. This study comprised of four groups: (a) the sedentary control group (CON, n=8) defined as participating in less than the recommended level (1) of physical activity (i.e., 30 min of moderate intensity exercise on most if not all days of the week); (b) a post bypass surgery group (CABG, n=17), none of which were using beta blockers; (c) a myocardial infarction (MI) group not taking beta blockers (MINBB, n=7); and (d) an MI group using beta blockers (MIBB, n=24). The myocardial infarction patients (MINBB and MIBB) were no more than 4 to 6 weeks post-event, and the coronary artery by-pass graft surgery patients (CABG) were no more than 6 to 8 weeks post-surgery (Table 1). Ethical approval was granted from the University of Chichester Research Ethics Committee as well as from the Wirral and West Cheshire NHS hospital trust. Subjects gave their written informed consent following a discussion outlining the study.

Procedures

Graded exercise tolerance test (GXT)

Prior to the graded exercise test (GXT) all subjects had a medical examination. This was part of the normal clinical work up at the Cardiac Rehabilitation Center, which is also in accordance with

published guidelines (1). Subjects completed a symptom-limited modified Bruce protocol continuing to volitional exhaustion. Testing for the study was carried out using a Marquette motorized treadmill (Marquette, Manchester, UK) interfaced to Marquette Centra acquisition module allowing for automatic protocol selection and continuous ECG monitoring. The test was terminated in accordance with established guidelines [1]. Throughout the GXT continuous electrocardiograph (ECG) monitoring of the heart was carried out.

Table 1. Subject Characteristics

Group	Age (yrs)	Height (m)	Mass (kg)	BMI ($kg \cdot m^{-2}$)
Control	53 ± 5	1.77 ± .03	80.33 ± 9.47	25.61 ± 3.29
CABG	60 ± 6	1.77 ± .03	83.97 ± 12.36	26.96 ± 4.18
MIBB	60 ± 7	1.75 ± .06	84.71 ± 9 .12	27.78 ± 2.55
MINBB	58 ± 8	1.78 ± .05	79.86 ± 9.01	25.11 ± 1.99

CON = Control group; CABG = post-bypass surgery group; MIBB = MI group using beta blockers; MINBB = myocardial infarction patients' group

Recovery of heart rate

On completion of the GXT, peak heart rate (HR_{peak}) and peak exercise treadmill time (PETT) were recorded. Then, the subjects spent 3 min in a cool-down period at a speed of 1.5 mph on a 0% grade (6). For the purposes of this study, heart rate recovery (HRR, $beats \cdot min^{-1}$) was calculated as HR_{peak} – HR recorded 1 min following completion of the GXT.

HRV acquisition

On a separate occasion, subjects laid supine for 5 min (22), during which a continuous 3 lead ECG was recorded using a MacLab 4e (AD Instruments Ltd, Oxfordshire, UK) interfaced to a Macintosh Powerbook 165C laptop computer running HRV graph module software version 2. To reduce variability in the data, this part of the study was completed in a quite room with no external disturbances. Subjects were made comfortable, and relaxed for 10 min prior to testing. The time domain measure, R-to-R interval (RR_{int}), and the following frequency domain measures were calculated: Total Spectral Power (TSP), High and Low Frequency Power (HFP, LFP), and the LF to HF ratio, (LF/HF a measure of sympathovagal balance).

Statistical Analyses

The data are presented as mean ± standard deviation. Group data were analysed using a one-way Analysis of Variance (ANOVA) and Tukey post hoc tests. A Pearson Product Moment Correlation Coefficient was used to determine relationships between PETT, HRR1, and indices of HRV. Statistical significance was set at P=0.05.

RESULTS

Exercise measurements

There were no significant differences among the groups for PETT, although the CON group had the lowest PETT of the four groups at 10.29 ± 0.39 min and the MINBB had the highest at 13.49 ± 0.80 min (Figure 1). Significant differences were shown between the groups for HRR ($F_{(3,52)} = 18.789$, P=0.0005), with the CON group having a statistically greater HRR (40 ± 4 $b.min^{-1}$) than the CABG (15 ± 2 $beats \cdot min^{-1}$), MIBB (16 ± 2 $beats \cdot min^{-1}$) and MINBB (16 ± 2 $beats \cdot min^{-1}$) groups. There was no difference between the patient groups (Figure 1).

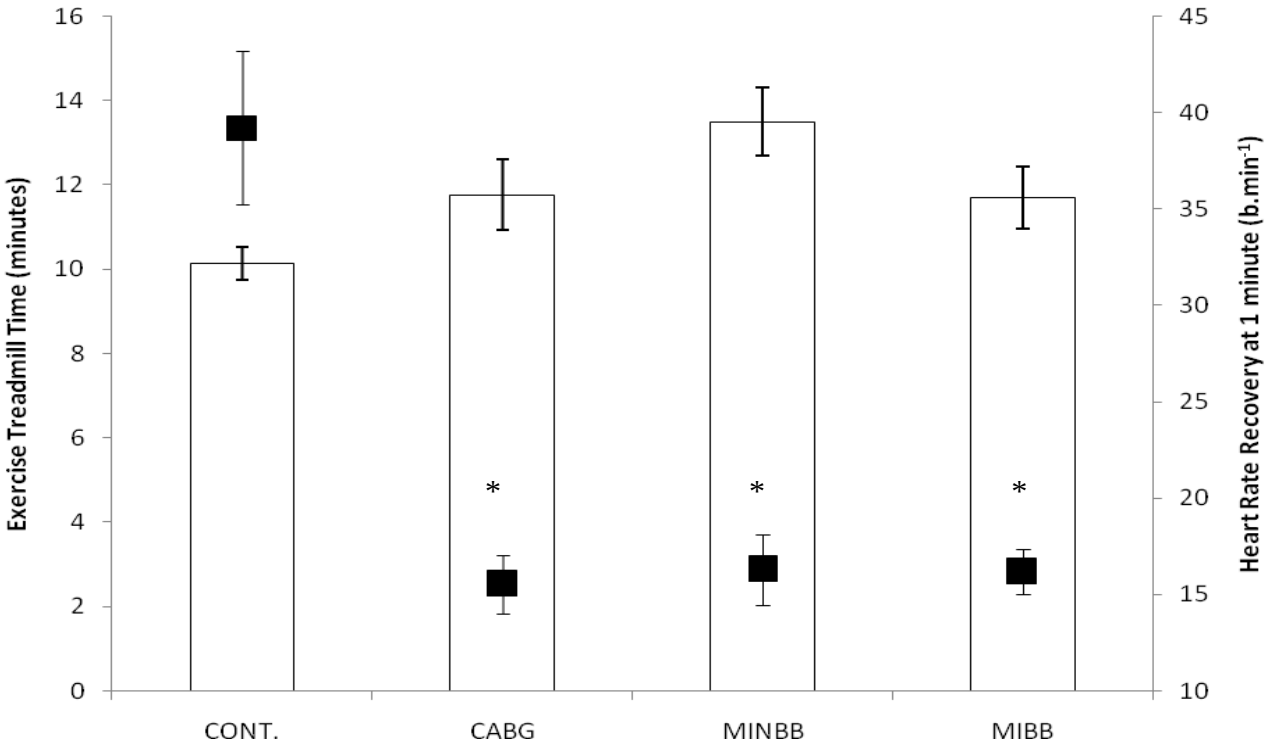

Figure 1. Peak Exercise Treadmill Time (open bars) and Heart Rate Recovery (HRR) from Peak Exercise (solid squares). *Indicates HRR significantly different from the Control group. Note: CON = Control group; CABG = post-bypass surgery group; MIBB = MI group using beta blockers; MINBB = myocardial infarction patients' group

Autonomic function

In general, the control group showed better global autonomic function in that the absolute values were significantly greater for most HRV components (Figures 2 through 6) with the exception of sympathovagal balance, where the LF/HF ratio was similar among all groups (P = 0.514, Figure 5). The MIBB also showed a significantly better HRV profile than the other cardiac groups for TSP, HFP and RRint (Figures 2,4 and 6), although the latter is probably a reflection of beta blockade therapy. The MIBB group showed no difference from the other cardiac groups for the LFP component of HRV (Figure 3), which was surprising given the primary affect of beta blocker medication. In addition, it would appear that the use of beta blockade improved the HFP component of HRV (Figure 4) as there was no significant difference between the control group and MIBB for this variable. The MIBB group differed significantly only from the control group in LFP.

Relationships between PETT & HRR and indices of HRV

Peak exercise treadmill time was not significantly associated with any indices of HRV or HRR. However, HRR showed a significant moderate positive association with indices of HRV; TSP r = 0.44, P=0.05, LFP r = 0.45, P=0.05 and HFP r = 0.356, P=0.05; but not the LF/HF ratio or RRint. This suggests that HRR is a function of both parasympathetic and sympathetic influence.

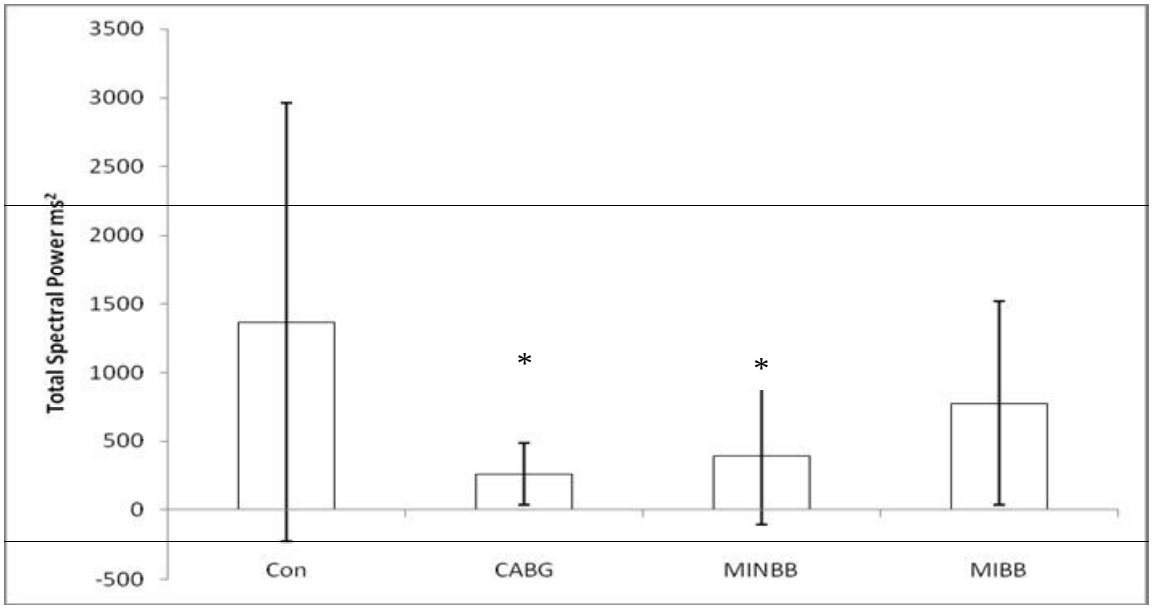

Figure 2. Differences in Total Spectral Power. *Indicates significantly different from the control group. CON = Control group; CABG = post-bypass surgery group; MIBB = MI group using beta blockers; MINBB = myocardial infarction patients' group.

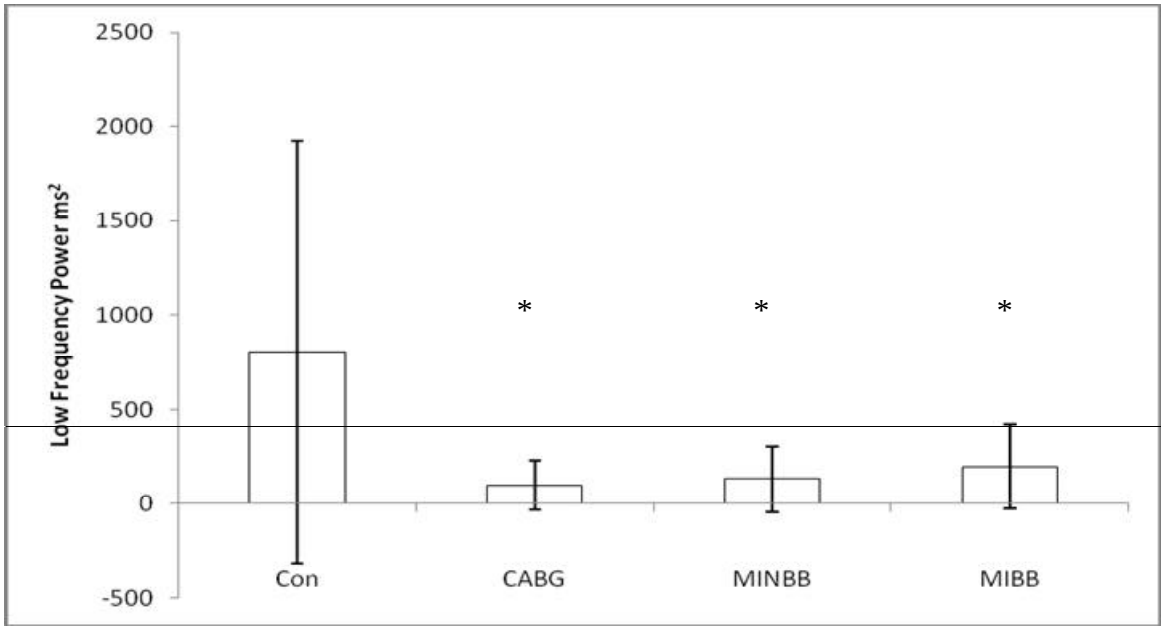

Figure 3. Difference in Low Frequency Power. *Indicates significantly different from the control group. CON = Control group; CABG = post-bypass surgery group; MIBB = MI group using beta blockers; MINBB = myocardial infarction patients' group

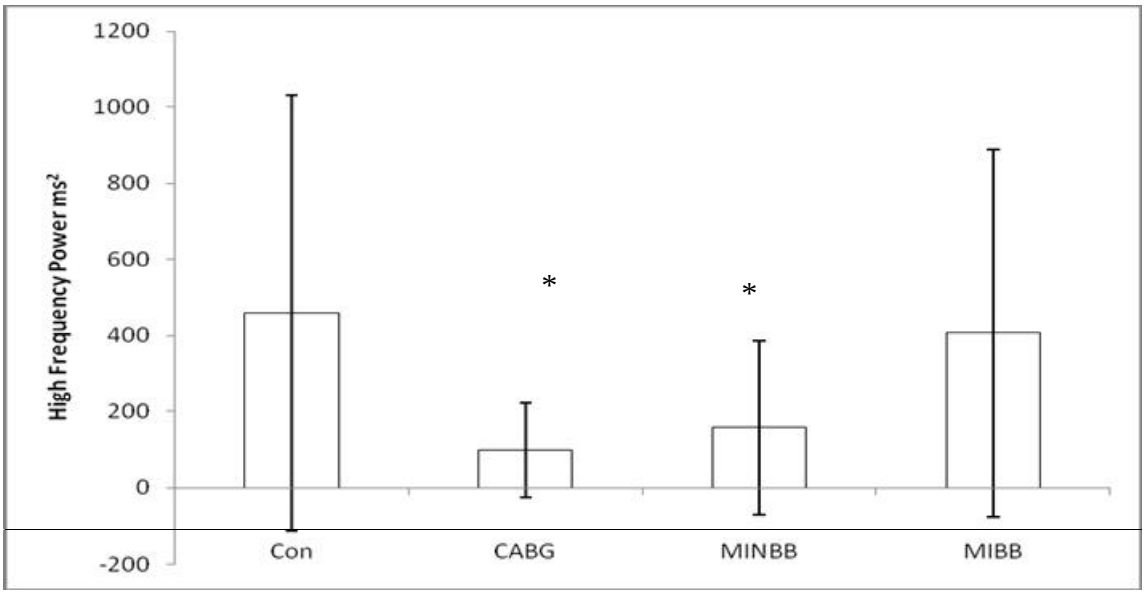

Figure 4. Difference in High Frequency Power. *Indicates significantly different from the control group. CON = Control group; CABG = post-bypass surgery group; MIBB = MI group using beta blockers; MINBB = myocardial infarction patients' group

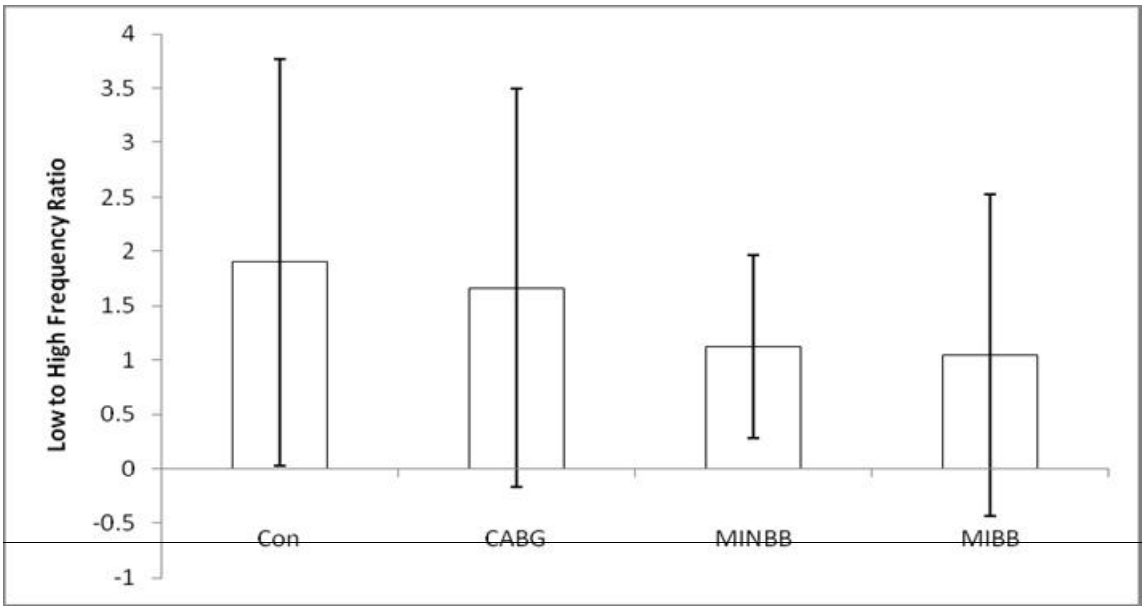

Figure 5. Difference in Low Frequency/High Frequency Ratio. CON = Control group; CABG = post-bypass surgery group; MIBB = MI group using beta blockers; MINBB = myocardial infarction patients' group

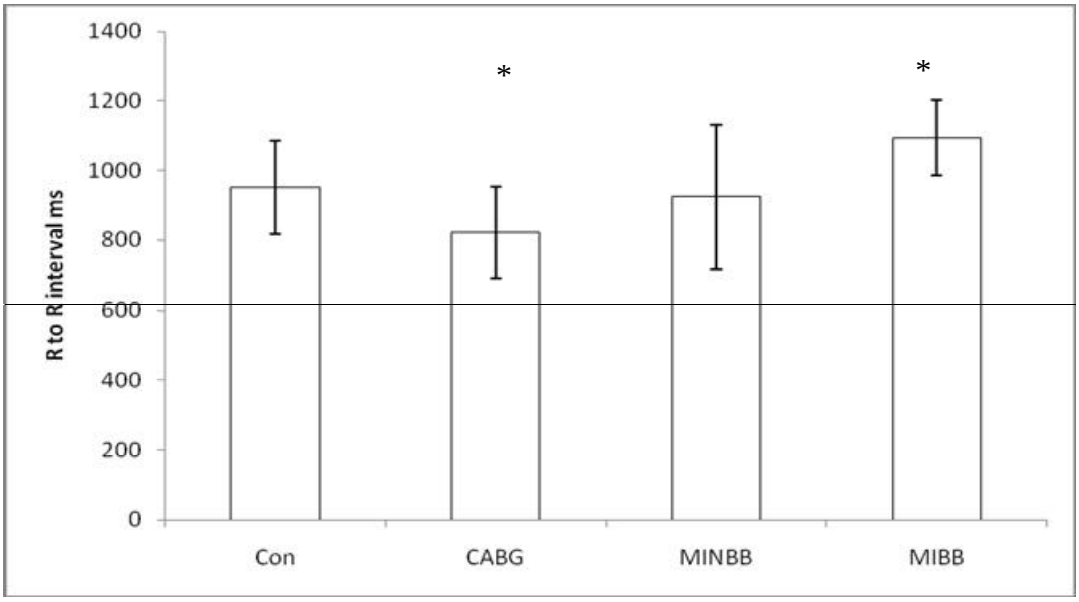

Figure 6. Difference in R-R interval. *Indicates significantly different from the control group.

DISCUSSION

This study found that the HHR following peak exercise is compromised in patients with CHD compared to sedentary controls despite similar levels of exercise capacity. Coronary heart disease patients showed a blunted HRR and diminished HRV, although the use of beta blocking drugs attenuated the latter to some extent. Heart rate recovery was moderately associated with resting measures of HRV while exercise capacity was not.

Exercise Capacity

The finding that the sedentary control group had a similar exercise capacity to CHD patients is somewhat surprising since it has been consistently demonstrated that CHD patients have a reduced exercise capacity. A reduced exercise capacity in CHD is a result of several changes occurring in the cardiovascular and muscular systems including a reduced mitochondrial content, a higher proportion of Type IIb muscle fibers, reduced maximal oxygen uptake (VO_2 max), reduced endothelium derived vasodilation, and reduced myocardial perfusion (3).

Heart Rate Recovery

The blunted HRR found in the present study in the CHD patients is more severe than that reported in other studies. Evrengul et al. (9) found a significantly reduced HRR in CHD patients of 23.6 ± 4.8 beats·min^{-1} during the first min following peak exercise compared to the controls (31.9 ± 9.4 beats·'min^{-1}). In the present study, the CHD groups showed a HRR of approximately 16 ± 2 b beats·'min^{-1}. This may be partly explained by the fact that none of the subjects in the Evrengul et al. Study (9) had suffered a prior MI or CABG, although they all had documented stable angina pectoris (whereas all subjects in this study had suffered from both). Furthermore, the subjects in Evrengul et al. (9) were not categorized as having an abnormal HRR response. That is, as defined by the work of the Cleveland clinic investigators (6) who have suggested 2 cut points: =12 beats·'min^{-1} or =18 beats·'min^{-1}, dependent on the mode of exercise testing. Our subjects demonstrated an abnormal response using the second criterion. This disparity between HRR in the two studies may also result

from the protocol used during recovery. Evrengul et al. (9) differed from the present study in that their subjects rested in a supine position immediately following maximal exercise; whereas, our subjects followed an active recovery of treadmill walking at a speed of 1.5 miles·hr^{-1} as described by the Cleveland investigators (6) and as advocated by Morise (15). Unfortunately, the variability in study protocols and the criterion for an abnormal response limit the generalizability between studies (15). The mode of recovery, active versus passive, is an important issue that needs to be standardized across future studies as Carter et al. (4) have shown a significant difference in post-exercise HR decline when using an active, inactive or passive recovery protocol in spite of subjects only exercising at 60% of their predicted HR_{max}.

The mechanisms responsible for the recovery of HR are not firmly established, although clearly an adjustment in autonomic balance is involved. Savin et al. (21) suggest that HRR is not solely dependent on the influence of the autonomic nervous system. They concluded that the post-exercise exponential decline in HR is an intrinsic property of the intact circulation. This was based on the results that HR declined after exercise in a similar fashion, irrespective of parasympathetic blockade, sympathetic blockade or a combination of both. Their data highlighted the contribution of sympathetic withdrawal in the initial stages of cardio-deceleration with increasing parasympathetic activation later in the recovery process. Other factors such as skeletal muscle pumping, total peripheral resistance, and mean arterial pressure also influence cardio-deceleration and autonomic regulation (4).

Heart Rate Variability

Kleiger and colleagues (13) demonstrated an association between increased mortality following acute MI and decreased measures of HRV that remained significant after adjusting for clinical, demographic variables, and left ventricular ejection fraction. The CHD subjects in the present study had suffered an AMI or had undergone CABG surgery. Frequency domain analysis showed group differences for all indices of HRV except for the HF/LF ratio. Total Spectral Power and HFP were significantly higher in the control group compared to the MINBB and CABG groups, which suggested superior autonomic parasympathetic function in the control group. This is consistent with others studies that have found similar results. Evrengul et al. (9) showed reduced high frequency power in 38 patients with CAD compared to controls and a reduction in PNN50 (a marker of parasympathetic activity). Interestingly, in the present study, the MIBB group showed no significant differences to the controls for TSP or HFP. Beta blockers have been shown previously to improve the recovery of parasympathetic tone following an acute MI (14). Reduced HFP in Lampert's study (14) was associated with an increased relative risk of death, AMI or CHF, with relative risk ratios (RR) of 0.48 in treated patients with low HFP versus RR 0 in treated patients with high HFP. The RR was increased still further in those who were not taking beta blockers. The effect of propranolol was also evident in the sub group of patients who had high HFP (i.e., RR 0.0 in the treated group compared to 0.18 in the untreated group). This randomized trial confirmed previous research suggesting a similar affect in subjects without CAD (7,17) and in patients with previous CAD (16).

In our study, all CHD groups had reduced LFP compared to the control group. This finding was expected as others studies have shown a reduction in LFP in CAD (23). Wennerblom et al. (23) showed significantly reduced low frequency power in uncomplicated coronary artery disease patients during night time and day time recording of HRV. They concluded that the reduction in LFP resulted from a general reduction in total power and reduced vagal activity; LFP is thought to encompass fluctuations in both parasympathetic and sympathetic tone. Their conclusion that LFP is mediated at least in part via vagal activity is supported by their finding that both HFP and LFP were higher during the day than during the night. Consistent with our study, LFP was reduced in the CABG patients compared to the controls (10). In Hougue's study (10), measures of HRV were 40 to 50% less following CABG as compared to patients undergoing other vascular surgery or a non-surgery control

group. Our data are consistent with these findings. However, Hogue's (10) study compared the differences in HRV following surgery for only a short period of follow up (i.e., 5 days in most cases). Demirel et al. (8) completed a long term analysis of HRV following CABG and concluded that post-operative measures of HRV dropped precipitously following surgery. But, they had recovered to near pre-operative values at 3 months and continued to recover during a 1 yr follow-up. Interestingly, their data revealed low frequency power recovered earlier than high frequency power. This was confirmed by a continual rise in the LF/HF ratio, thus implying that recovery of parasympathetic function is slower than that of sympathetic function. The high frequency component was still reduced at 1 year follow up.

While our study has found significant differences in measures of HRV between CHD patients and controls, the LF/HF ratios are similar in all groups. Therefore, although TSP may be reduced and the LFP and HFP components are reduced, CHD patients are still able to mount a functional shift in autonomic balance. Although this response may be blunted (and as previously shown), the effect was attenuated by the use of beta blockers. The MIBB group showed in some aspects a better profile than the control group.

CONCLUSIONS

This study found that despite showing similar levels of fitness, patients suffering from CHD have a reduced ability to recover HR following maximal treadmill exercise. This may be due to impaired autonomic function as evidenced by reduced indices of HRV and or as the result of a non-compliant vascular system. Future studies should attempt to assess changes in HRR and HRV in response to pharmacological intervention and exercise training and consider whether improved HRR translates into an improved clinical outcome.

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