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Faster Heart Rates During Early Graded Exercise May Account for Shorter Exercise Time Duration in Women

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Abstract: Recent data suggests that measures of autonomic dysfunction while differ with heart rate, gender and functional capacity are unaffected by body mass index (BMI); however none of these same parameters have been assessed during routine stress testing despite the well-known modulation of heart rate (HR) by the autonomic nervous system during dynamic exercise. In this study, data from 88 consecutive individuals who had a normal treadmill stress echo study was analyzed and differences in HR during and after exercise were recorded and examined with regards to gender, BMI and total exercise duration. An exercise capacity of less than 9 min identified individuals with significantly faster increments in HR during early stages of exercise ($p<0.02$ for 1 min, $p<0.0003$ at 2 min, $p<0.0001$ at 3 min) when compared to individuals who exercised longer. Although, no statistical difference was noted between HR response with either age or BMI, females had significantly higher increments in HR early during exercise than males (115±15 versus 103±15 beats per minute; $p< 0.0004$; respectively) at 1 min, (125±17 versus 109±16 beats per minute, $p<0.0001$) at 2 min, (129±17 versus 112±18 beats per minute, $p<0.00002$) at 3 min and (144±18 versus 130±18 beats per minute $p<0.001$) at 6 min even though both females and males attained similar peak HR. Rapid increments in HR early into exercise occur more commonly in females; that although independent of age and BMI, are associated with a shorter exercise time duration. Further studies are now required to assess the importance of these fast increments in HR early into exercise seen more commonly in females, in the absence of exercise-induced myocardial ischemia and with a preserved left ventricular systolic function, with relation to long term cardiovascular events.

Key words: Cardiac deconditioning, cardiovascular events, exercise stress testing, heart rate response, left ventricular ejection fraction

INTRODUCTION

It is well known that heart rate (HR) response to dynamic exercise is primarily modulated by the autonomic nervous system [1,3] A rapid increase in HR occurs during the first few seconds of exercise that is exclusively mediated by vagal inhibition that is independent of the exercise intensity [4]. As exercise continues there is a progressive acceleration in HR, which is usually proportional to the intensity of the exercise performed and is mediated by an increase in sympathetic activity. Then immediately upon cessation of exercise, there is a decrease in HR as a result of vagal reactivation and a reduction in the sympathetic stimulation[4].

Although changes in autonomic function, as measured by heart rate variability and baroreflex sensitivity, have been independently associated with adverse prognosis in patients with heartx failure and following acute myocardial infarction;[5] the potential role of autonomic dysfunction in otherwise healthy individuals has been less clear. However, compelling data recently published by Antelmi and associates using time- and frequency-domain indexes of heart rate variability, a marker of autonomic function published showed that not only there is an inverse correlation between heart rate variability and heart rate but also that heart rate variability indexes differed by gender, were higher in patients with higher functional capacity and were not associated to body mass index (BMI) [6]. Based on these results we designed a study to assess changes in heart rate response during exercise between males and females and the effect that both BMI and functional capacity have on this heart rate response.

MATERIAL AND METHODS

Study population: A total of 115 consecutive participants gave informed written consent and underwent a standard Bruce protocol followed by echocardiographic imaging after all beta or calcium antagonists with

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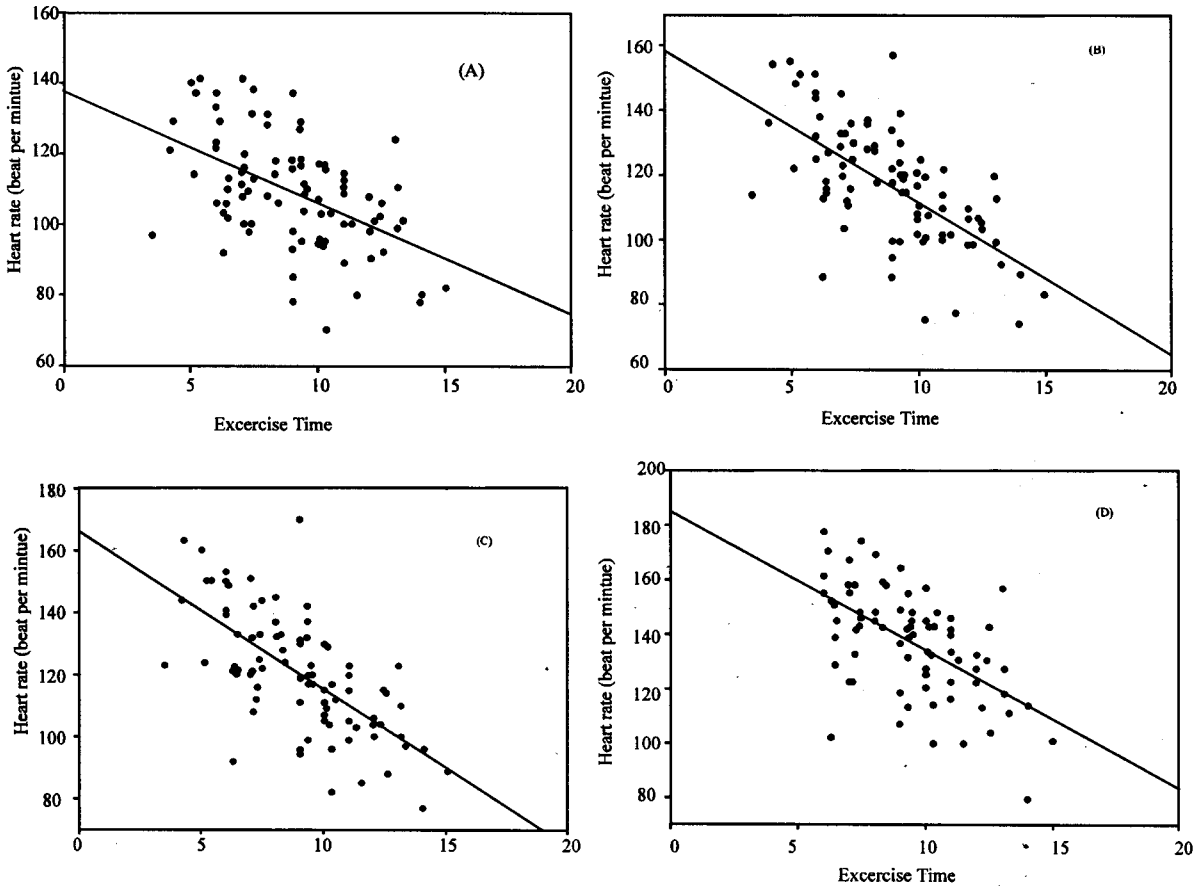

Fig.1: Indivisual heart rate expressed as beat per min at (A), 2 min (B) min (C) and (D) into excercise time duration

atrioventricular blocking properties were held for at least 48 hours before testing. Participants were ineligible if there was history of preexcitation syndrome, paced rhythms, sysmptoms of heart failure, left bundle branch block, ST-segment > 1mm depression in 2 consecutive leads on the resting electrocardiogram, digoxin or amiodarone use, congenital or valvular heart disease, persistent or permanent atrial fibrillation, uncontrolled hypertension (systolic blood pressure of more than 180 mm Hg or diastolic reading more than more than 110 mm Hg), pregnancy, significant peripheral vascular, pulmonary or musculoskeletal disease, or inadequate visualization of all 16 myocardial segments as recommended by the American Society of echocardiography [7]. A detailed interview was performed and included reason for the study, symptoms, coronary artery risk factors, prior cardiac events, list of all current medications and other pertinent medical history. Physical activity was assessed with the question: "Do you regularly engage in strenuous exercise or hard physical labor?" and participants were considered to engage in regular exercise if they answered affirmatively. The study had institutional review board approval from the University of Pittsburgh Medical Center.

After a supine rest electrocardiogram was obtained, symptom-limited exercise testing was conducted according to the standard Bruce protocol [8]. Target HR (THR) was determined prior to initiation of the exercise protocol using the conventional equation [9].

Maximal HR = 220-age (in years)

The test was concluded when either the age-predicted HR of at least 85% or maximal physical activity was attained.

ST-segment depression was defined as at least 1.0 mm horizontal or downsloping depression at 0.08 seconds after the J point in the lead with the greatest abnormality in the last stage of exercise or recovery. Peak exercise capacity was estimated from treadmill time and expressed in metabolic equivalents (METs) [10]. Data on symptoms, HR, rhythm and blood pressufe at rest, during each minute of exercise, at peak and 2 min into recovery were

collected. Differences in HR between rest and each minute into exercise and peak exercise were calculated. In addition, HR recovery was defined as the difference between the peak HR and the HR 2 min into recovery.

Two-dimensional echocardiography was performed before and immediately after exercise using standard methods as described elsewhere [11]. Interpretation was based on one attending physician. Left ventricular ejection fraction was estimated visually. The standard 16-segment model of the left ventricle was used to identify wall motion [12].

Statistical analysis: All continuous variables showed a normal distribution. Comparison between groups for pretest differences in independent variables was made using the Student's t test for unpaired samples. Statistical analysis on age, BMI, diabetes, obesity, dyslipidemia, hypertension, smoking, family history of premature coronary heart disease, left ventricular systolic function, METs achieved, blood pressure readings, differences in HR achieved and recovery HR were performed using analysis of variance. A value $p<0.05$ was considered significant. Stepwise forward and backward Cox regression analyses (at the .05 significance level) were used to statistically select which exercise test variables were independent predictors of risk. SPSS version 10.0 (SPSS Inc) was used for calculations.

RESULTS

Fifteen stress tests were excluded from the analysis based on predetermined criteria and another 12 additional studies were also excluded due to development of a new wall motion abnormality [12]. Thus, the study population included for final analysis was that of 88 individuals who were able to complete the exercise protocol (Table 1). None of the participants developed chest pain, significant arrhythmias, hypotension, or had any electrocardiographic changes.

A wide distribution in HR was noted during the first 3 min of exercise, which became less evident by 6 min. In particular, a specific correlation between a rapid increase in HR during the first few minutes of exercise and exercise duration was noted. (Fig. 1A-D) In general, individuals with an exercise capacity of less than 9 min had a statistically significant faster increase in HR during the first 3 min of exercise compared to those individuals who exercised for more than 9 min ($p<0.02$ for 1 min, $p<0.0003$ at 2 min, $p<0.0001$ at 3 min). In addition, as seen in Table 2, individuals who exercised less than 9 min had A significantly slower HR recovery when compared to patients who exercised more than 9 min (47±17 versus 63±29 beats per minute; $p<0.003$).

Table 1: Demographic data (BMI = Body Mass Index, PVD= Peripheral Vascular Disease, CAD = Coronary Artery Disease, ACE = Angiotensin Converting Enzyme, SOB= Shortness of Breath, DOE = Dyspnea On Exertion)

Variables	Results (n = 88)
Age	56±13
BMI	27±5
Gender	Females 44
Race	Whites 75
Hypertension	29
Diabetes Mellitus	8
Hyperlipidemia	34
Smoker	12
Ex-smoker	21
PVD	2
Prior History CAD	11
Family History of CAD	27
Pulmonary Disease	6
Musculoskeletal Disease	4
Medications	-
Beta-blockers	8
Calcium channel blockers	8
ACE inhibitors	13
Indication for testing	-
Chest pain	36
SOB/DOE	18
Palpitations	12
Abnormal ECG	6
Syncope	3
Other	13

Table 2: HR Recovery

Variables	HR. Recovery	p.value
All patients	56±26	-
Exercise	-	-
Less than 9 min	47±17	0.003
More than 9 min	63±29	-
Gender	-	-
Females	54±28	0.3
Males	59±23	-

No statistical difference between age and BMI between females and males as shown on Table 3. However, females had significantly faster HR as early as 1 min into exercise than males (115±15 versus 103±15 beats per minute; $p<0.0004$; respectively). These differences persisted at 2 min (125±17 versus 109±16 beats per minute, $p<0.0001$), 3 min (129±17 versus 112±18 beats per minute, $p<0.00002$) and 6 min (144±18 versus 130±18 beats per minute $p<0.001$) into exercise. Although both females and males attained similar THR (164±17 versus 164±14 beats per minute), females accomplished their total exercise sooner (7.9±2.2 min) than males (10±2 min, $p<0.0001$).

Consequently, the total workload attained by women was less (9.0±2 versus 11±2 METs; $p<0.0001$) than males.

Finally, no statistical difference was found between

Table 3: Gender differences (BMI = Body Mass Index, HR = HR, METs = Metabolic Equivalents, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure and LVEF = Left Ventricular Systolic Function)

Variables	Females (44)	Males (44)	p value
Age	56±13	56±13	NS
BMI	27±6	27±4	NS
Supine HR	74±12	71±10	NS
Standing HR	87±13	84±13	NS
Hyperventilation HR	90±15	91±14	NS
1 min Exercise HR	115±15	103±15	0.0004
2 min Exercise HR	125±17	109±16	0.0001
3 min Exercise HR	129±17	112±18	0.00002
6 min Exercise HR	144±18	130±18	0.001
Peak HR	164±17	164±14	NS
METs	9.0±2	11±2	0.0001
Total Exercise Time	7.9±2.2	10±2	0.0001
Baseline SBP	136±20	136±17	NS
Baseline DBP	81±9	82±10	NS
Peak SBP	177±24	194±29	0.005
Peak DBP	86±10	91±14	NS
LVEF	57±7	58±5	NS
HR recovery	54±28	59±23	NS

females and males (59±23 versus 54±28, p=NS, respectively) with regards to HR at 2 min post cessation of exercise. The peak systolic blood pressure was lower in females than males (177±24 versus 194±29 mmHg; p<0.004) with no difference noted in diastolic blood pressure readings (86±10 versus 91±14 mmHg; p=NS, respectively).

DISCUSSION

Heart rate responses in normal individuals before, during and immediately after cessation of exercise are modulated by a complex interaction between functional capacity and rhythmic fluctuations of the autonomic nervous system [13,18]. It is well known that both exercise capacity and each individual physical activity status are inversely related to the overall risk of cardiovascular disease[19,20] . In addition, both chronotropic incompetence or an attenuated HR response during exercise is a predictor of coronary heart disease events and total mortality as well as a delayed decrease in HR after exercise predicts all-cause mortality [22,27]. However, how changes in autonomic function might be related to other exercise variables that can be routinely measured in otherwise normal individuals with preserved left ventricular function and no demonstrable ischemia are less clear. We conducted a prospective study to analyze changes in heart rate during exercise and the effect of gender, BMI and overall exercise time given the provocative findings by Antelmi and associates that used frequency-domain indexes of heart rate variability, a marker of autonomic function and found not only an inverse correlation between heart rate variability and heart rate but also that heart rate variability indexes differ by gender and functional capacity but not by BMI [6].

Present results revealed a statistically significant time-dependent dichotomy that exists between HR response early into exercise and overall exercise time duration. Specifically, individuals that exercise for less than 9 min had faster increments in HR at low workloads with the strongest correlation seen during the first 3 min of graded exercise. Despite this time-dependent dichotomy, individuals were still able to reach their respective THR. In addition, these same individuals who exercised less than 9 min also had a significantly slower HR recovery when compared to individuals who exercised for more than 9 min. Such correlation was lost when examing this parameter between males and females. This specifc gender correlation has not been previoulsy adressed in other studies [28,29].

In addition, we noted that a shorter exercise duration predicted a slower HR recovery. Obvioulsy, the true significance of this association remains unclear and although suggests that patients with a slower HR recovery could be at risk of adverse cardiovascular outcomes given the results of recent reports [28,30] a longitudinal follow-up of these patients is definitively needed before any conclusions can be drawn.

A more significant finding is that women have faster increments in HR early during exercise than males of comparable age and BMI. These changes were readily appreciated as early as 1 min into exercise and persisted for the first 6 min of graded exercise. Although both males and females attained similar THR, it took females less time to accomplish the total workload than males. Finally, we also documented a gender specific difference with regards to HR recovery after cessation of exercise.

The small sample size is an obvious limitation, however, this study was intended to assess if indeed an intrinsic difference in HR response could be identified in order to incorporate these variables into a larger scale study. We also recognize that although exercise capacity was estimated on the results of a symptom-limited exercise test and this might inappropriately reduced our estimates of peak exercise capacity; exercise duration was not a limiting factor in our study. Therefore, we do not think that this would alter the association between HR response and total exercise duration. Lack of long-term follow-up data is another limitation that usually confers more validity for any given finding but we are simply making reference to its occurrence. Finally, since no standard measurements of autonomic function were used in this study, we can't make any specific correlation between our results and autonomic function' however our results are in complete agreement with the results published by Antelmi and associates[6].

Although there is a large body of literature demonstrating that women have higher resting heart rates,

higher cardiovascular reactivity, differing HR variability indicative of differing vagal and sympathetic tone and differing baroreceptor response to a variety of conditions when compared to men [31,36] no previous study has identified that woman also have rapid increments in HR early during regular graded exercise and that these changes in HR might be related to their reduced total exercise time duration when compared to males of similar age and BMI.

In summary, this study showed that in individuals with no documented ischemia and normal left ventricular systolic function, a reduced exercise time duration was associated with faster increments in HR early into exercise with a corresponding slower HR recovery after cessation of the exercise protocol. More importantly these faster increments in HR at low workloads, independent of age, BMI, resting or recovery HR, were particularly seen among women. These faster increments in HR with exercise not only is suggestive of a combination involving an intact vagal tone with an inordinate sympathetic activation but also may account for the previously reported physiological and functional differences between males and females in response to dynamic exercise[37].

CONCLUSION

A fast HR response during the first 3 min of graded exercise, as it might relate to cardiac deconditioning mediated by an altered autonomic response, could be used to further stratify women undergoing stress testing even when other traditional testing parameters are unremarkable. Further studies are now required to not only assess the importance of these fast increments in HR early into exercise seen more commonly in females, but also to determine the effect of both ischemia and abnormal left ventricular systolic function on these HR responses early with exercise as potential markers of adverse cardiovascular outcomes.

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