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Original Article

# Impact of Phase II cardiac rehabilitation on abnormal heart rate recovery

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#### Abstract

*Background*: A delayed decrease in heart rate recovery (HRR) following a maximal exercise test is a predictor of mortality in healthy adults and in those referred for diagnostic testing evaluation. Cardiac rehabilitation (CR) has been proven to be beneficial in the treatment of numerous diseases. The purpose of this retrospective study was to explore the relationship between CR and improvement of HRR and to determine which factors can be predictive for the improvement of abnormal HRR after Phase II CR.

*Methods*: We reviewed the medical histories of patients referred for symptom-limited cardiopulmonary treadmill testing with abnormal HRR. Each patient underwent exercise testing before and after Phase II CR, and parameters including functional aerobic impairment, metabolic equivalent, anaerobic threshold (AT), and %AT were recorded and compared.

*Results*: Of the 25 patients recruited, 13 patients showed no abnormal HRR after Phase II CR. The functional capacity of these patients was improved after Phase II CR, to a statistically significant extent; the aerobic capacity (as expressed with AT and %AT) showed improvement, but without statistical significance.

*Conclusion*: There are multiple factors of cardiopulmonary exercise tests that cannot be used to predict the effect of Phase II CR on the improvement of abnormal HRR. Forty-one percent of patients with abnormal HRR could improve after Phase II CR, but all of the patients could have improved exercise capacity regardless of whether or not HRR improved. We can conclude that HRR and exercise capacity change independently. However, it is important to closely follow-up during Phase III CR for patients with persistently abnormal HRR after Phase II CR has been completed. Copyright © 2014 Elsevier Taiwan LLC and the Chinese Medical Association. All rights reserved.

Keywords: abnormal heart rate recovery; cardiac rehabilitation; cardiopulmonary exercise testing

## 1. Introduction

There is mounting evidence that supports the inverse relationship between physical activity and premature mortality, hypertension, stroke, osteoporosis, type 2 diabetes, metabolic syndrome, obesity, colon cancer, breast cancer, depression, falls, and cognitive function.<sup>1</sup> Exercise-based Phase II 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.<sup>2,3</sup> Change in heart rate (HR) during exercise and recovery from exercise are mediated by the balance between sympathetic and vagal activity.<sup>2,4</sup> An attenuated heart rate recovery (HRR) after exercise, thought to be a marker of reduced parasympathetic activity,<sup>5,6</sup> has been established as an independent prognostic marker of overall mortality.<sup>2,7–12</sup>

Exercise training has been shown to increase resting parasympathetic tone and to decrease sympathetic tone in both humans and animals.<sup>13,14</sup> Parasympathetic activation is considered to be the main mechanism underlying exponential cardio-deceleration after exercise.<sup>15,16</sup>

A delayed decrease in HRR following a maximal exercise test is a predictor of mortality in healthy adults and in those referred for diagnostic testing or physical fitness evaluation.<sup>7,10,12</sup> These findings are independent of the workload achieved during the test, presence or absence of myocardial

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perfusion defects, and changes in heart rate during the exercise test.<sup>2,9,17</sup> In a review of the literature,<sup>2,3,7–10,18–21</sup> most of the achieving of peak workloads, expressed in metabolic equivalent (MET; 1 MET equals 3.5 mL of oxygen uptake/kg of body weight/minute), were estimated from treadmill speed and grade, not from collecting and analyzing expired gas during exercise testing. The direct measurement of peak VO<sub>2</sub> has been shown to be a more accurate predictor of survival than indirectly derived peak VO<sub>2</sub>.<sup>22</sup> There is no measure of aerobic capacity (measured as anaerobic threshold; AT).

The purpose of this retrospective study was to explore the relationship between CR and improvement of HRR and to determine which factors (directly measured from exercise testing) can be predictive of an improvement in abnormal HRR after Phase II CR.

## 2. Methods

#### 2.1. Patient sample

The cohort for this study was derived from chart records of patients referred for symptom-limited cardiopulmonary treadmill testing at our medical center hospital from January 2008 to December 2012. Patients were excluded if they had a history of pacemaker use, arrhythmia, heart transplantation, heart failure New York Heart Association (NYHA) class III/IV, use of digoxin/antiarrhythmic drugs, or diabetes mellitus with autonomic dysfunction. Our Institutional Review Board approved the use of this clinical database for purposes of our research.

HRR was defined as the difference between HR at peak exercise and exactly 1 minute or 2 minutes into the recovery period. A HRR value  $\leq$  12 beats/minute at 1 minute into the recovery phase or  $\leq$  22 beats/minute at 2 minutes into the recovery phase was considered abnormal on the basis of previously published and validated work.<sup>2,7,16,23</sup>

We identified 126 patients who had abnormal HRR during exercise testing before Phase II CR, and 25 consented to participate in Phase II CR. Each patient underwent exercise testing before and after Phase II CR during which abnormal HRR was prospectively recorded.

### 2.2. Cardiopulmonary exercise testing

Patients were in the standing position, and the pulmonary function test was performed with the V max pulmonary function analyzer (Carefusion, San Diego, CA, USA). If the predicted exercise heart rate (220 - age) was met, abnormal signs were found on electrocardiography, or any discomfort was felt by the patients, the test was terminated.

Aerobic threshold was identified using V-slope analysis.<sup>24,25</sup> Functional aerobic impairment (%FAI) was calculated as follows<sup>26</sup>:

#### 2.3. Phase II cardiac rehabilitation

The most important goal of Phase II CR is to assist patients in developing and implementing safe and effective formal exercises and lifestyle-based physical activity programs. Phase II CR consisted of a highly structured program in which patients followed a specific exercise program according to an established protocol.<sup>27,28</sup> Patients exercised under supervision for 12–16 weeks, typically involving two or three visits/week. Sessions generally consisted of a 10–15-minute warm-up and stretching period, followed by 30–50 minutes of continuous aerobic exercise at an intensity of 50–80% of HR reserve calculated from the entry exercise cardiopulmonary treadmill test.<sup>27–29</sup> Sessions ended with a 10–15-minute cool-down period.

## 2.4. Statistical analysis

Statistical analysis was performed using SPSS version 18.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to establish patient characteristics and continuous data were expressed as mean  $\pm$  standard deviation. Intergroup differences were presented using the analysis of variance test or paired *t* test. A *p* value < 0.05 was considered statistically significant.

### 3. Results

Twenty-five patients were recruited into this retrospective study (Table 1). Data comparing baseline HR, peak HR, HRR1, and HRR2 before and after CR are shown in Tables 2 and 3, respectively. The functional capacity (expressed as MET) and %FAI were improved after Phase II CR, to a statistically significant extent; the aerobic capacity (as expressed with AT and %AT) showed improvement, but without statistical significance (Table 4). Among the 12 patients in the subgroup with persistently abnormal HRR, functional capacity and %FAI improved with significance, but not aerobic capacity (measured as AT and % AT; Table 5). Phase II CR yielded the same results and characteristics in the group with an absence of abnormal HRR as in the persistently abnormal HRR group (Table 6). In the comparison between the two subgroups (persistent vs. absence), none of the variables were statistically significant (Table 7).

### 4. Discussion

This study used the direct collection of expired gas method for analysis (not the estimated method used in most reports) to seek factors that can be predictive of improvement in abnormal HRR after Phase II CR. Our study results show that the varying factors of cardiopulmonary exercise cannot be

Table 1 Patient characteristics.

Characteristics	Baseline leve	
Age (y)	$63.0 \pm 10.5$	
Sex (male/female)	15/10	
Height (cm)	$165.5 \pm 6.0$	
Body weight (kg)	$70.2 \pm 7.6$	
Body mass index (kg/m <sup>2</sup> )	$25.5 \pm 6.0$	
Duration of Phase II training (wk)	$13.0 \pm 3.5$	
Clinical diagnosis		
Post-CABG	6	
Post valvular heart disease	9	
CAD status post-PCI	3	
CHF	5	
COPD	2	

CABG = coronary artery bypass graft; CAD = coronary artery disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; PCI = percutaneous coronary intervention.

predictive of the effect of CR on improving abnormal HRR, although functional capacity significantly improved (as measured with MET and %FAI) after Phase II CR. This implies that HRR and exercise capacity changed independently.<sup>2</sup>

Approximately 130-150 patients receive exercise testing in our medical center per year. Due to the minimal recognition of Phase II CR as a therapeutic tool, limited referral from other specialists, and the fact that few medical centers are capable of executing CR, the percentage of patients that actually join cardiac rehabilitation is only around 20-30%. Furthermore, due to our exclusion criteria, only a small number of cases were included in this retrospective study. We also hope to promote Phase II CR by the publication of our study. In our hospital, not many patients enter the Phase II CR program at the conclusion of their Phase I rehabilitation. It is rare that patients with acceptable exercise testing results before entering Phase II cardiac rehabilitation enter the Phase III CR program directly. In Taiwan, fewer physicians evaluate physical fitness with exercise testing during Phase III follow-up. This is also the problem that we face when promoting the use of CR.

Table 2

Heart rate in patients with persistent abnormal heart rate recovery (HRR; 12 patients).

Heart rate (before/after CR; beats/min)	Baseline heart rate	Peak heart rate	HRR1	HRR2
A	115/110	162/160	157/150	150/141
В	89/91	152/162	146/151	140/142
С	69/72	123/135	115/125	103/114
D	101/110	122/132	115/121	102/102
E	96/90	151/146	140/136	131/123
F	75/80	139/136	129/125	114/113
G	103/114	151/160	141/149	130/140
Н	94/100	111/123	109/113	100/99
Ι	95/89	141/130	130/121	118/110
J	74/72	141/138	138/130	135/116
Κ	64/66	109/112	100/103	85/92
L	81/78	141/135	131/128	121/116

CR = cardiac rehabilitation.

Table 3									
Heart rate in	patients v	with im	proved	heart	rate	recovery	(HRR;	13	patients).

Heart rate (before/after CR; beats/min)	Baseline heart rate	Peak heart rate	HRR1	HRR2
M	78/84	123/130	113/117	100/106
N	96/100	162/158	151/145	133/130
0	105/100	123/130	115/117	102/100
Р	88/84	100/114	100/101	90/89
Q	83/88	146/140	135/120	126/103
R	106/108	137/140	128/125	118/112
S	88/86	113/105	110/90	101/78
Т	88/93	144/139	133/119	126/109
U	97/93	141/138	133/118	111/103
V	68/77	116/127	109/108	101/99
W	95/99	141/134	134/114	120/108
Х	94/100	119/128	109/110	105/99
Y	103/100	140/129	133/112	123/100

CR = cardiac rehabilitation.

Some controversy remains concerning the correct definition of "abnormal HRR". Most reports use an HRR value  $\leq 12$ beats/minute after the recovery phase or  $\leq 22$  beats/minute at 2 minutes into the recovery phase, as we used in this study. Some authors used "a reduction of 12 beats/minute after a slow cessation of exercise and < 18 beats/minute after a sudden cessation of exercise as abnormal".<sup>7,22,30</sup> Cole et al<sup>18</sup> used HRR after submaximal exercise testing to predict mortality in a cardiovascular-healthy cohort. They defined abnormal HRR as "a change of < 42 beats/minute from peak HR to that measured 2 minutes later". Overall, the threshold value for an abnormal (cut-point) standing exercise test still varies.

In this retrospective cohort of patients undergoing CR, HRR improved in 52% of patients with an abnormal baseline HRR before CR. Our results seemed better than those of Jolly et al,<sup>2</sup> wherein a 41% improvement in HRR was noted. However, the disparity in these results may be due to the small sample size in our study. The predictors of failure to improve HRR included older age, peripheral arterial disease, DM, prior heart failure, and the use of nitrates.<sup>2,9,18</sup> The strength of the predictor is still unknown and should be a subject for further study.

Impaired functional capacity and abnormal HRR were strongly associated with lower socioeconomic status and accounted for a major proportion of the correlation between socioeconomic status and mortality.<sup>11</sup> Jolly et al<sup>2</sup> found that those patients whose HRR normalized after CR had improved

Table 4				
Clinical data	after Phase I	I cardiac	rehabilitation	(CR).

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	Pre-CR (25)	Post-CR (25)	р
METs (3.5 mL/kg/min)	$5.1 \pm 1.0$	$6.1 \pm 1.3$	0.001
FAI (%)	$30.2 \pm 18.9$	$16.2 \pm 13.0$	< 0.001
AT (mL/kg/min)	$12.5 \pm 3.7$	$14.7 \pm 4.0$	0.249
% of AT (% of peak VO <sub>2</sub> )	$65.5 \pm 11.5$	$69.5 \pm 14.5$	0.488

AT = anaerobic threshold; FAI = functional aerobic impairment; MET = metabolic equivalent.

Table 5 Clinical data after Phase II cardiac rehabilitation (CR) for those with persistently abnormal heart rate recovery.

	Pre-CR	Post-CR	р
Number (person)	12	12	
METs (3.5 mL/kg/min)	$5.1 \pm 2.0$	$6.0 \pm 1.7$	0.048
FAI (%)	$30.3 \pm 22.1$	$17.3 \pm 13.4$	0.010
AT (mL/kg/min)	$13.4 \pm 4.7$	$13.6 \pm 3.6$	0.955
% of AT (% of peak VO <sub>2</sub> )	$70.0 \pm 4.4$	72.0 ± 17.7	0.884

AT = anaerobic threshold; FAI = functional aerobic impairment; MET = metabolic equivalent.

survival compared with those whose HRR remained abnormal. We should encourage those patients with persistently abnormal HRR after Phase II CR to take part in Phase III CR, and then closely follow them. HRR consistently improves only in association with Phase II CR, but functional capacity (as expressed by MET and %FAI) or aerobic capacity (as expressed as AT and %AT) can be improved both with or without formal exercise.<sup>2,31</sup>

Abnormal HRR has been observed to be associated with several risk factors for atherosclerosis.<sup>32</sup> Samad et al found a significant correlation of abnormal HRR with smoking, among all coronary artery disease factors.<sup>33</sup> We should strictly control coronary artery disease risk factors in Phase III CR for those patients with persistently abnormal HRR after Phase II CR.

An abnormal HRR reflects abnormal vagal tone and has been validated as an important prognostic variable in multiple patient populations, and is independent of symptoms, left ventricular ejection fraction, and the severity of coronary lesion.<sup>8,21,34</sup> Whether HRR is a modifiable risk factor or not is still unknown, but preliminary evidence suggests that CR improves HRR. Further study may use analysis of exercise recovery heart rate variability to provide useful information about autonomic control of the cardiovascular system.<sup>15</sup> We also can use the washout rate of presynaptic neuronal norepinephrine uptake to assess the degree of sympathetic activity. Messias et al<sup>20</sup> found that abnormal adrenergic activation was associated with abnormal HRR.

The main limitations of our study were the small sample size and varied diagnosis of the patients, because only a single medical center was involved. Additional studies should involve collected data from multiple medical centers and investigation of the factors in different etiologies of subgroups.

Our study showed in part that there are multiple factors of cardiopulmonary exercise tests that cannot be used to predict the effect of Phase II CR on the improvement of abnormal

Table 6

Clinical data after Phase II cardiac rehabilitation (CR) for those with no abnormal heart rate recovery.

	Pre-CR	Post-CR	р
Number (person)	13	13	
METs (3.5 mL/kg/min)	$5.1 \pm 1.1$	$6.0 \pm 1.0$	0.020
FAI (%)	$26.6 \pm 13.4$	$12.5 \pm 11.7$	0.011
AT (mL/kg/min)	$12.9 \pm 2.0$	$14.6 \pm 1.5$	0.120
% of AT (% of peak VO <sub>2</sub> )	$61.7 \pm 13.3$	$70.7 \pm 17.5$	0.346

AT = anaerobic threshold; FAI = functional aerobic impairment; MET = metabolic equivalent.

Table 7					
Comparison	of	the	two	groups.	

	Post-CR with persistently abnormal HRR	Post-CR with no abnormal HRR	р
Number (person)	12	13	
METs (3.5 mL/kg/min)	$6.0 \pm 1.7$	$6.0 \pm 1.0$	0.080
FAI (%)	$17.3 \pm 13.4$	$12.1 \pm 11.2$	0.369
AT (mL/kg/min)	$13.6 \pm 3.6$	$14.6 \pm 1.5$	0.846
% of AT (% of peak VO <sub>2</sub> )	72.0 ± 17.7	$70.0 \pm 17.5$	0.469

AT = anaerobic threshold; CR = cardiac rehabilitation; FAI = functional aerobic impairment; HRR = heart rate recovery; MET = metabolic equivalent.

HRR. Although only 41% of patients with abnormal HRR could improve after Phase II CR, all of the patients could have improved exercise capacity whether HRR improved or not. According to our study, we can deduce that HRR and exercise capacity change independently. However, it is important to follow-up closely during Phase III for those patients with persistently abnormal HRR after Phase II CR.

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