

Effect of cardiac rehabilitation on heart rate recovery in patients with coronary artery disease

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Ethics Committee Approval

The study was approved by the ethics committee of the Haydarpasa Numune Education and Research Hospital with the reference number HNEAH-KAEK 2020/KK/138.

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest

No conflict of interest was declared by the authors.

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Abstract

Background/Aim: It is well-established that individuals with coronary artery disease (CAD) often exhibit autonomic dysfunction and a reduction in vagal function is associated with increased mortality and morbidity. Vagally mediated heart rate recovery (HRR) can be assessed by analyzing the post-exercise heart rate (HR) decay. It is hypothesized that effective exercise-based cardiac rehabilitation (CR) can enhance post-exercise parasympathetic function. This study aims to evaluate the impact of CR on HRR and other cardiac parameters in CAD patients.

Methods: This retrospective cohort study was conducted at a single center. It included patients with CAD who were referred to the CR unit and completed either 30 or 60 sessions. These patients were free from angina or angina-equivalent symptoms at the time of enrollment and were receiving guideline-directed medical therapy for ischemic heart disease. A customized CR program was implemented for each patient. To calculate HRR, the maximum HR during the exercise test and HR values at 1, 2, and 3 minutes after exercise cessation were recorded. The differences between the maximum HR and the HR values at the end of the 1st, 2nd, and 3rd minutes after exercise were designated as HRR1, HRR2, and HRR3, respectively.

Results: This study enrolled 104 patients with CAD. Following CR, there was a significant improvement in functional capacity, as assessed by the 6-minute walk test (from 367.83 [56.58] to 381.61 [53.76], $P=0.001$), and endurance, as measured by the Cycle Ergometer Test Maximum Watts (from 63.22 [22.29] to 77.38 [19.87], $P<0.001$). CR also led to a noteworthy increase in HRR1, HRR2, and HRR3 ($P=0.036$, $P=0.015$, $P=0.002$, respectively).

Conclusion: In our study, both the functional capacity and endurance of CAD patients improved significantly after CR sessions. Additionally, HRR showed a substantial increase following CR, suggesting that exercise-based CR can enhance post-exercise parasympathetic function. HRR may serve as a potential prognostic marker for predicting outcomes in CR.

Keywords: coronary artery disease, cardiac rehabilitation, heart rate recovery

Introduction

Cardiovascular disease stands as one of the foremost contributors to global mortality and morbidity [1]. While the precise pathophysiology remains elusive, emerging evidence underscores the significant role played by the autonomic nervous system [2]. Notably, the vagus nerve may exert an influence on cardiovascular disease through its impact on inflammatory responses [3].

Exercise-based cardiac rehabilitation (CR) programs have been shown to enhance both the quality of life [4] and cardiovascular mortality outcomes in patients with coronary artery disease (CAD) [5]. It is hypothesized that effective exercise-based cardiac rehabilitation (CR) can lead to improvements in post-exercise parasympathetic function and reductions in inflammatory markers [6,7]. Vagally mediated heart rate recovery (HRR) is characterized by the difference in heart rate (HR) between the exercise peak and one or more minutes following exercise cessation [8]. Reduced HRR has been correlated with an elevated risk of both cardiovascular and all-cause mortality [9].

In this study, we assessed the impact of CR on HRR and various cardiac parameters in patients with CAD.

Materials and methods

Study design

This was a single-center, retrospective cohort study conducted between January 2016 and January 2020. The study included patients with CAD who were referred to the CR unit and completed both 30 and 60 sessions. At the time of enrollment, all patients were free of angina or angina-equivalent symptoms and were receiving guideline-directed medical therapy for ischemic heart disease.

The ethics committee of the Haydarpasa Numune Education and Research Hospital reviewed the study and determined that there were no ethical objections to conducting it, with the study being assigned the reference number HNEAH-KAEK 2020/KK/138. Additionally, the study received approval from the Istanbul Provincial Health Directorate, Health Services Presidency Research, Printed Publication, and Announcement Content Evaluation Commission, as indicated by their decision dated 10.11.2020 and reference number 2020/42. Furthermore, informed consent was obtained from all study participants.

The study population comprised patients aged 18 years and older who had coronary artery disease (CAD) and had completed all 30 and 60 sessions of the CR program. We included patients with CAD who had experienced a myocardial infarction, received a CAD diagnosis through angiography, or underwent revascularization procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

The exclusion criteria for this study encompassed several factors, including significant cognitive disorders, acute or chronic respiratory failure, the presence of angina or angina-equivalent symptoms, non-revascularized significant coronary stenosis, recent (within a month) acute coronary syndrome, residual myocardial ischemia, uncontrolled hypertension, coexisting valvular and/or peripheral vascular diseases, any

physical disabilities that could hinder ergometer bicycle training and acute or chronic heart failure. Notably, the use of medication classes that affect heart rate (HR), such as beta-blockers, was not considered an exclusion criterion. Participants were specifically instructed to continue their regular medication regimens throughout the study (Table 1).

Table 1: Medications of the patients (n=104).

Medications	n (%)
Beta-blocker	90 (87)
Calcium channel blocker	18 (17)
ACEI	49 (47)
ARB	8 (8)
Diuretics	7 (7)
Alfa blocker	3 (3)
Statin	80 (77)

Cardiac rehabilitation

All patients were invited to participate in the hospital-based CR program, which involved attending sessions three times a week for either 10 weeks (30 sessions) or 20 weeks (60 sessions) for those who wished to continue. A customized CR program was tailored to each patient based on their peak workload as determined through a cycle ergometer test. After the initial ten sessions, a physiatrist assessed and adjusted the patient's rehabilitation program using the Borg scale for exertion. Each exercise session commenced with a warm-up and concluded with a recovery period. To assess endurance, a submaximal cycle ergometer test was administered, increasing the wattage by 25 watts every 2 minutes, with patients self-reporting their exertion on the Borg scale. Throughout the exercise, continuous monitoring included electrocardiogram readings, HR, blood pressure, and oxygen saturation levels. Prior to engaging in the cycle ergometer program, patients performed supervised stretching exercises, with strengthening exercises introduced after two weeks. These strengthening sessions targeted the major muscle groups of the upper and lower extremities, involving ten repetitions at a load ranging from 60–80% of their maximum capacity.

Functional capacity was assessed using the 6-minute walk test (6MWT), during which patients were instructed to walk back and forth around cones on a 30-foot path for six minutes, allowing them to slow down or stop if necessary. Additionally, patients received dietary recommendations from nutritionists, psychosocial support from a psychologist, and educational guidance from CR nurses, along with educational materials. Smokers were referred to the tobacco cessation outpatient clinic as part of the comprehensive program.

Heart rate recovery

HRR is defined as the difference in HR between the peak of exercise and one or more minutes after exercise cessation. To calculate HRR, the maximum heart rate during the exercise test was initially recorded. Subsequently, HR measurements were taken again at 1, 2, and 3 minutes after the exercise test concluded. The disparities between the maximum HR and the HR recorded at the end of the 1st, 2nd, and 3rd minutes after exercise were designated as HRR1, HRR2, and HRR3, respectively.

Furthermore, we defined the differences in cycle ergometry watt values, HRRs, and 6-minute walk test (6MWT) results after completion of the CR program compared to their baseline values as Δ watt, Δ HRR, and Δ 6MWT, respectively.

Statistical analysis

Statistical analyses were conducted using SPSS 16.0 for Windows. To assess the data obtained in this study, descriptive statistical methods such as mean (standard deviation), frequency, and ratio values were employed. In-group comparisons of quantitative variables with a normal distribution were performed using the t-test, while the Wilcoxon signed-ranks test was utilized for in-group comparisons of quantitative variables that did not exhibit a normal distribution. Mean values of continuous variables were compared between groups using either the Student t-test or the Mann-Whitney U test, as appropriate. The relationships between parameters were determined using Pearson's coefficient of correlation.

To identify differences between the CABG, PCI, and medical treatment groups, an analysis of variance (ANOVA) test was employed. Statistical significance was established at a threshold of $P < 0.05$.

The study's statistical power and the minimum required patient count were calculated based on interim analysis, which evaluated the first 30 enrolled patients. To achieve 80% statistical power and account for a type 1 error rate of 0.05, a minimum of 92 patients were determined to be necessary to claim significant findings.

Results

In this study, a total of 104 patients were enrolled. Among them, 30 (29%) were female, and 74 (71%) were male. The average age of the patients was 58 years. The clinical findings of the subjects are presented in Table 2.

Table 2: Baseline characteristics of the study population.

		30 sessions (n=30)	60 sessions (n=74)	P-value
Age	58 (9)	58 (12)	59 (8)	0.640
Gender				
male	74 (71%)	22	52	0.755
female	30 (29%)	8	22	
Hypertension	68 (65%)	20	48	0.861
Diabetes mellitus	22 (21%)	7	15	0.729
Heart failure	15 (14%)	4	11	0.840

Data are presented as mean (SD) and n (%)

The patients' body mass index (BMI) showed a significant decrease after participating in the training program ($P=0.044$). Furthermore, functional capacity, as assessed through the 6-minute walk test, and endurance, as measured by the maximum watts achieved in a cycle ergometer test, both exhibited significant increases in patients following their participation in CR sessions (from 367.83 [56.58] to 381.61 [53.76], $P=0.001$; from 63.22 [22.29] to 77.38 [19.87], $P < 0.001$, respectively).

CR also resulted in significant improvements in heart rate recovery parameters: HRR1, HRR2, and HRR3 (from 22 [11] to 24 [9], $P=0.036$; from 28 [12] to 31 [9], $P=0.015$; from 29 [11] to 33 [10], $P=0.002$, respectively). Additionally, the mean HRR showed a significant improvement (from 26.24 [10.59] to 29.49 [8.61], $P=0.006$) (Table 3).

Out of the CR patients, 20 (19%) underwent CABG, 65 (62%) received PCI, while the remaining patients were medically followed. There were no significant differences observed between the treatment groups regarding changes in HRR, endurance, and distance following CR ($\Delta HRR1 P=0.404$,

$\Delta HRR2 P=0.174$, $\Delta HRR3 P=0.640$, $\Delta \text{Mean HRR } P=0.349$, $\Delta \text{watt } P=0.383$, $\Delta 6\text{MWT } P=0.882$).

Table 3: Evaluation of BMI, endurance and functional capacity, and heart rate recovery before and after cardiac rehabilitation.

	Before CR	After CR	P-value
BMI (kg/m ²)	28.81 (4.66)	28.55 (4.37)	0.044
Cycle ergometer test max WATT	63.22 (22.29)	77.38 (19.87)	<0.001
6MWT (meters)	367.83 (56.58)	381.61 (53.76)	0.001
HRR1	22 (11)	24 (9)	0.036
HRR2	28 (12)	31 (9)	0.015
HRR3	29 (11)	33 (10)	0.002
Mean HRR	26 (11)	29 (9)	0.006

BMI: body mass index, HRR: heart rate recovery, 6MWT: 6-minute walk test. Data are presented as means (standard deviation).

In the univariate correlation analysis, there was a significant correlation observed between the increase in wattage (Δwatt) and the improvements in HRR1, HRR2, and HRR3 ($r=0.229$, $P=0.019$; $r=0.328$, $P=0.001$; $r=0.330$, $P=0.001$, respectively).

There were no significant differences in the baseline characteristics between the groups undergoing 30 sessions and 60 sessions (Table 1). However, it's important to note that the improvements in HRR, endurance, and the 6-minute walk test (6MWT) were not statistically different between the two groups (Table 4).

Table 4: Comparison of the results of 30 session and 60 session groups.

	30 Session	60 Session	P-value
$\Delta HRR1$	0.43 (14.61)	3.60 (12.16)	0.258
$\Delta HRR2$	0.67 (13.83)	4.12 (12.49)	0.218
$\Delta HRR3$	0.67 (13.14)	5.26 (12.28)	0.094
$\Delta \text{Mean HRR}$	0.59 (12.67)	4.33 (11.50)	0.148
Cycle ergometer test ΔWATT	10.00 (19.25)	15.83 (22.10)	0.209
$\Delta 6\text{MWT}$ (meters)	4.00 (35.56)	17.74 (40.96)	0.111

HRR: heart rate recovery, 6MWT: 6-minute walk test. Data are presented as means (standard deviation).

Discussion

Resting HR in healthy individuals is primarily regulated by the vagus nerve [10]. Acute stress leads to vagal withdrawal, followed by sympathetic stimulation [11]. It is well-established that individuals with cardiovascular disease often exhibit autonomic dysfunction and a decrease in vagal function is correlated with increased mortality and morbidity [12,13].

Heart rate recovery (HRR), as an indicator of vagal function, is defined as the difference in HR between the peak of exercise and one or more minutes following the cessation of exercise. The elevation in HR during exercise is attributed to the interplay of parasympathetic withdrawal and sympathetic activation. The decline in HR immediately after exercise is believed to signify the reactivation of the parasympathetic system [11]. Impaired HRR has been demonstrated to be linked to an elevated risk of cardiovascular events [14,15].

In our study, we measured HRR in all patients during the initial and final sessions of the cycle ergometry exercise program. HRR showed a significant improvement following the CR program compared to its baseline measurements. Notably, there was an observed increase in HRR values at 1st, 2nd, and 3rd minutes, as well as the mean HRR. These findings align with previous studies that utilized treadmill exercise in CR programs [16,17]. Furthermore, a two-week residential CR study involving cycle ergometry exercise also reported an increase in HRR [18]. To the best of our knowledge, this is the first study to demonstrate the impact of hospital-based CR with cycle ergometry on HRR in patients with CAD.

Qiu et al. [19] reported that there was no significant difference in the predictive value of 2-minute HRR compared to 1-minute HRR concerning the risk of all-cause mortality. However, they noted that 2-minute HRR demonstrated greater sensitivity in predicting the risk of cardiovascular events. In a separate study [18], it was observed that HRR at 2 minutes significantly increased in CAD patients following a residential CR program. In our study, while all HRR measurements at 1, 2, and 3 minutes showed significant increases, the most pronounced increase was observed at the 2nd and 3rd minutes.

While there is an evident dose-response correlation between HRR and cardiorespiratory fitness [9], no significant disparity in HRR metrics has been identified between 30 and 60 workout sessions. Conversely, in another study, a 6-week program showed similar effects on HRR when compared to a 12-week program [20]. This suggests that the advantages of CR on HRR may be independent of the duration of the rehabilitation program.

We observed significant correlations between HRR and changes in cycle ergometer watts in response to the CR program. An increase in HRR was found to be significantly correlated with the magnitude of the wattage increase.

Limitations

The retrospective design of this study represents a limitation. Furthermore, the absence of a control group in the current study is another limitation. To obtain a more comprehensive understanding, future prospective studies should include a group of CAD patients who do not participate in CR as a comparison.

Conclusion

In our study, we observed improvements in the endurance and functional capacity of the patients. Furthermore, all HRR values at the 1st, 2nd, and 3rd minutes showed significant increases after the CR sessions. This increase in HRR following CR suggests an improvement in autonomic dysfunction among patients with CAD. Therefore, CR appears to be a valuable intervention for addressing autonomic dysfunction in this patient population. Additionally, HRR may serve as an effective predictor of CR outcomes.

References

- Nowbar AN, Gitto M, Howard JP, Francis DP, Al-Lamee R. Mortality from ischemic heart disease. *Circ Cardiovasc Qual Outcomes*. 2019;12:e005375.
- Olshansky B, Sabbah HN, Hauptman PJ, Colucci WS. Parasympathetic nervous system and heart failure: pathophysiology and potential implications for therapy. *Circulation*. 2008;118:863-71.
- Olshansky B. Vagus nerve modulation of inflammation. *Cardiovascular implications*. *Trends in Cardiovascular Medicine*. 2016;01:1-11.
- Conraads VM, Pattyn N, De Maeyer C, Beckers PJ, Coeckelberghs E, Cornelissen VA et al. Aerobic interval training and continuous training equally improve aerobic exercise capacity in patients with coronary artery disease: the SAINTEX-CAD study. *Int J Cardiol*. 2015;179:203-10.
- Anderson L, Oldridge N, Thompson DR, Zwisler AD, Rees K, Martin N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: Cochrane systematic review and metaanalysis. *J Am Coll Cardiol*. 2016;67:1-12.
- Rocamora AM, Ribeiro F, Sarabia JM, Íbias J, Oliveira NL, Vera-García FJ, et al. Exercise-based cardiac rehabilitation and parasympathetic function in patients with coronary artery disease: a systematic review and meta-analysis. *Clin Auton Res*. 2021;31:187-203. doi: 10.1007/s10286-020-00687-0.
- Kaya BB, Ozbilgin N. Effect of cardiac rehabilitation on mortality related inflammatory markers. *J Surg Med*. 2019;3(8):588-92. doi: 10.28982/josam.606487
- Peçanha T, Silva-Júnior ND, Forjaz CL. Heart rate recovery: autonomic determinants, methods of assessment and association with mortality and cardiovascular diseases. *Clin Physiol Funct Imag*. 2014;34:327-39.

- Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. *N Engl J Med*. 1999;341:1351-7.
- Jose AD, Collison D. The normal range and determinants of the intrinsic heart rate in man. *Cardiovasc Res*. 1970;4:160-7. doi: 10.1093/cvr/4.2.160.
- Imai K, Sato H, Hori M, H Kusuoka, H Ozaki, H Yokoyama, et al. Vagally mediated heart rate recovery after exercise is accelerated in athletes but blunted in patients with chronic heart failure. *J Am Coll Cardiol*. 1994;15;24:1529-35. doi: 10.1016/0735-1097(94)90150-3.
- Besnier F, Labrunee M, Pathak A, Pavy-Le Traon A, Galès C, Sénard JM, et al. Exercise training-induced modification in autonomic nervous system: an update for cardiac patients. *Ann Phys Rehabil Med*. 2017;60:27-35. doi: 10.1016/j.rehab.2016.07.002
- Thayer JF, Lane RD. The role of vagal function in the risk for cardiovascular disease and mortality. *Review Biol Psychol*. 2007;74:224-42. doi: 10.1016/j.biopsycho.2005.11.013.
- Vivekananthan DP, Blackstone EH, Pothier CE, Lauer MS. Heart rate recovery after exercise is a predictor of mortality, independent of the angiographic severity of coronary disease. *J Am Coll Cardiol*. 2003;42:831-8.
- Nishime EO, Cole CR, Blackstone EH, Pashkow FJ, Lauer MS. Heart rate recovery and treadmill exercise score as predictors of mortality in patients referred for exercise ECG. *JAMA*. 2000;284:1392-8.
- Tiukinhoy S, Beohar N, Hsie M. Improvement in heart rate recovery after cardiac rehabilitation. *J Cardiopulm Rehabil*. 2003;23:84-7. doi: 10.1097/00008483-200303000-00002.
- Hao SC, Chai A, Kligfield P. Heart rate recovery response to symptom limited treadmill exercise after cardiac rehabilitation in patients with coronary artery disease with and without recent events. *Am J Cardiol*. 2002;90:763-5. doi: 10.1016/s0002-9149(02)02607-3.
- Legramante JM, Iellamo F, Massaro M, Sacco S, Galante A. Effects of residential exercise training on heart rate recovery in coronary artery patients. *Am J Physiol Heart Circ. Physiol* 2007;292:H510-5. doi: 10.1152/ajpheart.00748.2006. Epub 2006 Sep 15.
- Qiu S, Cai X, Sun Z, Li L, Zuegel M, Steinacker JM, et al. Heart rate recovery and risk of cardiovascular events and all-cause mortality: a meta-analysis of prospective cohort studies. *J Am Heart Assoc*. 2017;9;6:e005505. doi: 10.1161/JAHA.117.005505.
- Missiri AE, Amin SA, Tawfik IR, Shabana AE. Effect of a 6-week and 12-week cardiac rehabilitation program on heart rate recovery. *Egypt Heart J*. 2020;72:69. doi: 10.1186/s43044-020-00107-8.

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