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Heart rate recovery in patients with inflammatory bowel disease in clinical remission

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Abstract

Aim: The purpose of this report was to assess Heart Rate Recovery (HRR) which is known to be a predictor of cardiovascular diseases in patients diagnosed with Inflammatory Bowel Disease (IBD).

Materials and Methods: Fifty-two patients (41 patients with Ulcerative Colitis (UC) and 11 patients with Crohn's Disease (CD)) in remission and 50 healthy volunteers were enrolled in the study. All participants was performed treadmill exercise testing. HRR was expressed as the decrease in the heart rate from peak exercise value to 1 min and 2 min after the exercise. The HRR index was calculated for the first (HRR1) and the second (HRR2) minutes of the recovery phase.

Results: The maximal and baseline heart rate during exercise stress test were the same in control groups ,UC and CD (156.6±13.3 vs. 153.8±12.7 vs 152.7±13.6, p=0.432; 93.18±16.37, 94.05±14.8 vs. 86.5±13.9, p=0.313, respectively). Also, there was no difference between the groups in means of the first and the second minute HRR indices (HRR1: 30.7±11.8, 34.5±8.8, 33.9±13.5, p=0.403; HRR2: 51.4±15.4, 54.1±14.6, 55.1±16.9, p=0.807).

Conclusion: Many systemic inflammatory diseases are thought to be related to an increased risk of cardiovascular diseases. This association has not been well determined in patients with IBD. We found that the HRR index was not different between the CD and UC patients in remission in this report. Further studies may be needed in this way, and all IBD patients should be suspected of the presence of cardiovascular risk factors to reduce mortality and morbidity.

Introduction

Inflammatory Bowel Disease (IBD) is a chronic inflammatory disease that involves Ulcerative Colitis (UC) and Crohn's Disease (CD) [1]. The etiology of IBD has not been clarified, and the interaction between the inflammatory cells, immunity and the autonomic nervous system has been implicated [2].

The autonomic nervous system has a leading function in the modulation of motility, secretion, microcirculation, mucosal immune and inflammatory responses of the gastrointestinal tract [3, 4]. Many studies have reported that hypo/hyperactivation of the autonomic nervous system is associated with chronic inflammatory bowel diseases. Numerous studies that examine autonomic functions in UC and CD emphasize the increase in sympathetic activity in these inflammatory diseases, while some studies claim a decrease in vagal activity [5-8].

Inflammation is thought to be the critical element for the increased risk of cardiovascular diseases [9]. Several systemic inflammatory conditions have been linked to an increased risk of cardiovascular diseases; however, this has not been well established in IBD. Increasing evidence of an association between IBD and adverse cardiovascular events including stroke and myocardial infarction emerged during the last decade [10]. Smoking, diabetes, poor diet, obesity, and drugs used to treat IBD may also contribute to cardiovascular diseases that are seen in IBD patients [9].

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Increased heart rate during exercise is known to be a result of sympathetic activation and parasympathetic withdrawal [11]. Decreased heart rate after exercise is the result of the reactivation of the parasympathetic nervous system which is related to a declining in the risk of death [12, 13].

Many protocols were developed for the autonomic functions. Calculating the Heart Rate Recovery (HRR) index is one of them, can be calculated by using an exercise stress test, and is known as the decreased in heart rate after maximal exercise [4]. Anormal HRR index was explained as no reduction in the heart rate of more than 12 beats per minute after termination of exercise [14]. As shown in the studies, HRR is an measurement of impaired parasympathetic tone, an estimator of cardiovascular morbidity and mortality [14].

In this study, we hypothesized that changes in the heart rate may be a crucial prognostic marker for cardiovascular diseases, and we investigated the presence of increased cardiovascular risk in patients with IBD in remission by calculating the HRR index.

Materials and Methods

A hundred and two consecutive patients (72 patients diagnosed with UC and 30 patients diagnosed with CD) admitted to the Internal Medicine clinic were recruited in the study. The patients, diagnosed with IBD were accepted as in remission according to European Crohn´s and Colitis Organisation (ECCO) guidelines [15]. A group of 70 healthy volunteers attending the internal medicine outpatient clinic with some complaints and with no known cardiovascular diseases were selected as the control group. The exclusion criteria in the study were; aged younger than 18 and older than 65 years, those having active IBD and extraintestinal involvement, and those having a history of ischemic heart disease, previous myocardial infarction, severe valvular pathology, left ventricular ejection fraction <50%, cardiac arrhythmia, cardiomyopathy and comorbidities, such as uncontrolled hypertension, anemia (Hgb <10 g/dl), chronic liver and renal disease, diabetes mellitus, neurologic disease, hyperthyroidism/hypothyroidism, autonomic nervous system disorder, and smoking. The patients with active IBD might not complete the exercise stress test due to disease symptoms, thus we could not evaluate these patients in the study. Based on the exclusion criteria, a total of 52 patients (UC: 41 and CD: 11) with IBD and 50 healthy volunteers were examined in the study.

Baseline Electrocardiograms (ECG) and transthoracic echocardiography were examined for study population. The exercise stress tests were performed in compliance with the modified Bruce protocol to calculate the HRR index. Maximum heart rate was determined as follows: maximum heart rate = 220-age of the subject. Patients who reached 85% of maximum heart rate were enrolled in this study. The ECG was documented during the exercise test continuously. The heart rates were documented at rest and also during the 2 minutes after the exercise. Heart Rate Recovery indices were determined by subtracting the heart rates at 1 (HRR1) and 2 (HRR2) minutes from the heart rate at peak exercise. The sociodemographic parameters and laboratory analyses were recorded from the hospital data system.

The study was approved by the local ethics committee (Kecioren Training and Research Hospital Clinical Research Ethics Committee, date: 08.04.2015, decision no: 782). All patients recruited in the study had given written informed consent.

Statistical analysis

All data were examined by using The Statistical Package for the Social Sciences software version 17 program (IBM Corp; Armonk, NY, USA). A hundred and two consecutive patients (72 patients diagnosed with UC and 30 patients diagnosed with CD) admitted to the Internal Medicine clinic and a group of 70 healthy volunteers attending the internal medicine outpatient clinic with some complaints and with no known cardiovascular diseases as the control group constituted the sample size. We used the non-probability consecutive sampling technique. The variables were determined by analytic tests if they were normally distributed. While normally distributed quantitative variables were expressed as mean values ± standard deviation, non-normally distributed quantitative variables were expressed as median values. Qualitative variables were expressed as proportions. Nonparametric values were examined by using Mann-Whitney U tests and Kruskal Wallis-H. The relationship between gender and UC, CD and the controls are determined by using Chi-square test. Some demographic, clinical features and laboratory parameters of the patients with UC, CD and the controls were examined by using Kruskal Wallis-H test and Mann-Whitney U test where appropriate. For the purpose of testing the hypothesis of differences in exercise stress test between UC, CD and the controls, Kruskal Wallis-H test and Mann-Whitney U test were used where appropriate. In the analyses, p values <0.05 was accepted as significant.

Results

The clinical characteristics of control groups, UC and CD are showed in Table 1. According to some basic demo-

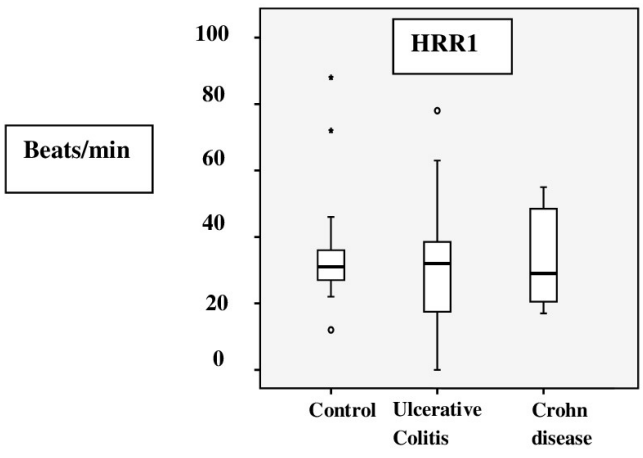

Figure 1. HRR indices of patients with UC, CD and controls at 1 min of recovery.

Table 1. Some Demographic, clinical features and laboratory parameters of the patients with UC, CD and the controls.

	UC group (n=41)	CD group (n=11)	Control group (n=50)	p value
Age (years)	43 (22-65)	40 (22-59)	44 (18-65)	0.69
Female Gender (n/%)	18/43.9	5/45.5	23/54	0.61
Body mass index (kg/m^2)	28.4 (20.1-45.6)	27.8 (20.2-42.3)	27.3 (20.3-37.5)	0.52
Duration of IBD, months	36 (1-180)	36 (1-120)	-	0.99
Plasma glucose (mg/dL)	104 (82-119)	103 (86-122)	102 (76-120)	0.30
Total cholesterol (mg/dL)	201 (120-334)	202 (124-342)	195 (133-353)	0.78
LDL cholesterol (mg/dL)	122 (38-216)	120 (60-224)	119 (70-264)	0.89
Triglyceride (mg/dL)	119.5 (42-435)	112 (52-306)	102 (37-297)	0.24
HDL cholesterol (mg/dL)	53 (28-94)	54 (30-102)	57 (35-108)	0.28

UC: Ulcerative Colitis, CD: Crohn Disease, IBD: Inflammatory bowel disease, LDL: Low-density lipoprotein, HDL: High-density lipoprotein.

Table 2. Comparison of exercise stress test results between the patients with UC, CD and the controls.

	UC group (n=41)	CD group (n=11)	Control group (n=50)	p value
Duration of exercise (min)	7.3 ±1.7	9.2 ±2.4	8.5 ±3.1	0.03
Initial systolic pressure (mmHg)	122.7 ± 18.1	123 ±12 1	23.7 ±12.7	0.70
Maximal systolic pressure (mmHg)	149.4 ±18.9	145.7 ±26.9	153.1 ±16.6	0.38
Baseline heart rate(bpm)	94.05 ±14.8	86.5 ±13.9	93.18±16.37	0.31
Maximum HR(bpm)	153.8 ±12.7	152.7 ±13.6	156.6 ±13.3	0.43
HRR1	30.7 ±11.8	34.5 ±8.8	33.9 ±13.5	0.40
HRR2	51.4 ±15.4	54.1 ±14.6	55.1 ±16.9	0.80

UC: Ulcerative Colitis, CD: Crohn Disease, HRR: Heart Rate Recovery.

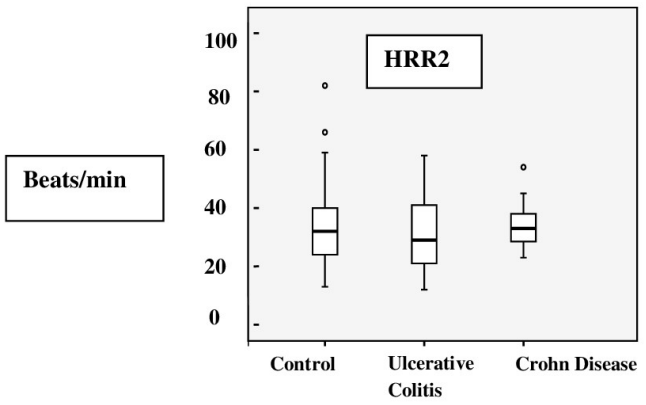

Figure 2. HRR indices of patients with UC, CD and controls at 2 min of recovery.

graphic, clinical characteristics and laboratory parameters, the groups were balanced with regard to gender; age, body mass index (BMI), and also lipid profile (Table 1). Also, there was no difference in means of duration of the disease between the patients with UC and CD. In addition, BMI and ejection fraction were similar between patients with the control group and IBD.

The healthy controls and IBD patients achieved the exercise stress tests. All IBD patients and the controls reached at least 85% of maximum heart rates. All study population had sinus rhythm with normal 12 lead ECG results at rest.

Comparison of the initial systolic blood pressure, maximal systolic blood pressure, maximal heart rate achieved during the exercise stress test, and exercise duration between participants are presented in Table 2. There was no difference between three groups in means of initial systolic blood pressure, maximal systolic blood pressure, maximal heart rate, and baseline heart rate during the test (Respectively; 122.7 ± 18.1 vs. 123 ± 12 vs. 123.7 ± 12.7, p=0.7; 149.4 ± 18.9 vs. 145.7 ± 26.9 vs. 153.1 ± 16.6, p=0.387; 153.8±12.7 vs. 152.7±13.6 vs. 156.6±13.3, p=0.432; 94.05±14.8 vs. 86.5±13.9 vs. 93.18±16.37, p=0.313).

The HRR indices of the UC, CD group, and the control group are shown in Table 2. The first and the second minute HRR indices of patients with UC and CD were the same as those of the control group (HRR1: 30.7±11.8, 34.5±8.8, 33.9±13.5, p=0.403; HRR2: 51.4±15.4, 54.1±14.6, 55.1±16.9, p=0.807) (Figure 1, 2).

Discussion

Inflammatory bowel diseases are chronic, systemic inflammatory conditions that affect the gastrointestinal tract with numerous extraintestinal manifestations caused by concomitant systemic inflammation [16]. As shown in other studies, the presence of autonomic dysfunction and IBD leads to the suggestion that autonomic dysfunction have a crucial role in the pathogenesis of IBD. While Ganguli et al. demonstrated that sympathetic activity was increased in patients with UC, Corruzzi et al emphasized that patients with IBD had significantly lower parasympathetic activity [17, 18]. In addition, Mouzas et al. released increased parasympathetic activity in patients with IBD [19]. Straub et al. couldn't find any autonomic dysfunction in IBD patients in the study [20]. As seen in these studies, the link between IBD and autonomic dysfunction has not been well determined.

Heart Rate Recovery was seen as the outcome of parasympathetic reactivation and sympathetic withdrawal [21], and impaired heart-rate recovery was thought to increase the risk of cardiovascular death [12]. Cole et al. showed that the absence of an expected decrease in the 1st minute after exercise was an indicator of decreased vagal activity, and this is a crucial indicator of overall mortality, presence of myocardial perfusion defect, independent of workload and heart rate changes [14]. Furthermore, Jauven et al. found that the risk of sudden death was 2 times higher in those with low heart rate recovery in their study with 5713 male participants [22].

Many cardiovascular abnormalities have been reported in IBD, such as pericarditis, endocarditis, myocarditis, cardiomyopathy, complete AV block, atrial fibrillation, and increased thromboembolism in the arterial and venous systems. However, there is insufficient information about the actual incidence and natural course of cardiac involvement in IBD. We released that the HRR index was not affected in UC and CD in this report. Our data doesn't indicate the presence of impaired autonomic nervous system function as a leading cause for increased cardiovascular disease risk in IBD patients as shown in previous studies.

There are some limitations of this report. Firstly, this study has small sample size. Furthermore, genetic predisposition to cardiovascular diseases can affect the HRR index. The previous studies did not analyze parameters in the patients with active disease and in remission. The inflammatory load of active disease is not similar that in remission. In our study, we selected the patients in remission to rule out the effect of inflammation on the HRR index. In our report, we record medical history including previous specific treatment targeting IBD and β-blocker usage in detail unlike in other studies, and we selected the patients who did not use any medication [23].

Conclusion

Although some systemic inflammatory diseases are known to be related to an increased risk of cardiovascular diseases, this hypothesis has not been well established in patients with IBD. In our study, data showed that the HRR index, which is associated with autonomic nervous system function and the presence of cardiovascular risk, is not affected in IBD patients during remission. Eventually, all IBD patients should be examined for the presence of cardiovascular risk factors to reduce mortality and morbidity.

Ethics approval

The study was approved by the local ethics committee (Kecioren Training and Research Hospital Clinical Research Ethics Committee, date: 08.04.2015, decision no: 782).

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