

# Heart Rate Recovery Index as a Novel Indicator of Autonomic Status in Irritable Bowel Syndrome

## İrritabil Barsak Sendromunda Otonomik Fonksiyon Değerlenirmede Yeni Bir Belirteç Olarak Kalp Hızı Toparlanma İndeksi

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### Abstract

Objective	There are numerous studies with conflicting results using heart rate variability as a marker for parasympathetic dysfunction in irritable bowel syndrome. In this study we aim to investigate heart rate recovery index which is derived from exercise ekg test as a dynamic new tool to document autonomic status in irritable bowel syndrome (IBS) patients.
Materials and Methods	We enrolled 35 IBS patients without documented cardiovascular disease and 35 healthy age and sex matched controls in the study. All patients underwent transthoracic echocardiography and exercise ekg test with modified Bruce protocol. Heart rate recovery measurements were taken at first and second minute after abrupt cessation of exercise.
Results	IBS and control group were similar with respect to age, sex, hypertension and smoking status except BMI which was lower in IBS group. ( $26\pm 3$ vs $28\pm 5$ , $p=0.028$ ). HRR values did not differ statistically between groups (IBS: $34\pm 11$ vs Control: $36\pm 11$ , $p=0.459$ ).
Conclusion	Our results suggest that autonomic imbalance might not be the primary pathophysiological mechanism in IBS patients according to HRR index.
Keywords	Heart rate recovery index; irritable bowel syndrome; autonomic dysfunction

### Öz

Amaç	İrritabil barsak sendromunda (IBS) otonomik fonksiyon değerlendirilmesi ile ilgili yapılan çalışmalarda sıklıkla ritim holter tetkikinden elde edilen kalp hızı değişkenliği indeksi kullanılmış ve çelişkili sonuçlar elde edilmiştir. Biz bu çalışmada egzersiz ekg testi (efor testi) ile dinamik olarak elde edilen kalp hızı toparlanma indeksini (KHTİ) bu hasta grubunda otonom fonksiyon değerlendirilmesinde yeni bir belirteç olarak önerdik ve çalıştık.
Gereç ve Yöntemler	Çalışmaya 35 adet bilinen kardiyovasküler hastalık öyküsü olmayan IBS hastası ile yaş ve cinsiyet açısından eşitlenmiş 35 adet sağlıklı bireyden oluşan kontrol grubu dahil edildi. Bütün hastalara transtorasik ekokardiyografi ve modifiye Bruce protokolü ile efor testi uygulandı. KHTİ ölçümleri egzersiz testi ani şekilde sonlandırıldıktan sonraki 1. ve 2. Dakikalarda ölçülerek kayıt altına alındı.
Bulgular	IBS ve kontrol hasta grubu yaş, cinsiyet, hipertansiyon ve sigara içiciliği açısından karşılaştırıldığında birbirlerine benzerdi. Vücut kitle indeksi ölçümlerinde IBS grubu istatistiksel anlamlı olarak daha düşük ölçümlere sahipti ( $26\pm 3$ vs $28\pm 5$ , $p=0.028$ ). KHTİ ölçümleri açısından iki grup arasında anlamlı fark saptanmadı (IBS; $34\pm 11$ vs Kontrol; $36\pm 11$ , $p=0.459$ ).
Sonuç	KHTİ göz önüne alındığında, otonom fonksiyon bozukluğu IBS hastalarında primer fizyopatolojik sebep olmayabilir.
Anahtar Kelimeler	Kalp hızı toparlanma indeksi; irritabil barsak sendromu; otonomik disfonksiyon

## INTRODUCTION

Irritable bowel syndrome (IBS) is a frequently diagnosed gastrointestinal motility disorder which is presented with symptoms of abdominal pain and bloating, altered bowel movements, and dynamic changes of these symptoms with time. Exclusion of other possible mechanisms that mimic same symptoms is very important during diagnosis process. Currently IBS is diagnosed with the symptom-based Rome III criteria. General pathophysiological explanations for this entity includes altered autonomic nervous system (ANS) functions and related gastrointestinal dysfunction.<sup>1</sup> Autonomic dysfunction in the pathophysiology of IBS is a popular subject and is usually measured with heart rate variability (HRV) as a quantitative scale for ANS functions among several studies.<sup>2-4</sup> Basically, HRV is defined as fluctuations of the intervals between two consecutive heart beats on an ECG record, or could be understood as beat to beat variations in heart rate.<sup>5</sup> Although it is a well-studied measure of ANS functions, HRV is not the only reliable parameter for autonomic function assessment. Heart rate recovery index (HRR) is another parameter that is used for measuring ANS effect on heart rate. It is based on the rate of decline in heart rate to its basal levels immediately after an exercise. Studies showed that especially during the first minute after cessation of exercise, the fall of heart rate is mostly under control of parasympathetic system.<sup>6,7</sup> A recent study from Emren et al. has demonstrated patients with cardioinhibitory syncope patients had significantly higher HRR values comparing to patients with other type of syncope.<sup>8</sup> HRR was used as a surrogate marker of parasympathetic function in this study. Consequently, we thought that HRR may be a new and valuable tool for assessment of autonomic functions in IBS apart from HRV which has been used for years. In this study, we aim to study HRR in IBS patients as a novel measure of autonomic dysfunction comparing with age matched healthy individual patient group.

## MATERIALS and METHODS

This is a case-control study. We studied 35 patients diag-

nosed with IBS according to the Rome III criteria from Sakarya University Medical School Hospitals, Gastroenterology outpatient clinics from November 2015 to January 2016 and the study had approval from Sakarya University Medical School Ethics Committee on November 2nd, 2015 (02-11-2015, 13651). All patients recruited for the study signed a written informed consent form. Data derived from patient group were compared to 35 age and sex matched healthy controls. Exclusion criteria for the study population were i) history of organic gastrointestinal and thyroid diseases ii) metabolic and psychiatric disorders iii) any kind of medication that alters autonomic system and heart rate (Beta blockers, calcium channel blockers, anti-depressants, SSRIs, medication with known anti cholinergic side effects etc.) iv) coronary artery disease, systolic and diastolic heart failure, more than mild valvular heart disease v) history of diabetes mellitus and medication. All patients were evaluated by an internal medicine specialist and a cardiologist with echocardiographic examination before the exercise stress test.

### Heart Rate Recovery Assessment

All patients underwent exercise treadmill test in accordance with modified Bruce Protocol until they reach %85 of age-predicted maximum heart rate. All patients are asked not to smoke, take alcohol or caffeine including soft drinks 4 hours preceding the test. After reaching the predicted heart rate, exercise is immediately stopped without a cool down period. Heart rate counts were noted before the exercise, at peak exercise, at the end of 1st minute of recovery period. Noted heart rate counts at the recovery period is then subtracted from maximal heart rate at peak exercise and this value is designated as HRR.

HRR values were divided to maximal heart rate counts and then calculated as a percentage and named as HRR ratio.

### Statistical Analysis

Data are expressed as mean  $\pm$  standard deviation for normally distributed continuous variables, as median and

interquartile ranges for skew distributed continuous variables, and as frequencies for categorical variables. Analysis of the normality of the continuous variables was performed using the Kolmogorov-Smirnov test. Propensity score matching according to age and sex was done to find appropriate pairs for IBS cases. Paired samples t test, Wilcoxon signed rank test and chi-square test were performed when comparing clinical and laboratory characteristics of patients and control subjects. A p value of <0.05 was considered statistically significant. Statistical analysis was done by using SPSS 20.0 for Mac statistical software.

### RESULTS

Subjects with IBS and control were similar with respect to age (41±10 vs 40±9, p=0.499) sex, presence of HT and smoking status (Table 1). Mean BMI was lower in IBS group as compared to control subjects (26±3 vs 28±5, p=0.028). There was no difference in HRR values (34±11 vs 36±11, p=0,459) and HRR ratio (21±7 vs 23±7, p=0,505). Statistical power analysis yielded a power of 0.85 with the current sample size and an alpha value of 0.05.

**Table 1.** Baseline demographics and comparison of two groups in terms of HRR values

	IBS (N=35)	Control group (N=35)	P value
Age (mean±SD)	41±10	40±9	0,750
Sex (Female-%)	25 (71)	23 (65)	0,607
HT (%)	4 (11)	2 (5)	0,393
Smokers (%)	16 (45)	17 (48)	0,597
BMI (mean±SD)	26±3	28±5	0,028
HRR (mean±SD)	34±11	36±11	0,459
HRR ratio (mean±SD)	21±7	23±7	0,505

BMI: body-mass index, HRR: heart rate recovery index, HRR ratio: heart rate recovery ratio, IBS: irritable bowel syndrome, SD: standart deviation

### DISCUSSION

In the current study we compared HRR as an overall indicator of autonomic status IBS patients with healthy age and sex matched control group. We tried to exclude patients with diseases or medication which might alter autonomic

functions.

Our study included 35 IBS patients who were diagnosed according to Rome III criteria and 35 healthy age and sex matched controls. Although mean HRR and HRR ratio values were smaller in IBS group, they did not reach statistical significance.

Historically, HRR has been validated as an independent measure of autonomic imbalance for determining cardiac mortality.<sup>9,10</sup> As autonomic dysfunction has been proposed as the underlying pathophysiological mechanism in IBS among several studies which was measured with HRV, HRR is another easily measurable autonomic function marker might be valuable in the same patient population. A meta-analysis including 392 patients with 263 controls analyzed data derived from HRV measures to analyze autonomic functioning in IBS patients.<sup>11</sup> This meta analyze revealed that an abnormal sympatho-vagal balance might play a role in the pathogenesis of IBS according to HRV measurements. Conversely, a detailed review about HRV in IBS selected 20 studies from the literature and revealed that HRV measurements from IBS patients are frequently similar to healthy controls.<sup>12</sup> It is also stated in the review that patients with severe abdominal pain, depression-anxiety symptoms and constipation predominant symptoms are more likely to have autonomic imbalance in favor of vagal activation. These findings lead us to investigate autonomic functions in IBS with HRR, another measurable noninvasive objective tool. We thought it would be valuable to provide information on the current subject with a new point of view.

This insignificant difference that we found might be important if a new study with a larger patient population is performed in the future. Certainly not conclusive, these results from our patient group does suggest an autonomic imbalance in IBS patients but number of patients included in the study is not enough to reach a final conclusion.

Our study has limitations. First, there was a small but significant difference at BMI values between two groups. BMI is an important factor which alters autonomic functions. Recent study from Azam et al. has demonstrated that study participants with high BMI and high body fat ratio values had significantly lower HRRI at second minute post exercise comparing to participants with normal or low BMI levels.<sup>13</sup> Secondly, we performed our study in a small study population and as we mentioned before, a larger population might show a statistically significant difference between groups. On the other hand, recent trials on IBS has used a negative colonoscopy scan in 2 years preceding their study as an inclusion criterion which we did not. Although it is still not required for the diagnosis of IBS, this is a weakness for the selection of the patient group in this study. In general, like HRV and heart rate count values, HRRI is based on the autonomic effect (mainly parasympathetic) on sinus node function and may not necessarily reflect vagal influence on the gut. However, we tried to exclude all the possible extra mechanisms which alters vagal effect on the sinus node so we think these results still might give us an idea about comparing two groups for the autonomic functions in general.

Autonomic dysfunction is a possible mechanism in the pathogenesis of IBS. There are several data in the literature regarding HRV as an indicator for the status of autonomic functions in this patient group. We suggested and studied a novel indicator of autonomic functions in IBS patients which did not reveal a statistically significant autonomic imbalance comparing to healthy control group. Further studies using HRRI in larger number of patients will give more conclusive data and a new point of view for the subject.

### **Fundings**

No fundings declared

### **Conflict Of Interests**

The authors of this paper declare that there is no conflict of interest

### **Ethics Approval**

**This study has been approved from Sakarya University Medical School Ethics Committee on November 2nd, 2015 (protocol number:13651)**

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