



## COMPARISON OF BLOOD PRESSURE VARIABILITY AMONG CLINICAL SUBTYPES IN IRRITABLE BOWEL SYNDROME PATIENTS WITH HYPERTENSION

### HİPERTANSİYONLU İRRİTABL BARSAK SENDROMLU HASTALARDA KLİNİK ALT TIPLER ARASINDA KAN BASINCI DEĞİŞKENLİĞİNİN KARŞILAŞTIRILMASI

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Geliş Tarihi / Received: 21.10.2022

Kabul Tarihi / Accepted: 23.12.2022

Yayın Tarihi / Published: 01.02.2023

#### Abstract

**Objective:** In this study, we aimed to compare blood pressure variability among irritable bowel syndrome subtypes.

**Methods:** Patients with newly diagnosed irritable bowel syndrome and existing hypertension were included in the study. Average real variability (ARV) was calculated by consecutive one week home blood pressure measurements. Groups were compared for blood pressure variability.

**Results:** While diastolic ARV was found to be similar among subtypes ( $p=0.919$ ), a significant difference was found between them in terms of systolic ARV ( $p<0.001$ ).

**Conclusion:** Since irritable bowel syndrome patients with constipation-predominant subtype have higher systolic blood pressure variability, these patients can be followed more closely for cardiovascular complications.

**Keywords:** Blood pressure, constipation, diarrhea, irritable bowel syndrome.

#### Öz

**Amaç:** Bu çalışmada, iritabl bağırsak sendromu alt tipleri arasında kan basıncı değişkenliğini karşılaştırmayı amaçladık.

**Yöntem:** Yeni tanı almış iritabl bağırsak sendromu ve mevcut hipertansiyonu olan hastalar çalışmaya dahil edildi. Ortalama gerçek değişkenlik (ARV), ardışık 1 haftalık ev kan basıncı ölçümleri ile hesaplandı. Gruplar kan basıncı değişkenliği açısından karşılaştırıldı.

**Bulgular:** Alt tipler arasında diyastolik ARV benzer bulunurken ( $p=0,919$ ), sistolik ARV açısından aralarında anlamlı fark bulundu ( $p<0,001$ ).

**Sonuç:** Kabızlık baskın alt tipi olan iritabl bağırsak sendromu hastalarının sistolik kan basıncı değişkenliği daha yüksek olduğundan, bu hastalar kardiyovasküler komplikasyonlar açısından daha yakından takip edilebilir.

**Anahtar Kelimeler:** Kan basıncı, kabızlık, ishal, iritabl bağırsak sendromu.

## Introduction

Irritable bowel syndrome (IBS) is characterized by abdominal pain and altered bowel habits.<sup>1</sup> Although it varies from region to region, it was revealed in a meta-analysis that the prevalence of IBS was around 11.5%.<sup>2</sup> Its prevalence is also quite high among patients admitted to internal medicine outpatient clinics. In a study conducted in Nigeria, the frequency of IBS was found to be 33% in patients who applied to general outpatient clinics.<sup>3</sup> The diagnosis of IBS can be made clinically according to the Rome IV criteria, and it is also possible to clinically classify IBS as IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), and IBS with mixed bowel habits (IBS-M).<sup>4</sup>

Hypertension is also an important public health problem, affecting one out of every 3 adults. Hypertension and its complications continue to be the most important causes of morbidity and mortality worldwide.<sup>5,6</sup> In recent years, many publications have suggested that blood pressure (BP) variability may be associated with complications as much as BP values.<sup>7-9</sup> Average real variability (ARV) is an important index of BP variability. The ARV can be calculated as the mean of the absolute differences in consecutive BP measurement values.<sup>10</sup>

Although IBS is considered a functional bowel disease, it may have a critical role in some systemic disorders. For example, there are publications reporting that IBS may be associated with a higher risk of dementia and that the risk of coronary artery disease increases 4 times in IBS patients.<sup>11,12</sup> Since different pathophysiological mechanisms play a role among IBS subtypes, we designed our study considering that different BP variability can be observed in IBS patients with hypertension according to subtypes. In this study, we aimed to compare BP variability in different subtypes of IBS in patients with hypertension and newly diagnosed IBS.

## Methods

### Patients

All patients with a diagnosis of hypertension and IBS symptoms who applied to the Internal Medicine outpatient clinic were informed about the study. The inclusion criteria for the study were: being older than 18 years old, diagnosed with hypertension, newly diagnosed with IBS, having their own FDA-approved and certified BP measurement device at home, volunteering to participate in the study, and having the ability to measure BP at home. Being younger than 18 years of age, not voluntarily participating in the study, not being able to take BP measurements at home, and not having an FDA-approved BP measuring device were determined as exclusion criteria from the study. It was checked whether the patients' BP measuring devices were FDA-approved on the <https://www.validatebp.org/> website. A signed informed consent form was obtained from all patients for their participation in the study.

### IBS Diagnosis and Subtypes

Rome IV criteria were considered for the diagnosis of IBS. IBS was diagnosed if two or more of the following were accompanied by recurrent episodes of abdominal pain at least once a week in the last 3 months; relief with defecation, change in stool frequency and change in stool form. The Bristol Stool Form Scale (BSFS) was used for IBS subtyping. Patients were divided into IBS-C, IBS-D, and IBS-M subgroups according to this scale. IBS-C; patients reporting

mostly constipation (type 1, and type 2 in the BSFS), IBS-D; patients reporting mostly diarrhea (type 6, and type 7 in the BSFS), and IBS-M; patients reporting both diarrhea, and constipation.

### BP Measurements and ARV

Verbal education and written brochures were given to all patients on how to measure their BP accurately. These brochures contained the following information;

- Do not exercise, do not eat, avoid caffeine-containing foods, and do not smoke half an hour before the BP measurement,
- Rest for 5 minutes before BP measurement,
- Never measure over your clothes,
- For BP measurement, keep your arm at heart level and support it with your other arm or a pillow,
- Release your hand on the BP side, do not punch,
- Do not talk during the measurement,
- Do not cross your legs during BP measurement,
- Take 3 measurements during the day preferably one in the morning, one in the afternoon and one in the evening in accordance with the specified rules, and record these 3 measurements on the BP follow-up forms given to you.

The average of these three measurements was used as the daily BP value of the patients. Seven-day BP measurements of the patients were recorded, and six  $\Delta$ BP measurements were obtained from these seven measurements by subtracting between consecutive measurements. ARV was calculated by taking the arithmetic mean of these six  $\Delta$ BP measurements. ARV formula=

$$ARV = \frac{1}{\sum w_k} \sum_{k=2}^n w_k \times |BP_k - BP_{k-1}|$$

$n$ = the number of BP measurements and  $w_k$  is the time interval between  $BP_k$  and  $BP_{k-1}$ .

### Statistical Analysis

Statistical analyzes were done with SPSS 26.0 (Statistics for Windows, version 26.0. Armonk, NY: IBM Corp.) package program. Categorical variables were expressed as percentages and frequency. The chi-square test was used to compare categorical variables between groups. The conformity of continuous variables to normal distribution was checked with the Shapiro-Wilk test. Continuous variables with normal distribution were presented as mean and standard deviation, and continuous variables without normal distribution were presented as median and interquartile range 1-3. One-way ANOVA or Kruskal Wallis test was used according to the presence or absence of normal distribution for continuous variable comparison between groups. The repeated measures test was used to determine the p-value for the trend of 7-day BP measurements. A pairwise comparisons test was used while performing post-hoc analysis for ARV values.  $p < 0.005$  is considered statistically significant.

## Results

One hundred and twelve patients were evaluated for the study. 104 patients with complete BP measurements were included in the analyses. The median age of the study group was 49 years (IQR1-3= 46-51.75 years). Of the patients 65.4% ( $n= 68$ ) were female. IBS symptoms accompanying abdominal pain are, in order of frequency; relief of symptoms with defecation in 78.8% ( $n= 82$ ), change in stool form in

74% (n= 77), and change in defecation frequency in 62.5% (n= 65). According to BSFS, 34.6% (n= 36) of the patients had IBS-D, 33.7% (n= 35) had IBS-M and 31.7% (n= 33) had IBS-C subtype. Table 1 shows the comparison of patients' age, gender, antihypertensive drugs, and IBS symptoms according to IBS subtypes.

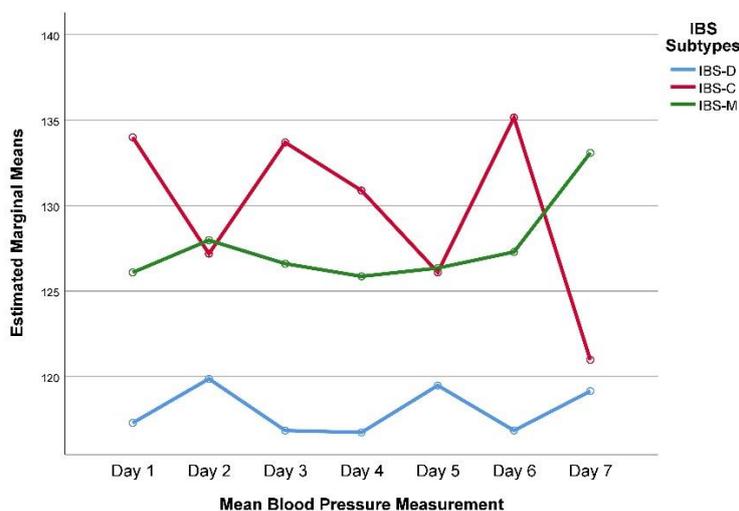
The course of BP in all three IBS subtypes was statistically significantly different ( $p<0.001$ ). Figure 1 shows the 7-day BP trends by IBS subtypes. While diastolic ARV was found

to be similar among IBS subtypes ( $p=0.919$ ), a significant difference was found between them in terms of systolic ARV ( $p<0.001$ ). The highest systolic ARV was found in the IBS-C group, while the lowest systolic ARV was found in the IBS-D group. Figure 2 shows the comparison of systolic and diastolic ARV among groups. In the pairwise comparisons test performed, the systolic ARV of all IBS subtypes were found to be statistically significantly different from each other ( $p<0.001$ ).

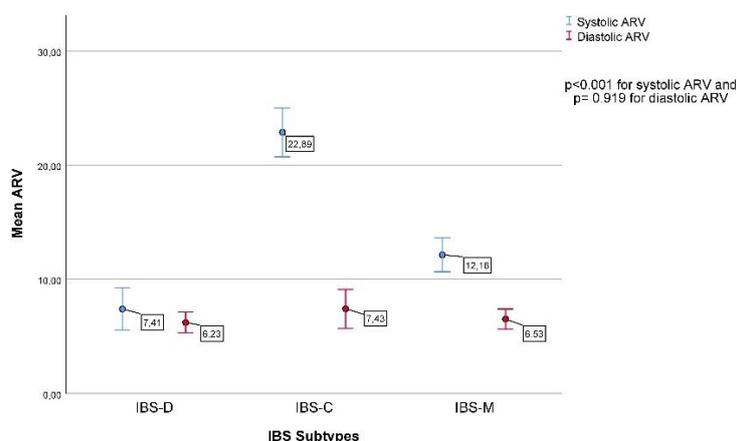
**Table 1.** Comparison of subgroups in terms of general characteristics

Characteristics	IBS-D (n= 36)	IBS-M (n= 35)	IBS-C (n= 33)	p
Age, median (IQR1-3)	49 (45-54)	48 (46-51)	49 (45-51)	0.699
Female gender, %-n	61.1-22	68.6-24	66.7-22	0.790
RAS blocker, %-n	88.9-32	85.7-30	90.9-30	0.795
CCB, %-n	13.9-5	25.7-9	21.2-7	0.456
Diuretics, %-n	25-9	14.3-5	21.2-7	0.523
Relief with defecation, %-n	86.1-31	77.1-27	72.7-24	0.379
Change in stool form, %-n	75-27	74.3-26	72.7-24	0.976
Change in defecation frequency, %-n	61.1-22	60-21	66.7-22	0.832

RAS= Renin Angiotensin System, CCB= Calcium Channel Blocker



**Figure 1.** The 7-day blood pressure trends by irritable bowel syndrome



**Figure 2.** The comparison of systolic and diastolic average real variability among groups

**Discussion**

While the gastrointestinal system has its own enteric nervous system, it is also stimulated by the autonomic nervous system through the sympathetic and parasympathetic nerves. It is thought that the interactions between these two nervous

systems and the gut may play an important role in the pathophysiology of IBS.<sup>13</sup> In a randomized controlled trial, Zhang et al showed that autonomic nervous system dysfunction is associated with an increase in the day-night systolic BP gradient.<sup>14</sup> In our study, we found that the 7-day BP trend varied significantly in all subtypes of IBS. We think

that autonomic nervous system dysfunction in IBS may play a role in the 7-day BP variability in IBS subtypes.

The parasympathetic nervous system exerts its effects on the gastrointestinal tract via the vagus and pelvic nerves. The main purpose of the parasympathetic nervous system is to regulate functions such as energy conservation and digestion, which are summarized with the words "rest and digest".<sup>15</sup> van Orshoven et al showed parasympathetic nervous system involvement in IBS and emphasized that new studies are needed to reveal its relationship with subtypes.<sup>16</sup> It has also been shown that there is a relationship between parasympathetic dysfunction and hypertension and blood pressure variability.<sup>14,17,18</sup> We found that BP variability in IBS patients with the IBS-C subtype was higher than in the IBS-D and IBS-M subtypes. Mazur et al showed that parasympathetic dysfunction and sympathetic overactivity were associated with constipation in IBS patients.<sup>19</sup> We think that our finding is probably due to parasympathetic dysfunction in IBS-C patients. The lowest BP variability in IBS-D patients may possibly be related to parasympathetic overactivity and sympathetic dysfunction, which may also explain the diarrheal symptom in these patients.

An increase in BP variability is associated with an increased risk of organ damage and cardiovascular mortality.<sup>8,20,21</sup>

Knowing that IBS-C patients with hypertension may be riskier in terms of cardiovascular disease may reduce the morbidity and mortality of these patients. According to the findings of our study, since IBS patients with the IBS-C subtype have higher systolic BP variability, these patients can be followed more closely for cardiovascular complications. Single-center, cross-sectional and small number of patients can be considered as limitations of our study. Since it is a cross-sectional study, it is not possible to establish a cause-effect relationship with the findings of our study. However, our study is important because it is the first study to investigate blood pressure variability in IBS subtypes.

## Conclusion

Our study showed that 7-day BP variability was higher in IBS patients with the IBS-C subtype compared to other subtypes. Larger studies investigating the clinical implications of this finding are needed.

## Conflict of Interest

We declare no conflicts of interest concerning the authorship and/or publication of this article.

## Compliance with Ethical Statement

Ethics Committee approval was received at the Local Ethics Committee meeting dated 07.10.2022 (code of ethics committee: 2011-KAEK-2, meeting number: 2022/12, decision number: 490).

## Financial Support

No financial support was received for the study.

## Author Contributions

Study idea/Hypothesis: EDK, SK, OT; Data preparation: EDK, SK; Analysis: SK; Literature search: EDK, OT; Manuscript writing: EDK, SK, OT; Critical review: SK, OT

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