Evaluation of Left Ventricular Function of Patients with Irritable Bowel Syndrome with Tissue Doppler and 2D Speckle Tracking Echocardiography

Hakan Tasolar[1], Selami Demirelli[2], Havva Yilmaz[3], Esra Poyraz[2], Husnu Degirmenci[4], Mehmet Balli[1], Mustafa Cetin[1]

[1] Adiyaman University, Training and Research Hospital, Department of Cardiology, Adiyaman, Turkey
[2] Erzurum Training and Research Hospital, Cardiology, Erzurum, Turkey
[3] Erzurum Training and Research Hospital, Internal Medicine, Erzurum, Turkey
[4] Erzincan University, Faculty of Medicine, Cardiology, Erzincan, Turkey

Abstract

We aimed to evaluate the systolic and diastolic functions of left ventricule in irritable bowel syndrome (IBS) by conventional echocardiography and two-dimensional (2D) speckle tracking echocardiography (STE) method. Thirty patients with IBS diagnosed with Rome III criteria were referred to our clinic. Standart echocardiographic and 2D-STE evaluation were obtained from all participants. C-reactive protein and erythrocyte sedimentation rate showing inflammation were significantly higher in patients with IBS compared to control group. Comparision of echocardiographic and tissue doppler imaging parameters measured from the septal mitral annulus demonstrated similar values between both groups. There were not any differences between the groups in terms of SRS-3C, SRE-4C, SRE-3C, SRE-2C, GLSRE, SRA-4C, SLA-3C, SLA-2C and GLSRA (p>0.05, for all). GLS (p=0.002), GLSRS (p=0.021), SRS-2C (p=0.030), S-4C (p=0.001), S-3C (p=0.025) and S-2C (p=0.012) values were significantly lower in IBS patients than in the control group. Our results suggest that IBS of which pathogenesis cannot be clearly elucidated is an inflammatory process and the heart may also be affected from this process. 2D-STE can also be useful in determination of subclinical left ventricular dysfunction in IBS patients.

Keywords: Irritable bowel syndrome, subclinical left ventricular dysfunction, strain, strain rate, two-dimensional speckle tracking echocardiography

(Rec.Date: Feb 25, 2015 Accept Date: March 30, 2015)

Corresponding Author: Dr. Hakan Tasolar. T.C. Sağlık Bakanlığı Adiyaman Üniversitesi Eğitim ve Araştırma Hastanesi, Hastane Cad. Merkez, Adiyaman, Turkey
Phone: +90 416 2161015 / 1387 **Fax:** +90 416 214 25 25
E-mail: hakantasolar@gmail.com

Introduction

Chronic disorder not only causes physical pain for humans, but also have serious effects on quality of life of people by affecting their social life and psychological dimensions [1]. Irritable bowel syndrome (IBS) is a prevalent and distressing problem which is diagnosed by symptoms of abdominal pain and discomfort along with disorder in excretion without any organic causes [2-4]. Epidemiologic studies showed the prevalence of this disease around the world has been reported as 10-20% among adults and adolescents and more women than men are affected [5]. At present the main mechanism behind IBS is considered to be dysfunction of the brain-gut axis associated with disturbed motor activity of the digestive tract, visceral hypersensitivity and disturbed neuroimmunologic response of the intestines [6]. Patients with IBS frequently present impaired outonomic regulation. Liu et al. [7] investigate heart rate variability (HRV) in patients with IBS. They found that difference of HRV in the general IBS population. For this reasons we hypothesized that there might be an association between left ventricule (LV) dysfunction and IBS.

Tissue Doppler Imaging (TDI) have major disadvantages such as angle dependence, limited spatial resolution and deformation analysis in one dimension. The recent development of two-dimensional (2D) speckle tracking echocardiography (STE) overcomes some of these limitations and its superiority to Doppler strain has been demonstrated [8]. This new echocardiographic approach allows the objective evaluation of both regional and global systolic and diastolic functions of myocardium in detail. According to our knowledge, no study has assessed LV functions in patients with IBS. Therefore, the aim of this study was to evaluate the systolic and diastolic functions of LV in IBS by conventional echocardiography and STE method.

Materials and Methods

Thirty patients with IBS who were first diagnosed according to the Rome III criteria [2] were referred from the gastroenterologist for considerations of inclusion in this study. Exclusion criteria were as follows: coronary artery disease, diabetes mellitus, hypertension, decreased LV function, valvular heart disease, pulmonary artery hypertension, arrhythmia, renal and hematological disorders, being on medications known to afffect the echocardiographic parameters and inadequate image quality. Age-sex matched 30 healty subjects were selected

as the control group. All of participants were informed about the procedure, and their written consents were obtained. The study protocol was approved by the local Ethical Committee and conducted according to the Helsinki Declaration.

Standard Echocardiographic Study

All echocardiographic measurements were performed by 2 experienced cardiologists blinded to each other. For each subject included in the study, echocardiographic measurements were performed at the left lateral position with Vingmed ultrasonund system (Vingmed System 7, General electric, Horten, Norway) using 2.5 MHz transducer. LV ejection fraction (EF) was measured with the Teichholz method [9]. Left ventricular end-diastolic volume, end-systolic volume, left atrial diameter and interventricular septum diastolic were measured from the parasternal long axis in accordance with the recommendations of American Society of Echocardiography's Guidelines [10]. Trans mitral Doppler velocities at the mitral valve level were measured by apical four chamber view. Early and late mitral inflow velocity, E/A ratio, and deceleration time were obtained. Systolic, early diastolic and late diastolic velocities were measured from the septal mitral annulus by TDI apical four chamber.

Strain and Strain Rate Measurements

The automated function imaging protocol was used to evaluate LV longitudinal strain (S), LV longitudinal strain rate systolic (SRS), LV longitudinal strain rate diastolic early filling (SRE), and longitudinal strain rate diastolic early filling (SRA) parameters [10]. 2D echocardiographic images were obtained from apical 4-chamber (4C), 2-chamber (2C) and 3-chamber (3C) views and images of LV were stored digitally. All images were obtained while the patients held their breath and the images were stored in a cineloop format from three consecutive beats. The position of the sample volume for velocity and strain measurements was manualy positioned in the myocardium throughout the cardiac cycle. Frame rates were recorded to include 60-100 frame/sec.Digital loops were stored and transferred to a work station (Echo PAC, GE Vingmed Ultrasound) for offline analysis. A line was traced along the endocardium of left ventricles at the frame where it was best defined. Strain and strain rate measurements were taken from a total of 5 spots at each long apical imaging with optional manual adjustment. The mean S, SRS, SRE and SRA values were calculated for each of the 3

views. The values for the global longitudinal LV strain (GLS), global longitudinal SR (GLSRS, GLSRE, GLSRA) were calculated as the arithmetical mean of the values.

Statistical analysis

Statistical analysis was performed using SPSS package program (Chicago, IL, USA). Results are reported as the mean ± SD or, frequency and percentage. Statistical analysis of clinical data between two groups consisted of unpaired t-tests for parametric data and Mann Whitney U test analysis for nonparametric data. Level of significance was established at the 0.05 level.

Results

Demographic data of the study population are presented in Table 1. Mean age and gender were comparable between the two groups. There were also no significant differences in systolic and diastolic blood pressure, body mass index and heart rate. C-reactive protein and erythrocyte sedimentation rate showing inflammation were significantly higher in patients with IBS compared to control group ($p<0.001$, for both of them).

Table 1. Demographic data of the study population

Variables	Patients with IBS (n=30)	Control group (n=30)	p Value
Age (years)	35.00±3.54	34.60±2.21	NS
Gender (male, %)	14 (47%)	16 (53%)	NS
BMI (kg/m^2)	23.00±2.74	22.34±3.10	NS
SBP (mmHg)	110.00±13.45	107.56±10.10	NS
DBP (mmHg)	72.00±11.69	69.04±10.70	NS
HR(beats/m)	68±4.54	69.30±5.17	NS
ESR (mm/h)	18.83±9.00	12.00±2.98	<0.001
CRP (mg/L)	1.74±0.45	0.49±0.13	<0.001

Data are expressed as mean ± SD; NS, not significant. BMI, body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; EDV, end-diastolic volume; ESV, end-systolic volume; ESR, erythrocyte sedimentation rate; HR, heart rate; IVSd, interventricular septum end diastolic diameter; LA, Left atrium; LVEF, left ventricle ejection fraction; SBP, systolic blood pressure.

Echocardiographic and transmitral Doppler parameters of the both group are shown in Table 2. Comparision of echocardiographic and TDI parameters measured from the septal mitral annulus demonstrated similar values between both groups ($p>0.05$, for all of them).

Table 2. Echocardiographic data of the study population

Variables	Patients with IBS (n=30)	Control group (n=30)	p value
EF (%)	68.30±2.83	69.47±3.62	NS
EDV (mL)	114.53±18.90	113.73±22.2	NS
ESV (mL)	36.80±11.09	38.6±10.93	NS
IVSd (mm)	9.80±1.20	8.91±1.96	NS
PWd (mm)	9.3±0.9	9.4±1.0	NS
LA (mm)	31.51±4.62	30.10±3.62	NS
E velocity (m/sec)	0.83±0.15	0.89±0.15	NS
A Velocity (m/sec)	0.54±0.12	0.57±0.15	NS
dT (msec)	192.00±34.5	179±26.12	NS
E/A ratio	1.53±0.12	1.56±0.18	NS
Em peak (cm/sec)	14.5±2.37	14.71±2.48	NS
Am peak (cm/sec)	8.1 ±2.37	8.36±1.11	NS
Sm (cm/sec)	11.42±1.39	11.47±1.44	NS
IVRT	80.7±6.0	80.8±3.7	NS
IVCT	42.1±8.0	41.0±3.7	NS

A=Mitral late diastolic velocity, Am=LV myocardial late diastolic velocity, dT=Mitral E-wave deceleration time, E=Mitral early diastolic velocity, Em=Left ventricule myocardial early diastolic velocity, EDV=End diastolic volume, EF=Ejection fraction, ESV=End systolic volume, IVCT=Isovolumetric contraction time, IVSd=Interventricular septal thickness, IVRT=Isovolumetric relaxation time, PWd=Posterior wall thickness, Sm= Left ventricule systolic myocardial velocity.

LV global longitudinal strain and strain-rate parameters are presented in Table 3. There were not any differences between the groups in terms of SRS-3C, SRE-4C, SRE-3C, SRE-2C, GLSRE, SRA-4C, SLA-3C, SLA-2C and GLSRA ($p>0.05$, for all). GLS ($p=0.002$), GLSRS ($p=0.021$), SRS-2C ($p=0.030$), S-4C ($p=0.001$), S-3C ($p=0.025$) and S-2C ($p=0.012$) values were significantly lower in IBS patients than in the control group.

Table 3. Comparison of longitudinal and global strain and strain rate parameters of patient and control groups

Variables	Patients with IBS (n=30)	Control group (n=30)	p Value
S-4C	-21.13±1.28	-22.56±1.27	**0.001**
S-3C	-21.79±1.31	-22.67±1.46	**0.025**
S-2C	-22.52±1.36	-23.96±1.45	**0.012**
GLS	-21.78±0.99	-23.03±1.23	**0.002**
SRS-4C	-1.10±0.15	-1.27±0.15	**0.004**
SRS-3C	-1.14±0.22	-1.17±0.13	0.213
SRS-2C	-1.12±0.21	-1.18±0.14	**0.030**
GLSRS	-1.12±0.14	-1.20±0.09	**0.021**
SRE-4C	1.84±0.17	1.86±0.08	0.487
SRE-3C	1.82±0.17	1.82±0.10	0.943
SRE-2C	1.77±0.20	1.80±0.15	0.431
GLSRE	1.81±0.18	1.83±0.86	0.554
SRA-4C	0.66±0.20	0.69±0.53	0.396
SRA-3C	0.71±0.17	0.74±0.08	0.467
SRA-2C	0.71±0.17	0.76±0.17	0.224
GLSRA	0.69±0.18	0.74±0.12	0.255

4C-3C-2C= apical four-, three-, and two-chamber views, GLS= Global longitudinal strain, GLSR=Global longitudinal strain rate, LS=Longitudinal strain, SRS=Systolic longitudinal strain rate, SRE=Early diastolic strain rate, SRA=Late diastolic strain rate.

Discussion

In our study, we found that S-4C, S-3C, S-2C and GLS values were lower in IBS patients compared to the control group. SRS-4C, SRS-2C and GLSRS values were also found to be lower in patients group. C-reactive protein and erythrocyte sedimentation rate values were higher in IBS patients.

IBS is reported to be an inflammatory process in several studies [11]. It has also been reported that IBS can be accompanied to the autonomic nervous system dysfunction in various publications [12-16]. These conditions may cause changes in the electrical activity and contraction problems of the heart. Changing of the contraction dynamics can lead to myocardial dysfunction. Furthermore the occurrence of inflammatory processes cause changes in the sequences of myocardial fibers via focal fibrosis [16]. This pathophysiological process may result in myocardial deformation. In addition, autonomic dysfunction is known to cause visceral hypersensitivity by changing levels of serotonin and noradrenaline [17]. We therefore consider that cardiac catecholaminergic toxicity can lead to deformation affecting

myocardial contractility. Not only autonomic dysfunction, but emotional stress accused in the pathogenesis of IBS can cause myocardial toxicity by causing catecholaminergic discharge as well [18]. Cardiac involvement may become apparent as a result of these existing pathological processes. If subclinical dysfunction is not detected, QT prolongation secondary to autonomic dysfunction may cause cardiac contractility disorders as a results of myocardial deformation [19]. Therefore it is extremely important to detect subclinical dysfunction.

Myocardial deformation can be detected by 2D-STE on which many studies recently performed [20,21]. Demirelli et al. [22] showed in their study that STE can be useful in determination of subclinical LV dysfunction in patients with Behcet's disease. In another study, Sitia et al. [23] stated that non invasive evaluation of LV function by STE appears to be useful to detect subclinical cardiac involvement in rheumatoid arthritis patients. Hereby, early diagnosis of cardiac dysfunction can be provided by the identification of cardiac involvement during the course of subclinical condition. That LV peak SRS negatively affected may be the result of the adversely affected of the contraction function of the myocardial mass. We consider that this situation may be a result of the autonomic nervous system dysfunction. In the present study, the same of diastolic strain rate parameters in the patient group as the control group may be due to the early diagnosis of IBS. Lack of long-term follow of the patients in this direction may be a limitation of our study. In addition inadequate number of patients is another limitation.

Conclusion

In conclusion, our results suggest that IBS of which pathogenesis cannot be clearly elucidated is an inflammatory process and the heart may also be affected from this inflammatory process. Furthermore 2D-STE can also be useful in determination of subclinical left ventricular dysfunction in IBS patients. Additional large-scale studies are needed for the clinical implementation of our study results.

References

1. Hanestad BR. Quality of life and insulin dependent diabetes mellitus. University of Bergen, Bergen, 1992;36.
2. Engsbro AL, Simrén M, Bytzer P. The Rome II and Rome III criteria identify the same subtype-populations in irritable bowel syndrome: agreement depends on the method used for symptom report. Neurogastroenterol Motil. 2012;24(7):604-11,e266.
3. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Müller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut. 1999;45 Suppl 2:II43-7.
4. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology. 2006;130(5):1480-91.
5. Pae CU, Masand PS, Ajwani N, Lee C. Irritable bawel syndrome in psychiatric perspective: A comprehensive review. Int J Clin Pract. 2007;61(10):1708-18.
6. Catanzaro R, Occhipinti S, Calabrese F, Anzalone MG, Milazzo M, Italia A, Marotta F. Irritable bowel syndrome: new findings in pathophysiological and therapeutic field. Minerva Gastroenterol Dietol. 2014;60(2):151-63.
7. Liu Q, Wang EM, Yan XL, Chen SL. Automatic functioning in irritable bowel syndrome as measured by heart rate variability: a meta-analysis. J Dig Dis. 2013;14(12):638-46.
8. Teske AJ, De Boeck BW, Melman PG, Sieswerda GT, Doevendans PA, Cramer MJ. Echocardiographic quantification of myocardial function using tissue deformation imaging, a guide to image acquisition and analysis using tissue Doppler and speckle tracking. Cardiovasc Ultrasound. 2007;5:27.
9. Teichholz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence of absence of asynergy. Am J Cardiol. 1976;37(1):7-11.
10. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1-39.e14.
11. Collins SM. Is the irritable gut an inflamed gut? Scand J Gastroenterol Suppl. 1992;192:102-5.
12. Wilder-Smith CH, Schindler D, Lovblad K, Redmond SM, Nirkko A. Brain functional magnetic resonance imaging of rectal pain and activation of endogenous inhibitory mechanisms in irritable bowel syndrome patient subgroups and healthy controls. Gut. 2004;53(11):1595–601.
13. van Orshoven NP, Andriesse GI, van Schelven LJ, Smout AJ, Akkermans LM, Oey PL. Subtle involvement of the parasympathetic nervous system in patients with irritable bowel syndrome. Clin Auton Res. 2006;16(1):33-9.

14. Jarrett ME, Burr RL, Cain KC, Hertig V, Weisman P, Heitkemper MM. Anxiety and depression are related to autonomic nervous system function in women with irritable bowel syndrome. Dig Dis Sci. 2003;48(2):386-94.
15. Heitkemper M, Burr RL, Jarrett M, Hertig V, Lustyk MK, Bond EF. Evidence for autonomic nervous system imbalance in women with irritable bowel syndrome. Dig Dis Sci. 1998;43(9):2093-8.
16. Karling P, Nyhlin H, Wiklund U, Sjöberg M, Olofsson BO, Bjerle P. Spectral analysis of heart rate variability in patients with irritable bowel syndrome. Scand J Gastroenterol. 1998;33(6):572-6.
17. Schäfermeyer A, Gratzl M, Rad R, Dossumbekova A, Sachs G, Prinz C. Isolation and receptor profiling of ileal enterochromaffin cells. Acta Physiol Scand. 2004;182(1):53-62.
18. Furlan R, Colombo S, Perego F, Atzeni F, Diana A, Barbic F, Porta A, Pace F, Malliani A, Sarzi-Puttini P. Abnormalities of cardiovascular neural control and reduced orthostatic tolerance in patients with primary fibromyalgia. J Rheumatol. 2005;32(9):1787-93.
19. Higham PD. Campbell RW. QT dispersion. BR Heart J. 1994;71(6):508-10.
20. Binnetoğlu FK, Yıldırım Ş, Topaloğlu N, Tekin M, Kaymaz N, Aylanç H, Karakurt H. Early detection of myocardial deformation by 2D speckle tracking echocardiography in normotensive obese children and adolescents. Anadolu Kardiyol Derg. 2015;15(2):151-7.
21. Altiok E, Neizel M, Tiemann S, Krass V, Becker M, Zwicker C, Koos R, Kelm M, Kraemer N, Schoth F, Marx N, Hoffmann R. Layer-specific analysis of myocardial deformation for assessment of infarct transmurality: comparison of strain-encoded cardiovascular magnetic resonance with 2D speckle tracking echocardiography. Eur Heart J Cardiovasc Imaging. 2013;14(6):570-8.
22. Demirelli S, Degirmenci H, Bilen H, Ermis E, Duman H, Arisoy A, Bakirci EM, Ipek E, Askin L. Left ventricular mechanics in Behcet's disease: a speckle tracking echocardiographic study. Bosn J Basic Med Sci. 2014;14(3):160-4.
23. Sitia S, Tomasoni L, Cicala S, Atzeni F, Ricci C, Gaeta M, Sarzi-Puttini P, Turiel M. Detection of preclinical impairment of myocardial function in rheumatoid arthritis patients with short disease duration by speckle tracking echocardiography. Int J Cardiol. 2012;160(1):8-14.