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Assessment of left ventricular function by strain–strain rate echocardiography in patients with celiac disease

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Background/aim: Celiac is predominantly a disease of the small intestine characterized by chronic malabsorption in genetically susceptible individuals who ingest grains containing gluten, such as wheat, barley, and rye. In the present study, we evaluate left ventricular function in patients with celiac disease by using strain and strain rate echocardiography imaging.

Materials and methods: Twenty celiac patients and 20 healthy controls were included in this study. Left ventricle systolic and diastolic functions were evaluated with standard 2-dimension, M-mode, conventional Doppler echocardiography. Strain and strain rate parameters were obtained for 8 segments of the left ventricle.

Results: There were no significant differences between patients and controls regarding left ventricle function as assessed by 2-dimensional, M-mode, conventional Doppler. Differences between strain rate values did not reach statistical significance, but when strain and average strain values were taken into consideration, statistically significant differences were found between the groups.

Conclusion: We determined the subclinical effect of celiac disease on left ventricular systolic function by using strain echocardiography imaging for the first time in the literature. We showed that evaluation of the cardiac involvement in celiac patients by sophisticated echocardiography techniques is essential.

Key words: Celiac disease, strain–strain rate echocardiography, cardiac involvement

1. Introduction

Celiac disease (CD), or celiac sprue, is a chronic inflammatory disease of the small bowel that is characterized by chronic malabsorption in susceptible individuals who ingest grains containing gluten and gliadin, such as wheat, barley, and rye. CD is often seen during childhood and adolescence with a classic malabsorption syndrome, but it may also develop in adulthood. CD prevalence can vary from 0.1% to 1% (1,2). The major clinical symptoms are chronic diarrhea, abdominal pain, and weight loss and many CD patients show atypical symptoms such as iron deficiency anemia, osteopenia, infertility, and oral findings. Ertekin et al. demonstrated a significantly different and increased prevalence of dental enamel defects among CD patients and healthy controls (3). In CD, intolerance to dietary wheat, gliadin, and gluten causes chronic mucosal inflammation in the proximal small intestine. In chronic inflammatory diseases like connective tissue disorders (rheumatoid arthritis, Behçet disease, and systemic lupus erythematosus), cardiac involvement is common. Thus, in CD, cardiac involvement is expected like in other chronic inflammatory diseases. Polat et al. showed, through tissue Doppler imaging (TDI), that subclinical cardiac dysfunction and cardiac involvement are present in CD during the childhood period (4). Another disorder frequently associated with CD is idiopathic dilated cardiomyopathy. In the literature, several studies evaluated the relationship between CD and autoimmune disorders (5). Curione et al. demonstrated an immunologic associative mechanism and an increased prevalence of CD in patients who have idiopathic dilated cardiomyopathy (6).

The strain and strain rate technique is an important alternative to the standard conventional and TDI methods. The strain and strain rate technique originates from the TDI technique. Strain and strain rate imaging defines myocardial deformation and the strain rate measurements define the rate of deformation. The TDI technique has

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some limitations such as tissue effects, tethering, and the rotation motion of the heart. With the strain and strain rate technique, these limitations may be reduced. As shown in the literature, some limitations of the TDI technique (like angle dependency and rotation motion of the heart) may be overcome with the strain and strain rate imaging (7). As far as we know, cardiac dysfunction in celiac patients has not been examined using the strain and strain rate technique before. Aksakal et al. showed that with strain and strain rate echocardiography it may be possible to determine early and subclinical left atrium myocardial dysfunction in patients with mitral stenosis (8). In light of the foregoing research, we tried to detect early and subclinical myocardial dysfunction through strain and strain rate echocardiography technique in celiac patients.

This trial was originally designed to identify myocardial function in patients with CD using the strain and strain rate technique to evaluate possible left ventricle myocardial involvement.

2. Materials and methods

This study was performed at a single center in collaboration with gastroenterology and cardiology clinics. Table 1 shows the exclusion criteria of the study and Table 2 compares the data of the 20 CD patients included and 20 healthy volunteers from the cardiology polyclinic who had similar baseline characteristics. Volunteers with normal echocardiographic findings were considered as controls. The patient group was matched 1:1 with the control group. Each patient in the celiac group was matched manually with a control individual for age, sex, body mass index, smoking habits, and other coronary artery disease risk factors (family history, hyperlipidemia, hypertension) in order to exclude factors that might possibly affect the analysis of the data. They were observed between September 2009 and February 2010 and incorporated into the study. The ethics board of the hospital approved the study and before the study enrollment informed consent was obtained from each subject.

Table 1. Exclusion criteria of the study.

- Significant (moderate to severe) valve disease
- <60% ejection fraction
- Arrhythmia
- Structural or congenital heart disease (HOCMP, ASD, VSD)
- Coronary artery disease
- Active infection, malignancy, or pregnancy
- Other systemic inflammatory diseases
- Diabetes mellitus
- Hypertension
- Renal insufficiency or high values of serum urea, creatinine
- Chronic obstructive pulmonary disease
- Unconscious patients
- BMI > 35 kg/m^2

2.1. Echocardiographic study

The echocardiographic examination (conventional echocardiography, strain–strain rate technique) was performed with a 2.5–3.5 MHz transducer and Vingmed 7 system (Vivid 7 Pro Ultrasound; Horten, Norway) echocardiography machine. All images were obtained from the parasternal long axis, apical 2 and 4 chamber views, and 3 consecutive waveforms represented a cardiac cycle. M-mode standard 2-dimensional measurements were performed according to the recommendations of the American Society of Echocardiography (9,10). The modified Simpson method and Teichholz formula were used to calculate the left ventricle ejection fraction. The echocardiographic recordings were obtained by a single observer.

For longitudinal strain and strain rate measurements, apical 2 and 4 chamber views were used and a minimum of 3 consecutive cardiac cycles were recorded in digital format. Dynamic images were put in a file at a rate of 160–210 frames/s in tissue velocity imaging mode. Peak systolic strain and peak systolic strain rate analyses were performed at middle and basal segments of the anterior, inferior, lateral, and septum walls. Apical segments were not evaluated because of insufficient parallel projection and limitations in getting clear images.

2.2. Statistical analysis

Statistical evaluation was done using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA). The Shapiro–Wilk test was used to test the normal distribution of permanent variables. Permanent variables were described as mean ± standard deviation or median (interquartile range), and nominal variables were expressed as number of patients and percentages. To compare the groups, Student's t-test for mean values and the Mann–Whitney U test for median values were used. The chi-square test was used for nominal variables. $P < 0.05$ was considered statistically significant.

3. Results

The study involved 20 patients with CD (2 males, 18 females) and 20 healthy volunteers (1 male, 19 females). The demographic and clinical characteristics of the studied patients are shown in Table 2. The 2 groups had similar features in terms of their body mass index, sex, age, possibility of having hyperlipidemia, and smoking habits (Table 2). The wall thicknesses and the left ventricular systolic and diastolic diameters were also similar. Furthermore, we found that the left ventricular ejection fraction was similar and in the normal range (67.8% and 68.5%, respectively; P: NS). There were no significant differences between the 2 groups in terms of conventional echocardiographic results.

Table 2. The demographic characteristics and conventional echocardiographic measurements of the subjects in the study population. EF: Ejection fraction, IVS: interventricular septum, PW: posterior wall, LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter.

Parameters	Patient group (n = 20)	Control group (n = 20)	P-value
Sex (male/female)	2/18	1/19	0.56
Age (years)	31.9 ± 9.2	30.5 ± 10.5	0.66
Body mass index (kg/m^2)	23.5 ± 4.4	21.8 ± 3.7	0.17
Total cholesterol (mg/dL)	165 ± 40	162 ± 44	0.78
HDL (mg/dL)	50.5 ±7.4	52.1 ± 12.5	0.61
LDL (mg/dL)	100 ± 22	108 ± 35	0.39
Triglyceride (mg/dL)	108 ± 44	98 ± 31	0.39
Smoking (%)	20	25	NS
LVEDD (mm)	4.49 ± 0.45	4.4 ± 0.3	0.67
LVESD (mm)	2.8 ± 0.3	2.7 ± 0.2	0.24
IVS (mm)	9.2 ± 0.8	9.1 ± 0.8	0.85
PW (mm)	9.0 ± 0.7	8.9 ± 0.1	0.60
EF (%)	67.8 ± 4.1	68.5 ± 4.1	0.59
Mitral E (cm/s)	0.88 ± 0.17	0.92 ± 0.12	0.35
Mitral A (cm/s)	0.68 ± 0.15	0.62 ± 0.1	0.12
Left atrium diameter (mm)	31.2 ± 3.3	29.2 ± 3.79	0.08

Mean strain value was calculated from the left ventricular strain and strain rate measurements. The differences in the strain rate values were not statistically significant (Table 3). When strain and average strain values were taken into consideration, statistically significant differences were found between the groups (Table 4). Strain values obtained from 3 of the 8 segments of the left ventricle (mid anterior wall, mid interventricular septum, basal interventricular septum) were significantly higher in the control patients than the celiac patients ($P < 0.05$). There was no significant difference between the groups in terms of the basal anterior wall or the basal and middle segments of the inferior and lateral wall. The average strain value of the left ventricle was less in controls than in CD patients (21.05 ± 2.29, 23.74 ± 1.51) and these values represent statistical significance ($P < 0.001$).

4. Discussion

In this study, we evaluated the strain and strain rate technique to define cardiac involvement in CD. Our findings reveal that strain and strain rate imaging were superior to conventional echocardiography to evaluate cardiac involvement in CD. In the literature, several studies have shown the relationship between CD and idiopathic dilated cardiomyopathy (5,6). Frustaci et al. diagnosed an increased prevalence of CD in patients with idiopathic congestive heart disease or myocarditis and these results indicate that this is related to the association of inflammatory myocardial diseases with autoimmunity. All patients in the study (187 patients in total) were examined and they found autoantibodies related to CD in 13 patients and serum IgA antiendomysium antibody positivity in 9 patients (4.4%) (5).

To explain the evolution of cardiomyopathy and left ventricular systolic and diastolic dysfunction, many theories have been suggested in CD. One possible explanation is for chronic malabsorption, which is common in CD, to have caused nutritional deficits, thereby leading to cardiomyopathy. According to another theory, intestinal absorption abnormalities may develop an increased absorption of infectious agents and antigens, which triggers immune mechanisms and leads to myocardial injury (11,12). Finally, another possible explanation for the cardiac involvement is the direct immune response that occurs both in the myocardium and small intestine and may cause myocardial damage and chronic malabsorption (13).

Table 3. Strain rate (SR) value results of the study groups.

Parameters	Patient group (n = 20)	Control group (n = 20)	P-value
Basal septum SR (1/s)	1.41 ± 0.28	1.41 ± 0.2	0.974
Mid septum SR (1/s)	1.54 ± 0.31	1.56 ± 0.26	0.825
Basal lateral SR (1/s)	1.46 ± 0.38	1.52 ± 0.3	0.578
Mid lateral SR (1/s)	1.29 ± 0.41	1.26 ± 0.29	0.832
Basal anterior SR (1/s)	1.76 ± 0.74	1.73 ± 0.32	0.869
Mid anterior SR (1/s)	1.2 ± 0.43	1.47 ± 0.45	0.082
Basal inferior SR (1/s)	1.41 ± 0.27	1. 46 ± 0.33	0.623
Mid inferior SR (1/s)	1.52 ± 0.35	1.53 ± 0.35	0.94
Mean SR (1/s)	1.45 ± 0.19	1.49 ± 0.13	0.43

Table 4. Strain (S) value results of the study population.

Parameters	Patient group (n = 20)	Control group (n = 20)	P-value
Basal septum S (%)	22.7 ± 4.5	25.8 ± 2.7	0.011
Mid septum S (%)	23.5 ± 4.7	26.7 ± 4.0	0.029
Basal lateral S (%)	20.3 ± 5.77	21.2 ± 6.43	0.639
Mid lateral S (%)	20.07 ± 4.59	21.6 ± 7.19	0.422
Basal anterior S (%)	22.8 ± 5.37	24.01 ± 4.84	0.457
Mid anterior S (%)	17.48 ± 5.52	23.6 ± 5.9	0.002
Basal inferior S (%)	20.5 ± 4.01	21.5 ± 4.24	0.438
Mid inferior S (%)	22.5 ± 4.5	25.2 ± 4.8	0.074
Mean S (%)	21.05 ± 2.29	23.7 ± 1.51	0.0001

In our study, none of the celiac patients had left ventricular systolic and diastolic dysfunction on conventional echocardiography. The possible reason for this might be that our study population was relatively small and our adult patients had been diagnosed long before the study, and so an appropriate diet could block myocardial damage and cardiac involvement. We found that left ventricle strain values were significantly lower in 3 out of 8 segments in the patient group in comparison to the controls. Regional distribution of segmental involvement did not exhibit any correlation with coronary artery distribution. Strain rate values were higher in the control group patients, but there was no significant difference between the 2 groups. One possible explanation for this finding is that our study population was small and the exclusion of apical segments might cause a failure in detecting any statistical significant difference. We found that in celiac patients, the mean strain value was lower in comparison to the control group, but these findings did not show any statistical significance.

Some limitations of our study should be noted. First of all, we used TDI-derived strain to evaluate the cardiac functions and did not use speckle tracking-derived 2D strain. The lack of angle dependency and lower interobserver variability is a great advantage of the 2D-strain imaging in comparison to TDI-derived strain data. Although 2D strain and TDI strain calculations do not give the same values (2D strain imaging gives lower strain rate values), strain and strain rate measurements obtained by these 2 different imaging techniques correlate well (14). A further study is required to determine left ventricular functions by using speckle tracking-derived 2D strain imaging echocardiography in adult patients with CD. Secondly, our study population was very small. We did power analysis, but unfortunately our study was not of sufficient strength since there was not a sufficient-number of patients to work with. This study power is inadequate for making a judgment. Future studies to examine this issue that have a large study population are needed.

In CD, the presence of antibodies has a positive interaction between the disease severity and its prognosis. Polat et al. showed that in antiendomysium antibody positive patients, systolic velocity is higher than in seronegative patients (4). This is another limitation of our study, as we did not group the patients according to the presence of antibodies.

In this study, we aimed to investigate cardiac functions in patients with CD by conventional echocardiography and strain–strain rate imaging. As noted above, we have found that strain and strain rate echocardiography is more valuable than conventional echocardiography in detecting cardiac involvement in patients with CD.

In conclusion, we tried to find subclinical effects of CD on the left ventricular systolic function by using strain echocardiography imaging. We found that an evaluation of the cardiac involvement in celiac patients by sophisticated echocardiography techniques is essential. These results indicated that, to evaluate cardiac involvement in patients with CD, a global assessment of left ventricular functions through mean strain and strain rate technique is more effective.

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