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Assessment of aortic and left ventricular functions in children with celiac disease

Ajda Mutlu Mıhcıoglu[1*], Hasret Ayyıldız Civan[2]

[1]Division of Pediatric Cardiology, Department of Pediatrics, University of Health Sciences Bakırköy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey.

[2]Division of Pediatric Gastroenterology, Department of Pediatrics, University of Health Sciences Bakırköy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey.

[*]**Corresponding author:** Ajda Mutlu Mıhçıoğlu, Division of Pediatric Cardiology, Department of Pediatrics, University of Health Sciences Bakırköy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey, Tel: 905057479765; E-mail: ajdamutlu@yahoo.com

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INTRODUCTION

Celiac disease (CD) is an autoimmune disease characterized with immune response to gluten in genetically predisposed people with inflammation, villous atrophy, crypt hyperplasia of the intestine effecting girls predominantly with a prevelance of 1-2% [1,2]. Genetic, immune, envoirenmental factors effect development of the disease. Autoimmune responses to tissue transglutaminase and endomysium are used for serological evaluation to identify the disease [3]. Gluten free diet (GFD) is suggested for reducing symptoms. Patients may be asymptomatic or severe symptomatic secondary to malabsorption. Extraintestinal clinical findings effecting hematologic, endocrinologic and neurologic systems also may be present. One another effected system is cardiovascular system. There are cases published with dilated cardiomyopathy (DCM) mostly in adults, but a casual relation between CD and DCM has not been proven yet. The inflammation in CD is systemic, effecting not only intestines but also extraintestinal tissues and is thought to be responsible from endothelial dysfunction that shows progression to atherosclerosis reflected by arterial stiffness and thicness [3]. Therefore our aim in this study is to evaluate the patients cardiac systolic and diastolic functions of the left ventricle and elasticity parameters of the adjacent aortic wall and to determine whether there is a clinical or subclinical cardiac involvement or not [1,2].

MATERIAL AND METHODS

We performed a prospective study among 45 patients with CD who were evaluated from pediatric gastroenterology outpatient polyclinic and 45 patients referred to pediatric cardiology polyclinic for murmur without any cardiac disorder. The diagnosis of CD was made according to European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) criteria [1,4]. Intestinal biopsy was performed to patients with CD and the specimens were evaluated according to Modified Marsh Classification according to histologic findings [1,5]. Their MARSH classification is and the duration CD is reported.

Patients were evaluated with physical examination, cardiac examination and laboratory parameters. The weight, height, sysolic and diastolic blood pressures of all of the patients were measured . Laboratory measurements that were routinely performed for evaluating the effects of the disease were used for the patients with CD. Anti tissue transglutaminase immunglobulin A and G (anti TTG IgA and anti TTG IgG, anti endomysium antibody IgA and IgG (anti EMA IgA and IgG), serum IgA were taken into consideration among these parameters and TTG and EMA IgA were used in the study. Cardiac examinations were performed with transthorasic echocardiography with 2D echocardiographic measurements, M-mode and tissure Doppler imaging. Also 12 channel electrocardiography was performed to each patient.

2D echocardiographic measurements

Patients were evaluated with echocardiography (EPIQ 7 Ultrasound System, Philips, Heide, Netherlands) machine, by using, S8 and S5 probes, while the patient was laying on the left lateral decubitis position. Conventional echocardiographic imaging was performed to declare if there is a structural heart diseases, valvular stenosis, insufficiency or other disorders. M-mode showed systolic functions of the left ventricle using Teichholz Formula [6,7]. M- mode was also performed to investigate the elasticity parameters of the ascending aorta by placing the cursor over ascending aorta perpendicularly at RPA level by using the following formulas [8]. Maximum diameter measured was accepted as the systolic diameter while the beginning of the QRS complex on electrocardiography was accepted as the diastolic diameter. The measurements were performed from inner edge to inner edge.

Aortic strain (AS) (%) = 100 (AoS - AoD)/AoD

Distensibility (DIS) (10-6 cm2.dyn-1) = [2(AoS - AoD)/AoD x100 / (PP)]

Beta stiffness index (SI) = ln(SBP/DBP)/[(AoS - AoD)/AoD]

Tissue Doppler echocardiographic measurements

Patients were evaluated with tissue Doppler imaging (TDI) with a sample volum of 2-5 mm, Nyquist limit between -20 and +20 cm/s and monitor rate between 50-100 mm/s for high temporal resolution [9]. The measurements were obtained when the cursor was placed on the mitral anulus on apical four

chamber view. Mitral early diastolic flow velocity (E) and late diastolic flow velocity (A) velocity, E wave deceleration time (EDT), A wave duration were measured with pulse wave Doppler and E/A was calculated. Then the cursor was placed on the conjuction of mitral anulus and interventricular septum at apical four chamber view and peak early diastolic wave velocity septal (E'septal), peak late diastolic wave velocity septal (A'septal), isovolumetric relaxation time septal (IVRT septal), isovolumetric contraction time septal (IVCT septal), mitral annular peak systolic velocity (S') were measured, E/E' septal, E'/A' septal and miyocardial performance index septal (MPI septal) were calculated. Afterwards the cursor was placed on the conjuction of mitral anulus and left ventricular free wall. E',A', S',IVCT, IVRT, E/E', E'/A', MPI were obtained as lateral measurements. MPI was calculated as IVCT+IVRT /Ejection time for both septal and lateral side. All of the measurements were repeated 3 times and the means of them were calculated and used in the study.

Informed constant was obtained from all the patients and their parents. Patients with hypertension or with other chronic diseases like diabetes mellitus, dyslipidemia, patients with structural heart disease, arrhythmia, systemic inflamatuar diseases were not included in the study [8]. Informed consent was obtained from all individual participants included in the study.

STATISTICS

Analyses were performed with NCSS 11 (Number Cruncher Statistical System, 2017 Statistical Software) Programme. Frequency and percentage were used for categorical variables. Mean, standard deviation, median, minimum and maximum values were used for continuous variables. Normal distribution of continuous variables was evaluated with Kolmogorov Smirnov test. The relationship between categorical variables was assessed with chi square test. Fisher exact and Fisher Freeman Halton tests were used for categorical variables when needed. Continuous independent variables that showed normal distribution were evaluated with T test for comparison of two groups, and ANOVA test for comparison of more than two groups. The variables that did not show normal distribution were assessed with Mann Whitney U test for comparison of independent two groups and Kruskall Wallis test for comparison of more than two groups. Correlation analysis for the variables without normal distribution were performed with Spearman correlation analysis. Regression analyses were used to detect the causal relationships between the findings. P<0,05 was accepted for statistical significance.

RESULTS

Totally 90 patients consisting of 45 celiac and 45 controls were included in the study. Girls were 51.1% of the patient group, while they were 35.6% of the control group. Both of the groups were similar in terms of age, gender, height, weight, BMI. The mean weight of the patient group was lower than the controls but this difference was not significant. Besides heart rate, systolic and diastolic blood pressures were similar between the groups. Histopathological analysis revealed MARSCH type 3a in 17 patients, 3b in 14 patients and 3c in 14 patients. Mean duration of the illness was 2.47 years (0.25- 8 years) in the patient group. 24 of the patients had TTG IgA and EMA IgA positive and the remained 21 had TTG IgA and EMA IgA negative serology (table 1).

		PATIENTS (n=45) (mean±SD) number	CONTROLS (n=45) (mean±SD)	p
Age (year)		10,70±4,40	10,20±2,60	0,373
Gender	M	22 (48,9%)	29 (64,4%)	0,202**
	F	23 (51,1%)	16 (35,6%)	
Height (cm)		139,00±22,10	142,60±15,90	0,383*
Weight (kg)		36,00±14,20	38,10±12,60	0,511
BMI (kg/m2)		17,90±3,10	18,20±2,90	0,519
Heart rate (min)		93,00±18,00	87,00±16,00	0,113
SBP (mmHg)		99,00±9,00	101,00±12,00	0,479
DBP (mmHg)		64,00±7,00	65,00±8,00	0,526
Duration of Celiac disease (year)		2.47±2.59	-	
MARSH 3a/3b/3c		17/14/14	-	
TTG IgA and EMA IgA (+)/(-)		24/21	-	

Table 1: Demographic characteristics of the patient and control group.

Mann-Whitney U test, Student t test*, Chi-square test**

BMI: Body mass index, DBP: Diastolic blood pressure, EMA IgA: Endomysium Immunglobulin A, F: female, M: Male, SBP: Systolic blood pressure, TTG IgA : Tissue Transglutaminase Immunglobulin A

IVSd was higher in patients with celiac disease rather than controls. Ejection fraction and the other diameters of the left ventricle were similar between the groups (Table 2). There was 1 patient with bicuspid aortic valve with mild insufficiency and mild stenosis, 1 patient with a small atrial septal defect, 2 patients with patent foramen ovale and 3 patients with mild mitral insufficiency among the patients with CD.

	PATIENTS (n=45)	CONTROLS (n=45)	p
IVSDd (cm)	0,70±0,11	0,64±0,09	0,018
LVEDd (cm)	3,83±0,51	3,92±0,42	0,371*
LPWDd (cm)	0,67±0,08	0,65±0,10	0,074

IVSs (cm)	0,83±0,11	0,84±0,09	0,744
LVEDs (cm)	2,32±0,35	2,34±0,30	0,720*
LPWDS (cm)	0,86±0,11	0,85±0,09	0,400
EF (%)	71,00±4,00	71,00±5,00	0,890
FS (%)	40,00±5,00	40,00±4,00	0,919

Table 2: 2D and M-mode echocardiographic measurements of the patient and control group

Mann-Whitney U test, Student t test*

EF: Ejection fraction, FS: Fractional shortening, IVSDd: Interventricular septal diastolic diameter, IVSDs: interventricular septal systolic diameter, LPWDd: Left posterior wall diastolic diameter, LPWDs: Left posterior wall systolic diameter, LVEDd: Left ventricular end diastolic diameter, LVEDs: Left ventricular end systolic diameter

E' lateral was lowerand E/E' lateral was higher in the patient group than controls with similar results of the other Doppler and tissue Doppler parameters (table 3).

	PATIENTS (n=45)	**CONTROLS (n=45)**	**p**
E (cm/s)	98,10±15,00	95,50±13,50	0,377*
A (cm/s)	60,50±13,60	58,60±13,80	0,413
E/A	1,67±0,37	1,68±0,39	0,942*
EDT (ms)	109,00±21,00	105,00±13,00	0,292*
A duration (ms)	112,20±18,40	107,20±13,20	0,139*
S'septal (cm/s)	7,93±1,01	8,24±1,42	0,472
E' septal (cm/s)	14,50±2,10	14,34±2,52	0,747*
A'septal (cm/s)	7,53±1,59	7,24±1,29	0,354*
IVCT septal (ms)	55,00±9,00	55,00±7,00	0,533
IVRT septal (ms)	58,00±9,00	59,00±6,00	0,576
E/E' septal	6,87±1,33	6,84±1,18	0,888*
E'/A'septal	2,00±0,49	2,02±0,44	0,805
MPI septal	0,42±0,07	0,43±0,06	0,557
S' lateral (cm/s)	19,30±3,40	20,40±3,30	0,762
E' lateral (cm/s)	10,67±2,31	10,82±2,41	0,034
A' lateral (cm/s)	7,96±1,69	7,90±2,25	0,505
IVCT lateral (s)	57,00±9,00	55,00±7,00	0,371*
IVRT lateral (s)	60,00±7,00	58,00±8,00	0,235
E/E' lateral	5,18±0,92	4,77±0,94	0,006
E'/A' lateral	2,49±0,58	2,70±0,61	0,104
MPI lateral	0,43±0,05	0,41±0,05	0,089*

Table 3: Doppler and tissue Doppler measurements between the groups

Mann-Whitney U test, Student t test* (Mann-Whitney U p<0,05).

A: Late diastolic flow velocity, A': Peak late diastolic wave velocity, E: Mitral early diastolic flow velocity, E': Peak early diastolic wave velocity , EDT: Mitral E wave deceleration time, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, ms: milisecond, MPI: Miyocardial performance index, s: second

The difference between systolic and diastolic diameters of aortic wall was higher in the patients. The components of elasticity parameters AS, DIS, SI were similar between the groups (Table 4).

	PATIENTS (n=45)	**CONTROLS (n=45)**	**p**
AoS (cm)	1,88±0,35	1,98±0,22	0,148
AoD (cm)	1,54±0,32	1,65±0,21	0,072
AoS-AoD (cm)	0,34±0,12	0,32±0,10	0,009*
AS (%)	23,69±10,49	19,84±6,39	0,121
DIS (10-6 cm2.dyn-1)	1,50±0,75	1,15±0,46	0,069
SI	2,21±1,19	2,49±1,03	0,119

Table 4: Aortic measurements and elasticity parameters between the patient and control group.

Mann-Whitney U test, Student t test* (Mann-Whitney U p<0,05).

AoD: Diastolic aortic diameter, AoS: Systolic aortic diameter, AoS - AoD: Difference in aortic diameter AS: Aortic strain, DIS: Distensibility, SI: Beta Stiffness index

Patients we classified according to serological findings of TTG IgA and EMA IgA. AS and E/E' lateral parameters were different between the three groups (p=0.020, p=0.008, respectively) (Table 5). The difference was evaluated with Mann-Whitney U test, Tukey test (p<0,016 Bonferroni correction) and it was present in AS between the antibody negative patients and controls (p= 0.015), while the difference in E/E' lateral was between antibody positive patients and controls (p=0.002).

	TTG/EMA IgA (+) Patients (n=24)	**TTG/EMA IgA (-) Patients (n=21)**	**CONTROLS (n=45)**	**p**
AoS (cm)	1,79±0,36	1,98±0,32	1,98±0,22	0,097
AoD (cm)	1,49±0,32	1,59±0,32	1,65±0,21	0,105
AoS-AoD (cm)	0,31±0,11	0,38±0,13	0,32±0,1	0,069*
AS (%)	21,41±8,73	26,30±11,87	19,84±6,39	0,020*
DIS (10-6 cm2 dyn-1)	1,38±0,74	1,65±0,75	1,15±0,46	0,079
SI (%)	2,38±1,05	2,02±1,33	2,49±1,03	0,053
E (cm/s)	102,30±14	93,40±15,1	95,50±13,5	0,075*

A (cm/s)	63,10±13,10	57,60±14,00	58,60±13,80	0,212
E/A	1,59±0,34	1,78±0,37	1,68±0,36	0,226*
EDT (ms)	105,00±19,00	113,00±23,00	105,00±13,00	0,214*
A duration (ms)	110,10±19,80	114,60±17,00	107,20±13,20	0,226
S'septal (cm/s)	7,80±0,93	8,09±1,09	8,24±1,42	0,451
E' septal (cm/s)	14,88±1,93	14,07±2,25	14,34±2,52	0,483*
A'septal (cm/s)	7,56±1,86	7,49±1,27	7,24±1,29	0,645*
IVCT septal (ms)	55,00±9,00	54,00±9,00	55,00±7,00	0,716
IVRT septal (ms)	59,00±10,00	58,00±7,00	59,00±6,00	0,850
E/E' septal	6,98±1,29	6,75±1,39	6,84±1,18	0,825*
MPI septal	0,43±0,07	0,42±0,04	0,43±0,06	0,842
S' lateral (cm/s)	10,25±1,98	11,14±2,60	10,82±2,41	0,638
E' lateral (cm/s)	19,40±3,40	19,20±3,60	20,40±3,30	0,104
A' lateral (cm/s)	7,76±1,78	8,18±1,59	7,90±2,25	0,554
IVCT lateral (ms)	55,00±8,00	59,00±9,00	55,00±7,00	0,187
IVRT lateral (ms)	59,00±8,00	61,00±6,00	58,00±8,00	0,270
E/E' lateral	5,36±0,83	4,98±1,00	4,77±0,94	0,008
MPI lateral	0,43±0,05	0,43±0,06	0,41±0,05	0,197*
Duration of disease (year)	2,23±2,41	2,75±2,83	-	0,605**

Table 5: The comparison of patients according to antibody persistance and controls according to Doppler, tissue Doppler and elasticity parameters (Table 5).

Kruskal Wallis test, One-Way ANOVA*,Mann-Whitney U test**, Fisher's Exact test***(One-Way ANOVA, Kruskal Wallis).

A: Late diastolic flow velocity, A': Peak late diastolic wave velocity, AoD: Diastolic aortic diameter, AoS: Systolic aortic diameter, AoS - AoD: Difference in aortic diameter AS: Aortic strain, DIS: Distensibility, E: Mitral early diastolic flow velocity, E': Peak early diastolic wave velocity, EDT: Mitral E wave deceleration time, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, MPI: Miyocardial performance index, SI: Beta Stiffness index

When AS was accepted as dependant variable and age, BMI, MARSH histopathologic stage, E/A, E/E' septal, E/E' lateral, MPI septal, MPI lateral, SBP, DBP, TTG IgA(+), duration of disease were accepted as variables, multivariate regression model was detected as meaningless, therefore the results were not declared on a table (p=0,064>0,05). When DIS was accepted as dependant variable and the other parameters were evaluated, Backward variable selection method was used and the model in the table was accepted as significant (p=0,031<0,05). Age and SBP showed significance (p=0.023, 0.049, respectively) stating that 1 unit increase in age decreases DIS 0,462 unit and 1 unit increase in SBP decreases DIS 0,411unit. When SI was the dependant variable and the same parameters were evaluated, Backward variable selection method was used and the model in the table was accepted as significant (p=0,012<0,05). E/E' septal, SBP showed significance (p=0.016, p=0.005, respectively), stating that 1 unit increase in E/E'septal increases SI 0,433 unit and 1 unit increase in SBP increases SI 0,544 unit (Table 6 and Table 7).

	DIS	
	β	**p**
Age (year)	-0,463	0,023
BMI (kg/m2)	0,303	0,090
E/E'septal	-0,265	0,088
MPI septal	0,334	0,070
MPI lateral	-0,324	0,089
SBP (mmHg)	-0,411	0,049
DBP (mmHg)	0,370	0,057

Table 6. Parameters effecting DIS in the patient group

(p=0,031<0,05)

BMI: Body mass index, DBP: Diastolic blood pressure, MPI: Miyocardial performance index, SBP: Systolic blood pressure

	SI	
	β	**p**
E/E'septal	0,433	0,016
SBP (mmHg)	0,554	0,005
DBP (mmHg)	-0,361	0,059

Table 7: Parameters effecting SI in the patient group

(p=0,012<0,05)

DBP: Diastolic blood pressure, SBP: Systolic blood pressure

MARSH classification of the histopathologic findings in patents with CD did not show correlation with MPI septal and lateral (r=0.171,p=0.261; r=0.211,p=0.164, respectively) (Figure 1).

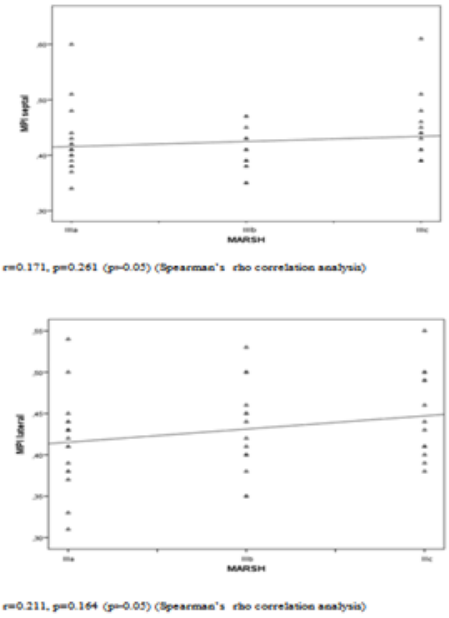

Figure 1: Correlation between MARSH classification and MPI septal and MPI lateral

DISCUSSION

Cardiovascular system involvement is one of the important extraintestinal manifestations of celiac disease which is responsible from cardiac morbidity and mortality. The presentation characteristics may differ among the patients having cardiovascular involvement. Some of the patients had systolic and/or diastolic dysfunction resulted with DCM while some of them had arrhytmias like atrial fibrillation. Also there are case reports declaring pericarditis or sudden death especially in adults. The different involvement may arise from variation of the disease severity, duration of the disease and genetic tendency [1].

DCM related with CD is not very frequent even in adults [10]. Curione et al. [11]included 52 patients included in the study with DCM and CD incidance was 5.8% . Prati et al. [12] included 275 patients with heart failure in the study and CD incidance was 1.9% among them while it was 0.35% in the control group. Fortunately, the cases in pedaitric population presented with DCM related with CD were lesser than adults. Doğan et al. [13] stated an 8 year old girl with DCM and CD. Frustaci et al. [14] stated some cases with myocarditis and CD. The probable mechanism of DCM may be, chronic malabsorption and nutritional deficiencies , especially carnitine with the additive effect of hypoxia. Hypoxia increases the permeability of intestine and allows various luminal antigens or infectious diseases to transit in through so that causing myocardial damage [10].

In the lights of these knowledge because these lifethreatening cardiac disorders appear predominantly in adults, but also in childhood, patients with CD should be evaluated earlier may be after they get the diagnosis to detect subclinical findings. According to the studies performed in the patients with CD in childhood, Polat et al. [15] stated that patients with CD and controls did not have any differences between cardiac dimensions. Saylan et al. [6] reported that pediatric patients with CD and controls do not have any differences between EF and FS, with different E, A, E/A in the patient group than controls but not declaring diastolic dysfunction. Fatty et al. [1] evaluated Tei index of both RV and LV and they were higher in children with CD than controls. Karadaş et al. [16] stated similar FS , mitral E, A, E/A measurements between the patient and control group but with different tissue Doppler parameters between the groups in terms of E/E'. It was lower in the patient group with similar E'/A', IVRT, EDT and MPI [16]. In our study the demographic features were similar between the patient and control group also with similar SBP, DBP, heart rate and normal electrocardiographic findings. M-mode echocardiography declares similar ventricular dimensions and ejection fraction with fractional shortening except interventricular septal diastolic diameter (IVSD). IVSD was higher in the patient group than controls. This finding may be related with subclinical hypertrophy of the septum and may have an effect over left ventricular systolic and diastolic functions. When we evaluate left ventricular Doppler and tissue Doppler parameters E' lateral was lower and E/E' lateral were higher in the patient group than controls without any differences in the other parameters also with similar MPI lateral measurements.

E' is a measure of myocardial relaxation and is one of the earliest markers of diastolic dysfunction [17-19]. E' decreases when there is impairment in myocradial relaxation [18]. E/E' is related with left ventricular filling pressures [20]. Nagueh et al. [18] stated that, E/E' correlates with pulmonary capillary wedge pressure and with left ventricular diastolic pressures [21]. When it increases it states elevated LV filling pressures [21,22]. When diastolic dysfunction is present E' decreases, and E'/A' also decreases with elevation of E/E' parameter. Besides with the effect of the other doppler parameters like IVRT, EDT, E/A, A wave velocity and A wave duration. But they are similar between the two groups in our study. The impairment of the paremters we detected may be related with subclinical thickening of IVSD. The systolic functions of the left ventricle assessed by ejection fraction, Doppler and tissue Doppler parameters like IVCT,S' parameters were also similar declaring us that systolic functions were protected. Miyocardial performance index combines time intervals related to systolic and diastolic function that reflects global cardiac function. It is a sensitive indicator for the severity of cardiac dysfunction. It is not affected from heart rate and blood pressure,preload and afterload. In our study MPI septal and lateral were similar between the two groups [23].Our results showing decrease in E' and increase in E/E' in the patient group were compatible with the literature.

Left ventricular systolic and diastolic functions are also related with aortic elasticity parameters incuding aortic strain, aortic stiffness, distensibility. Systemic inflammation plays important role in cardivascular involvement. Bayar et al. [24] showed that patients with CD had increased SI, decreased DIS and similar AS compared to controls. Also systolic and diastolic diameters of aorta were lower in CD group. They stated that the increase in SI was not only atrributed to systemic inflammation like other autoimmune diseases. Folic acid and B12 deficiency were present as a result of malabsorption with an increase in homocysteine levels triggering oxidative stress and lowering nitric oxide synthesis from endothelial cells causing endothelial dysfunction in patients with CD effecting the distensibility and

stifness and afterwards increasing the thickness of the wall [3,24, 25]. Carotid intima media thickness is a marker used for evaluating atherosclerozis [25]. Sarı et al [8]. declared that,endothelial dysfunction triggers AS and AS triggers atherosclerozis and showed that AS and DIS was lower and SI was higher in adult patients with CD with normal ventricular diameters but increased left atrium diameter. Korkmaz et al. [26] showed that 58 adults with CD had increased stiffness with increased CRP, sedimentation, insulin and insulin resistance. Demir et al. [25] investigated preclincal atherosclerozis in pediatric patients with CD by measuring arterial stiffness and CIMT and demonstrated that there was no difference in arterial stiffness and thickness between CD and controls. We detected similar AS, DIS and SI and similar aortic diameters between the groups except difference in aortic diameter. Difference in systolic and diastolic diameter was higher in the patient group than the control group. But the patient group is expected to be lower because of the impaired endotelium derived dilatation if there was impairment in the elascticity indexes therefore this finding does not indicates any deterioration to us.

TTG IgA positivity shows inflammatuar activity and it is related with increased CIMT [25]. We evaluated our patients cardiovascular parameters according to serological antibody positivies declaring adherence to GFD or not. Adhering to GFD reduces inflammation and therefore makes the antibodies negative. Saylan et al. [6] stated that mitral E, E/A, E',A'were similar between EMA (+) and EMA (-) group but all of theseparameters were higher in both of the subgroups than controls . EMA(+) group had higher IVRT and MPI than controls and EMA(-) group. They offered to use mitral MPI and IVRT for evaluating the effectiveness of the treatment especially between EMA (+) and EMA (-) patients indicating early cardiac dysfunction. Karadaş et al. [16] stated that mitral EDT and mitral IVRT were shorter in newly diagnosed CD patients with GFD (-), compared to previously diagnosed GFD (+) patients and controls indicating diastolic dysfunction. Also both of the subgroups had lower E/E' ratio than controls. Polat et al. showed [15] that mitral S' was lower in patient group with EMA(-) than controls. They also declared that EMA IgA had negative correlation with S'. Bayar et al. [24] showed that GFD (+) and (–) did not show difference in terms of AS, SI, DIS indicating that GFD reduces inflammatuar parameters but not all the cardivascular risks. Demir et al. [25] determined that arterial stiffness and thickness parameters were similar between patients with CD and controls and between TTG IgA (+) and TTG IgA (-) group after 47 months follow up. Similar results were present in studies of Korkmaz et al. [26] and Sarı et al. [27]. Patients with CD who were strictly adherent to GFD had significantly lower CIMT compared to controls suggesting that being away from gluten had a positive effect on atherosclerotic risk factors [25]. Polat et al. [15] stated that when the patients obey their gluten free diet, their cardiac abnormalities showed regression, probably because of improvement of the permability and the absorbtion of intestines also effecting the efficacy of the cardiac drugs by increasing absorbtion of them [2,15]. De Marchi et al. [28] stated that CIMT and flow characteristics improved after GFD. Chicco et al. [29] showed recovery in ejection fraction after GFD in 3 patients with CD among 104 patients with DCM. We determined in our study that demographic findings, aortic diameters and elasticity parameters except AS were similar between the subgroups and controls. Also left ventricular systolic and diastolic parameters except E/E'lateral were similar between the subgroups and controls. AS was higher in the TTG and EMA IgA(-) group than controls and E/E' was higher in the TTG and EMA IgA (+) group. AS was higher in the antibody negative CD group than controls declared us that reducing inflammation was not reducing all the cardivascular risk factors, like it was stated previously by Bayar et al. [24]. Also it is expected for E/E' lateral to be high in the TTG IgA (+) group who do not adhere to GFD than controls because exposure to gluten continues the inflammation and this inflammation impairs diastolic function like in our study compatible with the literature.

Sarı et al. [8] stated that age, CD were correlated with AS, DIS. CD was correlated also with SI. Therefore, CD was the independent factor correlated with all the elasticity parameters. Bayar et al. [24] determined that, systolic and diastolic aortic diameters, SI and AS showed association between CD. Demir et al. [25] showed that arterial stiffness parameters evaluated with PWV showed correlataion with BMI and SBP and DBP in patients with CD. Fathy et al. (1) determined significant positive correlation with MARSH classification and right ventricular MPI. There was also positive but non significant correlation between MARSH and left ventricular MPI. We did not show significant correlation between MARSH classification left ventricular MPI septal and lateral. We did not show correlation for AS with any parameter while DIS showed negative correlation with age and SBP, SI showed positive correlation with E/E'septal and SBP. These findings declare us that as age, SBP, E/E' increases elasticity parameters of the aorta shows deterioration. Therefore the parameters effecting elasticity indexes known in general like age, blood pressure and cardiac diastolic dysfunction also were risk factors in our study like the literature. The importance of SBP and E/E' parameters came apparent that can be easily evaluated in the polyclinic follow-ups.

CONCLUSION

CD is associated with increased risk of atherosclerozis but it may not be easy to detect in childhood or after a short while the patients get diagnose because of the young age of the pateints or relatively short duration of illness than adults. Therefore we have to use other technics rather than conventional methods to evaluate subclinical cardiac involvement. These technics may be Doppler, tissue Doppler parameters and aortic elasticity parameters. We stated in our study that there was impairment in E' lateral, E/E' lateral with an increase in IVSd than controls declaring us early diastolic dysfunction of the left ventricle. E/E' lateral was higher in TTG IgA (+) group supporting that exposure to gluten with increasing inflammation disturbs diastolic function without a detoriation in the other diastolic and systolic findings. SBP and E/E' parameters and age of the patient had negative effects on aortic elasticity parameters. Aortic elasticity parameters did not show significant impairment at this stage. Therefore patients with CD should be followed up for myocardial dysfunction.

REFERENCES

1. Fathy A, Abo-Haded HM, Al-Ahmadi N, El-Sonbaty MM, (2016), Cardiac functions assessment in children with celiac disease and its correlation with the degree of mucosal injury: Doppler tissue imaging study. Saudi J Gastroenterol. Nov;22(6):441-447.
2. Zahmatkeshan M, Fallahpoor M, Amoozgar H, (2014), Prevalence of celiac disease in children with idiopathic dilated cardiomyopathy. Iran J Pediatr. Oct;24(5):587-92.
3. Santoro L, De Matteis G, Fuorlo M, Giupponi B, Martone AM, Landi F, Landolfi R, Santoliquido A et al, (2017), Atherosclerosis and cardiovascular involvement in celiac disease: the role of autoimmunity and inflammation. Eur Rev Med Pharmacol Sci. Dec;21(23):5437-5444.
4. Husby S, Koletzko S, KorponaySzabo IR, Mearin ML, Phillips A, Shamir R, et al, (2012), European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. J PediatrGastroenterolNutr; 54:13660.
5. Oberhuber G, Granditsch G, Vogelsang H, (1999), The histopathology of coeliac disease: Time for a standardized report scheme for pathologists. Eur J GastroenterolHepatol;11:118594.
6. Saylan B, Cevik A, Kirsaclioglu CT, Ekici F, Tosun O, Ustundag G et al, (2012), Subclinical cardiac dysfunction in children with coeliac disease: is the gluten-free diet effective? ISRN Gastroenterol. ; 2012:706937
7. Teichholz LE, Cohen MV, Sonnenblick EH, Gorlin R, (1974), Study of left ventricular geometry and function by B-scan ultrasonography in patients with and without asynergy. N Engl J Med. Dec 5;291(23):1220-6.
8. Sari C, Ertem AG, Sari S, Efe TH, Keles T, Durmaz T, Ertem S, Bozkurt E, (2015), Impaired aortic function in patients with coeliac disease. Kardiol Pol. 73(11):1108-13.
9. Waggoner AD, Bierig SM. (2001), Tissue Doppler imaging: a useful echocardiographic metod for the cardiac sonographer to assess systolic and diastolic ventricular function. J Am Soc Echocardiogr; 14: 1143-52.
10. Boskovic A, Kitic I, Prokic D, Stankovic I. (2012), Cardiomyopathy associated with celiac disease in childhood. Case Rep Gastrointest Med. 2012:170760.