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# Investigation of cardiac functions and aortic stiffness in children with type 1 diabetes mellitus: A prospective study

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## Abstract

**Objective:** Cardiovascular diseases represent the most serious complications in the patients with type 1 diabetes mellitus (DM). Endothelial dysfunction and increased aortic stiffness play role in the occurance of these disorders. Aim of this study is to evaluate the patients cardiac functions and aortic elasticity parameters in children with type 1 DM.

**Materials and methods:** Thirty nine patients with type 1 DM and 39 controls were included in the study. After physical examination, cardiac evaluation was performed with conventional echocardiography, Doppler and tissue Doppler echocardiography. Aortic elasticty parameters were calculated.

**Results:** Systolic blood pressure, mean arterial pressure (MAP), pulse pressure (PP) and heart rate (HR) were higher in the patients than controls ($p<0.05$, for all). Mitral E wave velocity, E/A, E'/A' lateral were decreased, while E wave deceleration time, A' lateral, myocardial performance index (MPI) lateral and septal were increased in the patient group than controls ($p>0.05$, for all). Aortic systolic and diastolic diameters and aortic elasticity parameters were similar with controls ($p>0.05$, for all). Echocardiographic parameters and aortic elasticity parameters were similar in the patients who were grouped according to hemoglobin A1c and duration of diabetes ($p>0.05$, for all). E wave velocity was positively related with PP, while E'/A' was positively associated with HR and negatively associated with MAP and diastolic blood pressure ($p<0.05$, for all).

**Conclusions:** Diastolic dysfunction findings were stated in the diabetic children. Even though aortic compliance did not show impairment, periodic cardiac evaluation should be performed in case of progression. Patients with type 1 diabetes should be monitored for endothelial dysfunction and aortic stiffness when the prolonged life expectancy was taken into account for diabetic children.

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## Introduction

Type 1 diabetes is one of the most common endocrine and metabolic disorder in childhood (1). Cardiovascular diseases are the main reasons for mortality in the patients with type 1 diabetes. Microvascular and macrovascular complications are prevalent in the presence of hyperglycemia resulting with endothelial dysfunction with decreased vascular compliance. Studies stated early functional and structural abnormalities in the patients with type 1 diabetes before significant clinical findings resulted with heart failure (1,2). Diabetes accelerates arteriosclerotic process and arterial stiffness and it is an early sign of arteriosclerosis (3). Low grade inflammation, accumulation of advanced glycation end products and endothelial dysfunction are the reasons for this situation. Modifiable risk factors including blood pressure, increased pulse pressure (PP), dyslipidemia, microalbuminuria, hyperglycemia and its end products are independent risk factors for impaired vascular health in youth with type 1 diabetes (4).

In the light of these knowledge, evaluating arterial stiffness is important for detecting subclinical arteriosclerosis to make a better cardiovascular prediction for the patients with type 1 diabetes (3). The most common finding of arterial stiffness is impaired diastolic function. Cardiovascular diseases are the important causes of mortality and morbidity in diabetic patients, therefore controlling glucose levels is very crucical. But it is not sufficient to decrease the vascular complications, without evaluation of endothelial functions and vascular compliance. Nowadays preventing or treating the increased cardivascular risk has become one of the new approaches during the follow-ups of these patients (2,5). Cardiac evaluations were conducted using echocardiographic assessments. Most studies were focused on cardiac functions and arterial stiffness of the adults with type 1 diabetes, examining cardiac functions and arterial stiffness, but there are limited and conflicting reports that evaluate these parameters together in children. Notably, these children typically have a shorter duration of illness compared to adults.

The aim of this study is to evaluate cardiac functional deterioration of mycocardium and aortic elasticy parameters in diabetic children.

## Materials and methods

A prospective study was performed among 39 patients with type 1 diabetes who were evaluated in the pediatric endocrinology department and 39 sex and age matched patients who were evaluated in the pediatric cardiology department for murmur with normal electrocardiographic and echocardiographic patients. Inclusion criteria for the study group include the children between 0-18 years old with type 1 diabetes who have normal blood lipids, enflammatory parameters without any other chronic diseases. Exclusion criteria for the study group include the patients with hypertension, dyslipidemia, enflammatory disease, arrhythmia, structural heart disease.

Inclusion critereria for the control group include the children between 0-18 years old with normal echocardiographic and electrocardiographic findings. Exclusion criteria for the control group include the patients with arrhythmia, structural heart disease, chronic diseases, hypertension, patients who were taking any medication.

All of the participants were evaluated with physical examination, electrocardiography and echocardiography. Systolic blood pressure (SBP) and diastolic blood pressure (DBP), heart rate (HR) were measured. Mean arterial pressure (MAP) was calculated according to the formula 2DBP +SBP/3. Body mass index (BMI) was calculated according to the formula (kg/m$^2$). The laboratory findings for routine evaluation of type 1 diabetic patients including celiac serology, hemoglobin A1c (HgbA1c), urine albumin to creatinin ratio were evaluated in the patient group (17). Microalbumuria is defined if two of three consecutive measurements had urine albumin to creatinine ratio <30 mg/g. Microalbumuria or macroalbuminuria is defined if urinary albumin excretion ratio was between 30 and 300 mg/24h or >300 mg/24h, (4). Celiac serology was defined as positive or negative.

HgbA1c is usually <6% in nondiabetic patients, 6-7.9% is good metabolic control in diabetics, 8-9.9% fair metabolic control, ≥10 represent poor metabolic control (1). Patients were grouped according to HgbA1c level as <8% and ≥ 8% (1) and according to duration of diabetes as <3 years and ≥ 3 years (6).

### Echocardiographic evaluation

After 12 lead electrocardiographic evalution, echocardiographic evaluation was performed. Transthorasic echocardiograophic evaluation was performed with echocardiography (EPIQ 7 Ultrasound System, Philips, Heide, Netherlans) machine, by using S5 and S8 probes, while the patient is on the left lateral decubitis position. Conventional echocardiographic measurements by using two-dimensional, standard M-mode and Doppler echocardiographic evaluations were performed. Modified Simpson method was used to evaluate left ventricular systolic functions (7). Doppler parameters of mitral and tricuspid valve include early diastolic flow velocity (E), late diastolic flow velocity (A), E wave deceleration time (EDT) were measured, E/A was calculated. Tissue Doopler echocardiographic examinations were performed by placing the cursor on lateral side of the mitral annulus, basal interventricular septum and RV free wall segments at apical four chamber view. Peak early diasyolic wave velocity septal (E' septal), peak late diastolic wave velocity septal (A' septal), peak systolic wave velocity (S'), isovolumetric relaxation time (IVRT), isovolumetric contraction time (IVCT) were measured. E/E', E'/A', MPI were calculated. MPI was calculated according to the formula IVRT+IVCT/Ejection time. All of the measurements were performed by repeating them 3 times and calculating the average values of them. The sector angle was 30 derece or less, tissue Doppler frame rate was 170-220/s (8). Informed consent was obtained from all the patients and their parents. The study was approved by the Institutional Ethical Committee.

### Elasticity parameters of aorta

Aortic strain (AS) refers to the changes in the aorta's shape caused by the pulse pressure acting as a stress factor. Aortic stiffness (SI) denotes the resistance against such deformation. This stiffness is influenced by the relationship between vascular smooth muscle cells and the extracellular matrix, which consists of the elements like elastin, collagen, and fibrillin. Aortic distensibility (DIS) is described as the proportional compliance or the proportional alteration in diameter when there's a rise in pressure (9,10).

To assess the elasticity attributes of the ascending aorta, an M-mode examination was conducted by positioning the cursor directly over the ascending aorta. The systolic aortic diameter (AoS) was determined when the aortic valve was open, while the diastolic aortic diameter (AoD) was determined at the height of the QRS complex seen in electrocardiography. These dimensions were calculated from one inner boundary to the other (9,10).

1. Aortic strain (AS) (%) = 100X (Aos-AoD) / AoD
2. Beta Stiffness Index (SI)= In (SBP/DBP) / (AoS-AoD) / AoD
3. Distensibility (DIS) ($10^{-6}$ $cm^2$ $dyn^{-1}$) = 2 x (AoS-AoD/AoD) X 100/PP

### Statistical analysis

Frequency and percentage values are given for categorical variables, mean, standard deviation, median minimum and maximum values are given for continuous variables. Evaluation of normal distribution was performed with the Shapiro-Wilk test separately for each group in each analysis. Analysis between two independent groups was performed with the Independent sample t test in case of normal distribution, otherwise the Mann Whitney U test was used. Chi-square analysis was used in the analysis of categorical variables. Spearman correlation coefficient was calculated in order to examine the relationships between variables. All analyzes were done with SPSS 29 software. $p<0.05$ was considered significant.

### Results

The mean age of the diabetic patients was 11.42±3.22 years and most of the patients were male (M/F: 24/15). Mean of diabetes mellitus duration was 3.52±1.2 years, mean value of HgbA1c was 8.79±3.10%. Two of the patients had microalbuminuria, and 3 of the patients had positive celiac serology. SBP, MAP, PP, HR of the patients were significantly higher than controls ($p$=0.002, $p$=0.033, $p$=0.002, $p$=0.003, respectively) (**Table 1**).

The 2D echocardiographic findings were similar between the patient and control groups. Ejection fraction (EF) and fractional shortening (FS) were similar between the patient and control group (**Table 2**).

Mitral E velocity, E/A were lower, E deceleration time was higher in the patients than controls ($p$=0.001, for all). A' lateral was higher in the patient group ($p$=0.009), E'/A' lateral and septal were lower in the patient group ($p$=0.016, $p$=0.003, respectively). MPI lateral was higher in the patients ($p$=0.004) and MPI

septal was also higher in the patients with treshold significancy ($p$=0.058) (**Table 3**).

AoS, AoD, AoS-AoD, AS, SI, DIS were similar between the groups ($p$>0.05, for all) (**Table 4**).

Doppler, tissue Doppler parameters of left and right ventricle were similar between the patients with diabetes duration <3 years and ≥3 years. HgbA1c was higher in the patients with duration of diabetes ≥ 3 years than the patients with duration of diabetes <3 years ($p$=0.024). Aortic diameters and aortic elasticity parameters were similar between the patients and controls with duration of diabetes shorter and longer than 3 years (**Table 5**).

Doppler, tissue Doppler parameters of left ventricle were similar between the patients with HgbA1c <8% and HgbA1c ≥8%. Aortic diameters and aortic elasticity parameters were similar between the patients and controls with HgbA1c <8 %and ≥8 % (**Table 6**).

A positive relationship was stated between mitral E wave velocity and PP (rho=0.350, $p$=0.029). A positive relationship was also present between mitral E'/A' lateral and HR (rho=0.361, p=0.024). A negative relationship was present between mitral E'/A' septal and DBP and between MAP (rho=-0.366, $p$=0.022; rho=-0.360, $p$=0.024) (**Table 7**).

**Table 1:** Sociodemographic features and laboratory findings of the participants

| | Control group (n=39) Mean±SD | Patient group (n=39) Mean±SD | p-value |
|---|---|---|---|
| Age (year) | 11.93±3.19 | 11.42±3.22 | 0.487 |
| Gender (M/F) | 25/14 | 24/15 | 0.815 |
| Height (cm) | 149±18.48 | 145.18±20.13 | 0.386 |
| Weight (kg) | 42.14±14.47 | 41.26±16.51 | 0.803 |
| BMI (kg/m$^2$) | 18.35±2.84 | 18.71±3.42 | 0.712 |
| SBP (mmHg) | 100.08±9.34 | 107.1±9.56 | 0.002 |
| DBP (mmHg) | 63.69±6.41 | 66.1±7.45 | 0.104 |
| MAP (mmHg) | 76.03±7.3 | 79.64±7.48 | 0.033 |
| PP (mmHg) | 36.13±6.03 | 41.23±7.65 | 0.002 |
| HR (min) | 79.21±15.51 | 92.67±22.28 | 0.003 |
| HgbA1c (%) | | 8.79 ± 3.10 | |
| Duration of type 1 DM (year) | | 3.52 ± 1.2 | |
| Microalbuminuria (+)/(-) | | 2/37 | |
| Celiac serology (+)/(-) | | 3/36 | |

BMI: Body mass index, DBP: Diastolic Blood Pressure, DM: Diabetes mellitus, F: Female, HgbA1c: Hemoglobin A1c, HR: Heart rate, M: Male, MAP: Mean Arterial Pressure, PP: Pulse pressure, SD: Standart deviation, SBP: Systolic blood pressure

**Table 2:** The 2D echocardiographic measurements of the participants

| | Control group (n=39) Mean±SD | Patient group (n=39) Mean±SD | p-value |
|---|---|---|---|
| IVSDd (cm) | 0.76±0.18 | 0.75±0.12 | 0.708 |
| LVEDd (cm) | 3.97±0.53 | 3.84±0.48 | 0.256 |
| LPWDd (cm) | 0.72±0.15 | 0.73±0.11 | 0.475 |
| IVSSd (cm) | 1.03±0.24 | 0.95±0.14 | 0.570 |
| LVESd (cm) | 2.37±0.31 | 2.34±0.37 | 0.620 |
| LPWSd (cm) | 1.05±0.26 | 1.19±1.45 | 0.294 |
| EF (%) | 70.74±4.42 | 70.79±5.46 | 0.920 |
| FS (%) | 39.64±3.7 | 39.77±4.76 | 0.924 |

EF: Ejection fraction, FS: Fractional shortening, IVSDd: Interventricular septum diastolic diameter, IVSSd: Interventricular septum systolic diameter, LVEDd: Left ventricular end diastolic diameter, LVESd: Left ventricular end systolic diameter, LPWSd: Left posterior wall diastolic diameter, LPWDs: Left posterior wall systolic diameter

**Table 3:** Doppler and Tissue Doppler Imaging parameters of the participants

| | Control group (n=39) Mean±SD | Patient group (n=39) Mean±SD | p-value |
|---|---|---|---|
| Mitral E (cm/s) | 99.82±14.37 | 88.42±14.76 | **0.001** |
| Mitral A (cm/s) | 57.84±11.58 | 63.25±14.23 | 0.108 |
| Mitral EDT (ms) | 107.72±15.22 | 130.56±26.35 | **0.001** |
| Mitral E/A | 1.78±0.4 | 1.44±0.3 | **0.001** |
| E' lateral (cm/s) | 19.12±3.2 | 19.03±3.9 | 0.909 |
| A' lateral (cm/s) | 7.31±1.46 | 8.41±1.96 | **0.009** |
| S' lateral (cm/s) | 10.09±1.69 | 10.88±2.62 | 0.118 |
| IVRT lateral (ms) | 60.72±8.22 | 62.23±7.04 | 0.386 |
| IVCT lateral (ms) | 56.69±8.3 | 56.62±6.45 | 0.964 |
| E/E' lateral | 5.32±1.18 | 4.79±0.99 | 0.118 |
| E'/A' lateral | 2.68±0.5 | 2.37±0.7 | **0.016** |
| MPI lateral | 0.42±0.04 | 0.45±0.05 | **0.004** |
| E' septal (cm/s) | 14.25±2.21 | 12.9±2.19 | **0.008** |
| A' septal (cm/s) | 7.27±1.62 | 7.72±1.55 | 0.110 |
| S' septal (cm/s) | 8.66±1.54 | 8.28±1.18 | 0.273 |
| IVRT septal (ms) | 61.31±7.66 | 61.46±8.86 | 0.935 |
| IVCT septal (ms) | 55.69±7.2 | 58.67±9.71 | 0.105 |
| E/E' septal | 7.37±1.88 | 7.04±1.09 | 0.617 |
| E'/A' septal | 2.04±0.53 | 1.74±0.5 | **0.003** |
| MPI septal | 0.43±0.06 | 0.46±0.07 | 0.058 |

EDT: E wave deceleration time, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, MPI: Myocardial performance index

**Table 4:** Aortic measurements and elasticity parameters of the participants

| | Control group (n=39) Mean±SD | Patient group (n=39) Mean±SD | p-value |
|---|---|---|---|
| AoS (cm) | 2.1±0.29 | 2.05±0.28 | 0.416 |
| AoD (cm) | 1.77±0.25 | 1.74±0.28 | 0.516 |
| AoS-AoD (cm) | 0.33±0.09 | 0.32±0.15 | 0.244 |
| AS (%) | 18.89±4.92 | 17.61±5.92 | 0.303 |
| SI | 2.59±0.84 | 3.32±1.83 | 0.096 |
| DIS ($10^{-6}$ $cm^2$ $dyn^{-1}$) | 1.07±0.37 | 0.89±0.36 | 0.061 |

DIS: Distensibility, AoD: Aortic diastolic diameter, AoS: Aortic systolic diameter, AS: Aortic strain, SI: Beta stiffness index

## Discussions

Prolonged lifle expectancy in childhood increases the importance of cardiovascular health in diabetic patients (2). Glucose residues or metabolites can react non-enzymaticallty with proteins to form advanced glycation end products (AGEs). They make cross-links with collagen and contribute to the development of cardiac stiffness and arterial stiffness. AGEs are also present in healthy people but they are markedly increased in diabetic patients due to increased availability of glucose (8). In diabetic patients impaired endothelial functions and increased arterial wall stiffness results with increased afterload results with diastolic dysfunction of left ventricle and subendocardial ischemia. This process becomes prevalent with impaired relaxation of the myocard with diminishing left ventricular compliance accompanied with interstitial fibrosis (5). Suys et al. (11) noted a significant reduction in the left ventricular posterior wall diameter. This can be attributed to the increased dimension of the left ventricular posterior wall, especially when assuming that systemic resistance remained the same or was even greater. Posterior wall Doppler parameters are important, but the normal range is wide and classification of the values is difficult in children, therefore, the findings can be different (1,12). Abd-el Aziz et al. (1) stated in their study larger left ventricular end diastolic diameter (LVEDd) and left ventricular end systolic diameter (LVESd) with increased but in normal range interventricular septum (IVS) and left ventricular posterior wall diastolic diameters (LPWDd). Çiftel et al. (2) and Deveci et al. (5) stated in their study that left ventricular wall thickness and diameter were similar like the controls. Our results were also in concordance with them without any significat difference between the patients and controls. Hyperglycemia may decrease the expression of sarcoplasmic reticulum $Ca^2$-ATPase (6,13). Aepfelbacher et al. (14) stated that, controlling hyperglycemia improves cardiac functions and reduces left ventricular mass in type 1 diabetes. Abd-el Aziz et al. (1) declared that S' velocities were reduced in diabetic patients. S' represents mildly impaired systolic functions even EF is normal (1). The patients in our study had normal sytolic functions supported with normal EF and FS, S' septal and S' lateral, IVCT septal and lateral.

It is known that the combination of transmitral flow velocities and annular velocities are useful tools for evaluation of left ventricular filling pressures (11,15,16). E/E' is a marker of elevated diastolic left ventricle and left atrium pressure. E'/A' is also a parameter to evaluate diastolic functions (6). MPI is an index evaluating the global function of the ventricle including systolic and diastolic functions. Evaluation of filling velocities is performed by measurement of E wave and A wave velocities, IVRT and calculation of E/A ratio (17). E' is correlated with left ventricular relaxation, preload, and filling pressures. In normal hearts, left atrial pressure exerts a powerful effect on E' velocity. In addition to decrease in E', increase in E/E' is expected with diastolic dysfunction (15,16).

Suys et al. (11) stated that left and right ventricular filling abnormalities with conventional and tissue Doppler parameters including increased A wave velocity, decreased E/A ratio with smaller E' velocities and higher E/E' ratio with higher IVRT and Tei index in

**Table 5:** Echocardiographic findings of the patients according to the duration of diabetes mellitus.

| | Duration of DM <3 years (n=20) Mean±SD | Duration of DM ≥3 years (n=19) Mean±SD | p-value |
|---|---|---|---|
| Duration of DM (years) | 1.55±0.6 | 5.61±2.84 | **0.001** |
| HgbA1c (%) | 8.06±1.84 | 9.57±2.16 | **0.024** |
| EF (%) | 70.95±5.26 | 70.63±5.8 | 0.858 |
| FS (%) | 39.8±4.73 | 39.74±4.92 | 0.968 |
| Mitral E (cm/s) | 86.15±15.45 | 90.81±14.02 | 0.331 |
| Mitral A (cm/s) | 60.97±14.44 | 65.65±13.99 | 0.238 |
| Mitral EDT (ms) | 104.6±16.18 | 111±13.81 | 0.193 |
| Mitral E/A | 1.46±0.29 | 1.42±0.32 | 0.448 |
| E' lateral (cm/s) | 18.63±4.22 | 19.45±3.58 | 0.517 |
| A'lateral (cm/s) | 8.45±2.13 | 8.36±1.83 | 0.888 |
| S'lateral (cm/s) | 10.29±2.04 | 11.5±3.05 | 0.153 |
| IVRT lateral (ms) | 61.7±6.74 | 62.79±7.49 | 0.636 |
| IVCT lateral (ms) | 57.55±7.01 | 55.63±5.82 | 0.360 |
| E/E' lateral | 4.81±1.07 | 4.78±0.93 | 0.832 |
| E'/A' lateral | 2.31±0.73 | 2.43±0.68 | 0.602 |
| MPI lateral | 0.45±0.05 | 0.45±0.05 | 0.995 |
| E' septal (cm/s) | 12.96±2.47 | 12.85±1.91 | 0.878 |
| A' septal (cm/s) | 7.66±1.52 | 7.79±1.62 | 0.790 |
| S' septal (cm/s) | 8.18±1.32 | 8.38±1.04 | 0.182 |
| IVRT septal (ms) | 62.55±9.32 | 60.32±8.44 | 0.438 |
| IVCT septal (ms) | 59.55±12.5 | 57.74±5.67 | 0.567 |
| E/E' septal | 6.98±1.34 | 7.09±0.79 | 0.757 |
| E'/A' septal | 1.77±0.6 | 1.7±0.39 | 0.725 |
| MPI septal | 0.47±0.08 | 0.45±0.05 | 0.428 |
| AoS (cm) | 2.01±0.26 | 2.08±0.31 | 0.922 |
| AoD (cm) | 1.71±0.26 | 1.78±0.3 | 0.431 |
| AoS-AoD (cm) | 0.31±0.09 | 0.34±0.2 | 0.476 |
| AS (%) | 17.92±6.33 | 17.29±5.61 | 0.742 |
| SI | 3.27±1.72 | 3.36±1.98 | 0.725 |
| DIS ($10^{-6}$ $cm^2$ $dyn^{-1}$) | 0.89±0.35 | 0.89±0.38 | 0.995 |

AoD: Aortic diastolic diameter, AoS: Aortic systolic diameter, AS: Aortic strain, DIS: Distensibility, DM: Diabetes mellitus, EDT: E wave deceleration time, EF: Ejection fraction, FS: Fractional shortening, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, IVSDd: Interventricular septum diastolic diameter, IVSSd: Interventricular septum systolic diameter, LVEDd: Left ventricular end diastolic diameter, LVESd: Left ventricular end systolic diameter, LPWDd: Left posterior wall diastolic diameter, LPWSd: Left posterior wall systolic diameter, MPI: Myocardial performance ındex, SI: Beta stiffness index

diabetic patients. These findings indicate disturbance in early diastolic filling. Çiftel et al. (2) also stated increased mitral EDT, mitral decreased E/A, decreased E', increased IVRT and MPI in mitral lateral, basal septal

**Table 6:** Echocardiographic findings of the participants according to HgbA1c.

| | HgbA1c <8% (n=18) Mean±SD | HgbA1c ≥8% (n=21) Mean±SD | p-value |
|---|---|---|---|
| Duration of DM (years) | 3.06±30 | 3.93±2.75 | 0.063 |
| EF (%) | 71.72±5.51 | 70±5.42 | 0.333 |
| FS (%) | 40.56±4.63 | 39.1±4.88 | 0.346 |
| Mitral E (cm/s) | 91.44±13.86 | 85.82±15.35 | 0.241 |
| Mitral A (cm/s) | 62.28±14.7 | 64.08±14.13 | 0.632 |
| Mitral EDT (ms) | 107.89±13.95 | 107.57±16.58 | 0.949 |
| Mitral E/A | 1.52±0.35 | 1.38±0.24 | 0.151 |
| E' lateral (cm/s) | 19.7±4.41 | 18.46±3.4 | 0.327 |
| A' lateral (cm/s) | 8.31±1.72 | 8.49±2.19 | 0.785 |
| S' lateral (cm/s) | 11.63±2.39 | 10.23±2.69 | 0.096 |
| IVRT lateral (ms) | 60.5±6.94 | 63.71±6.95 | 0.158 |
| IVCT lateral (ms) | 57.61±6.84 | 55.76±6.12 | 0.379 |
| E/E' lateral | 4.79±0.91 | 4.8±1.08 | 0.976 |
| E'/A' lateral | 2.48±0.84 | 2.26±0.56 | 0.338 |
| MPI lateral | 0.45±0.05 | 0.46±0.05 | 0.567 |
| E' septal (cm/s) | 13.13±2.34 | 12.71±2.09 | 0.553 |
| A' septal (cm/s) | 7.52±1.5 | 7.9±1.6 | 0.454 |
| S' septal (cm/s) | 8.5±1.26 | 8.09±1.11 | 0.296 |
| IVRT septal (ms) | 61.22±10.43 | 61.67±7.51 | 0.878 |
| IVCT septal (ms) | 57.22±7.97 | 59.9±11.02 | 0.692 |
| E/E' septal | 7.07±1.05 | 7.01±1.16 | 0.875 |
| E'/A' septal | 1.84±0.64 | 1.65±0.32 | 0.253 |
| MPI septal | 0.45±0.07 | 0.48±0.07 | 0.127 |
| AoS (cm) | 2.03±0.19 | 2.06±0.35 | 0.789 |
| AoD (cm) | 1.72±0.21 | 1.76±0.33 | 0.659 |
| AoS-AoD (cm) | 0.36±0.2 | 0.3±0.09 | 0.360 |
| AS (%) | 18.16±6.61 | 17.15±5.38 | 0.360 |
| SI | 3.45±2.01 | 3.2±1.69 | 0.670 |
| DIS ($10^{-6}$ $cm^2$ $dyn^{-1}$) | 0.87±0.33 | 0.9±0.39 | 0.778 |

AoD: Aortic diastolic diameter, AoS: Aortic systolic diameter, AS: Aortic strain, DIS: Distensibility, DM: Diabetes mellitus, EDT: E wave deceleration time, EF: Ejection fraction, FS: Fractional shortening, HgbA1c: Hemoglobin A1c, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, IVSDd: Interventricular septum diastolic diameter, IVSSd: Interventricular septum systolic diameter, LVEDd: Left ventricular end diastolic diameter, LVESd: Left ventricular end systolic diameter, LPWDd: Left posterior wall diastolic diameter, LPWSd: Left posterior wall systolic diameter, MPI: Myocardial performance ındex, SI: Beta stiffness index

**Table 7:** Correlation between echocardiographic parameters and sociodemographic parameters

| | | HgbA1c | Duration of DM | BMI | BMI-SDS | Age | SBP | DBP | MAP | PP | HR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mitral E Velocity | r | -0.241 | 0.100 | 0.130 | 0.235 | 0.044 | 0.216 | -0.045 | 0.100 | .350* | -0.181 |
| | p | 0.140 | 0.543 | 0.430 | 0.149 | 0.791 | 0.187 | 0.785 | 0.544 | 0.029 | 0.269 |
| Mitral EDT | r | -0.086 | 0.204 | 0.155 | 0.055 | 0.170 | 0.261 | 0.108 | 0.108 | 0.219 | -0.106 |
| | p | 0.605 | 0.213 | 0.347 | 0.739 | 0.301 | 0.108 | 0.514 | 0.514 | 0.180 | 0.521 |
| Mitral A Wave Duration | r | -0.267 | -0.146 | -0.044 | -0.062 | 0.097 | 0.155 | 0.221 | 0.130 | -0.080 | -0.134 |
| | p | 0.100 | 0.377 | 0.791 | 0.708 | 0.559 | 0.345 | 0.177 | 0.431 | 0.629 | 0.416 |
| Mitral A' Lateral | r | 0.185 | 0.122 | 0.115 | -0.081 | 0.273 | 0.190 | 0.140 | 0.118 | 0.080 | -0.255 |
| | p | 0.258 | 0.458 | 0.486 | 0.625 | 0.092 | 0.246 | 0.395 | 0.473 | 0.627 | 0.118 |
| Mitral E'/A' Lateral | r | -0.177 | 0.005 | -0.045 | 0.161 | -0.212 | -0.145 | -0.238 | -0.146 | 0.021 | .361* |
| | p | 0.281 | 0.977 | 0.784 | 0.328 | 0.196 | 0.379 | 0.145 | 0.374 | 0.901 | 0.024 |
| MPI Lateral | r | 0.041 | 0.058 | -0.223 | -0.276 | 0.085 | -0.193 | 0.002 | -0.023 | -0.309 | 0.084 |
| | p | 0.802 | 0.725 | 0.173 | 0.089 | 0.606 | 0.238 | 0.991 | 0.891 | 0.055 | 0.613 |
| Mitral E' Septal | r | -0.073 | -0.156 | 0.058 | 0.266 | -0.166 | -0.063 | -0.087 | -0.096 | 0.048 | -0.087 |
| | p | 0.658 | 0.342 | 0.725 | 0.101 | 0.313 | 0.705 | 0.600 | 0.559 | 0.772 | 0.597 |
| Mitral E'/A' Septal | r | -0.054 | -0.108 | -0.205 | -0.018 | -0.252 | -0.293 | -.366* | -.360* | -0.012 | 0.171 |
| | p | 0.742 | 0.512 | 0.211 | 0.912 | 0.122 | 0.071 | 0.022 | 0.024 | 0.941 | 0.297 |
| MPI Septal | r | 0.226 | 0.039 | -0.003 | -0.164 | 0.129 | -0.105 | 0.049 | 0.048 | -0.251 | 0.049 |
| | p | 0.166 | 0.812 | 0.986 | 0.319 | 0.434 | 0.524 | 0.767 | 0.773 | 0.123 | 0.768 |

measurements of diabetic patients. Although there are studies in the literature reflecting deteriation of myocardium resulting with heart failure (6,18,19), there are other studies declaring normal diastolic functions (6,20) in diabetic patients. The studies with normal diastolic functions of diabetic patients could be related with patients'younger age and shorter duration of the illness. Abd-el Aziz et al. (1) stated lower mitral E and A wave velocities while E' and A' velocities were normal with higher MPI of the left ventricle in diabetic patients. Bradley et al. (21) declared that E' was lower, E/E' was higher in patients with type 1 diabetes. Brunvard et al. (8,22) showed increased stiffness with reduced E'/A' with similar E/E' and E/A in diabetic patients than controls. We stated decreased E and E/A with prolonged EDT than controls. Tissue Doppler findings demonstrated decreased E'/A' lateral and septal with increased A' lateral and MPI lateral. MPI septal was also increased in the diabetic group than controls but the increase was at treshold significancy. E/E' was similar with controls like the study performed by Brunvard et al. (7). E/E' is a predictor of elevated diastolic left ventricle and left atrium pressure. It was similar between the patient and control groups in our study, as a probable result of the limited number of the patients included in the study. Our findings support diastolic dysfunction of the left ventricle as a the result of diabetes like the other studies in the literature.

Increased aortic stiffness, causes left vetricular hypertrophy with diastolic dysfunction and remodelling that causes the principles of cardiovascular disease (5). The main mechanism for aortic stiffening is fracture and fragmantation of elastin fibres with repetative stretch, leading to the transfer of stress to less extensible collageous fibers in the vessel. The

loss of pulsatile flow damping by the proximal aorta may result in increased structural and functional microvascular damage, particularly in the heart, brain, retina and kidney (23,24.) Matrix metalloproteinases (mmps) are enzymes that degrade extrcellular matrix. Higher levels of mmp-9 are related with increased stiffness and these patients were reported to have hypertension and DM (25). Decreased aortic elasticity increases santral pulse pressure and wall stress that causes endothelial dysfunction and atherosclerosis (5). Bjarnegård et al. (25) stated higher HR, SBP, DBP, MAP, but similar PP in their study. Çiftel et al. (2) also stated similar PP and AoS. Deveci et al. (5) also showed similar AoD and AoS and PP in their study between the diabetic patients and controls. Bradley et al. (21) stated higher SBP, DBP, MAP but similar PP than controls. The blood pressures were higher than controls but they were still in normal range (21). We stated higher SBP, MAP, PP and HR in the patients with diabetes mellitus than controls in concordance with the literature. An increased sympathetic tone often accompanies an increasing HR. Autonomic neuropathy with a reduced parasympathetic effects might also play a role for this situation (25). There was a deteriation of aortic elasticity parameters, which can be related with short duration of illness and limited number of the patients included. Also deteriation of aortic elasticity parameters can become apparent in time, during follow-ups. We also did not detect a difference in systolic, diastolic parameters and elasticity indexes among the patients with good metabolic control (HgbA1c<8%) and poor metabolic control (HgbAc≥8%). There was also similar results in these same parameters among the patients with shorter duration of illness (<3 years) and longer duration of illness (≥3 years). Bjanegard et al. (25) stated that HgbA1c was positively associated with HR. Suys et al. (11) did not detect any influence of HbA1c and diabetes duration on the measured parameters. Brunvard et al. (7) also did not find an association between diastolic functions and duration of diabetes. But Holzmann et al. (26) reported that left ventricular diastolic function is related to glucose and glycated hemoglobin in middle-aged population like other studies (27). The studies that did not show correlation between diastolic functions and HgbA1c can be attributed to the usage of only one measurement of HgbA1c in the study rather than mean values of several measurements.

Kim et al. (6) stated left ventricular systolic and diastolic dysfunction as duration of diabetes prolongs. From et al. (28) also stated a longer duration higher than 4 years was correlated with significant left ventricular diastolic dysfunction. Deveci et al. (5) stated that diastolic dysfunction was not correlated with diabetes duration. Turbey et al. (23) stated a study on 879 patients with type 1 diabetes and they declared that hyperglycemia was the main risk factor in the study. The other risk factors were age, duration of diabetes. Bunvard et al. (8) showed that E'/A' was negativley associated with SBP and DBP and BMI, but there was no association with sex, years, HgbA1c. From et al. (28) showed that higher HgbA1c was associated with lower DT and E'/A'. In our study, A positive relationship was stated between mitral E wave velocity and PP. Also there was a positive relationship between mitral E'/A' lateral and HR, while a negative relationship was present between mitral E'/A' septal and DBP and between MAP. There was not a relationship between age, BMI, duration of diabetes and HgbA1c and diastolic parameters. One of the probable mechanism for absent relation between HgbA1c and diabetes may be related with using only one measurement in the study instead of multipl measurements. One other potential mechanism for absent relation with duration of diabetes may be related of the short duration of the illness.

One of the limitation of this study was that the number of the patients included in the study was limited. Another limitataion was the use of single HgbA1c value instead of using a mean the values of several months.

## Conclusions

Cardiac diasolic dysfunction findings were found in diabetic children. Even though aortic compliance does not show impairment but periodic cardiac evaluation should be performed. Patients with type 1 diabetes should be monitored for endothelial dysfunction and aortic stiffness and protection of arterial elasticity properties and early treatment of endothelial dysfunction should be performed when the prolonged life expectancy was taken into account.

## Conflict of interest:

The authors report no conflict of interest.

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**Ethical approval:**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (University of Health Sciences, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (decision number: 2023-11-11, date:05.06.2023) and with the1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent:**

Written informed consent was obtained from all individual participants and/or their gaurdians.

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**Data availability**

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Contributions**

Research concept and design: **AMM, ECB**
Data analysis and interpretation: **AMM**
Collection and/or assembly of data: **AMM, ECB**
Writing the article: **AMM**
Critical revision of the article: **AMM, ECB**
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