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Tissue Doppler-Derived Left Ventricular Myocardial Performance Index in Children with Type 1 Diabetes Mellitus

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ABSTRACT
Background: Diabetes Mellitus (DM) is a serious global health problem currently reaching epidemic proportions. It may be complicated with cardiomyopathy. Pulsed wave tissue Doppler can provide quantitative diagnostic information for the assessment of myocardial systolic and diastolic velocity.
Objective: Our study aimed to assess ventricular myocardial performance in type I diabetes mellitus using tissue Doppler echocardiography.
Patients and Methods: This study was carried out at Pediatric Cardiology Unit, Zagazig University Hospitals. 64 age- and sex-matched children were classified into case group included 32 type 1 DM and control group included 32 healthy children. They underwent complete history and conventional and tissue Doppler echocardiographic examination.
Results: E` wave velocity was lower in cases compared to control children (p <0.001). A positive correlation was found between mitral annular À wave velocity and left ventricular myocardial performance index (LV MPI) measured by tissue Doppler imaging.
Conclusion: Early diastolic dysfunction was found in our patients evidenced by reduced E` wave velocity measured by tissue Doppler imaging. The absolute value of LV MPI was higher in patients compared to control children. A finding designating that statistical significance may be found at a longer term follow up study of our diabetic children. LV tissue Doppler-derived MPI was found to have significant positive correlation with mitral annular À wave velocity although systolic LV function was normal in patients when measured by traditional echocardiography in terms of EF and FS.
Keywords: Diabetes mellitus, Tissue Doppler echocardiography, Myocardial performance index.

INTRODUCTION
Type 1 diabetes mellitus (DM) is a metabolic disease characterized by sustained hyperglycemia that leads to diabetic cardiomyopathy. While the diagnosis rests on a simple measurement of blood glucose, accurate classification is often more involved [(1)]. Type 1 diabetes diagnosed in childhood often has an abrupt onset with significant acute symptoms and is thus easily identified but the progression of autoimmune diabetes is often more insidious in adults [(2)].

It remains hard to prove that uncomplicated diabetes mellitus already affects myocardial function in asymptomatic children at an early stage of the disease. Hence, children with uncomplicated diabetes may serve as an ideal model to study the cardiac effect of diabetic metabolic conditions in the absence of potentially confounding ischemic events [(3)].

Tissue Doppler Echocardiography can provide quantitative diagnostic information for the assessment of myocardial deformation [(4)]. Therefore, our study aimed to assess ventricular myocardial performance in type I diabetes mellitus using tissue Doppler echocardiography.

PATIENTS AND METHODS
This study was performed at Pediatric Cardiology Unit, Zagazig University Hospitals on 64 participants divided equally into patients and control groups through the period from January 2019 to July 2021.

Study population: 32 patients with type I diabetes, who were followed up at Outpatient Clinic of Ministry of Health, Zagazig, Egypt, were retrospectively recruited. The control group included 32 asymptomatic healthy children selected at outpatient clinic of Pediatric Cardiology from children who were being investigated for cardiac murmur and whose echocardiography showed no structural heart disease.

Patients: Thirty-two children with type I diabetes mellitus that was diagnosed according to the World Health Organization criteria [(5)] together with a permanent need for insulin therapy

Control subjects: Thirty-two healthy children of comparable age and gender to cases. Children in the control group had to have no congenital heart disease, hypertension, hypercholesterolemia, or diabetes.

Inclusion criteria: Patients had type I diabetes mellitus below 18 years of age.

Exclusion criteria:
- Patients with congenital or rheumatic heart disease.
- Patients with type 2 diabetes mellitus.
- Patients with acute heart failure, dilated cardiomyopathy, chronic renal failure, hypertension and/or previous cardiac surgery.
- Family history of hypercholesterolemia

All patients were subjected to the following:
1- Full history taking.
2- Full general examination.

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3- Local cardiac examination.
4- Laboratory investigations as CBC and estimation of HgA1c.
5- Echocardiography using conventional and tissue Doppler techniques.

Echocardiography:

All patients and controls underwent an echocardiographic examination. Echocardiography with a simultaneous ECG tracing was performed with a Mylab Six (Esáote) machine using a 3-11 MHz transducer. Pulmonary artery systolic pressure was estimated from tricuspid regurgitation jet velocity [(6)].

1-Cardiac dimensions:

A) Aortic (AO) and left atrial (LA) dimensions were measured from the parasternal short axis view.

B) The main pulmonary artery, right and left pulmonary branches diameters were measured from the parasternal axis view.

C) Interventricular septum (IVS), left ventricular posterior wall (LVPW) thickness and left ventricular end systolic (LVESd) dimensions were measured from the parasternal axis view.

At the end of diastole, the septal wall thickness, posterior LV wall thickness and the diastolic diameter of the left ventricle were measured by 2D echocardiography.

2-Conventional LV systolic function:

A) The left ventricular end diastolic (LVED), and left ventricular end systolic (LVES) dimensions parameters were measured from M- mode (MM) images in parasternal short axis view just below the level of the mitral valve [(7)].

B) FS (%) were calculated through M-mode: FS (%) = (LVEDd - LVESd) / LVEDd * 100

Where LVEDd is left ventricular end diastolic dimension, LVESd is the left ventricular end systolic dimension [(8)].

LV ejection fraction was assessed using the biplane Simpson's method in apical 4 chamber view [(9)].

Echocardiographic examinations were read and analyzed offline using a dedicated Esáote software program by an observer blinded to patient history and laboratory test results. Three consecutive heart cycles were recorded. Pulsed wave tissue Doppler was used to measure the peak systolic velocity wave, peak early diastolic velocity, and peak late diastolic velocity. The pulsed wave sample volume was placed at medial and lateral mitral annulus and average of the two recordings was used in the statistical analysis [(10)].

Tissue Doppler-derived LV myocardial performance index (MPI):

The time interval from cessation of mitral inflow in one cardiac cycle to onset of mitral inflow in the subsequent cycle (A) was measured including isovolemic contraction time (IVCT): from the beginning of the first positive deflection after the Q-wave to the onset of the S-wave. Aortic ejection time (B) was measured from the beginning to the end of the S-wave. Isovolemic relaxation time (IVRT): from the end of the S-wave to the beginning of E-wave. Myocardial performance index of LV (MPI) was calculated as A-B divided by B.

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, entered, presented, and analyzed by computer using a data base software program [Statistical Package for Social Science (SPSS) version 20]. For quantitative variables mean ± standard deviation (SD) and median with interquartile range (for not normally distributed data) were computed and independent t-test (t) was used for detection of difference between different normally distributed quantitative variables. While, nonparametric data was evaluated by Mann-Whitney U test. Pearson and Spearman's correlations (r) were used to correlate LV GLS and MPI to LV findings and remaining parameters. The results were considered statistically significant and highly statistical significant when the significant probability (P value) was ≤ 0.05 and ≤ 0.001 respectively. The relationship between two variables is generally considered strong when their r value is larger than 0.7. The correlation r is always a number between (-1 and 1) Positive r values indicate positive association between the variables, and negative r values indicate negative associations.

RESULTS

We found a statistically significant difference between control group and case group regarding early diastolic mitral È wave velocity (0.14 ± 0.03 vs 0.1 ± 0.03 m/sec, $p < 0.001$, table 1 & figure 1) indicating early left ventricular diastolic dysfunction in our patients. There were no significant differences between the studied groups regarding LV myocardial performance index, systolic pulmonary artery pressure and S wave velocity (p values more than 0.05, table 1).

The absolute value of LV myocardial performance index was higher in patients compared to control children, a finding designating that statistical significance may be found at a longer term follow up study of our diabetic children. In our study, LV tissue Doppler derived-MPI was found to have significant positive correlation with mitral annular À wave velocity while no correlation was reported with any of the other studied parameters (Table 2).

Table (1): Tissue Doppler findings of the studied groups

Variable	Case group (n=32)	Control group (n=32)	Tests	
			t/Z	***P*** **value**
Á (M/ sec) Mean ± SD	0.05 ± 0.02	0.08 ± 0.04	-3.590	0.001*
É (M/ sec) **Mean ± SD**	0.1 ± 0.03	0.14 ± 0.03	4.427	<0.001*
É/ Á	2.7±0.41	1.6±0.41	-4.09	0.001*
LV MPI Mean ± SD	0.48 ± 0.13	0.45 ± 0.19	-0.746	0.459
Systolic pulmonary artery press (mmHg) Median (IQR)	31.5±4.81	16.85±2.31	-1.88	0.060
S. wave (M/sec) Mean ± SD	0.06 ± 0.01	0.07 ± 0.01	-1.873	0.066

A`:** late diastolic wave, **E`: early diastolic wave, **M/sec**: meter per second, **mmHg:** millimeter of mercury, **MPI**: myocardial performance index, ***: Significant (p value<0.05*), S wave**: systolic wave, ***(t)*** independent sample t-test,(z): Mann Whitney U test

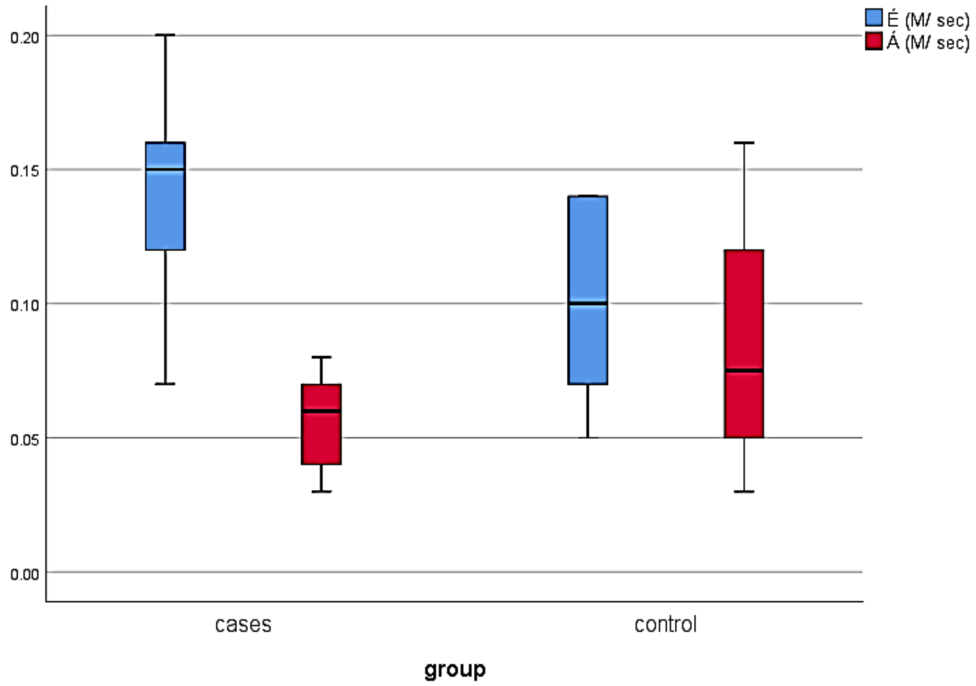

Figure (1): Box blot of tissue Doppler findings of mitral early and late diastolic velocities (A` and E`) of the studied groups.

Table (2): Correlation between LV myocardial performance index and other parameters

Variable	LV Myocardial performance index	
	r	P
Duration of illness	-0.170	0.369
Hb A1C	0.072	0.707
EF %	0.154	0.424
FS %	-0.138	0.466
Á (M/ sec)	0.383	0.037*
É (M/ sec)	-0.011	0.953
S. wave (M/ sec)	-0.066	0.730
Systolic pulmonary artery pressure	0.152	0.423

DISCUSSION

Diabetic cardiomyopathy in diabetes mellitus patients, ranges from 19% to 26%, and its incidence in type 1 diabetes mellitus is growing [11, 12]. Nevertheless, these changes are usually subclinical in children [13].

We found a statistically significant difference between control group and case group regarding early diastolic mitral È wave velocity (0.14 ± 0.03 vs 0.1 ± 0.03 m/sec, $p < 0.001$) indicating early left ventricular diastolic dysfunction in our patients. There were no significant differences between the studied groups regarding LV myocardial performance index, systolic pulmonary artery pressure and S wave velocity ($p > 0.05$, table 1). However, the absolute value of LV myocardial performance index was higher in patients compared to control children, a finding designating that statistical significance may be found at a longer term follow up study of our diabetic children. In our study, LV tissue Doppler derived-MPI was found to have significant positive correlation with mitral annular À wave velocity while no correlation was reported with any of the other studied parameters. These are in agreement with a prospective case control study conducted by **El-Razaky *et al.*** [14] where they reported lower mitral È/À ratio in asymptomatic children with type I diabetes mellitus compared to control children. On the other hand, they found higher LV MPI in patients than in control group (0.6 ± 0.3 vs 0.4 ± 0.1, p value of 0.001). Diabetes mellitus duration was 5 years or more in 40% of their studied patients.

Brunvand *et al.* [15] conducted a population-based case control study that included 173 patients with type I diabetes mellitus and 62 age-matched controls using tissue Doppler imaging. They found lower E'/A'-ratio in all registrations. Overall mean mitral E'/A'-ratio was 2.3 ± 0.5) in diabetic patients and 2.7 ± 0.6) in the controls ($p < 0001$). They concluded that diabetic children using intensive insulin therapy had echocardiographic signs of impaired diastolic myocardial function despite short duration of disease (5.6 ±3.4 years) with HbA1c of 8.4 ± 1.3 gm/dl.

Al-Biltagi *et al.* [16] demonstrated that tissue Doppler detected RV systolic and diastolic dysfunction as there were a significant reduction in E′/A′ wave of tricuspid annulus that indicated RV diastolic dysfunction ($p<0.0001$). S wave velocity of tricuspid annulus was also reduced that indicated RV systolic dysfunction ($p<0.0001$). Right ventricular MPI showed significant impairment in the diabetic children than in the control group ($p<0.0001$). In contrast with **Hensel *et al.*** [17] and **Bakhoum *et al.*** [18] who aimed to assess subclinical cardiac dysfunction in diabetic patients and found no statistically significant difference between type I diabetes mellitus pediatric patients and controls regarding early and late diastolic waves velocity.

Acar *et al.* [19] studied the effects of glycemic control in children and adolescents with type 1 diabetes on cardiac functions. Their diabetic patients were divided into two groups as well-controlled and poorly-controlled patients. All patients underwent M-mode, two-dimensional, pulsed wave Doppler, and tissue Doppler echocardiography to evaluate systolic and diastolic functions. Early diastolic mitral flow velocity (Em) and the ratio of early to late diastolic mitral flow velocity (Em/Am) obtained with TDI were found to be significantly lower in the well-controlled than in the control group and significantly lower in the poorly-controlled group than in the well-controlled group. Myocardial performance index was significantly higher in the poorly-controlled group. The ratio of early mitral diastolic flow velocity obtained with PW traditional Doppler (E) to that obtained by tissue Doppler (E/Em) was significantly higher in the diabetic group. Concerning mitral valve PW Doppler results, 13.6% of the well-controlled group and 31% of the poorly-controlled group had type 1 diastolic dysfunction. Regarding mitral TDI results, 18% of the well-controlled group and 40.4% of poorly-controlled group had type 1 diastolic dysfunction. They reported that conventional and TDI echocardiography revealed impairment in left ventricular functions in some patients. Tissue Doppler echocardiography also revealed diastolic impairment in some patients who appeared normal with PW Doppler echocardiography. In their study, impairment of left ventricular diastolic function was directly related to glycemic control and the rate of diabetic cardiomyopathy was higher in children with poor metabolic control.

Ramadan *et al.* [20] assessed LV systolic and diastolic functions in children with type 1 diabetes mellitus and its relation to the glycemic control and duration of the disease. Their results showed early cardiomyopathic changes in the form of diastolic dysfunction and impaired relaxation using E/A ratio measured by conventional Doppler mitral flow in 7.5% of the diabetic children, whereas by using pulsed TDI, they found diastolic dysfunction of the septal or medial segment of the LV in 52.5%, and of the lateral segment in 42.2% of the diabetic patients. There was a significant negative correlation between the duration of diabetes and E/A ratio. A significant negative correlation was found also between the LV diastolic dysfunction and the duration of the diabetes, whereas no significant correlation was found with the glycated hemoglobin% or age of the patients. The systolic function was normal in their diabetic patients.

CONCLUSION

Early diastolic dysfunction was found in our patients evidenced by reduced E` wave velocity measured by tissue Doppler imaging. The absolute value of LV myocardial performance index was higher in patients compared to control children, a finding designating that statistical significance may be found at a longer term follow up study of our diabetic children. In our study, LV tissue Doppler-derived MPI was found to have significant positive correlation with mitral annular À wave velocity although systolic LV function was normal in patients when measured by traditional echocardiography in terms of EF and FS.

RECOMMENDATIONS

Tissue Doppler imaging is recommended at baseline evaluation of diabetic children. Further studies are needed for confirmation of our findings using higher numbers of study participants. Long-term follow up studies are needed to evaluate the value of tissue Doppler echocardiography regarding serial assessment of LV function and monitoring of glycemic control.

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