

Original Research Article

Assessment of Subclinical Left Ventricular Systolic and Diastolic Dysfunction in Patients with Type 1 DM with and without Good Metabolic Control

Abstract

Background: Diabetic patients with normal left ventricular ejection fraction are frequently associated with diastolic dysfunction. However, LVEF is known not to be a sensitive marker for the detection of subclinical LV systolic dysfunction. This study aimed to assess left ventricular systolic and diastolic function in asymptomatic type 1 diabetic patients by conventional, tissue Doppler and two-dimensional speckle tracking echocardiography to assess subclinical left ventricular systolic and diastolic dysfunction.

Methods: Case-control study was conducted at 150 patients aged 15-35 y were subdivided into three equal groups: Group A: with type 1 diabetes mellitus (T1DM) with good metabolic control (Hb A1C <7.0), Group B: T1DM with poor metabolic control (Hb A1C >7.0), and Group C: Control group: included 50 normal healthy subjects.

Results: Tissue Doppler, diastolic function and strain parameters, AP4C LS, AP2C LS, AP3C LS, and GLS were significantly impaired among the three groups. AP4C LS, AP2C LS, AP3C LS, and GLS were significantly decreased in group B than group A and group C and was significantly decreased in group A than group C, A velocity was significantly impaired among the three groups. A velocity was significantly increased in group B

than group A and group C and was insignificantly impaired in group A than group C.

Conclusion:Conventional echocardiography parameters were insignificantly different between the study groups. 2D speckle tracking and tissue Doppler echocardiography showed that subclinical left ventricular systolic function may be affected even before affection of diastolic function. Longer duration and poor glycemic control of diabetes significantly affect GLS.

Keywords:Two-Dimensional Speckles Tracking, Type 1 Diabetes, tissue Doppler echocardiography

Introduction

Type 1 diabetes mellitus (T1DM) is a disorder characterized by autoimmune-mediated destruction of pancreatic β cells which results in an absolute insulin deficiency and it is most commonly diagnosed in children and adolescents who require exogenous insulin replacement. As it affects all pancreatic β cells, diabetes mellitus (DM) complications may involve almost all organs (especially the eyes, kidneys, heart, and the vascular system)^[1].

Although DM is associated with serious microvascular and macrovascular complications, they are usually subclinical during the early stages of life. DM is also associated with a 10-fold increase in the risk of cardiovascular diseases as compared with normal non-diabetic people of the same age/sex group. Cardiovascular diseases are now among the most common comorbidities and causes of death in patients with DM^[2, 3].

DM does not only result in abnormalities of the vasculature but also leads to structural and functional abnormalities of the myocardium. T1DM is associated with higher incidence rates of heart failure compared to a 10-year-old population, and the risk of death due to cardiovascular diseases is increased 6- to 12-fold^[4, 5].

The most well-known heart disease in DM is the premature development of coronary atherosclerosis, which leads to ischemic heart disease, however, a special subset of heart failure in diabetes has been proposed, the diabetic cardiomyopathy (DCM), which is dysfunction of the myocardium not caused by ischemia, hypertension nor valvular disease^[6].

Although the pathogenesis of DCM is unclear, many believe it is multifactorial. It is generally accepted that the most important factors are hyperglycemia, increased free fatty acids, activation of the rennin

angiotensin system, microangiopathy, increased oxidative stress, and cardiac autonomic neuropathy [7].

All of these underlying pathogenic conditions can change the cardiac structure and may lead to cardiac fibrosis. The duration of diabetes, glycemic control, and age are important factors to contribute towards the development of such complications [2, 8].

In the clinical setting, the systolic function of the left ventricle is usually assessed visually, by M-mode, or by Simpson's biplane method which is usually normal in the early stages of the disease. It is greatly important to identify early subclinical systolic or diastolic dysfunction of the left ventricle. Speckle tracking echocardiography (STE) has emerged as an accurate quantitative method to assess global and regional myocardial deformation parameters [9, 10].

The assessment of myocardial deformation allows early detection of subclinical Left ventricular systolic and diastolic dysfunction in different cardiac diseases which may appear normal by conventional echocardiography during this stage of the disease. In several studies, it has been shown that left ventricular diastolic dysfunction is an early sign of DCM and usually precedes systolic dysfunction while recent investigations have found that left ventricular longitudinal myocardial systolic dysfunction, rather than diastolic dysfunction, is to be considered the first sign of preclinical DCM in adults [11-13].

This study aimed to assess left ventricular systolic and diastolic function in asymptomatic type 1 diabetic patients by conventional, tissue Doppler and two-dimensional STE to assess subclinical left ventricular systolic and diastolic dysfunction.

Patients and Methods

A prospective case-control observational study was performed in the Cardiology Department at Tanta University Hospital from January to December 2020. Participants were recruited from the Cardiology and Internal Medicine Clinics of Tanta University Hospital. A written informed consent was obtained from all participants. No risk for the subjects who share in this study. Any unexpected risks that appeared during this study were cleared to participants. The study was approved by the Ethics Committee of the Faculty of Medicine at Tanta University. Privacy of participant and confidentiality of the data by putting code numbers to every patient and name were kept in a special file. Using the results of the study only in a scientific manner. Patients were subdivided into three groups: Group A: included 50 patients (age 15-35 years) with T1DM with good metabolic control (Hb A1C <7.0). Group B: included 50 patients (age 15-35 years) with T1DM with poor metabolic control (Hb A1C >7.0). Group C (Control group): included 50 healthy, non-diabetic age and sex-matched subjects who are normotensive and non-smoker subjects with no other comorbid conditions. The inclusion criteria were: age category between 15 and 35 years old. T1DM patients. While our exclusion criteria were: ages less than 15 years old and more than 35 years. As well as hypertensive patients, smokers, individuals with chronic kidney illness and history of documented coronary artery, congenital heart, and valvular heart diseases. In addition, patients with left ventricular ejection fraction (LVEF) <50 % by conventional echocardiography. As well as people with atrial fibrillation and other types of arrhythmias. All patients and controls were subjected to: clinical evaluation based on full history taking including duration of diabetes for the diabetic groups (Excluding presence of chest pain, dyspnea, or any cardiac complaint) and clinical examination were done to all 3 groups. $BMI = \text{Weight (kg)} / \text{height}^2 \text{ (m}^2\text{)}$ ^[14]. Moreover,

conventional, tissue doppler and two-dimensional speckle tracking echocardiography (2D-STE) were performed on the three groups. All echocardiographic examinations were performed according to the recommendations of the American Society of Echocardiography. Echocardiography was done using General Electric (GE) Vingmed ultrasound Vivid E 9 system equipped with an M5S probe (frequency 1.7–3.3 MHz) for echocardiography. The Conventional Echocardiography for the left atrium and aortic root dimensions were measured in the left parasternal long-axis view. Left ventricular diameters and wall thicknesses were measured in the left parasternal long-axis view at the level of the mitral valve tips, ensuring a measurement perpendicular to the long axis of the ventricle.

Ejection fraction (EF) and fractional shortening (FS) were determined using 2D guided M mode echocardiographic tracings at the parasternal long-axis view using the Teichholz formula. Pulsed wave Doppler was used to recording trans-mitral flow at the tips of the mitral leaflets in the apical four-chamber view. Continuous-wave Doppler was used to recording velocity of tricuspid regurg systolic jet in apical four-chamber view. Peak velocity of early (E) and late (A) atrial diastolic filling of the doppler Mitral flow, E/A ratio, and E wave deceleration time (DT) were calculated.

Regarding the tissue Doppler imaging (TDI), in the apical four-chamber view, pulsed wave TDI across septal and lateral mitral annulus was used to obtain the following parameters: Peak diastolic velocity during the early filling stage at septal and lateral mitral annulus (e'). As well as average E/ e' velocities, and peak systolic myocardial velocity (S) at septal and lateral mitral annulus.

Concerning the two-dimensional speckle tracking, speckle tracking is an offline technique that is applied to previously acquired 2D images. The longitudinal strain was measured using software on 2D grayscale images of LV from standard apical four-chamber, two-chamber, and three-chamber views. The peak systolic (PS) global longitudinal strain (GLS) was calculated as the average of the LS of the 17 LV segments obtained from 4-CH, 2-CH, and 3-CH views. Global Longitudinal Strain (GLS) was used to detect subclinical left ventricular systolic dysfunction. Septal e' , lateral e' , average E/e' , LAVI, TR velocity were used to assess diastolic function.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences version 25 (IBM Inc., Chicago, IL, USA). Quantitative variables were expressed as mean, standard deviation (SD), and range and were compared using ANOVA (F) test among the study groups with post hoc (Tukey) test to compare every two groups. Qualitative variables were expressed as frequency and percentage and were statistically analyzed by the Chi-square test. A two-tailed p -value ≤ 0.05 was considered statistically significant.

Results

Regarding demographic data, SBP, and DBP measures shows insignificant difference among the studied groups. Table 1

Table 1: Comparison between study groups regarding demographic data, and blood pressure measures

		Group A (n = 50)	Group B (n = 50)	Group C (n = 50)	P value
Age (years)	Mean \pm SD	26.68 \pm 5.78	26.50 \pm 5.65	25.76 \pm 6.02	0.705

	Range	15-35	16-35	15-35	
Gender	Male	20 (40%)	27 (54%)	23 (46%)	0.371
	Female	30 (60%)	23 (46%)	27 (54%)	
Weight (kg)	Mean ± SD	76.48 ± 17.63	78.90 ± 19.47	79.46 ± 18.25	0.693
	Range	46-110	46-110	45-110	
Height(cm)	Mean ± SD	161.80 ± 13.14	164.24 ± 15.01	164.24 ± 13.53	0.600
	Range	142-187	142-187	142-187	
BMI(Kg/m ²)	Mean ± SD	28.70 ± 2.26	28.66 ± 2.24	28.93 ± 2.36	0.907
	Range	22.81-31.49	22.81-31.8	22.32-31.8	
BSA(m ²)	Mean ± SD	1.89 ± 0.33	1.84 ± 0.29	2.01 ± 0.32	0.518
	Range	1.43-2.46	1.39-2.39	1.42-2.46	
SBP (mmHg)	Mean ± SD	117.40 ± 9.60	117.70 ± 8.70	118.90 ± 8.41	0.674
	Range	100-130	100-130	105-130	
DBP (mmHg)	Mean ± SD	70.60 ± 6.67	72.80 ± 5.54	71.60 ± 4.57	0.151
	Range	60-80	60-80	65-80	

Regarding DM duration, there was insignificantly different between diabetic groups. But, HBA1c was significantly decreased in group A than group B. Table 2

Table 2: Duration of DM and HBA1c level in group A and group B

		Group A (n = 50)	Group B (n = 50)	P value
Duration of DM(years)	Mean ± SD	9.38 ± 4.81	10.80 ± 5.14	0.157
	Range	2-19	2-19	
HBA1c	Mean ± SD	6.32 ± 0.40	8.62 ± 0.64	<0.001*

	Range	5.6-6.8	7.5-9.6	
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Regarding conventional echocardiography parameters (LVEDD, LVESD, IVST, PWT, LA, Ao, EF, FS), there were insignificantly different among the study groups. Table 3

Table 3: Comparison between study groups regarding conventional echocardiography parameters:

		Group A (n = 50)	Group B (n = 50)	Group C (n = 50)	P value
LVEDD (cm)	Mean ± SD	4.73 ± 0.61	4.49 ± 0.69	4.65 ± 0.85	0.150
	Range	3.7-5.6	3.4-5.6	3.7-5.7	
LVESD (cm)	Mean ± SD	2.86 ± 0.47	2.87 ± 0.48	2.91 ± 0.35	0.490
	Range	2.2-3.6	2.1-3.7	2.3-3.5	
IVST (cm)	Mean ± SD	0.86 ± 0.17	0.84 ± 0.19	0.88 ± 0.12	0.460
	Range	0.6-1.1	0.6-1.1	0.7-1.1	
PWT (cm)	Mean ± SD	0.87 ± 0.13	0.82 ± 0.16	0.85 ± 0.17	0.295
	Range	0.7-1.1	0.6-1.1	0.6-1.1	
LA (cm)	Mean ± SD	3.23 ± 0.49	3.05 ± 0.49	3.16 ± 0.42	0.187
	Range	2.3-3.9	2.2-3.9	2.4-3.9	
Ao (cm)	Mean ± SD	2.73 ± 0.42	2.85 ± 0.42	2.77 ± 0.46	0.335
	Range	2.1-3.4	2.1-3.4	2-3.4	
EF (%)	Mean ± SD	67.00 ± 4.87	66.78 ± 6.18	69.00 ± 4.87	0.076
	Range	59-76	57-76	61-77	

FS (%)	Mean ±	37.24 ±	36.36 ±	37.30 ±	0.515
	SD	4.74	4.34	4.58	
	Range	30-45	30-44	30-44	

regarding tissue Doppler, diastolic function and strain parameters, AP4C LS and AP2C LS were significantly impaired among the study groups. AP4C LS and AP2C LS were significantly decreased in group B than group A and group C and was significantly decreased in group A than group C. Also, AP3C LS and GLS were significantly impaired among the study groups. AP3C LS and GLS were significantly decreased in group B than group A and group C and was significantly decreased in group A than group C. Furthermore, A velocity was significantly different among the study groups. A velocity was significantly increased in group B than group A and group C and was insignificantly different in group A than group C. On the other hand, Sep S, Lat S, E velocity, Sep e', lat e', E/A ratio, Average E/e', TR velocity, DT, and LAVI were insignificantly different among the study groups. Table 4

Table 4: Comparison between study groups regarding tissue Doppler, diastolic function and strain parameters

		Group A (n = 50)	Group B (n = 50)	Group C (n = 50)	P value		
Sep S (cm/s)	Mean ±	8.97 ±	8.55 ±	8.83 ±	0.240		
	SD	1.22	1.47	0.98			
	Range	6.9-10.7	6.2-10.7	7.2-10.6			
Lat S (cm/s)	Mean ±	11.35 ±	10.93 ±	11.01 ±	0.524		
	SD	1.90	2.21	1.73			
	Range	7.8-14.5	6.8-14.8	8.1-13.9			
AP4C LS (%)	Mean ±	-20.34 ±	-17.46 ±	-22.47 ±	<0.0	P	<0.0
	SD	2.55	3.14	2.26			

	Range	-24.6: -16	-22.7: -12.9	-26.1: -18.4		P 2	<0.0 01*
						P 3	<0.0 01*
AP2C LS (%)	Mean ± SD	-20.48 ± 2.63	-17.76 ± 2.94	-23.16 ± 3.06	<0.0 01*	P 1	<0.0 01*
	Range	-24.7: -16	-22.6: -12.6	-28.4: -17.9		P 2	<0.0 01*
						P 3	<0.0 01*
AP3C LS (%)	Mean ± SD	-20.77 ± 2.62	-16.87 ± 3.20	-22.29 ± 3.02	<0.0 01*	P 1	<0.0 01*
	Range	-25.7: -17.2	-21.8: -11.5	-27.2: -17.4		P 2	<0.0 01*
						P 3	<0.0 01*
GLS (%)	Mean ± SD	-19.55 ± 1.43	-16.64 ± 2.84	-21.69 ± 1.50	<0.0 01*	P 1	<0.0 01*
	Range	-21.8: -17.1	-21.8: -12.3	-24.1: -19.3		P 2	<0.0 01*
						P 3	<0.0 01*
E velocity (cm/s)	Mean ± SD	99.74 ± 15.73	104.12 ± 18.83	98.74 ± 15.70	0.239		
	Range	69-125	67-131	70-123			
A velocity (cm/s)	Mean ± SD	65.68 ± 17.53	75.98 ± 21.98	60.04 ± 14.76	<0.0 01*	P 1	0.00 6*
	Range	37-95	40-114	35-90		P 2	0.12 6
						P 3	<0.0 01*
Sep e` (cm/s)	Mean ± SD	13.60 ± 2.82	13.04 ± 2.57	14.19 ± 2.78	0.114		
	Range	9-17.9	8.8-17.6	9-18.9			
lat e`	Mean ± SD	17.48 ± 3.84	18.72 ± 3.24	18.85 ± 3.63	0.113		
	Range	12.5-24.9	12.7-24.8	12.9-25.5			
E/A ratio	Mean ± SD	1.65 ± 0.58	1.50 ± 0.54	1.75 ± 0.56	0.568		
	Range	0.8-2.95	0.63-2.82	0.96-3.24			
Average	Mean ± SD	7.67 ±	8.22 ±	7.27 ±	0.075		

E/e`	SD	2.06	2.09	2.06	
	Range	4.5-12.86	4.41-13.46	4.4-13.52	
TR velocity(m/s)	Mean ±	2.16 ±	2.02 ±	2.18 ±	0.060
	SD	0.40	0.28	0.41	
	Range	1.6-2.8	1.6-2.6	1.5-2.9	
DT(ms)	Mean ±	216.02 ±	228.10 ±	195.14 ±	0.056
	SD	44.19	67.51	46.60	
	Range	147-295	111-332	118-266	
LAVI (ml/m ²)	Mean ±	21.32 ±	21.30 ±	22.64 ±	0.219
	SD	4.52	3.84	4.74	
	Range	15-30	14-27	16-31	

Discussion

The presence of impaired longitudinal function in diabetic patients has been reported when using TDI. However, TDI has its limitations included angle dependency and the one-dimensional nature of its measurement. The recent development of 2D-STE overcomes some of these limitations, and its accuracy and clinical usefulness have been reported ^[15].

In several studies, it has been shown that left ventricular diastolic dysfunction is an early sign of DCM and usually precedes systolic dysfunction ^[16].

On the other hand, recent investigations have found that left ventricular longitudinal myocardial systolic dysfunction, rather than diastolic dysfunction, should be considered the first sign of preclinical DCM in adults ^[17].

Sherwani et al., 2016 ^[18] suggested that HbA1c is an important indicator of long-term glycemic control with the ability to reflect the cumulative glycemic history of the preceding two to three months. HbA1c not only

provides a reliable measure of chronic hyperglycemia but also correlates well with the risk of long-term diabetes complications.

In the study of Sherwani et al. 2016^[18], they concluded that the HbA1c is an accurate and easy-to-administer test with on-the-spot results availability and can be an effective tool in establishing the diagnosis of diabetes, especially in low- and middle-income countries and hard-to-reach populations. Even though HbA1c has been endorsed for the diagnosis of diabetes, in most countries worldwide, some testing strategies and cutoff ranges are still being debated. The prognostic potential of HbA1c lies in its unique ability to assess retrospective glycemetic control as well as predicting the lipid profile in diabetic patients. As the epidemic of diabetes continues to grow worldwide, the HbA1c test may continue to be implemented as part of the diagnostic and prognostic tool, leading to better patient care and successful clinical outcomes.

Additionally, in the study of Zaidi et al., 2019^[19] they concluded that HbA1c is an accurate and easy-to-manage test with onsite results availability. It can be an effective tool for diagnosing and prognosis of diabetes, especially in low- and middle-income countries and in hard-to-reach populations. Although HbA1c has been approved for the diagnosis of diabetes, certain screening strategies and reduction intervals are still under discussion in most countries around the world. However, the combination of fasting glucose tolerance test (FGT) and HbA1c significantly increases the diagnostic accuracy of these individual tests. The prognostic potential of HbA1c lies in its unique ability to evaluate retrospective glycemetic control and to predict the lipid profile in diabetic patients. As the diabetes epidemic continues to grow worldwide, the HbA1c test can continue to be implemented as part of the

diagnostic and prognostic tool, improving patient care and improving patient outcomes to achieve good clinical results.

Our results regarding conventional echocardiographic parameters showing no statistically significant difference between them (p -value > 0.05) agree with Sameh et al., 2016, Tamer et al., 2017 and Ahmed et al., 2018 ^[20-22].

In parallel with our results, the study of Ahmed et al., 2018 ^[22], studied the early left ventricular and left atrial dysfunction in T1DM using 2D-STE a statistically significant decrease in the average peak LV global longitudinal strain was found in diabetics compared to nondiabetics and in LV TDI strain rate were found. A statistically significant peak atrial longitudinal strain decreases in the average in diabetics compared to nondiabetics. There were no significant differences between the two groups concerning the functional capacity of the parameters. They concluded that, Since T1DM is associated with early (subclinical) LV and LA dysfunction, 2D-STE becomes an important and sensitive tool for the early detection of subclinical LV and LA myocardial dysfunction.

Similarly, the study of Boyer et al., 2004^[23] who have evaluated the LV diastolic dysfunction using transmitral LV filling pattern (i.e., abnormal relaxation and/or pseudo-normal filling) and found that 47–75% of asymptomatic normotensive patients with well-controlled T2DM had diastolic LV dysfunction. They also found that TDI showed LV diastolic dysfunction in 63% of asymptomatic T2DM patients, while conventional Doppler echocardiography could diagnose only 46% of patients with diastolic dysfunction.

Boyer et al., 2004^[23] suggested that although the prevalence of subclinical LV longitudinal systolic dysfunction in diabetic patients with reserved LVEF varied among studies, this may depend on the patient characteristics, such as

the severity of DM or DM-related complications. Many previous studies have claimed that diastolic dysfunction is an early detectable parameter for DCM. These also are concordant with the current study as Group CDoppler, diastolic function and strain parameters differed significantly from other groups included in the study.

In the study of Abdelfattah et al., 2019^[24], they made a case-control study to detect subclinical Left Ventricular Dysfunction by Two-Dimensional Speckle Tracking and Tissue Doppler Echocardiography in young patients with T1DM. Their study was a case-control study that was done on 100 participants who were divided equally into 2 groups, the diabetic group, and the healthy control group. There was a highly statistically significant difference between the 2 groups regarding A wave velocity, E/A ratio, AP2C LS, AP3C LS, AP4C LS, and GLS with a p-value < 0.001 and a statistically significant difference in deceleration time DT with p-value 0.023. It also revealed that there was a positive significant correlation between duration of diabetes, HBA1c level, and GLS%. They concluded that GLS appears to be a good tool for early detection of subclinical LV systolic dysfunction. Long duration and poor control of DM are important factors for developing DCM.

The present results are in agreement with results obtained from Sameh et al., 2016, Tamer et al., 2017 and Ahmed et al., 2018^[20-22] studies regarding the correlation between HBA1c level, duration of diabetes, and longitudinal strain parameters. They showed that poor glycemic control (as indicated by elevation of HBA1c level) and longer duration of diabetes had a statistically significant correlation with longitudinal strain parameters. According to data obtained from the current study, the diabetic group had lower values of GLS which was used as the main indicator for detection of subclinical systolic dysfunction GLS (%) -18.95 ± 2.02 .

The ECAVI NORRE study by Sugimoto et al., 2017^[26] is a big study that evaluated reference ranges of normal left ventricular 2D strain. According to the current study, the average GLS for the current study age groups is: -21.8: -17.1, -21.8: -12.3, -24.1: -19.3 (for groups A, B, and C respectively). So according to the study, some diabetic patients who had GLS less than the values in ECAVI NORRE study may have subclinical left ventricular systolic dysfunction and are at risk for progression to overt DCM.

The results are also concordant with Ernande et al., 2011^[27] who proved the presence of LV longitudinal dysfunction in DM patients with preserved LVEF of at least 55% when assessed by GLS, despite their normal diastolic function. This indicates that diastolic dysfunction should not be considered

Similarly, Cameli et al., 2012^[28] revealed that global LA strain is a strong and independent predictor of cardiovascular events, even superior to LA conventional parameters (indexed LA volume, LA total emptying fraction, LA area, and LA diameter) in diabetic patients with the highest predictive value of cardiovascular events for global longitudinal LA strain. Also, Kadappu et al., 2012^[29] revealed that longitudinal strain in all six segments of the LA is lower in diabetic patients compared to the controls.

From all the aforementioned data, it could be concluded that conventional echocardiography parameters were insignificantly different between the study groups. 2D speckle tracking and tissue Doppler echocardiography showed that subclinical left ventricular systolic function may be affected even before affection of diastolic function. Longer duration and poor glycemic control of diabetes (evaluated by HBA1C, which is considered an indicator for diabetes control) significantly affect GLS.

Recommendations: Further clinical research on the mechanisms of subclinical cardiac dysfunction in young patients with T1DM will be able to

clarify the prevention and treatment of this entity. Additional studies included a large number of patients are required for generalization of these results. Good control of diabetes is essential for prevention of diabetic cardiomyopathy. All diabetic patients especially those with poor glycemic control or with longer period of diabetes should be screened for presence of subclinical systolic or diastolic dysfunction. Periodic follow up and early detection of left ventricular functional deterioration in young patients with T1DM may help to prevent the natural progression of the disease.

Limitations: The study evaluated a relatively small number of patients. Thus, our results cannot be extrapolated to the general diabetic population. Diabetic patients were considered to have a low probability of coronary artery disease based on clinical grounds and normal resting echocardiography; our enrolment criteria did not rule out definitively the possibility of epicardial coronary artery stenosis in some of the patients. Invasive coronary angiography was not justified in all patients, because it was not clinically indicated in this population.

Conclusion

Conventional echocardiography parameters were insignificantly different between the study groups. 2D speckle tracking and tissue Doppler echocardiography showed that subclinical left ventricular systolic function may be affected even before affection of diastolic function. Longer duration and poor glycemic control of diabetes (evaluated by HBA1C, which is considered an indicator for diabetes control) significantly affect GLS.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References

1. Haller MJ, Silverstein JH, Rosenbloom AL. Type 1 diabetes in the child and adolescent. *Pediatric Endocrinology*, New York, Informa Healthcare. 2006;5:63-81.
2. Brink SJ. Complications of pediatric and adolescent type 1 diabetes mellitus. *Curr Diab Rep*. 2001;1:47-55.
3. Laing SP, Swerdlow AJ, Slater SD, Burden AC, Morris A, Waugh NR, et al. Mortality from heart disease in a cohort of 23,000 patients with insulin-treated diabetes. *Diabetologia*. 2003;46:760-5.
4. Soedamah-Muthu SS, Fuller JH, Mulnier HE, Raleigh VS, Lawrenson RA, Colhoun HM. High risk of cardiovascular disease in patients with type 1 diabetes in the U.K.: a cohort study using the general practice research database. *Diabetes Care*. 2006;29:798-804.
5. Lind M, Bounias I, Olsson M, Gudbjörnsdóttir S, Svensson AM, Rosengren A. Glycaemic control and incidence of heart failure in 20,985 patients with type 1 diabetes: an observational study. *Lancet*. 2011;378:140-6.
6. Fang ZY, Prins JB, Marwick TH. Diabetic cardiomyopathy: evidence, mechanisms, and therapeutic implications. *Endocr Rev*. 2004;25:543-67.

7. Voulgari C, Papadogiannis D, Tentolouris N. Diabetic cardiomyopathy: from the pathophysiology of the cardiac myocytes to current diagnosis and management strategies. *Vasc Health Risk Manag.* 2010;6:883-903.
8. Miki T, Yuda S, Kouzu H, Miura T. Diabetic cardiomyopathy: pathophysiology and clinical features. *Heart Fail Rev.* 2013;18:149-66.
9. Ersbøll M, Valeur N, Mogensen UM, Andersen MJ, Møller JE, Velazquez EJ, et al. Prediction of all-cause mortality and heart failure admissions from global left ventricular longitudinal strain in patients with acute myocardial infarction and preserved left ventricular ejection fraction. *J Am Coll Cardiol.* 2013;61:2365-73.
10. Mondillo S, Galderisi M, Mele D, Cameli M, Lomoriello VS, Zacà V, et al. Speckle-tracking echocardiography: a new technique for assessing myocardial function. *J Ultrasound Med.* 2011;30:71-83.
11. Imbalzano E, Zito C, Carerj S, Oreto G, Mandraffino G, Cusmà-Piccione M, et al. Left ventricular function in hypertension: new insight by speckle tracking echocardiography. *Echocardiography.* 2011;28:649-57.
12. Vazeou A, Papadopoulou A, Miha M, Drakatos A, Georgacopoulos D. Cardiovascular impairment in children, adolescents, and young adults with type 1 diabetes mellitus (T1DM). *European journal of pediatrics.* 2008;167:877-84.
13. Nakai H, Takeuchi M, Nishikage T, Lang RM, Otsuji Y. Subclinical left ventricular dysfunction in asymptomatic diabetic patients assessed by two-dimensional speckle tracking echocardiography: correlation with diabetic duration. *Eur J Echocardiogr.* 2009;10:926-32.
14. Peterson CM, Thomas DM, Blackburn GL, Heymsfield SB. Universal equation for estimating ideal body weight and body weight at any BMI. *Am J Clin Nutr.* 2016;103:1197-203.

15. Cho GY, Chan J, Leano R, Strudwick M, Marwick TH. Comparison of two-dimensional speckle and tissue velocity based strain and validation with harmonic phase magnetic resonance imaging. *Am J Cardiol.* 2006;97:1661-6.
16. Khattab AA, Soliman MA. Biventricular function and glycemic load in type 1 diabetic children: Doppler tissue-imaging study. *Pediatr Cardiol.* 2015;36:423-31.
17. Mochizuki Y, Tanaka H, Matsumoto K, Sano H, Toki H, Shimoura H, et al. Clinical features of subclinical left ventricular systolic dysfunction in patients with diabetes mellitus. *Cardiovasc Diabetol.* 2015;14:37.
18. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights.* 2016;11:95-104.
19. Zaidi A, Singh SP, Raza ST, Mahdi F. Role of hba1c in the diagnosis of patients with diabetes mellitus. *Era J Med Res.* 2019;6:78-83.
20. Sameh W, Heba A, Ibrahim N, Mary N. Assessment of left ventricular function in young type 1 diabetes mellitus patients by two-dimensional speckle tracking echocardiography: relation to duration and control of diabetes. *Egypt Heart J.* 2016;68:217-25.
21. Tamer Y, Utku A, Elif S, al e. Subclinical left ventricular systolic and diastolic dysfunction in type 1 diabetic children and adolescents with good metabolic control. *Echocardiography.* 2017;10:1037.
22. Ahmed TA, Hassan MN, Mazen AA, Hegazy SA. Detection of early left ventricular and left atrial dysfunction in type I diabetes mellitus using two dimensional speckle tracking echocardiography. *Sci J Al-Azhar Med Fac Girls.* 2018;2:106.

23. Boyer JK, Thanigaraj S, Schechtman KB, Pérez JE. Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus. *Am J Cardiol.* 2004;93:870-5.
24. Abdelfattah ME, Biomy R, Hamouda M, Ebaid HH. Detection of Subclinical Left Ventricular Dysfunction by Two-Dimensional Speckle Tracking and Tissue Doppler Echocardiography in Young Patients with Type 1 Diabetes Mellitus. *JOCCT.* 2019;13:65-72.
25. Sugimoto T, Dulgheru R, Bernard A, Ilardi F, Contu L, Addetia K, et al. Echocardiographic reference ranges for normal left ventricular 2D strain: results from the EACVI NORRE study. *Eur Heart J Cardiovasc Imaging.* 2017;18:833-40.
26. Ernande L, Bergerot C, Rietzschel ER, De Buyzere ML, Thibault H, Pignonblanc PG, et al. Diastolic dysfunction in patients with type 2 diabetes mellitus: is it really the first marker of diabetic cardiomyopathy? *J Am Soc Echocardiogr.* 2011;24:1268-75.e1.
27. Cameli M, Lisi M, Focardi M, Reccia R, Natali BM, Sparla S, et al. Left atrial deformation analysis by speckle tracking echocardiography for prediction of cardiovascular outcomes. *Am J Cardiol.* 2012;110:264-9.
28. Kadappu KK, Boyd A, Eshoo S, Haluska B, Yeo AE, Marwick TH, et al. Changes in left atrial volume in diabetes mellitus: more than diastolic dysfunction? *Eur Heart J Cardiovasc Imaging.* 2012;13:1016-23.