Detection of early left ventricular and left atrial dysfunction in type I diabetes mellitus using two dimensional speckle tracking echocardiography

Taghreed A. Ahmed, Mona N. Hassan, Adel A. Mazen, SHreen A. Hegazy

Background Occult left ventricular (LV) systolic and diastolic dysfunction is not uncommon among young adults with type I diabetes mellitus (T1DM). Early detection in the subclinical phase may enhance different preventive strategies. The two-dimensional speckle tracking echocardiography (2D-STE) is a novel and promising tool for the detection of early changes in LV and left atrial (LA) myocardial performance.

Aim To detect early LV and LA dysfunction in young adults with T1DM by 2D-STE and its correlation with their functional capacity using the treadmill stress test.

Patients and methods Thirty patients with T1DM and 15 nondiabetics acting as controls were enrolled. Conventional 2D echo, tissue Doppler imaging (TDI), and 2D-STE were done. Peak LV global longitudinal strain and peak LA global longitudinal strain were obtained. The functional capacity was assessed using the treadmill stress test.

Results A statistically significant decrease in the average peak LV global longitudinal strain was found in diabetics compared to nondiabetics (15.8±6.8 and 23.9±2.7, respectively; $P<0.001$) and in LV TDI strain rate (19.7±5.4 and 23±2.7, respectively? $P<0.05$) were found. A statistically significant peak atrial longitudinal strain decrease in the average in diabetics compared to nondiabetics (34.40±12.9 and 42.3±3.9, respectively, $P<0.05$). There were no significant differences between the two groups with respect to the functional capacity of the parameters.

Conclusion Since T1DM is associated with early (subclinical) LV and LA dysfunction, 2D-STE becomes an important and sensitive tool for an early detection of subclinical LV and LA myocardial dysfunction.

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Cardiology Department, Al-Azhar University, Cairo, Egypt

Correspondence to Taghreed. A. Ahmed, MD, Cardiology Department, Al-Azhar University, Cairo, Egypt. Tel: +201064936260;
e-mail: taghreedahm40@hotmail.com

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Introduction

Type I diabetes mellitus (T1DM) is a chronic illness characterized by the body's inability to produce insulin due to the autoimmune destruction of the pancreatic β cells. It accounts for only 5–10% of those with diabetes. Onset most often occurs in childhood, but the disease can also develop in late 30's and early 40's [1].

Diabetes mellitus (DM) is associated with increased risk of cardiac diseases 'heart failure (HF) and coronary artery disease (CAD)' and its prevalence is assuming epidemic proportions due to the presence of metabolic abnormalities that affect the whole body with its profound impact on healthcare [2].

Early detection of diabetic heart disease is of paramount importance, because timely lifestyle modifications and medical interventions can prevent or delay the subsequent development of overt HF [3].

Prevalence of HF remains high in diabetic patients irrespective of age, hypertension, obesity, hypercholesterolemia, and CAD, which leads to the proposal of primary myocardial disease known as diabetic cardiomyopathy (DCM) [4].

The left ventricular ejection fraction (LVEF) is known not to be a sensitive marker for the detection of subclinical LV systolic dysfunction. Early manifestation of diabetic LV systolic dysfunction can appear longitudinally, because subendocardial fibers that are vulnerable to myocardial ischemia have a longitudinal trajectory [5].

The presence of impaired longitudinal function in diabetic patients has been reported when using tissue Doppler imaging (TDI). However, TDI has its own limitations including angle dependency and the one-dimensional nature of its measurement. The recent development of two-dimensional speckle tracking echocardiography (2D-STE) overcomes some of these limitations, and its accuracy and clinical usefulness have been reported [6].

Aim

To detect early LV and left atrial (LA) dysfunction in young adults with T1DM by 2D-STE and its correlation with their functional capacity using the treadmill stress test.

Patients and methods

Study cohort

This study conducted on 30 (10 males and 20 females) patients, their mean age was 20.9±2.02 years, with T1DM and had low risk for CAD who presented to the cardiology outpatient clinic in Ain Shams University Students Hospital with chest pain and fulfilled the inclusion criteria. They attended Al-Zahra University Hospital (Cairo, Egypt) during the period from September 2014 till September 2015, in whom treadmill exercise ECG had proved to be negative within a month of the study. Another group of 15 (five males and 10 females) healthy participants, with their mean age of 23.8±3.3 years had been enrolled as a control group. All the patient and control groups accepted an oral consent, and the study was approved by FMG ethical committee.

Excluded from this study were patients with history of documented cardiac disease: myocardial infarction or ischemia, HF, rheumatic or congenital heart disease, hypertension, arrhythmias, chronic pulmonary disease, and smoking or ex-smoking.

Methods

Detailed history: medical therapy, assessment of quality of life using heart quality of life (QOL), and Duke Activity Status Index (DASI) score [7]. Clinical examination, laboratory investigations (complete blood picture, fasting blood sugar, postprandial blood sugar, glycated heamoglobin (HbA1c), total lipid profile, urine analysis, liver and renal function tests, and erythrocyte sedimentation rate] 12 lead ECG, and stress exercise ECG, were performed on all cases.

Heart QOL was translated into Arabic and included 14 questions. Scoring of the questionnaire was done by summating the responses to all 14 questions where each question was scaled from 0 (highest impact on QOL) to 3 (no effect on QOL) where lower scores reflected poorer QOL. DASI was translated into Arabic and included 12 questions; score was calculated at the end according to the formula: functional capacity in metabolic equivalents= [(DASI score×0.43)+9.6]/3.5.

Assessment of the left ventricle

Transthoracic echocardiography:

Conventional transthoracic echo-Doppler examination was performed for all patients in both supine and left lateral position using Vivid-7 GE system with TDI capability; EchoPAC, GE version 110-1-2, (General Electric Healthcare, Wauwatosa, USA). All cases were examined using multifrequency (2.5–3.5 MHz) matrix probe M3S with simultaneous ECG physio-signal displayed with all recorded echo images and loops. All parameters were taken according to the American Society of Echocardiography standards [8]. Examinations were made by the same operator to minimize interobserver variability.

The 2D guided M-mode echocardiography was used to assess LV end diastolic dimension, LV end systolic dimension, interventricular septal diameter, LV posterior wall diameter, LVEF%, LV fractional shortening, LV mass, and mass index were calculated using linear measurements derived from 2D targeted M-mode by applying modified Devereaux's formula: 0.8×[1.04×(LVEDd+PWTd+SWTd)3(LVEDd)3] +0.6/body surface area (normal range: 49–115 g/m^2 in males, 43–95 g/m^2 in females) [9].

The 2D echocardiography was used for assessment of segmental wall motion abnormalities, LV systolic function (Simpson's method) and examination of any associated valvular lesions [9].

Conventional echo-Doppler using continuous wave Doppler was performed first to assess transmitral velocities to ensure that maximal velocities were obtained at 1–3 mm, sample volume was then placed between mitral leaflet tips during diastole to record velocity profile [10]. Pulsed wave Doppler echocardiography was used for mitral inflow assessment and measurement of peak early diastolic filling velocity (*E* vel) (normal range: 72±14 m/s), peak late diastolic filling velocity (*A* vel) (normal range: 40±10 m/s) [11] the ratio between the *E* velocity and *A* velocity (*E*/*A* ratio) [12] (normal range: 1.5±0.40) and deceleration time of early mitral flow (normal range: 138–194 m/s).

TDI was activated and images were obtained from the apical four and apical two chamber views. For image acquisition; three-cardiac cycles were taken in each view with the patient holding breath. All images were digitally stored for offline analysis (EchoPAC. GE version 110-1-2).

Offline analysis of the digitally stored loops was done by trace profile displacement through placing the TDI

sample volume at the four mitral annular sites (septal and lateral annular sites from the apical four chamber view and anterior and inferior annular sites from the apical two chamber view) to obtain: peak systolic myocardial velocity, early diastolic velocity (Em velocity), late diastolic myocardial velocity (Am velocity), and the average $E/\grave{E}$ (normal<8 m/s).

The average LV longitudinal strain was obtained by offline analysis of the stored images from the basal segments of the four walls (anterior, lateral, anterior, and inferior walls) of the LV.

Two-dimensional speckle tracking echocardiography:

Speckle tracking analysis performed on LV was obtained from the apical 2, 3, and 4 chambers views. The left ventricular global longitudinal strain (LVGLS), circumferential (global circumferential strain), and radial (global radial strain) strains were assessed using 2D-STE analysis with QRS onset as the reference point, applying a commercially available LV strain software package to the LV.

The left ventricular global circumferential strain (LVGCS) and left ventricular global radial strain (LVGRS) were obtained from the short axis view at the level of the papillary muscle. During analysis the endocardial border was manually traced at end systole and the width of the region of interest was adjusted to include the entire myocardium. The LV deformation parameters in each of 18 segments were assessed. Global strain assessed by averaging strain and strain rate of all segments.

Normal ranges for LV strain by 2D-STE: recent guidelines for normal GLS value are at least 21.7%, GCS is at least 22.1%, and GRS is at least 48.1% as reported by the American Society of Echocardiography and the European Association of Cardiovascular Imaging [13].

Assessment of left atrial by echocardiography

Conventional echocardiography was done to assess LA anteroposterior diameter, aortic root diameter (using M-mode), LA diameters (medial–lateral and superior–inferior diameters) and LA volumes (by the 2D study).

Assessment of left atrial function

Maximal LA volume, minimal LA volume, and precontractile LA volume were calculated. Indexed LA volume was calculated as LA volume divided by body surface area [14] the normal maximal LA volume is 25±9 ml/m^2; minimal LA volume is 11±4 ml/m^2; and precontractile LA volume is 15±5 ml/m^2 [15]. LA reservoir, conduit, and contractile functions were also calculated.

Tissue Doppler imaging

TDI was applied to assess the LA velocities by placing a small sample volume at the LA segment of interest (septal, lateral, anterior, and inferior) to measure: peak LA systolic myocardial velocity (LA-Sm vel), early diastolic velocity (LA Em velocity), and late diastolic myocardial velocity (LA Am velocity) then global LA function was assessed by averaging velocities of the four LA sites. The average LA longitudinal strain was measured at the end systole.

Two-dimensional speckle tracking echocardiography

LA longitudinal strain was assessed using 2D-STE analysis with QRS onset as the reference point, applying a commercially available LV strain software package to the LA (EchoPAC version 110.1.2). The region of interest was adjusted to include the LA myocardium in both four and two chamber views. Manual correction was performed to optimize tracking results if needed.

QRS-timed analysis to obtain peak atrial longitudinal strain (PALS), which is the first positive peak measured at the end of the reservoir phase; and the peak atrial contraction strain (PACS) measured just before the start of the active atrial contractile phase, which is the second positive peak were calculated by averaging values observed in all LA segments (global PALS and PACS) [16]. The analysis of the LA strain curve was done using QRS onset as the reference point to measure:

(1) Peak atrial strain during ventricular systole measured just before mitral valve opening and it is surrogate of the reservoir function.
(2) Late peak strain just before the active atrial contractile phase begins, at the onset of the P wave on the ECG, surrogate of the contractile function.

The average LA strain was obtained after averaging the six segments in each view.

Statistical analysis of the data

Numerical variables were expressed as mean and SD, the following statistical tests were used for analysis of data by SPSS version 19 (IBM company, Armonk, New York, United States):

(1) Independent *t*-test: for testing statistical significant difference between means of the two groups in each classification.
(2) Pearson's correlation test with the determination of the correlation coefficient (*r*) to test a positive or negative relationship between two variables ($P<0.05$, statistically significant).

Results

This study was conducted on 30 (10 males and 20 females) patients with type I diabetes and low risk for CAD presented with chest pain, their mean age was 20.9±2.02 years and BMI was 25.7±4.5. The study also included 15 (five males and 10 females) healthy individual as a control group, their mean age was 23.8±3.3 years and BMI was 24.1±4.5. We found no statistically significant difference between the studied groups with respect to the BMI.

There were statistically significant differences between the two groups as regard fasting blood sugar, postprandial blood sugar, HbA1c, total cholesterol, low density lipoprotein (LDL), high density lipoprotein, and triglycerides levels, in contrast to high density lipoprotein cholesterol, erythrocyte sedimentation rate, uric acid, and serum creatinine levels where differences were not significant (Table 1).

Diabetes profile

The mean disease duration was 10±4 years, the mean insulin dose was 75.2±18.4 U, and the mean HbA1c level was 8.6±1.7% for the diabetic group with significant negative correlation between HbA1c level and PALS ($r=-0.390$, $P< 0.05$), also there was a significant negative correlation between LDL cholesterol level and LVGLS ($r=-0.373$, $P< 0.05$).

Functional capacity parameters

There were no statistically significant differences between the two groups regarding the functional capacity evaluated by either DASI or treadmill scores as shown in Table 2.

Echocardiographic data

Conventional echocardiography:

There were no statistically significant differences between the two groups regarding the conventional LV and LA echo-Doppler parameters as shown in Table 3.

Left ventricular function assessment

LV function assessed by TDI:

There was statistically significant decrease in the average S wave velocity denoting impairment of LV systolic function in the diabetic group in comparison to the control group ($P<0.05$). A highly significant difference between the two groups was found when assessing the diastolic function ($P<0.001$), taking into consideration that diastolic dysfunction affected about 60% of the diabetic group (Table 4).

LV function assessed by 2D-STE:

LVGLS was significantly impaired in the diabetic group ($P< 0.001$), also the strain assessed by TDI is significantly lower in the diabetic group ($P< 0.05$). However, LVGCS and LVGRS showed no statistically significant differences between the two groups although being lower in diabetics (Table 4 and Fig. 1).

Prevalence of subclinical LV dysfunction in the diabetic group:

In this study impairment of both systolic and diastolic functions were found in 60% of examined patients (all diabetic patients with diastolic dysfunction had systolic dysfunction). In contrast, isolated systolic dysfunction

Table 1 Shows a comparison between the two groups with respect to the mean laboratory values

Variables	Control (mean±SD)	Patient (mean±SD)	*P* value
FBS (mg/dl)	83.1±7.9	165.3±59.2	0.0001
PPBS (mg/dl)	102.6±12.5	190.2±54	0.0001
HbA1c (%)	5.8±0.4	8.6±1.7	0.0001
Total cholesterol (mg/dl)	124.9±10.3	157.3±25.1	0.0001
LDL (mg/dl)	58.7±7.2	91±20.7	0.0001
HDL (mg/dl)	48.2±4.6	46.4±2.8	0.11
TG (mg/dl)	82±13	77.3±26.4	0.52
Serum creatinine (mg/dl)	0.64±0.1	0.73±0.2	0.109
Uric acid (mg/dl)	5.0±0.9	4.8±0.7	0.421
ESR (mm/h)	20.5±4	19.3±5	0.423

ESR, erythrocyte sedimentation rate; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; PPBS, postprandial blood sugar; TG, triglycerides.

Table 2 Showing a comparison between the two groups with respect to the functional capacity parameters

Variables	Control group (mean±SD)	Diabetic group (mean±SD)	*P* value
DASI score	49±2.5	47.9±9.7	0.67
DASI METs	8.8±3.12	8.6±1.2	0.76
Treadmill METs	11.9±1.4	12.3±2.5	0.57

DASI, Duke Activity Status Index; METs, metabolic equivalents.

Table 3 Showing the comparison between the study groups with respect to the left ventricular and left atrial conventional echo-Doppler parameters

Variables	Control group (mean±SD)	Diabetic group (mean±SD)	*P* value
EF M-mode (%)	68.5±3.2	70.8±6.8	0.22
EF 2-D (Simpson's method)	64.6±2.8	62.3±4.5	0.078
FS (%)	37.7±2.4	40.1±5.7	0.13
IVSd (mm)	8.3±1.1	8.4±2.3	0.87
LVPWd (mm)	8.8±1.1	7.9±2.4	0.17
LVEDD M-mode (mm)	43.3±3.8	44.7±7.8	0.52
LVESD M-mode (mm)	27.7±3.02	25.6±4.6	0.12
LA M-mode (mm)	32.2±3.1	29±4.2	**0.012**
MV *E* wave velocity (cm/s)	0.88±0.1	0.8±0.14	0.055
MV *A* wave velocity (cm/s)	0.58±0.13	0.6±0.12	0.61
MV *E*/*A* ratio	1.6±0.25	1.4±0.5	0.15

E/*A*, peak early diastolic velocity/peak late diastolic velocity; EF, ejection fraction; FS, fraction shortening; IVSd, interventricular septal diameter; LA, left atrium; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; LVPWd, left ventricular posterior wall diameter; MV, mitral valve.

was detected in 33% of the patients and only 7% of the patients had normal LV function (Fig. 2), which may indicate affection of the systolic function in the diabetic patients before the diastolic function.

Left atrial function assessment

LA volume parameters by 2D echo-Doppler:

The study showed a highly significant difference between the studied groups as regarding LA volumes ($P< 0.001$) for the three LA-indexed volumes. The mean values of LA volume parameters of the studied groups are shown in Table 5.

LA tissue Doppler parameters:

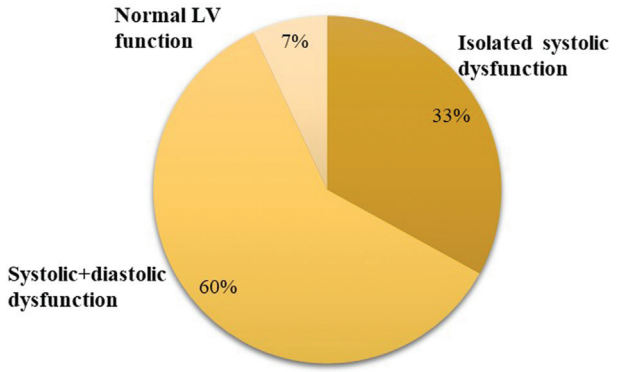
With respect to the LA TDI parameters, there was a statistically significant decrease in average Sa ($P< 0.05$). Moreover, there was a highly significant decrease in the average Ea wave ($P<0.001$) in the diabetic group. No significant difference was found

Table 4 Shows comparison between the two groups with respect to the left ventricular function assessed by tissue Doppler imaging and speckle tracking echocardiography

Variables	Control group (mean±SD)	Diabetic group (mean±SD)	*P* value
Avg S (cm/s)	11±1.1	6.6±1.1	**0.0001**
Avg E. (cm/s)	11.9±1.3	10.1±1.4	**0.0001**
E/*È* ratio	7.4±0.5	8.4±1.3	**0.006**
LVGLS%	–23.9±2.7	–15.8±6.8	**0.0001**
LVGCS%	–19±2.4	–16±9.9	**0.25**
LVGRS%	44.8±17.9	44.3±21.4	**0.94**
LVTD strain%	–23±2.7	–19.7±5.4	**0.031**

Avg, average (lateral, anterior, septal, and inferior walls); *E*, mitral inflow peak early velocity; *E*/*È*, peak early diastolic velocity/peak early mitral annular diastolic velocity; LVGCS, left ventricular global circumferential strain; LVGLS, left ventricular global longitudinal strain; LVGRS, left ventricular global radial strain; LVTD strain, left ventricular Tissue Doppler strain; S, peak systolic mitral velocity.

Figure 1



A pie chart comparing systolic and diastolic functions of the LV in the diabetic group. LV, left ventricle.

Table 5 Showing a comparison between the studied groups with respect to the left atrium parameters

Variables	Control group (mean±SD)	Diabetic group (mean±SD)	*P* value
LA maximal indexed volume (ml)	22.1±3.6	15±5.4	0.0001
LA minimal indexed volume (ml)	7.3±2.4	3.8±1.5	0.0001
LA precontractile indexed volume (ml)	13.5±4.6	7.4±2.8	0.0001
Sa avg. (cm/s)	6.2±0.6	5.6±1	0.039
Ea avg. (cm/s)	–9.8±1.5	–7±1.5	< **0.001**
Aa avg. (cm/s)	–5.3±1	–5.3±1.5	1
Avg PALS%	42.3±3.9	34.40±12.9	**0.026**
Avg PACS%	12.8±2.6	11.34±4.6	0.26
LATD strain%	41±7	28±12.8	< **0.001**

Aa, late atrial diastolic velocity; Avg, average; Ea, early atrial diastolic velocity; LA, left atrial; PACS, peak atrial contraction strain; PALS, peak atrial longitudinal strain; Sa, early atrial systolic velocity; TD-strain, Tissue Doppler strain.

between the two groups as regard the average Aa wave as shown in Table 5.

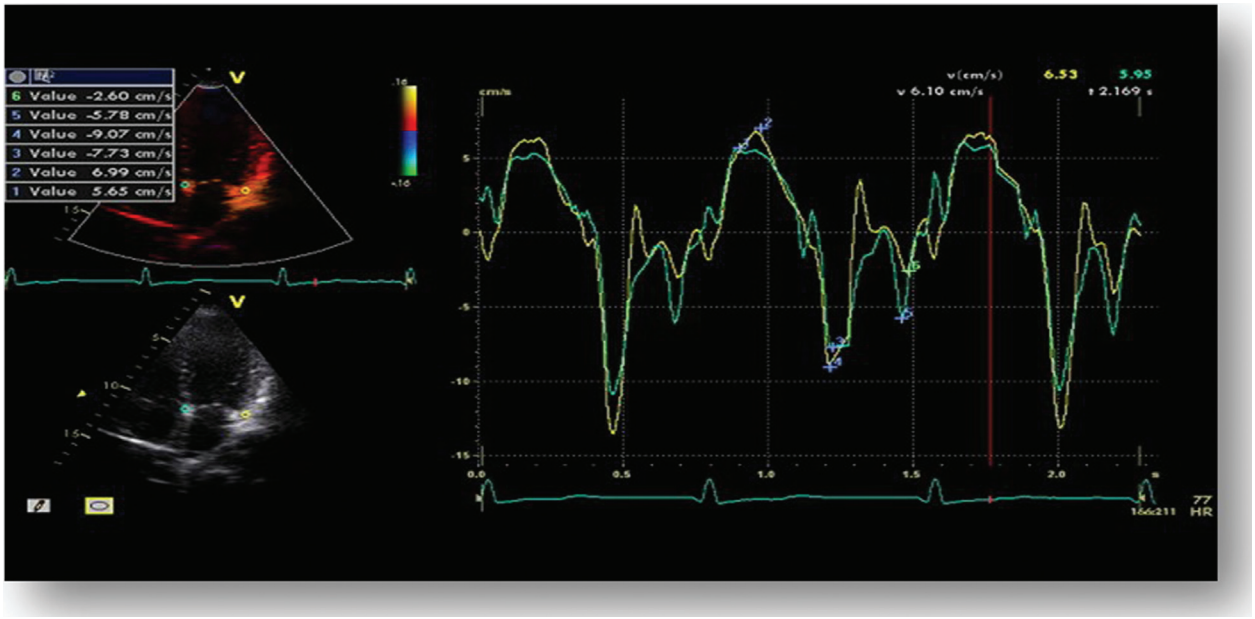
LA strain study:

There was significant decrease in LA strain in the diabetic group assessed by TDI study (41±7 in the control group vs. 28±12.8 in the diabetic group) and 2D-STE (average LA PALS 42.3±3.9 in the control group vs. 34.40±12.9 in the diabetic group), *P* value less than 0.05 for both, but there was no significant difference between the two groups as regard average LA PACS as shown in Figs 3–5 and Table 5 although being lower in the diabetic group.

Left ventricular function and peak atrial longitudinal strain

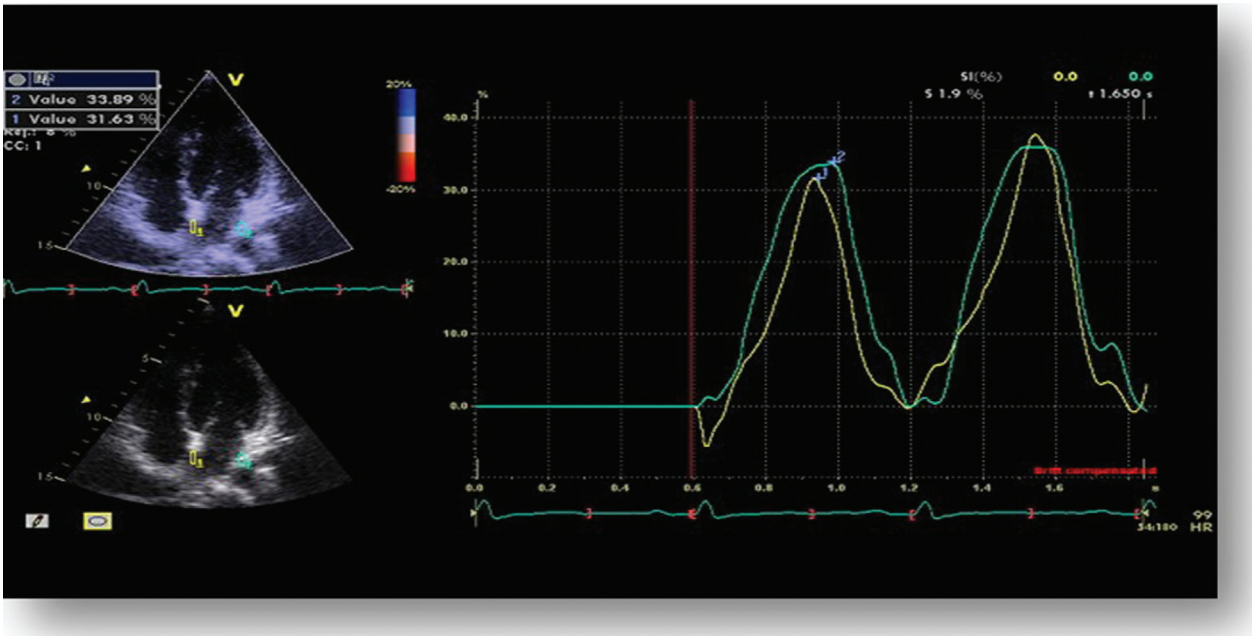
As we mentioned; 60% of the diabetic group showed impaired diastolic function as indicated by the elevated *E*/*È* ratio of 8, among them 83% showed impaired LA strain measured by 2D-STE evidenced as reduced

Figure 2



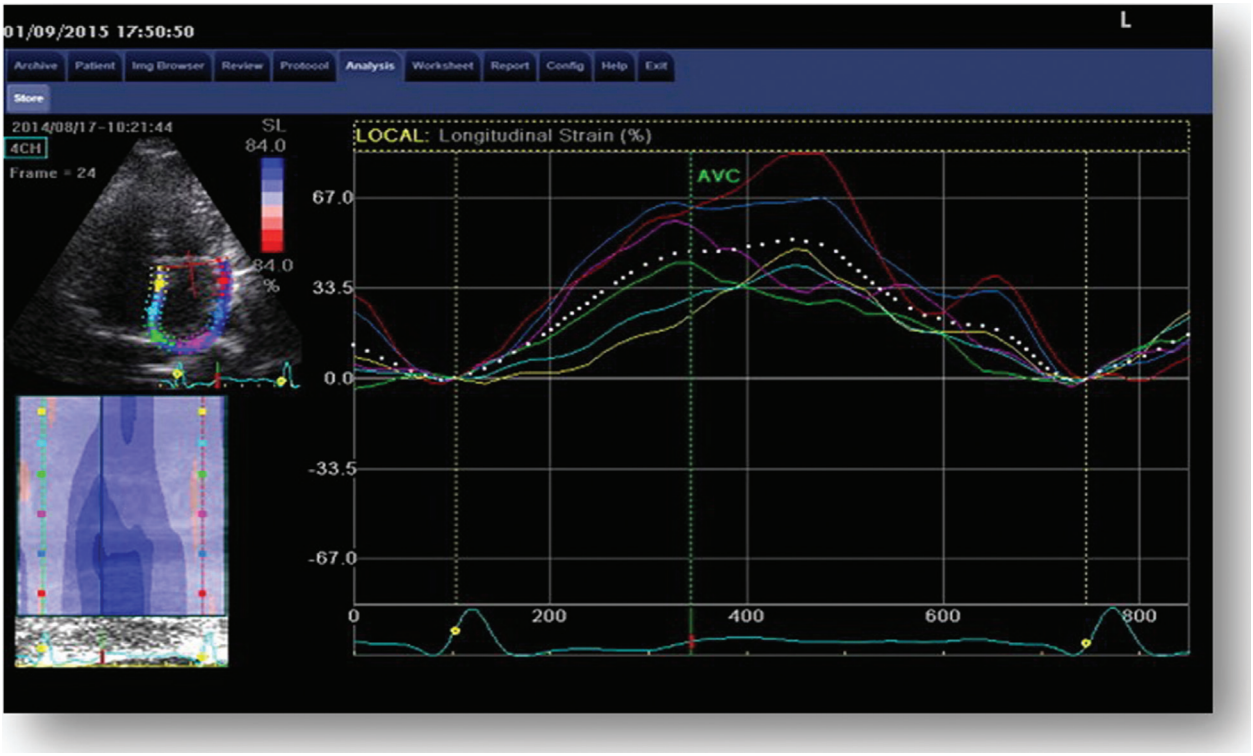
Colour Tissue Doppler Imaging for assessment of LV function at septal and lateral. LV, left ventricular.

Figure 3



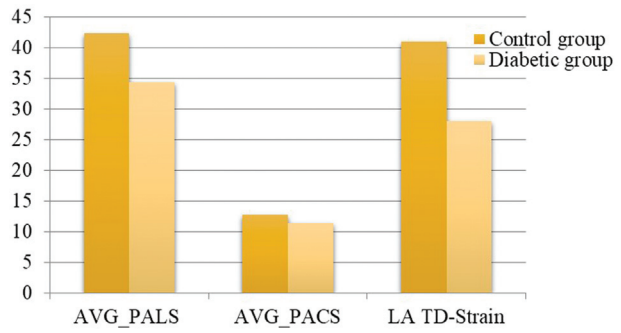
LA strain by TDI from apical four chamber view (patient no. 3). LA, left atrial; TDI, tissue Doppler imaging.

Figure 4



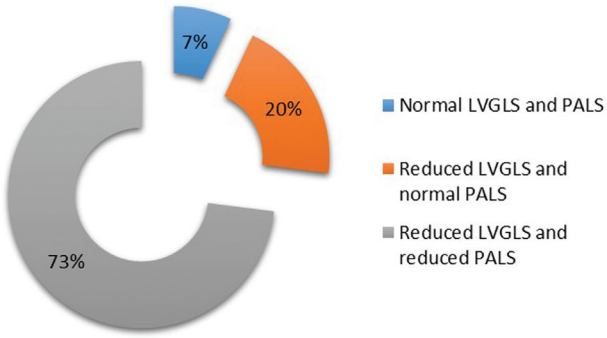
LA strain by 2D-STE from apical four chamber view (patient no. 3). 2D-STE, two-dimensional speckle tracking echocardiography; LA, left atrial.

Figure 5



A bar chart showed a comparison between the two groups regarding the LA strain by TDI and 2D-STE. 2D-STE, two-dimensional speckle tracking echocardiography; LA, left atrial; TDI, tissue Doppler imaging.

Figure 6



A pie chart showing the relation between PALS and LVGLS. LVGLS, left ventricular global longitudinal strain; PALS, peak atrial longitudinal strain.

PALS and only 17% had normal PALS. Also about 93% of the diabetic group had reduced LVGLS, 21% of them had preserved PALS, and 79% had impaired PALS (Fig. 6). A strong negative correlation was also found between PALS and LVGLS (r=–0.55, P<0.001).

Discussion

Myocardial involvement in type 2 diabetes mellitus (T2DM) has been proved as subclinical LV and right ventricular systolic dysfunction [17], but T1DM-induced DCM is a different entity as it relies on different pathophysiological mechanisms [18] and rarely coexists with hypertension and obesity, therefore; DCM in T1DM needs individual assessment [19].

Our result was concordant with Boyer *et al.* [20] 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% patients with diastolic dysfunction.

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 the early detectable parameter for DCM [20].

In this study, a statistically significant reduction in the LV TDI-derived strain was found (19.7±5.4% in the diabetic group vs. 23±2.7% in the control group, $P< 0.05$), also STE-derived LV strain was lower in the diabetic group, especially LVGLS, which showed a highly significant difference (15.8±6.8% in diabetic group vs. 23.9±2.7% in the control group) while the conventional echo revealed preserved EF. There was also reduction in both LVGCS (16±9.9% for diabetics vs. 19±2.4% for control) and LVGRS (44.3±21.4% for diabetics vs. 44.8±17.9% for control) but differences were not significant statistically. Comparable results were reported by Jędrzejewska *et al.* [21] who studied T1DM patients and found that LVGLS was 20.3 ±2.0% in diabetics versus 22.2±1.8% in the control group ($P<0.001$), LVGCS 22.1±2.5% in diabetics versus 22.2±2.4% in the control group ($P<0.05$), and LVGRS 47.1±10.8% in diabetics versus 50.9±11.5% in the control group with statistically insignificant difference.

Now it is well known that hyperglycemia contributes to cardiac remodeling as it induces metabolic disturbances that cause oxidative damage and deregulated cytokine signaling that results in cellular injury, impairment of cell–cell coupling, and apoptosis of myocardial cells. These events in turn activate collagen deposition and remodeling of the extracellular matrix. The cumulative result is the stiffening of cardiac tissues that impairs normal contractile functions. Therefore, structural abnormalities in the LV (such as interstitial and perivascular fibrosis) are common hallmarks that are attributed to DCM [22].

Some studies explained pathophysiological causes of LV longitudinal dysfunction in DM patients as microvasculopathy, myocardial hypertrophy, and cardiac fibrosis. The transforming growth factor beta, aberrant differentiation of fibroblast progenitor cells due to hyperinsulinemia and dysregulation of extracellular matrix due to hyperglycemia are also recognized as causes of not only renal but also cardiac fibrotic mechanism [23].

Our results are also concordant with Ernande *et al.* [24] 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 as the first marker of a preclinical form of DCM.

In our study, the only factor that showed a significant correlation with LVGLS was LDL cholesterol levels. Similar result was proved by Jędrzejewska *et al.* that highlights the importance of tight cholesterol control in this group of patients.

The relationship of LDL with LV systolic function may be explained by several mechanisms, one of them is the direct influence of hypercholesterolemia on cardiomyocytes that occurred in the absence of coronary atherosclerosis. An experimental study demonstrated that hypercholesterolemia reduces the level of connexin 43 protein, which is the main gap junctions component, decreases myocardial conduction velocity, and subsequently impairs the ventricular contractile function [25].

Interestingly, we found that PALS had a strong negative correlation with LVGLS and a strong positive correlation with LVGRS, which indicates the association between LA and LV strains.

This result was consistent with Mondillo *et al.* [26] found that PALS was lower in patients with hypertension (29.06±6.5%) and in patients with diabetes (24.76±6.4%) than in controls (39.66±7.8%) and was further depressed in patients with both diabetes and hypertension (18.36±5.0%) even in the presence of normal LA size, and so changes in LA strain precedes the 2D change in LA parameters.

Cameli *et al.* [27] 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.* [28] revealed that longitudinal strain in all six segments of the LA is lower in the diabetic patients compared to the controls.

Limitations

The study was applied on a relatively small number of patients because of the challenging selection of patients in absence of comorbidities of cardiac history.

ECG stress test was done to exclude CAD although the reference method is coronary angiography, which was not performed because of ethical reasons and lack of indication.

Conclusion

In asymptomatic patients with T1DM; LV diastolic function measured by TDI as well as global longitudinal systolic LV function measured by 2D-STE and TDI; were impaired in comparison to normal participants. Impaired LV global longitudinal strain is an early marker for detection of DCM in young adults with T1DM even before affection of diastolic function. Also LA systolic function was significantly impaired in diabetic patients and was strongly related to LVGLS. Tight glycemic control and LDL cholesterol adjustment could alter the natural history in those patients and hinder or at least delay the development of DCM.

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Conflicts of interest

There are no conflicts of interest.

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