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Original Article

Detection of occult right ventricular dysfunction in young Egyptians with type 1 diabetes mellitus by two-dimensional speckle tracking echocardiography

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ABSTRACT

Background: Type 1 diabetes mellitus (T1DM) is a common chronic disorder of childhood and adolescence. T1DM induced cardiomyopathy has a different entity than T2DM as it relies on different pathophysiological mechanisms, and rarely coexists with hypertension and obesity. Evaluation of right ventricular (RV) function in diabetic patients has been neglected despite the important contribution of RV to the overall cardiac function that affects the course and prognosis of diabetic cardiomyopathy (DCM).
Objective: To assess RV myocardial performance in asymptomatic T1DM using speckle tracking and standard echo parameters and correlate it with functional capacity using treadmill stress test.
Patients and methods: Thirty-nine patients with TIDM (Group 1, mean age 18.2 ± 1.7y, BMI = 26.2 ± 3.9kg/m^2), without cardiac problems and 15 apparently healthy matched subjects as a control group (Group 2, mean age 18.8 ± 2.3 y, BMI = 22.8 ± 3.3kg/m^2) were enrolled. RV function was evaluated using conventional, tissue Doppler and 2D speckle tracking echocardiography (2D-STE). The peak RV global longitudinal strain (RV-GLS) was obtained. Functional capacity was assessed by treadmill exercise test and estimated in metabolic equivalent (METs).
Results: In this study; the diabetic group showed statistically highly significant decrease in the average RV-GLS (−14.0 ± 6.9 in group 1 vs. −22.7 ± 2.5 in group 2, $P < 0.001$), significant decrease in RV S velocity (9.5 ± 2.2 in group 1 vs. 11.5 ± 1.8 in group 2, $P < 0.05$), significantly reduced E/A ratio (1.0 ± 0.2 in group 1 vs. 1.1 ± 0.1 in group 2, $P < 0.05$), and highly significant increased E/Em ratio (7.9 ± 3.2 in group 1 vs. 5.2 ± 0.7 in group 2, $P < 0.001$). We did not found any significant differences between the two groups regarding the other echocardiographic or functional capacity parameters.
Conclusion: In asymptomatic patients with T1DM, in addition to RV diastolic dysfunction, early (subclinical) RV systolic dysfunction is preferentially observed with normal RV and left ventricular (LV) ejection fraction (EF). 2D-STE has the ability to detect subclinical RV systolic dysfunction.

1. Introduction

Diabetes mellitus (DM) may lead to diabetic cardiomyopathy (DCM) defined as myocardial dysfunction independent of coronary artery disease (CAD) and hypertension.[1] Type 1 diabetes mellitus (T1DM) is ranging among the most common chronic disorders of childhood and adolescence.[2] Early detection of diabetic heart disease is of paramount importance, because timely life-style modifications and medical interventions could prevent or delay the subsequent development of heart failure.[3,4] Right ventricular (RV) dysfunction has been recognized to be clinically and prognostically significant in various pathological settings, such as heart failure, which may be expected also in diabetes.[5]

Most of the previous studies regarding myocardial dysfunction in diabetic patients were dedicated to the left ventricle (LV), ignoring the role of the right side, which has an important contribution to the overall cardiac function, affecting both the course and prognosis in patients with DCM.[6] The assessment of RV function remains difficult, because of its complex anatomy, the non-uniform contraction and the retrosternal position.[7] So limited data are available regarding RV involvement in T1DM.[8]

Echocardiography can sufficiently assess RV structures and functions and predict the prognosis in presence of pulmonary

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hypertension, especially with the use of modern imaging techniques.[9] Strain/strain rate imaging provides extensive information about regional myocardial function which may be applicable to the RV.[10] Recent development of speckle tracking echocardiography (STE) can provide quantitative diagnostic method for the assessment of myocardial deformation[11] and feature promising inter- and intraobserver reproducibility.[12]

2. Objective

The aim of this work was to assess RV myocardial performance in the course of asymptomatic T1DM using STE, and standard echo parameters and to correlate the RV function with functional capacity using treadmill stress test in Egyptian young adolescents.

3. Patients and methods

3.1. Study cohort

This study was conducted on 39 patients with TIDM (Group 1, mean age 18.2 ± 1.7y, BMI = 26.2 ± 3.9kg/m^2), with no history of cardiac disease and 15 apparently healthy subjects matched for age and BMI as a control group (Group 2, mean age 18.8 ± 2.3 y, BMI = 22.8 ± 3.3kg/m^2) with low risk for CAD who presented to the endocrinology and pediatric out clinic at Al-Zahra university hospital (Cairo- Egypt) by chest pain and fulfilled the inclusion criteria during the period from October 2014 till September 2015, whom treadmill exercise electrocardiogram (ECG) was proved to be negative within 1 month of the study. All the patient and control groups accepted an oral consent, and the study was approved by FMG ethical committee.

Excluded from this study cases with history of documented cardiac disease (myocardial infarction [MI], episodes of ischemia, heart failure [HF]), inducible ischemia evaluated by exercise ECG or stress echocardiography performed within 1 year of the study, rheumatic heart disease, congenital heart disease, hypertension, arrhythmias, chronic pulmonary disease, smoking or ex-smoking.

3.2. Method

Detailed history, medical therapy, assessment of quality of life (using heart QOL (HQOL), Duke Activity Status Index (DASI)),[7] clinical examination, 12 lead ECG, and stress exercise ECG were done in all cases.

Baseline measurements of weight, height were recorded, and body mass index (BMI) was calculated according to Quetelet index: BMI = weight (kg)/height (m).[2]

DASI was translated into Arabic and included 12 questions; score was calculated at the end according to the formula

Functional capacity in METs = ((DASI score $\times$ 0.43)+9.6)/3.5.[13]

3.2.1. Laboratory investigations

We asked for fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycosylated hemoglobin (HbA1c),total serum cholesterol level (TC), serum triglycerides level (TG), low density lipoprotein level (LDL), high density lipoprotein level (HDL), complete blood picture (CBC), liver enzymes (alanine transferase, aspartate transferase), renal function (serum creatinine, urine analysis), inflammatory markers (erythrocyte sedimentation rate [ESR], C reactive protein) and uric acid for all the patients.

3.2.2. Trans-thoracic echocardiography

All examinations were performed by one physician to minimize interobserver variability. Conventional transthoracic echo-Doppler examination was performed for all patients in both supine and left lateral position using Vivid-7GE system with tissue Doppler imaging (TDI) capability. All cases were examined using multi frequency (2.5–3.5 MHz) matrix probe M3S with simultaneous ECG physio signal displayed with all recorded echo images and loops. For image acquisition, 3- cardiac cycles were taken in each view with the patient holding his breath. All images were digitally stored for off line analysis (EchoPAC.GE VERSION 110-1-2).All parameters were taken according to the American Society of Echocardiography standards and recommendations of the European Association of Cardiovascular Imaging.[14]

3.2.2.1. Assessment of the LV. LV assessment was done using 2-D guided M-mode echocardiography to assess LV end diastolic dimension (LVEDD), end systolic dimension (LVESD), Inter ventricular septal diameter (IVSD), posterior wall diameter (LVPWD), ejection fraction (EF%), and fractional shortening (FS).

2D-echocardiography was used for assessment of EF (Sympson's method),[14] segmental wall motion abnormalities and evaluation of any associated valvular lesions. Conventional echo-Doppler using continuous wave Doppler was performed first to assess transmitral velocities to ensure that maximal velocities were obtained at 1 mm–3 mm, sample volume was then placed between mitral leaflet tips during diastole to record velocity profile.[15] Pulsed wave Doppler echocardiography was used for mitral inflow assessment by measuring peak early diastolic filling velocity (E), normal range 72 ± 14 m/s, peak late diastolic filling velocity (A) normal range 40 ± 10 m/s,[16] the E/A ratio (normal range = 1.5 ± 0.40) and deceleration time of early mitral flow (normal range = 138–194 m/s).[17]

Tissue Doppler imaging (TDI) was activated and images were obtained from the apical four (4CH) and apical two chambers (2CH) views.

3.2.2.2. Assessment of the RV

3.2.2.2.1. Conventional and Doppler echocardiography. 2D echocardiography was used for measurement of RV end-diastolic diameters from parasternal long-axis (PLAX), parasternal short-axis (PSAX), and apical 4CH views. RV outflow tract (RVOT) was measured in PLAX (RVOTprox) and PSAX (RVOTdyst) views; RV basal diameter (RVD1), RV mid-cavity diameter (RVD2), and RV longitudinal dimension (RVD3) were measured in apical 4CH view.[18] Tricuspid plane systolic excursion (TAPSE) was obtained from apical 4CH view as the difference between end-diastolic and end-systolic positions of tricuspid annulus. RV fractional area change (FAC) was calculated as the RV area difference (diastolic–systolic) divided by RV end-diastolic area in apical 4CH view.[19]

Pulsed wave Doppler echocardiography was used for tricuspid inflow assessment and measurement of peak early diastolic filling velocity (Et vel) (normal range is 72 ± 14 m/s) and peak late diastolic filling velocity (At vel) (normal range is 40 ± 10 m/s).[16] The ratio between the E velocity and A velocity (E/A ratio) was obtained (normal range is 1.4 ± 0.30).[17]

Pulse-wave TDI was used to measure septal peak systolic velocity (S'spt), septal early diastolic velocity (E'spt), septal late diastolic (A'spt)velocity, lateral peak systolic velocity (S'lat),lateral early diastolic velocity (E'lat), lateral late diastolic velocity (A'lat) and the average E/È ratio (normal$<$ 6 m/s) in the apical 4CH view.

The average RV longitudinal strain was obtained by offline analysis of the stored images from the basal segments of the two walls (lateral, septal walls) of the RV.

3.2.2.2.2. Two dimensional speckle tracking echocardiography (2D-STE). For speckle tracking analysis of RV chambers, standard gray scale 2D images were acquired in the apical 4CH view, with a stable electrocardiographic recording, to measure global systolic RV myocardial strain. We applied a commercially available LV strain

software package to assess the RV strain through recording and averaging three consecutive heart cycles. RV endocardial surface of the RV septum and RV free wall were manually traced in apical 4CH view by a point and click approach using novel speckle-tracking software. An epicardial surface tracing was then automatically generated by the system that tracks the characteristic pattern of natural acoustic markers present in the myocardial wall ("speckles") of the RV from frame to frame throughout the cardiac cycle. Myocardial strain was then calculated by the change in position of the speckle pattern from the initial position. Peak systolic longitudinal strain was calculated by averaging the peak systolic values of the six segments. For myocardial strain; regional thickening or lengthening was expressed as a positive value and thinning or shortening as a negative value. Peak systolic longitudinal strain was calculated by averaging the peak systolic values of the six segments for myocardial strain.[20,21]

3.2.2.2.3. Normal ranges for RV strain by 2D –STE. Recent guidelines for normal GLS value is $\geq -20\%$, as reported by the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[14]

3.3. Statistical analysis

Numerical variable was expressed as mean and standard deviation (SD).The following statistical tests were used for analysis of data by SPSS version 19: Independent *t*-test was used for testing statistically significant difference between means of the two groups in each classification. Pearson's correlation test with the determination of the correlation coefficient (r) was used to test a positive or negative relationship between two variables. P value less than 0.05 was considered statistically significant.

4. Results

The current study was conducted on 39 patients, (13 males and 26 females) with T1DM, the disease duration was 9.6 ± 3.9, their mean age was 18.2 ± 1.7 years and BMI was 26.2 ± 3.9 kg/m^2 as group 1. The study also included 15 healthy individual (5 males and 10 females) as a control group, their mean age was 18.8 ± 2.3 years and their BMI was 22.8 ± 3.3 kg/m^2 as group 2. They all had low risk for CAD and presented with chest pain to the outpatient clinic.

In our study, there were statistically significant differences between the two groups as regard BMI (26.2 ± 3.9 vs 22.8 ± 3.3 kg/m^2, P=<0.05), FBS (170.8 ± 55.8 vs 81.1 ± 8.6 P=<0.01), PPBS (205.7 ± 61.1 vs 103 ± 9.9, P=<0.01),HbA1c (8.9 ± 1.7 vs 5.7 ± 0.4, P= <0.01), HDL (45.9 ± 6.2 vs 51.1 ± 5.9,P=<0.01), uric acid (4.8 ± 5.5 vs 0.9 ± 0.8,P=<0.01) and Hb levels (13 ± 1.3 vs 12.4 ± 0.5, P=<0.01), ESR (23.2 ± 6.1 vs 17.7 ± 3.9, P=<0.01), SBP (120.7 ± 7.4 vs 115 ± 74,P=<0.05), and DBP (78.7 ± 5.7 vs 74.7 ± 6.4, P=<0.05). Other parameters showed non-significant difference as shown in Table 1.

4.1. Functional capacity parameters

There were no statistically significant differences between the two groups regarding the functional capacity evaluated by either DASI or treadmill scores, but higher heart rate at rest was found in group 1 when compared to group 2 (96.1 ± 13.8 vs 80.1 ± 11.2 P=<0.01) as shown in Table 2.

4.2. Echocardiographic data

4.2.1. Conventional echocardiography

The two groups did not show any significant differences regarding the conventional LV, RV echo-Doppler parameters, both groups had normal LV and RV dimensions and function measured by M-mode and 2D echoes shown in Table 3.

Table 1
Demographic data and laboratory data in the studied groups.

Variable	Patients	Control	P value
Gender (male/female)	13/26	5/10	–
Age	18.2 ± 1.7	18.8 ± 2.3	NS
Insulin dose	77.3 ± 17.3	–	–
Disease duration	9.6 ± 3.9	–	–
BMI	26.2 ± 3.9	22.8 ± 3.3	<0.05
SBP	120.7 ± 7.4	115 ± 74	<0.05
DBP	78.7 ± 5.7	74.7 ± 6.4	<0.05
TC	156.2 ± 20.1	149.5 ± 25.8	NS
LDL	81.3 ± 24.1	77.8 ± 11.8	NS
HDL	45.9 ± 6.2	51.1 ± 5.9	<0.01
TG	82.8 ± 29.9	90.7 ± 12.6	NS
FBS	170.8 ± 55.8	81.1 ± 8.6	<0.01
PPBS	205.7 ± 61.1	103 ± 9.9	<0.01
HbA1c	8.9 ± 1.7	5.7 ± 0.4	<0.01
Hb	13 ± 1.3	12.4 ± 0.5	<0.01
Uric acid	4.8 ± 5.5	0.9 ± 0.8	<0.01
S.cr	0.9 ± 0.2	0.8 ± 0.2	NS
ESR	23.2 ± 6.1	17.7 ± 3.9	<0.01

Table 2
Functional capacity parameters in the studied groups.

Variable	Patients	Control	P value
RHR	96.1 ± 13.8	80.1 ± 11.2	<0.01
PHR	183.4 ± 29.2	179.7 ± 11.1	NS
METs	12.2 ± 2.3	11.9 ± 1.4	NS

4.2.2. RV function assessment

4.2.2.1. RV diastolic function assessed by Doppler and tissue Doppler-echo:-. We observed a statistically significant decrease in E/A ratio<1 (1.0 ± 0.2 in group 1 vs. 1.1 ± 0.1 in group 2) with P value < 0.05 in this study, also a highly significant increase in E/Em in group 1 (7.9 ± 3.2) compared to group 2 (5.2 ± 0.7) who had normal diastolic function (P value < 0.01) as shown in Table 4.

In group 1; 20.5% had normal diastolic function measured by both Doppler and tissue Doppler studies, 30.7% had impaired diastolic function by the two modalities and 13.9% had impaired diastolic function by Doppler (E/A < 1) while normal by TDI (E/Em<6.0). Interestingly; 35.9% of those who had normal E/A ratio; had impaired diastolic function indicated by increased E/Em ratio >6.0 m/s (Fig. 1)

Table 3
The conventional echocardiographic parameters for the studied groups.

Variable	Patients	Control	P value
LVSd	8.5 ± 1.8	8.3 ± 1.1	NS
LVPWd	8.2 ± 1.8	8.8 ± 1.1	NS
LVEF	69.2 ± 13.1	68.6 ± 2.6	NS
LVFS	39.3 ± 8.3	40.2 ± 4.6	NS
LVEDD	44.95 ± 6.5	43.5 ± 3.5	NS
LVESD	24.4 ± 4.6	23.4 ± 2.5	NS
EF	54.9 ± 4.3	54.9 ± 4.7	NS
AoD	25.3 ± 2.7	26.2 ± 2.3	NS
RVOT prox(cm)	25.4 ± 4.4	25.7 ± 3.4	NS
RVOT dist(cm)	18.4 ± 3.0	19.6 ± 2.2	NS
RVD1	32.7 ± 5.8	31.8 ± 6.0	NS
RVD2	26.4 ± 4.6	29.4 ± 6.7	NS
RVD3	68.2 ± 7.1	64.9 ± 6.2	NS
TAPSE	23.4 ± 4.1	23.8 ± 2.7	NS
RVEDD	17.3 ± 3.3	18.2 ± 3.9	NS
RVESD	9.8 ± 2.3	10.3 ± 2.2	NS
RV FAC	43.4 ± 6.7	43.1 ± 6.2	NS

Table 4
Doppler, and TDI for LV and RV in the studied groups.

Variable	Patients	Control	P value
Doppler			
RV A vel	76.2 ± 19.5	55.2 ± 15.1	<0.05
RV E vel	67.1 ± 15.8	62.0 ± 12.8	NS
RV E/A	1.0 ± 0.2	1.1 ± 0.1	<0.05
LV E vel	82.6 ± 11.1	87.2 ± 8.9	NS
LV A vel	62.2 ± 10.4	69.0 ± 11.7	NS
LV E/A	1.4 ± 0.1	1.3 ± 0.1	NS
TDI			
RV Smv	9.5 ± 2.2	11.5 ± 1.8	<0.01
RV Emv	−8.7 ± 4.5	−8.4 ± 8.1	NS
RV Amv	−8.0 ± 3.4	−5.5 ± 3.5	<0.05
E/Em ratio	7.9 ± 3.2	5.2 ± 0.7	< 0.01

Also; there were significant differences in group 1 as regard TAPSE, RVESD, RV E velocity, RV A velocity, TD A velocity, and RV Em velocity between patients who had normal diastolic function and those who had diastolic dysfunction by tissue Doppler as predefined (Table 5), but only TDA velocity was found to be the independent predictor by univariate analysis for RV diastolic dysfunction in young patients with T1DM [(OR = 0.887, at 95%CI: 0.806–0.977)P < 0.05]

4.2.2.2. RV systolic function assessed by 2D-STE and TDI. RV-GLS assessed by 2D-STE was significantly impaired in group1 compared to group 2 (−14.0 ± 6.9 vs. −22.7 ± 2.5, respectively) with P value <0.01,although RV systolic function by TDI showed a statistically significant decrease in average S wave velocity in the diabetic group when compared to control group (9.5 ± 2.2 vs 11.5 ± 1.8) with P value <0.01. On the other hand; the RV systolic function assessed by strain was normal with non-significant difference with a trend towards being lowering in group 1 than group 2 (−26.0 ± 17.1vs. −32.4 ± 8.2, respectively) (Table 6, Figs. 2 & 3)

4.2.2.3. Prevalence of subclinical RV dysfunction in the diabetic group. We found a strong positive correlation between RV-GLS and diastolic dysfunction measured by TDI; as about 62% of the diabetic patients had both; impaired systolic function measured by STE with decreased RV-GLS and diastolic dysfunction measured by TDI (E/Em ratio › 6.0) with P value <0.01as shown in Fig. 4.

BMI and RV E velocity were the only independent predictors for RV systolic dysfunction measured by STE [OR = 1.39, at 95% CI: 1.032–1.869 and OR = 1.07at 95% CI: 1.008-:1.146, respectively] with P value < 0.05. Interestingly; FBS was found to be significantly lower in patients with normal RV-GLS (177.7 ± 56.4 in patients with decreased RV-GLS vs. 112 ± 35.3 in patients with normal RV-GLS, P value < 0.01) which makes it a valuable modifiable additional factor related to RV-GLS as shown in Fig. 5.

Table 5
Factors that are significantly related to RV diastolic dysfunction in the diabetic group assessed by TDI.

Variable	E/Em>6.0	E/Em< 6.0	P value
TAPSE	24.4 ± 3.9	21.5 ± 3.8	<0.05
RVESD	10.4 ± 2.4	8.7 ± 1.8	<0.05
RV E velocity	74.2 ± 12.1	52.9 ± 12.6	<0.01
RV A velocity	72.6 ± 17.7	56.5 ± 19	<0.05
RV Em velocity	−7.1 ± 4.6	−11.8 ± 2	<0.01
TD A velocity	59.8 ± 10.05	67.1 ± 9.7	<0.05

Table 6
Comparison between the two groups as regards the RV function assessed by TDI and strain.

Variable	Patients	Control	P value
RV GLS	−14.0 ± 6.9	−22.7 ± 2.5	<0.01
RV Smv	9.5 ± 2.2	11.5 ± 1.8	<0.01
RV TDI strain	−26.0 ± 17.1	−32.4 ± 8.2	NS

5. Discussion

DM leads to increased cardiovascular mortality that is evident in all age groups, particularly in children and adolescents with T1DM. This group of patients may be in need for specific cardiovascular risk estimation models.[22]

It is well known that myocardial involvement in T2DM has been proved as subclinical LV and RV systolic dysfunction.[23,24] Hence type 1 DCM is a different entity as it relies on different pathophysiological mechanisms,[25] and rarely coexists with hypertension and obesity, factors that independently influence cardiac function, therefore; type 1 DCM needs individual assessment.[26]

The RV dysfunction is associated with a worse prognosis in a variety of cardiovascular diseases, including acute MI and HF. Although most investigators studied the effect of diabetes on the functionality and geometry of the LV, there are also scanty data indicating that diabetes is equally detrimental for the RV,[27]attributed to the complex anatomy, non-uniform contraction and its retrosternal position. Strain/strain rate imaging provides extensive information about regional myocardial function which may be

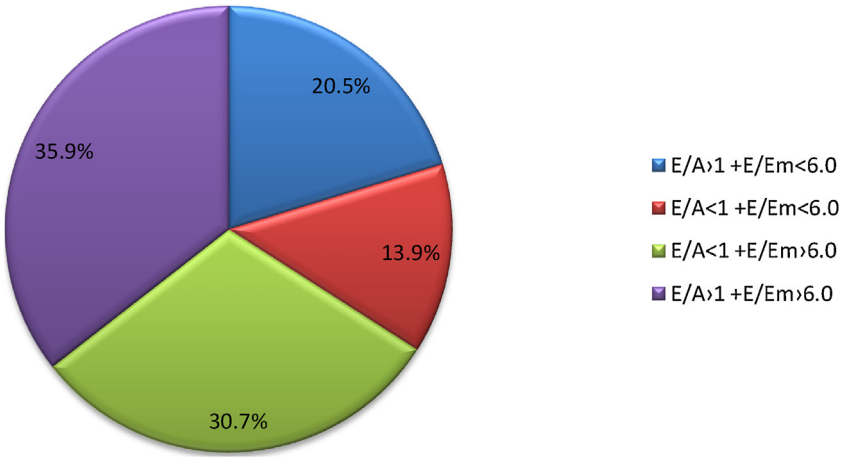

Fig. 1. Representing relation between diastolic function in group 1 assessed by Doppler and tissue Doppler echo.

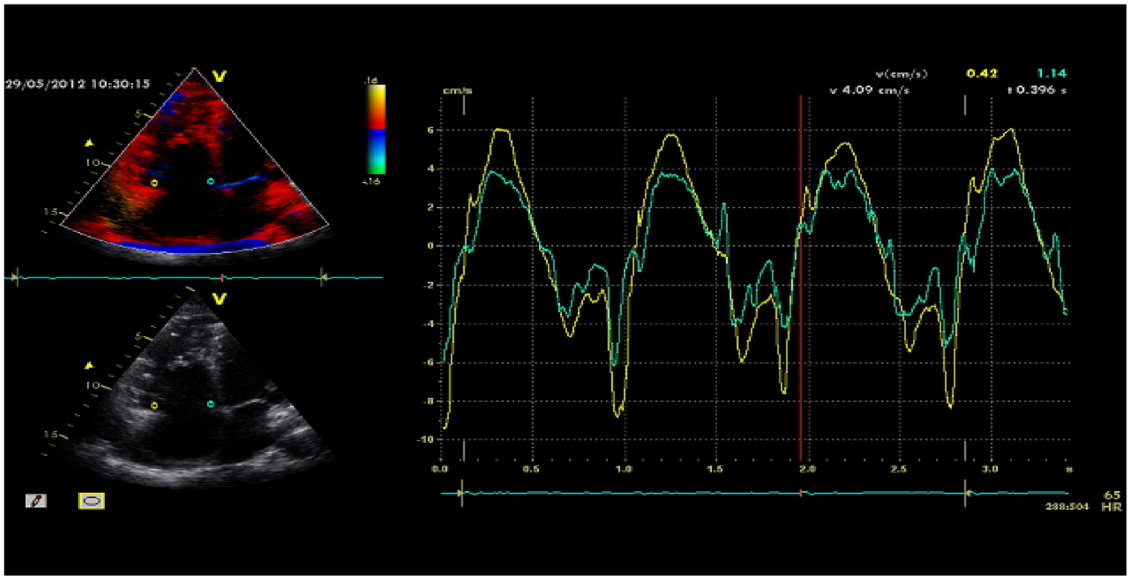

Fig. 2. Colour Tissue Doppler Imaging for assessment of RV function at septal &lateral Tricuspid annulus from the apical 4Ch view (patient No 16).

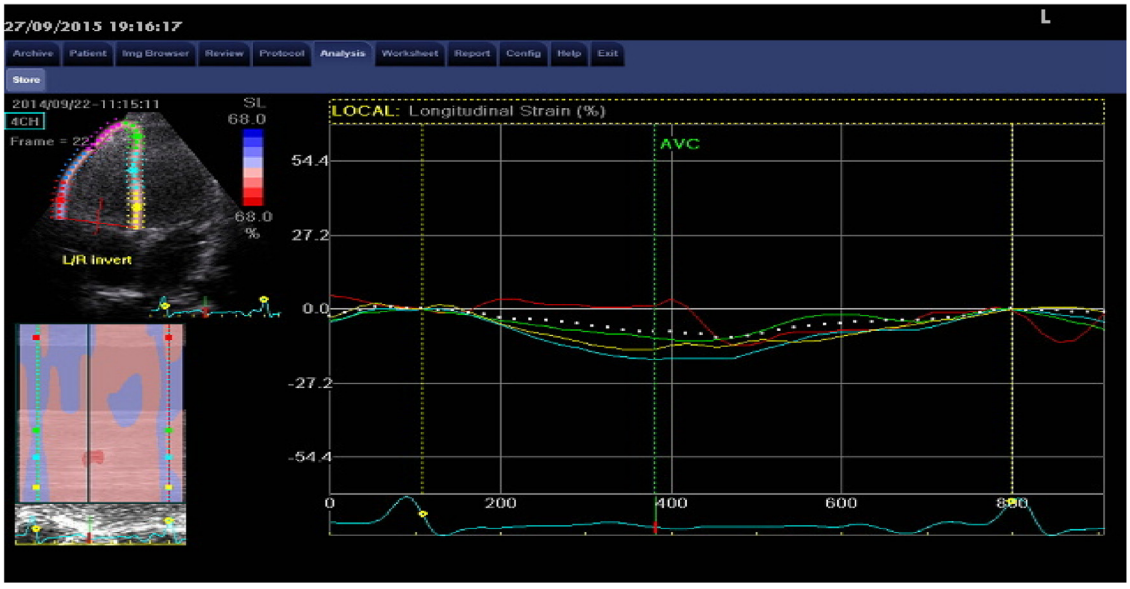

Fig. 3. RV strain by2D **STE** from apical 4Ch view shows impaired RV-GLS in patient No 3.

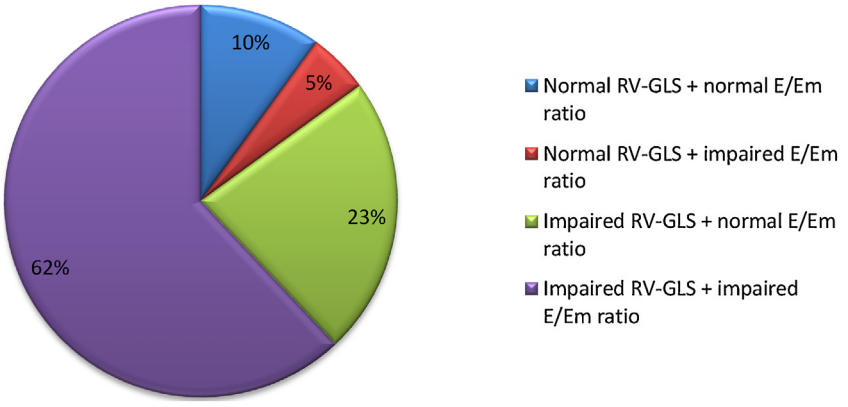

Fig. 4. The relation between RV-GLS and RV diastolic function assessed by TDI.

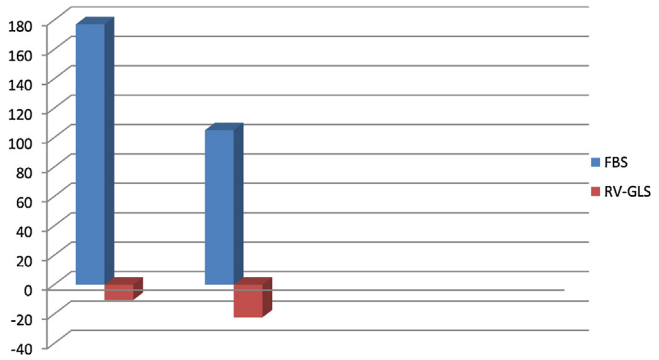

Fig. 5. Relation between FBS and RV systolic function within the diabetic group.

applicable to the right ventricle.[28] We can assume that in patients with DCM the RV is influenced by both the LV, via a biventricular interaction mechanism, and the diabetes mellitus. Interestingly, it has been demonstrated that in diabetic patients both the systolic and diastolic functions of the RV are affected.[29]

Al-Biltagi et al found a significant increases in BMI, random blood sugar, HbA1c, and resistin level (an adipocytokine hormone that regulates insulin sensitivity and exerts pro-inflammatory activities) in the diabetic children compared with the control group.[30] In addition to these parameters, in our study we found HDL, uric acid, ESR, SBP, DBP, and Hb levels significantly differs in diabetics than healthy subjects.

In the present study, we could not find any significant correlations between the duration of diabetes and the severity of RV dysfunction, which is consistent with the findings of Kosmala et al[31] and Soliman et al.[32]

Also, we could not find any discrepancy in functional capacity measured by exercise stress ECG test between the studied groups, Comparable results were reported by Stettler et al who found that in subjects with type 1 diabetes, exercise capacity is not influenced by hyperglycemia.[33] While Silmara et al reported comparable results with ours as they found in their study on 53 adolescents with type 1 diabetes that they have reduced exercise capacity and display alterations in cardiac function compared with nondiabetic control subjects, associated with reduced stroke volume during exercise.[34]

We observed a statistically significant decrease in E/A ratio <1 between the studied groups (1.0 ± 0.2 in diabetic group vs. 1.1 ± 0.1 in control group) in addition to a highly significant increase in E/Em in diabetic group (7.9 ± 3.2) compared to the control group (5.2 ± 0.7)which are concordant with Soliman et al who revealed in their study on 45 diabetic children a significant differences in right ventricular diastolic filling patterns between patients with type 1 diabetes and healthy subjects (diabetics have had higher A wave velocity and lower E/A ratio compared with controls) (0.48 ± 0.13 vs 0.38 ± 0.12, p value 0.004, 1.37 ± 0.24 vs 1.73 ± 0.41, p value 0.001 respectively).[32]

Also our study is concordant with Karamitsos et al, as conventional Doppler in their study revealed significant differences in RV diastolic filling patterns, that is in agreement with our results that showed impairment of RV A velocity (76.2 ± 19.5 in diabetic group vs. 55.2 ± 15.1 in control group) and RV E/A ratio (1.0 ± 0.2 in diabetic group vs. 1.1 ± 0.1 in control group) with significant difference.[35]

Al-Beltagi et al in 2015 agreed with our results and confirmed the presence of subclinical RV systolic and diastolic dysfunction in 30 children with T1DM, as they found significant differences in the mean value of TAPSE, pulmonary artery pressure, RV GLS), MPI, and RV EF between the studied groups. Moreover; they confirmed a positive correlation between resistin level and RV dysfunction among these patients and significant negative correlation of resistin with both TAPSE and RV GLS values. Yet, no significant differences in E/A ratio and S value were observed between the two groups.[30]

According to our study, we found that BMI and RV E velocity were independent predictors for RV dysfunction in patients with T1DM (OR = 1.39, at 95% CI: 1.032–1.869 and OR = 1.07 at 95% CI: 1.008-:1.146 respectively), the results that were concordant with Ilona et al who found that in patients with T1DM; RVGLS correlated with BMI (r = 20.33, P = 0.019) and LVGLS (r = 0.38, P = 0.006), but they didn't found any relationship between RVGLS and age, diabetes duration, serum lipids, HbA1c, TAPSE, or S't.[24]

STE is novel technique that analyzes motion by tracking natural acoustic reflections and interference patterns within an ultrasonic window. This technique resolved angle-independent 2D sequences of tissue motion and deformation. STE showed that our patients had abnormal systolic function presented by significant lower RVGLS compared with the controls. These results are matched with previous studies that demonstrated the ability of TDI and STE to detect presence of subclinical diastolic or systolic dysfunction in asymptomatic diabetic patients.[36]

DM is associated with subclinical RV systolic and diastolic dysfunction, regardless of coexisting hypertension. Similar results were reported by Kosmala et al, who detected impairment of both diastolic and systolic functions in diabetic patients compared to healthy subjects assessed by STE as decreased strain and strain rate values.[31]

With the development of new echocardiographic techniques; we could detect the subclinical affection of the myocardium in the course of diabetic pathology. 2D-STE is a new emerging promising echocardiographic modality that could overcome a lot of the tissue Doppler limitations. We were made sure that all our patients had a normal LV and RV function assessed by conventional echocardiography. With the application of the STE we found that most of our patients (85%) had impaired systolic function indicated by reduced RVGLS that was in concordant with Ilona et al who did not find significant difference between young patients with T1DM & healthy controls as regards RVD and TAPSE, however when the same patients were examined by 2D-STE; RV systolic dysfunction in diabetic patients was identified (indicated by reduction in RV global and segmental "basal, mid and apical" longitudinal strain).[24]

5.1. Clinical implication

The study results show that the RV functions in T1DM patients may be altered even in the absence of clinical symptoms and CAD. This indicates that echocardiographic assessment with 2D-STE should be considered in T1DM to detect subclinical RV dysfunctions. The correlation between RV-GLS and BMI in addition to the significantly lower FBS level that could be seen in the T1DM patients with normal RV-GLS may highlight the role of blood sugar control, diet and lifestyle modification in delaying the development of RV dysfunction in this sector of patients.

5.2. Limitations

The study was applied on a relatively small number of patients because the challenging selection of patients in absence of co-morbidities of cardiac history. ECG stress test done to exclude CAD while the reference method is coronary angiography while was not performed because of ethical reasons and lake of indication.

6. Conclusion

Finally, we can conclude that children and adolescence with T1DM had combined subclinical RV systolic and diastolic

dysfunctions despite the apparently preserved cardiac function. We assume from our results that the RV systolic function might be affected by the pathology of diabetes mellitus even before the diastolic function that had beenassessed by TDI.

The authors declare that there are no potential conflicts of interest.

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