RESEARCH ARTICLE

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The role of Speckle Tracking Echocardiography and Three-dimensional Echocardiography in the Assessment of Left Ventricular Systolic Function in Type II Patients with diabetes with Negative Myocardial Perfusion Imaging in Correlation to Multi-gated Acquisition Scan

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Abstract

Background and Aim: Two-dimensional (2D) speckle tracking echocardiography (STE) has shown promising results being a recent technology to assess "myocardial performance" in cardiac patients. Three-dimensional echocardiography 3DE has been shown to be accurate in the assessment of left ventricular (LV) systolic function. The multigated acquisition (MUGA) scan provides a more accurate quantification of the ventricular ejection fraction To Assess the role of 2D-STE and 3DE in the assessment of LV systolic function in type II patients with diabetes with negative myocardial perfusion imaging in correlation with the MUGA scan.

Materials and Methods: The study included 30 patients with type 2 diabetes mellitus (T2DM) [Group 1, 25 (83%) female and 5 (16%) males with mean age 48.40 ± 7.44], their stress myocardial perfusion imaging was negative for coronary ischemia. The control group included 15 apparently healthy age and sex-matched subjects, [Group 2, 11 (73%) females and 4 (26%) males with mean age 50.20 ± 7.74], LV systolic function was evaluated using conventional, TDI, 2D-STE (LV-GLS), 3-DE and MUGA scan.

Results: The group with diabetes showed statistically highly significant reduction in LV-GLS (-18.07 ± 2.73 in group 1 vs -21.24 ± 1.29 in group 2, $P < 0.001$), and in 3D LVEF (52.30 ± 5.28 in Group 1 vs 58.93 ± 4.69 in Group 2, $P < 0.001$). We found an agreement between three modalities (speckle tracking, 3DE and MUGA scan) by 33% in 10 patients [3 patients (10%) had impaired LV functions and 7 patients (23%) had preserved LV functions]. There was an agreement between speckle tracking and 3D echo by 76.6% in 23 patients [16 patients (53.3%) had impaired LV functions and 7 patients (23.3%) had preserved LV functions].

Conclusion: T2DM is associated with subclinical LV systolic dysfunction that can be assessed by different noninvasive modalities (speckle tracking, 3DE and the MUGA scan). 2D speckle tracking and 3DE might have an edge compared with MUGA scan in the detection of subclinical LV systolic dysfunction.

Keywords: DM, 2D-STE, 3D Echo, MPI, MUGA scan

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INTRODUCTION

Early detection and proper treatment of diabetic heart disease are important because focusing on early lifestyle interventions and proper updated guideline - directed medical therapy could prevent or delay the complications including heart failure, with the drawbacks and burdens to the national healthcare systems.

Two-dimensional (2D) speckle tracking echocardiography (STE) has the advantage of being accurate, reproducible, and angle independent, and it enables a complete assessment of regional and global cardiac function.

2D STE has shown promising results being a recent technology to assess "myocardial performance" in cardiac patients.[1]

Real time 3DE has the advantages of being a relatively low cost, available, and offering the option of live 3D imaging acquisition. It has shown a particular edge by being more accurate for the assessment of LV-volumes and functions.[2]

Myocardial perfusion imaging (MPI) single photon emission computed tomography has been found to be a very helpful diagnostic and prognostic tool for the evaluation of subtle LV systolic dysfunction in asymptomatic patients with diabetes without known coronary artery disease.[3]

The MUGA scan was first introduced in the early 1970s and since then has been one of the standard methods for measurement of the left ventricular ejection fraction (LVEF).[4]

Aim of the work

This research aimed to assessing the role of 2D-STE and three -dimensional 3DE in the assessment of LV systolic function in type 2 patients with diabetes with negative myocardial perfusion imaging for coronary ischemia in correlation to MUGA scan.

Patients

This study was conducted on 30 patients with type 2 diabetes presented to the cardiology clinic presenting with chest pain or dyspnea with negative stress myocardial perfusion imaging (MPI) for ischemic coronary artery disease (Group 1).

The control group (Group 2) included 15 healthy subjects, they were aged and sex matched.

Group 1 was further sub-classified in to 3 subgroups (A, B & C) according to their MUGA LVEF, LV-GLS, and 3D LVEF respectively.

All patients included in the study accepted oral and written consent, and the study was approved by the Ethical Committee of Al-Azhar University Faculty of Medicine for Girls, approval number 202209/543 (date: 28.09.2022).

Patients with documented ischemic heart disease, valvular heart disease or congenital heart disease, hypertension, arrhythmias, chronic pulmonary disease, and patients with associated co-morbidity were excluded from the study.

MATERIALS AND METHODS

All patients included in this study were subjected to through history taking and clinical examination.

Echocardiography

All patients underwent conventional transthoracic echocardiography in both the supine and left lateral positions using the Vivid-9GE system. All cases were examined using multifrequency (2.5-3.5 MHz) matrix probe M3S with simultaneous ECG recording. For image acquisition, three cardiac cycles were recorded in each view with the patient holding breath.

All images were digitally stored for off-line analysis.

The following data were obtained:

a- Using 2D and 2D guided M-mode to assess: LV end-systolic and end-diastolic volumes (mL^3), LVEF (%), fractional shortening (%), interventricular septum end-diastolic diameter (mm), and LV posterior wall end-diastolic diameter (mm).

b- Using convention Doppler echo to assess: mitral E and A wave Velocities (cm/s), E/A ratio.

c- Using tissue Doppler imaging to assess: S velocity, E' velocity, A' Velocity, and E/E' ratio.

Two-dimensional speckle tracking

Speckle tracking analysis for the left ventricle was recorded in apical 4, 2, and 3 chambers. The LV longitudinal strain was measured using 2D speckle tracking analysis with QRS onset as the reference point. During analysis, the endocardial border was manually traced at end systole and the region of interest width was adjusted to include the entire myocardium, The LV deformation parameters in each of 18 segments were assessed. Then the global strain was calculated by averaging the strain of all segments.

Real time 3-dimensional echocardiography

RT3DE imaging was performed from the apical window with the patient in the left lateral decubitus position. The data sets were acquired using the wide-angled mode to include the entire LV cavity within the scan volume, where in 4 wedge-shaped sub-volumes were acquired during a single breath-hold. The technique for the acquisition of each sub-volume was triggered by the ECG R wave of every other heartbeat (total of 6 heart

beats) to allow sufficient time for each sub-volume to be stored. Six automatically selected long-axis planes rotated around the long axis of the left ventricle at 30° steps were subsequently used to analyze LV function. LV end diastolic volume (LVEDV), LV end systolic volume (LVESV), and LVEF (EF %) were quantified accordingly.[5]

MUGA scan

Radionuclide angiography was performed using a Philips Cardio-MD system by labeling autologous erythrocytes, performed by injecting the patients with 1.5 mg stannous pyrophosphate. After twenty minutes, thirty MCi technetium-99m pertechnetate was injected. Ten minutes later, imaging acquisition was performed in the left anterior oblique (30° to 40°) view with a digital Gamma camera with the collimator positioned at a caudal angulation of 30°. Processing of the data was followed using standard software and background correction. The LVEF was calculated by digital or manual tracing of the LV end-diastolic and end-systolic images. Planar ECG - gated images of the left ventricle were obtained over multiple cardiac cycles. Each cardiac cycle was then separated into a predetermined number of intervals (16 or 32), according to the number of frames (images) per cardiac cycle. The frame with the highest count represented the end-diastole, and the frame with the lowest count represented the end-systole.[6]

LVEF was then calculated from the equation: net counts in the end-diastolic frame - net counts in the end systolic frame divided by net counts in end-diastole. Net counts are determined by subtracting counts from the background region of interest (next to the left ventricle) from measured LV counts.[6]

This was followed by calculation of the left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), and LVEF.[6]

Statistical analysis

The numerical variable was expressed as mean and standard deviation, independent t-test was used for testing statistically significant differences between the means of the two groups. Pearson's correlation test and correlation coefficient (r) were used to test a positive or negative relationship between two variables. P-value less than 0.05 was considered statistically significant and ≤0.001 highly significant.

RESULTS

The study included (30) patients, (25) females and (5) males with mean age of (48.40 ± 7.44 y) and the control group included 15 healthy individuals (11 female and 4 male) with mean age (50.20 ± 7.74).

As regard the different echo modalities (conventional, 2D strain & 3D Echo) and MUGA parameters: There were a statistically significantly lower values of LV-GLS and 3D-EF in the patient group and higher values of 3D LV ESV and 3D LV EDV in the same group compared with the control group, and a non-significant difference between the two groups as regard the following parameters (2D-EF, 2D LVESV, 2D LVEDV, IVSD, PWD, MUGA-EF, MUGA LV ESV and MUGA EDV), as shown in Table 1.

Left ventricular systolic function in the patients' group

We assessed the LV systolic function of all 30 patients with diabetes by the different echo modalities (conventional, 2D strain & 3D Echo) and by MUGA scan.

We found that 23 patients (76.67%) with impaired LV-GLS (5 of them had impaired LV EF measured by MUGA and 16 patients had impaired LVEF by 3D Echo), 17 patients (56.67%) with impaired LVEF by 3D Echo (3 of them had impaired LV EF measured by MUGA and 16 patients had impaired LV-GLS), 5 patients (16.67%) with impaired MUGA LVEF all of them had impaired LV-GLS, and 3 patients had impaired LVEF by 3D Echo.

There was an agreement between three techniques (2D strain, 3D Echo and MUGA scan) by 33% in 10 patients [3 patients (10%) with impaired function and 7 patients (23%) with preserved function]. Also there was an agreement between the two techniques (2D speckle tracking, 3D echo) by 76.6% in 23 patients [16 patients (53.3%) with impaired function and 7 patients (23.3%) with preserved function], as shown in Figure 1.

We divided the group with diabetes into three groups (A, B, C) according to their MUGA LVEF, LV-GLS, and 3D LVEF, respectively.

Table 1: Comparison between the different echo modalities (conventional, 2D strain & 3D Echo) and MUGA parameters in the patient and the control groups

Variable	Patient	Control	*P*
2D-EF	70.77±7.9	70.27±4.89	0.796
2D LVESV	28.03±3.9	28.6±2.6	0.569
2D LVEDV	47.40±3.96	45±6.09	0.118
IVSD	9.50±1	9.13±.743	0.176
PWD	9.13±1.1	9.60±2.67	0.410
LV-GLS	-18.07±2.73	-21.24±1.29	<0.001
3D-EF	52.30±5.28	58.93±4.69	<0.001
3D LV EDV	67.73±13.32	60.13±11.079	0.051
3D LV ESV	31.87±6.11	25.53±7.15	0.003
MUGA EF	65.50±9.164	67.07±5.66	0.485
LV MUGA EDV	113.20±54.74	92.73±17.64	0.07
LV MUGA ESV	40.83±22.91	37.27±9.13	0.462

A) Comparison between the diabetic subgroups as regard MUGA LVEF

We divided the group with diabetes into two groups according to their LV EF measured by MUGA:

Group 1A: Included 5 patients (4 females and 1 male) with impaired MUGA LVEF <50% (50.2% ± 4.44%).

Group 2A: Included 25 patients (21 females and 4 males) with preserved MUGA LVEF ≥50% (68.56% ± 6.3%).

Patients with impaired LV function by MUGA (group 1): All patients with impaired MUGA LV EF had preserved function by conventional echo and impaired LV GLS, but only 3 patients (60%) had impaired systolic function by 3D Echo, as shown in Table 2.

Patients with preserved LV EF by MUGA (Group 2): (LV EF =67.44% ± 5.7%), were found to be with the following parameters: LV GLS (-17.27 ± 1.9) LV 3DEF (51.2% ± 5.9%)

Comparing the two groups (1A & 2A) as regard the different echo modalities (conventional, 2D strain & 3D Echo) and MUGA parameters: There were a statistically significant higher values of IVSD, MUGA LV ESV and EDV in group 1A and lower value of LV-GLS in the same group compared to the group 2A ($P < 0.05$) and a non-significant difference between the two groups as regard the following parameters (2D-EF, LVESV, LVEDV, PWD, 3D EF, 3D LV ESV and EDV), as shown in Table 3.

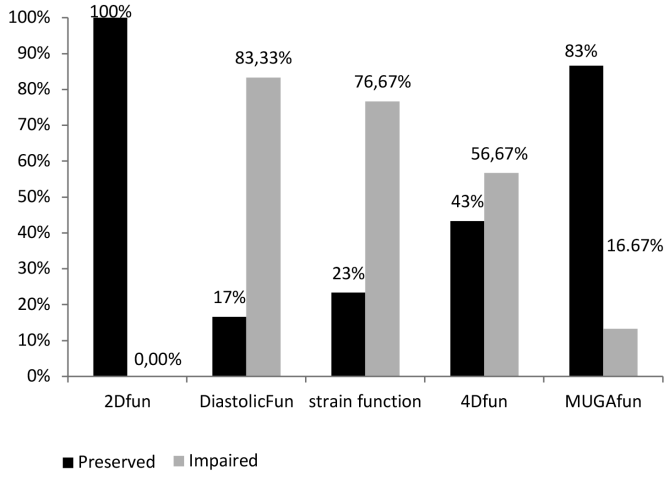

Figure 1: LV function in the study group by different modalities

Table 2: Showing the relationship between group 1A and group 2A regarding other different parameters

Variable		MUGA LV EF		*P*
		Impaired	Preserved	
LV GLS	Impaired	5	18	0.177
	Preserved	0	7	
LV 3D EF	Impaired	3	14	0.869
	Preserved	2	11	

Correlation between MUGA LV EF and different parameters: There was a positive correlation between the MUGA LVEF and LV-GLS at the value of (r=0.511, P = 0.004), a positive correlation with 3D LVEF at the value of (r=0.395, P = 0.031) and a negative correlation with HbA1c value of (r= 0.384, P = 0.036), as shown in Table 4.

B) Comparison between the diabetic subgroups as regard LV-GLS

We divided the group with diabetes as regard LV-GLS into: group 1B: Included 23 patients (18 females and 5 male) with impaired LV-GLS <-20 (-16.94±1.9).

Group 2B: Included 7 patients (all are females) with preserved LV-GLS function >-20 (-21.78±1.9)

Patients with impaired LV function by LV-GLS: All patients with impaired LV-GLS had preserved function by conventional echo, but only (5 patients) with impaired MUGA LVEF and (16 patients) had impaired systolic function by 3D Echo, as shown in Table 4.

There was a statistically significant relationship between both groups in 3D LVEF with (p<0.05).

Correlations between the LV-GLS and different parameters

There was a positive correlation between the LV-GLS and MUGA LVEF at value of (r=0.511, P = 0.004) and a negative correlation with MUGA LVESV at value of (r=0.491, P = 0.006) and MUGA LVESV at value of (r=0.456, P = 0.011), as shown in Table 5.

Table 3: Showing the comparison between group 1A and group 2A regarding the different echo modalities (conventional, 2D strain & 3D Echo) and MUGA parameters

Variable	Group 1A	Group 2A	*P*
2D-EF	68.00±3.32	71.32±8.51	0.16
2D LVESV	28.20±1.79	28.00±4.23	0.866
2D LVEDV	45.60±4.33	47.76±3.87	0.273
IVSD	10.20±.45	9.36±1.03	0.01
PWD	9.00±.71	9.16±1.18	0.694
LVGLS	-15.78±1.47	-18.53±2.71	0.009
EF3D	52.32±5.55	52.20±4.15	0.957
3D LV EDV	66.60±18.02	67.96±12.64	0.839
3D LV ESV	32.00±10.42	31.84±5.19	0.958
LVMUGA EDV	166.80±83.23	102.48±41.81	0.014
LV MUGA ESV	79.00±30.6	33.20±10.67	<0.001

C) Comparison between the diabetic subgroups as regard to LV-3DEF

Patients were classified into two groups according to their LV 3DEF: Group 1C: Included 17 patients (15 females and 2 male) with impaired function <54% (49.76 ± 5.5).

Group 2C: Included 13 patients (10 females and 3 males) with preserved function ≥54 (55.61 ± 2.4).

Patients with impaired LV function by 3D Echo

All patients with impaired LV-3DEF had preserved function by conventional echo, but only (3 patients) with impaired MUGA LVEF and (16 patients) had impaired LV-GLS, as shown in Table 6. There was a statistically significant relation between both groups in LV-GLS with ($P < 0.05$)

Table 4: Showing the correlation between the MUGA LVEF and 3D-EF, LV-GLS and HgbA1C

Variables		Person correlation	Significance
MUGA LVEF	3D-EF	0.395*	0.031
	LV-GLS	0.511*	0.004
	HbA1c	-0.384**	0.036

*Positive correlation, **Nagative correlation

Table 5: Showing the correlation between the LV-GLS and MUGA-LVEF, MUGA-LVEDV and MUGA-LVESD

Variables		Person correlation	Significance
LV-GLS	MUGA-LVEF	0.511*	0.004
	MUGA-LVEDV	-0.456**	0.011
	MUGA-LVESD	-0.491**	0.006

*Positive correlation, **Nagative correlation, MUGA: Multigated acquisition

Table 6: Showing the relationship between group 1C and group 2C regarding other different parameters

Variable		LV-3DEF		*P*
		Impaired	Preserved	
LV-GLS	Impaired	16	7	0.01
	Preserved	1	6	
MUGA LVEF	Impaired	3	2	0.869
	Preserved	14	11	

MUGA: Multigated acquisition, LVEF: Left ventricular ejection fraction

Table 7: Showing correlations between the 3D-LVEF and different parameters

Variables	Person correlation		Significance
3D-LVEF	MUGA LVEF	0.395*	0.031
	LDL	-0.378*	0.039

LDL: MUGA: Multigated acquisition, LVEF: Left ventricular ejection fraction, *Positive correlation

Correlations between the 3D-LVEF and different parameters

There was a weakly positive correlation between 3D LVEF and MUGA LVEF at the value of (r=0.395, P = 0.031) and a weakly negative correlation with LDL at a value of (r=0.378, P = 0.039) and, as shown in Table 7.

DISCUSSION

Subclinical myocardial involvement in type 2 patients with diabetes has been proved as a form of subclinical LV and RV systolic dysfunction.[7]

Our results agreed with that of Labombarda *et al*.[9] who, suggested that LV longitudinal function is impaired in patients with T2D, and glycemic control may be the main risk factor for the myocardial changes. In contrast, the same time, our results disagreed with Di Cori *et al*.,[10] who did not find a relationship between HbA1c and LV systolic strain.

In our study, we found that the LVEF by MUGA was below normal in 16.67% of the patients with diabetes.

There was a little difference between our result and that of Hazra *et al*.,[11] who studied thirty type 2 subjects with diabetes without cardiac symptoms and thirty prediabetic who were assessed by MUGA and pulse rheography, the LVEF was below normal in 29% of diabetics and 16.6% of prediabetic. Our explanation to this difference is that most of our patients were under strict control of their diabetes as their HbA1c was 6.7 ± 1.2%.

In our study results, we found that there was no correlation between 2DE EF% and that by MUGA and this finding was concordant to the finding of Naik *et al*.,[12] who compared 2DE and MUGA in the determination of LVEF and concluded that the 2D method demonstrated these results because of its geometric assumptions for assessing LVEF.

In our study, we found that all patients with impaired MUGA LVEF had impaired LV-GLS and we found that even in patients with diabetes with preserved LVEF by MUGA, 72% had impaired LV-GLS. On the other hand, Ernande *et al*.,[13] results were discordant with our; they found that only 23% (14/60) of study diabetic patients with impaired LVEF by MUGA had LV longitudinal systolic dysfunction determined as their LV-GLS < -18, and our explanation to our finding is the high ability of 2D-STE to predict subclinical LV systolic dysfunction, which is unmasked by the alteration of longitudinal strain.[14]

Also, we found a moderately positive correlation between EF by MUGA and LV-GLS. Gopal *et al*.[15] in 1995 conducted a comparative study between 3DE and MUGA. In that study, LVEF measured by MUGA ranged from 9% to 75%, with a mean of 47% ± 19%, they showed an excellent correlation between the

3DE method and MUGA and this was consistent with our results as we found a 60% of patients with impaired MUGA LVEF with impaired 3D LVEF and we found a weakly positive correlation between these two methods.

We found that even in patients with diabetes with preserved LVEF by MUGA, 56% had impaired 3D LVEF. In our study, we found a statistically significant reduction in the LV-GLS in the group with diabetes compared to in the control group. Moreover, LV-GLS was lower in the diabetic group with impaired MUGA LVEF. Also, LV-GLS was lower in the diabetic group with impaired 3D LVEF, and all those patients with preserved 2D LVEF being concordant to our results the result of Nakai *et al*., [14] they reported that GLS in patients with diabetes mellitus (DM) was significantly lower than that in age-matched normal subjects despite of similar 2D LVEF, and 43% (26/60) of patients with DM showed LV longitudinal systolic dysfunction determined as GLS <17.2%.

Mochizuki *et al*.[16] studied 144 patients with diabetes without overt heart failure or and cardiac disease including type 1 and type 2 patients with diabetes found that 37% of the patient group had reduced GLS, but this result was associated with diabetic complications, especially diabetic nephropathy and neuropathy and hypertriglyceridemia.

Jędrzejewska *et al*. [17] studied LV in 50 patients with type 2 DM (T2DM) and found that there was a statistically significant reduction in LVGLS in the patients with diabetes compared with the control group.

Some studies have explained the pathophysiological causes of LV longitudinal dysfunction in patients with DM patients as microvasculopathy, myocardial hypertrophy, and cardiac fibrosis due to hyperinsulinemia, and dysregulation of the extracellular matrix due to hyperglycemia.[18]

Ceyhan *et al*.[19] found that all LV-GLS were reduced in patients with uncontrolled DM, which is consistent with our study results.

In our study, a significant correlation between LV-GLS and HbA1c was observe; our results agreed with Labombarda *et al*. [9] who, suggested that LV longitudinal function is impaired in patients with T2D, and glycemic control may be the main risk factor for the myocardial changes. This finding was discordant with Di Cori *et al*., [10] who did not find a relationship between HbA1c and LV systolic strain or velocity.

Wang *et al*.[20] studied 82 patients with type 2 diabetes including 46 subjects with diabetes alone and 36 subjects with diabetes and hypertension; their study results showed that despite a similar 2D LVEF, 3D LVEF was significantly lower in patients with diabetes only than in control ($P < 0.001$). We agree with that, as in our study results, we found a significantly lower 3D LVEF in patients with diabetes than in control and all those patients were with preserved 2D LVEF, 94% impaired LV-GLS, and 17.6% with impaired MUGA LVEF. Vinereanu *et al*.[21] observed an inverse correlation between LDL and subclinical left ventricular dysfunction by real-time 3D echocardiography and found that LDL was an independent determinant of systolic function. In our study, a weakly negative correlation between 3D LVEF and LDL was observed, and this was concordant with the result of the previous study.[21]

Study limitations

The main limitation is the limited number of patients studied; further studies including a larger number of patients might be needed in the future.

CONCLUSION

T2DM is associated with subclinical left ventricular systolic dysfunction that can be assessed by different non-invasive modalities (speckle tracking, 3D echocardiography and MUGA scan). New noninvasive modalities like speckle tracking and 3D echocardiography might be more powerful than MUGA scan in the detection of subclinical left ventricular systolic dysfunction, for further evaluation. Therefore, we recommend that STE should be considered a routine investigation in the assessment of patients with T2DM.

Ethics

Ethics Committee Approval: The study was approved by the Ethical Committee of Al-Azhar University Faculty of Medicine for Girls, approval number 202209/543 (date: 28.09.2022).

Informed Consent: All patients included in the study accepted oral and written consent.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.A., M.N., T.S., Concept: T.A., M.N., T.S., Design: T.A., M.N., T.S., Data Collection or Processing: T.A., M.N., T.S., Analysis or Interpretation: M.Z., Literature Search: M.Z., Writing: M.Z.

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