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EVALUATION OF SUBCLINICAL LEFT VENTRICULAR MYOCARDIAL DYSFUNCTION AND SUBCLINICAL CORONARY ARTERY DISEASE IN PATIENTS WITH TYPE TWO DIABETES MELLITUS BY THREE-DIMENSIONAL SPECKLE TRACKING VERSUS CONVENTIONAL TWO-DIMENSIONAL AND SPECKLE TRACKING ECHOCARDIOGRAPHY

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Abstrct

Background: Type 2 diabetes mellitus (T2DM) is a major global health concern related to subclinical cardiac dysfunction, particularly diabetic cardiomyopathy. Early detection of left ventricular (LV) dysfunction is crucial to prevent progression to overt heart failure.

Aim: To evaluate the diagnostic value of 3D speckle tracking echocardiography compared to conventional 2D echocardiography and 2D speckle tracking echocardiography for the early recognition of subclinical left ventricular myocardial dysfunction and Diabetic cardiomyopathy in patients with Type II diabetes mellitus.

Patients and methods: This was Cross-sectional research in which T2DM cases and matched healthy controls have been evaluated using different types of Echocardiography modalities. Two hundred Patients and 200 healthy controls have been recruited for the study at Al-Azhar University Hospitals - Assuit, and Sohag General Hospital, Sohag.

Results: 3D-STE detected significantly lower LV strain values in T2DM patients than controls. 3D-GLS illustrated stronger reproducibility and correlation with 2D-GLS than other strain parameters. 2D-STE consistently overestimated strain values compared to 3D-STE. Diabetes status was the most significant predictor of impaired strain, while HbA1C and disease duration showed no significant correlation.

Conclusion: 3D-STE is a reliable and superior modality for detecting subclinical LV dysfunction in T2DM cases. GLS is the most consistent and reproducible strain parameter, outperforming conventional echocardiography and 2D-STE in early myocardial assessment.

Key words: Type two diabetes mellitus, subclinical coronary artery disease, subclinical left ventricular myocardial dysfunction, Three-Dimensional Speckle Tracking Echocardiography.

INTRODUCTION

T2DM is known to be one of the most prevalent and fastest-growing chronic medical conditions worldwide involving approximately 463 million patients. It is also the predominant type of diabetes representing 90% of cases and around 6% of males and 5% of females in the general population **(1)**. In Egypt, about 10.9 million adult patients are suffering from diabetes mellitus (DM) and about 6.2 million cases are still undiagnosed **(2)**.

Long-term T2DM is associated with many complications that could be categorized into; macrovascular complications increasing the risk of atherosclerosis, Stroke, myocardial infarction (MI), and peripheral arterial disease (PAD), and

microvascular complications including neuropathy, retinopathy, and nephropathy due to involving small arterioles and capillaries **(3)**.

The frequency of heart failure (HF) among diabetic cases is significantly higher (39%) compared to non-diabetic cases (23%) and this higher association between HF and DM is independent of previously mentioned associated risk factors like obesity, CAD, dyslipidemia, and hypertension **(4)**.

In 1972, Rubler et al. first introduced Diabetic cardiomyopathy (DMCMP) as a complication of DM in which cardiac structure and function could be altered leading to ventricular dysfunction in the absence of alterations in blood pressure and CAD **(5)**.

In the initial stages, a subclinical period of DMCMP could be described as functional and structural abnormalities, involving left ventricular hypertrophy (LVH), cell signaling anomalies, and myocardial fibrosis. These abnormalities which cause subclinical diastolic dysfunction usually evolve into heart failure with preserved ejection fraction (HFpEF) and eventually impaired systolic function and HF reduced ejection fraction (HFrEF) **(4)**.

Echocardiography is the first line, cheapest, and most widely available tool for evaluating cardiac structure and function. Although left ventricular ejection fraction (LVEF) assessed with two-dimensional (2D) echocardiography is the easiest, most simple, and most applied parameter for the determination of left ventricular function in daily practice, clinical research, and guidelines, it also has many limitations. It relies on geometrical assumptions, is easily affected by geometrical changes (hypertrophy or dilatation of LV), is insensitive to declining LV function, and is extremely load dependent which declines its reproducibility **(6)**.

Recently, 2D speckle tracking echocardiography (2D-STE) offered a more sensitive instrument for evaluating early myocardial dysfunction through assessment of myocardial strain **(7)**. Although global longitudinal strain (GLS) gives the best prognostic and diagnostic data, radial and circumferential strain could also help assess regional and global active LV deformation **(8)**.

Nowadays, Three-dimensional speckle tracking echocardiography (3D-STE) is thought to provide a better quantitative assessment of myocardial work and overcome the difficult tracking of speckles frame by frame by 2D-STE because of out-of-plane cardiac motion **(9)**.

Our study aimed to evaluate the diagnostic value of 3D speckle tracking echocardiography compared to conventional 2D echocardiography and 2D speckle tracking echocardiography for the early recognition of subclinical LV myocardial dysfunction and Diabetic cardiomyopathy in cases with Type II diabetes mellitus.

Patients and methods

This was Cross-sectional research in which T2DM cases and matched healthy controls have been evaluated using different types of Echocardiography modalities. Two hundred cases and 200 healthy controls have been recruited for the study at Al-Azhar University Hospitals - Assuit, and Sohag General Hospital, Sohag.

Inclusion criteria: Patients group: Adult cases ≥ eighteen years old and diagnosed with T2DM as per the guidelines of the international diabetes federation (IDF) and WHO, 2017. **Controls group:** Healthy adults with no history or clinical evidence of T2DM according to IDF guidelines matched to age and other risk factors to the patient group.

Exclusion criteria: History or clinical proof of hypertension, smokers and previous history or clinical evidence of CAD, MI, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), history or clinical evidence of HF, valvular heart disease and congenital heart disease, history or clinical evidence of T1DM, left bundle branch block (LBBB), or right bundle branch block (RBBB) in electrocardiogram (ECG) and significant persistent arrhythmias or cardiac pacing, chronic renal failure; thyroid dysfunction, glomerular filtration rate under 60 mL/min/1.73 m^2 and history or clinical evidence of PAD, malignancy or cardiotoxic drug intake and poor echocardiography window.

Sampling method: Simple random sampling.

Sample size: The sample size for this research has been determined depending on the assumption that GLS in patients with T2DM differs significantly from healthy controls. According to **Liu et al. (10),** a threshold GLS value of > -17.9% predicts cardiovascular events in this population, with an effect size of around 0.55. Utilizing a significance level of 0.05 and a power of eighty percent, the needed sample size was approximately 53 participants per group. However, with 200 participants per group, the study's power increases to 99.98%, ensuring robust detection of even smaller differences in myocardial strain.

METHODS

All patients were subjected to the following:

Complete history taking: Demographic criteria, risk factors like hypertension, smoking, dyslipidemia, and family history of CAD and DM, time of diagnosis and duration of T2DM, Level of glycemic control, and compliance to medical therapy and symptoms suggesting CAD or HF. **physical examinations:** Full clinical examination including

the general examination (mainly pulse, blood pressure, head and neck, chest, Abdominal, upper and lower extremities examination) and local cardio-vascular examination were performed for every study participant and **Investigational Studies: Routine laboratory investigations:** Complete blood count (CBC), lipid profile including LDL and cholesterol levels, glycosylated hemoglobin (HbA1C) level, fasting and postprandial blood glucose and renal and thyroid function.

Resting 12-leads ECG: Twelve leads ECG was obtained for every patient using a Proper ECG machine (Biocare IE 3 channels ECG machine, SHHENZEN Biocare©, China) for exclusion of signs of IHD, conduction abnormalities, and cardiac arrhythmias.

Echocardiography: Echocardiography was performed using a well-equipped machine (GE Vivid E95; GE Healthcare©, Horten, Norway) with a 4V phased-array matrix transducer (1.5-4.0 megahertz) as follows; Patient was at left lateral decubitus position, ECG tracing was obtained during the study and full views including PLAX, PSAX, A2CV, A3CV, A4CV, A5CV, and subcostal views were obtained, LV dimensions, volumes, and systolic and diastolic function were assessed using the following modalities: M-Mode of PLAX view, Simpson's method, PW Doppler, TDI, 2D-STE including GLS, and 3D echocardiography, LA dimensions and volumes were assessed through the M-Mode of PLAX view, Area tracing, 2D volume estimation, and 3D volume quantification, 3D echocardiography has been measured, LVEF has been measured automatically utilizing 4D Auto LVQ and 4-beats acquisition was used for analysis. Automatic detection of the LV cavity and endocardial border was used unless it has been judged as inaccurate by the examiner. In this case, borders were manually adjusted in a multiplanar layout (3 apical and 3 transverse planes) followed by secondary automated refinement and LV myocardial segment definition and segmentation models were interpreted as per the frequent standard for 2D speckle tracking echocardiography. Normal values of 3D-STE derived parameters including LV end-systolic, End-diastolic, LVEF, GCS, and GLS were defined as published by **Addetia et al. (11)**

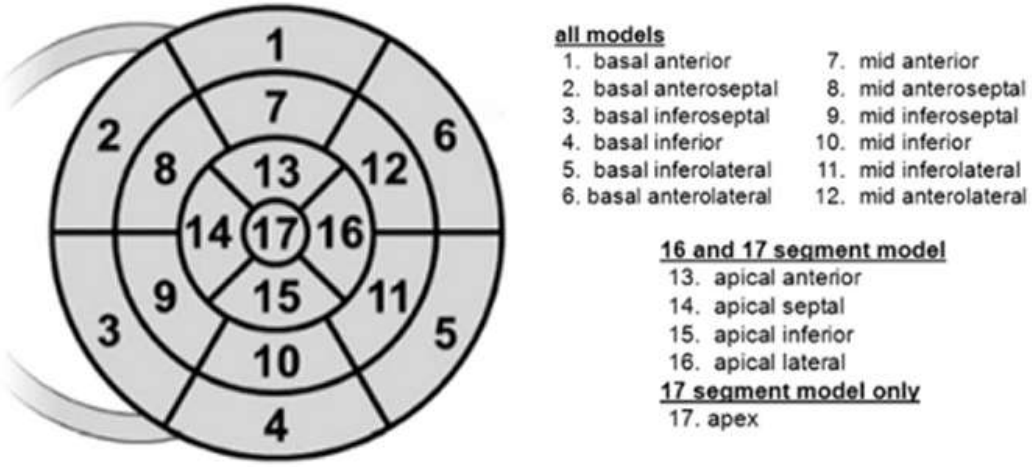

Figure (1): 17-myocardial segments model forming the bull's eye map.

Ethical considerations: The procedures of blood sampling, ECG, and echocardiography were explained thoroughly to the participants and written consent was obtained before participant inclusion. Participation is voluntary, every patient and healthy control participated without coercion. All collected data including personal and medical information is confidential. There is no opportunity for participants to be identified. No form of harm including any physical or psychological harm (stress, pain, or anxiety) was allowed to happen to any participant during the study.

Statistical Analysis: Statistical analysis has been carried out utilizing SPSS software version 26 (IBM©, Chicago, IL, united state of America) and GraphPad Prism software version 10.3.1 (GraphPad©, California, USA) for bland-Altman analysis. The normality of distribution has been checked utilizing the Shapiro-Wilk test and visual tools like histograms or Q-Q plots. For Continuous variables, the Mann-Whitney U Test has been utilized to compare the 2 groups in the case of non-parametric data, and results have been reported primarily as Mean ± SD, Median, and IQR. The Independent Sample T-test has been utilized for comparing the parametric data. For Dichotomous variables, Pearson's Chi-Square or Fisher's Exact test has been utilized. The Chi-square test has been utilized for the comparison of dichotomous variables. The comparison of the paired data has been done using the Wilcoxon Signed-Rank test. The correlation of non-parametric data was performed using the Spearman correlation. The diagnostic accuracy calculation

was performed using the McNemar test. The receiver operating curve (ROC) has been utilized for plotting the performance of the diagnostic test. Regression was done using Multivariate linear regression.

RESULTS

Table (1): Baseline characteristics of the two groups; cases (DM patients) and controls (Non-DM controls)

Parameter	DM Group		Control Group		P-value
	Mean	± SD	Mean	± SD	
Age	51.57	9.99	53.05	10.58	0.154
Height (m)	1.70	0.10	1.67	0.09	**0.002***
Weight (Kg)	78.18	7.69	75.31	9.0	**0.000***
Body Mass Index (Kg/m^2)	27.19	3.63	27.08	3.10	0.990
Body Surface Area (m^2)	1.92	0.12	1.866	0.14	**0.000***
Systolic Blood Pressure (mmHg)	114.53	10.13	116.15	10.7	0.127
Diastolic Blood Pressure (mmHg)	78.08	9.8	79.23	9.7	0.276
Total Cholesterol (mg/dl)	220.87	86.71	192.69	34.46	0.156
Low-density Lipoprotein (mg/dl)	145.69	70.13	135.63	29.46	0.872
High-density Lipoprotein (mg/dl)	32.63	8.60	30.17	4.97	**0.002***
Triglycerides (mg/dl)	207.33	85.45	134.54	53.72	**0.000***
Hemoglobin A1C Level (%)	8.90	2.55	5.0	0.49	**0.000***
Duration of Diabetes (y)	8.31	4.155	0.0	0.0	**0.000***
Serum Creatinine (mg/dl)	1.53	0.3	1.07	0.34	**0.000***
Heart Rate (b/m)	77.63	12.53	77.09	13.338	0.626

Table 1 shows that the participants involved in the research have been classified into two groups; **the DM (patients) group [200 cases]** and **the Control group [200 participants]**. There was **a statistically insignificant variance** among the DM group and the control group regarding Age, BMI, SBP, DBP, Total cholesterol, LDL, or HR. On the other hand, Height, weight, BSA, HDL, Triglycerides, HbA1C, Duration of diabetes, and serum creatinine **were significantly different** among both groups

Table (1): Conventional echocardiography, M-Mode, PWD, and TDI findings of the DM group and the control group

Parameter	DM Group		Control Group		P-value
	Mean	± SD	Mean	± SD	
LV end-diastolic diameter (cm)	4.96	0.45	4.9	0.47	0.646
LV end-systolic diameter (cm)	3.5	0.38	3.4	0.39	**0.012***
Inter-ventricular septal thickness (cm)	0.85	0.13	0.88	0.17	0.121
LV posterior wall thickness (cm)	0.84	0.13	0.88	0.16	0.056
Mitral E/A ratio [PWD]	1.4	0.7	1.3	0.65	0.530
Septal E' velocity [TDI]	5.8	2.14	5.8	1.97	0.690
Lateral E' velocity [TDI]	5.77	2.12	5.8	2.04	0.777
Septal E/E' ratio	10.59	3.97	10.15	3.67	0.272
Lateral E/E' ratio	10.46	3.92	10.2	3.8	0.721
Mean E/E' ratio	10.5	3.86	10.2	3.64	0.430
Tricuspid regurge peak velocity (m/s)	2.55	0.499	2.53	0.489	0.855

Table 2 shows that **a statistically significant variance** has been observed among both groups considering **LV end-systolic diameter only** from all M-Mode measurements. All other 2D-echo parameters were **statistically insignificant** between the 2 groups.

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Table (3): Comparison of LV Mass, LVEF, LV volumes, and LA dimensions

Parameter		DM Group				Control Group				P value
		Mean	± SD	Median	IQR	Mean	± SD	Median	IQR	
EF	2D LVEF	**63.7**	9.6	64	16	**65.78**	8.6	67	12	**0.018***
	3D LVEF	**55.9**	4.99	55	6	**61.62**	4.65	62	8	**0.000***
LVM	3D LV Mass	**163.8**	36.5	165.3	54.3	**142.4**	39.8	139.2	53.6	**0.000***
	Indexed 3D LV Mass	**85.4**	18.8	84.7	29.5	**76.5**	21.1	74.5	30.3	**0.000***
Volumes LV [Simpsons]	LVEDV [Simpson's]	**122.7**	24.4	121.8	37.5	**108.5**	25.7	106.2	32.6	**0.000***
	LVESV [Simpson's]	**51.9**	13	50.9	21	**48.4**	13.1	47.4	20.2	**0.012***
	Indexed LVEDV [Simpson's]	**63.7**	11.2	62.5	14.9	**57.9**	11.7	56	64.2	**0.000***
	Indexed LVESV [Simpson's]	**27.0**	6.8	27.3	11.6	**26.0**	7.2	26.0	10.6	**0.141***
3D-LV Volumes	3D LVEDV	**142**	24.7	138.9	34.6	**114.9**	24.9	118.2	38	**0.000***
	3D LVESV	**62.4**	12.7	61	18.2	**44.2**	11.2	43.8	16.3	**0.000***
	Indexed 3D LVEDV	**74.0**	12.5	72.9	15.6	**61.9**	14.0	60.6	21.0	**0.025****
	Indexed 3D LVESV	**32.5**	6.4	32	9.4	**23.8**	6.3	23.8	9.0	**0.000***
LA Volumes	LA diam. [M-Mode]	**3.8**	0.6	3.8	0.8	**3.7**	0.6	3.8	1.0	0.595
	LA Area [2D]	**20.59**	4.3	18.9	8.2	**20.7**	4.6	18.4	8.4	0.669
	3D LA volume	**62.8**	9.0	62.3	13.5	**60.4**	8.9	59.8	12.4	**0.005***
	Indexed 3D LA Volume	**32.7**	4.1	32.7	6.2	**32.3**	3.8	32.0	6.0	0.349**

Table 3 shows that regarding systolic function, both 2D and 3D LVEF were significantly different amongst both groups. Yet the 3D-LVEF in the patients' group (55.9 ± 4.9) is ***significantly lower*** than the 2D-LVEF (63.7 ± 9.6) of the same group. This difference was not the same in the case of the control group where the variance between the 2D LVEF (65.78 ± 8.6) and 3D LVEF (61.62 ± 4.65) was much lower than in the patient group.

Table (4): Comparison of 3D and 2D STE parameters among the DM group and the control group.

Parameter	DM Group				Control Group				P-Value
	Mean	± SD	Median	IQR	Mean	± SD	Median	IQR	
2D GLS	**-16.5**	1.62	-16.6	2.2	**-19.6**	1.3	-19.5	1.7	**0.000***
2D GCS	**-18.2**	1.6	-18.2	2.7	**-21.1**	1.8	-21.0	3.3	**0.000***
2D GRS (%)	**37**	5.2	36.7	9.2	**42.3**	6.1	42.4	9.8	**0.000***
3D GLS	**-15.7**	2.0	-15.6	3.3	**-19.3**	1.7	-19.2	2.7	**0.000***
3D GCS	**-18.1**	1.4	-18.2	1.9	**-20.8**	1.8	-20.8	2.9	**0.000***
3D GRS (%)	**34.8**	4.5	35.2	6.0	**40.7**	3.1	40.5	4.3	**0.000***

*** Mann-Whitney U test** was used for comparing variables, P value under 0.05 is considered significant

Table 4 shows that regarding 2D and 3D speckle tracking imaging of both groups; all parameters of speckle tracking using 2D-STE or 3D-STE were found to be ***significantly different*** among both groups.

Table (5): Bland-Altman analysis of paired STE parameters.

Parameters	Mean difference	± SD	Limit of agreement	
			From**	To**

2D GLS	**3D GLS**	0.5634*	1.151	-1.693	2.82
2D GCS	**3D GCS**	0.2281*	2.282	-4.245	4.701
2D GRS	**3D GRS**	-1.913*	7.044	-15.72	11.89

Table 5 shows that these results show that 2D-STE parameters (2D-GLS, 2D-GCS, and 2D-GRS) systematically overestimate results compared to 3D-STE parameters (3D-GLS, 3D-GCS, and 3D-GRS correspondingly). The narrow limits of agreement in the case of GLS indicate that the differences between the two measurement methods are small and consistent across most of the data points (better agreement between the 2 parameters). The wide limits of agreement in the GRS indicate that the differences between the 2D-GRS and 3D-GRS methods are larger and more variable. This suggests poorer agreement between 2D and 3D methods regarding GRS and GCS compared to GLS

Table (6): Correlation of 2D-STE and 3D-STE derived parameters

Correlated parameters		Correlation coefficient	Correlation	P-Value
2D GLS	**3D GLS**	.891	Strong	0.000*
2D GCS	**3D GCS**	.451	Weak	0.000*
2D GRS	**3D GRS**	.213	Very weak	0.000*

Table 6 shows that a ***strong positive correlation has been observed*** between ***2D-GLS and 3D-GLS***, which was ***statistically significant***, the association between ***2D-GCS and 3D-GCS*** revealed *a* ***significant, weak, and positive correlation***. On the other hand, the association analysis between 2D-GRS and 3D-GRS revealed *a* ***very weak positive correlation*** despite being significant.

Table (7): Regression analysis of covariates on 3D-STE parameters

Covariates	3D-GLS		3D-GCS		3D-GRS	
	Regression Coefficients (B)	P-value	Regression Coefficients (B)	P-value	Regression Coefficients (B)	P-value
Gender	-0.110	0.632	-0.223	0.260	0.135	0.776
Diabetes status	**-3.584**	**0.000***	**-2.485**	**0.000***	**5.458**	**0.000***
Age	0.005	0.796	-0.015	0.388	0.007	0.869
Height (m)	-30.039	0.026*	-5.270	0.651	16.858	0.547
Weight (Kg)	-0.263	0.367	-0.012	0.962	0.321	0.596
Body Mass Index (Kg/m^2)	-0.384	0.156	-0.060	0.797	0.097	0.863
Body Surface Area (m^2)	31.843	0.135	2.504	0.892	-26.523	0.549
Systolic Blood Pressure (mmHg)	0.000	0.968	-0.004	0.663	0.004	0.859
Diastolic Blood Pressure (mmHg)	-0.014	0.172	0.010	0.281	0.020	0.359
Total Cholesterol (mg/dl)	-0.028	0.410	-0.004	0.883	-0.008	0.910
Low-density Lipoprotein (mg/dl)	0.023	0.497	0.004	0.880	0.018	0.795
High-density Lipoprotein (mg/dl)	0.032	0.372	0.014	0.648	-0.053	0.477
Triglycerides (mg/dl)	0.008	0.240	0.001	0.914	-0.002	0.875
Hemoglobin A1c Level (%)	-0.012	0.820	-0.016	0.725	-0.047	0.666
Duration of Diabetes (y)	0.007	0.837	0.006	0.852	-0.001	0.986
Serum Creatinine (mg/dl)	-0.246	0.696	0.582	0.284	0.283	0.828
Heart Rate (b/m)	0.008	0.265	0.005	0.393	0.000	0.991

Table 7 shows that Multiple linear regression assessed the relationship between various clinical factors and **3D-GLS**. The overall regression model was **significant** (p -value under 0.001) and **explained 49.4% of the variance in 3D-GLS**. Among the independent variables, **Diabetic status (p -value under 0.000) and height (p-value equal 0.026)**

were significant predictors of 3D-GLS. Other variables were **not statistically significant predictors of 3D-GLS**. In the case of **3D-GCS**, the overall model was **significant** (p -value under 0.001), **explaining approximately 42.2% of the variance in 3D-GCS** ($R^2 = 0.422$). The overall model of **3D-GRS** was also **significant** ($p < 0.001$), **explaining approximately 38.1% of the variance in 3D-GRS** ($R^2 = 0.381$). Among all the variables included in the analysis, **the DM status was the most significant predictor of all strain parameters in the three models**.

DISCUSSION

We recruited 200 DM patients in the DM group and 200 Age-matched controls in the control group to compare conventional echocardiography and 2D-STE to 3D-STE results as a tool to identify subclinical LV dysfunction. The 3D-LV volumes (even after indexing to BSA) were significantly greater in the DM group than the control group. The 3D-LVM was also significantly elevated in the DM group (And the same after indexing to BSA). Although all 2D-STE and 3D-STE parameters were significantly diminished in the DM group, The association between 2D-STE and 3D-STE revealed a strong association in the case of GLS only, the correlation was weak in the case of GCS and GRS. The 3D-GLS tended to be a more accurate and consistent parameter than 2D-GLS (Generally, 2D-STE parameters tended to overestimate results compared to 3D-STE parameters). Moreover, we found the 3D-STE parameters weren't significantly related to any demographic parameter including HbA1C, duration of the disease, serum cholesterol, LDL, HDL, or serum creatinine.

Comparable outcomes have been reported by **Tadic et al (12).** in a cross-sectional study investigating LV mechanics by 2D-STE and 3D-STE in T2DM cases. They included 50 normotensive T2DM patients and 50 Age-Matched controls in their study. They reported increased parameters of LVH in the DM group. The 2D-STE analysis of the LV mechanics illustrated impaired GLS, GCS, and GRS in the DM group in comparison with the control group. The 3D-STE assessment also confirmed 2D-STE findings. 3D-LVEF was comparable in the observed groups, whereas LVMi was elevated in the DM group. all four 3D-STE components (GLS, GCS, GRS, and GAS) were significantly diminished in the DM patients than the control group. They also reported that HbA1C was independently related to 3D-LVMi, 3D-GLS, and 3D-GAS.

The first study that used 3D-STE to evaluate LV dysfunction in T2DM patients was reported by **Zhang et al. (13)**. They recruited 31 patients with controlled DM, 37 patients with uncontrolled DM, and 63 matched controls to their study. Although LVEF was not different among groups, cases with uncontrolled DM had reduced peak systolic strain in all directions in comparison with the other two groups, as proved by GLS, GCS, GAS, and GRS. On the other hand, the difference between controlled and uncontrolled DM groups was only seen in the case of GLS.

In 2015, **Wang et al. (14)** recruited 82 patients with controlled T2DM (46 with T2DM alone and 36 with T2DM and controlled hypertension) and forty matched controls. Using 3D-STE, they reported a significantly lower GLS in the T2DM group than controls. Moreover, the T2DM+hypertension group illustrated significantly lower systolic strains in all directions in comparison with controls and cases with T2DM only.

Our results also agreed with the other study of **Wang et al. (15)** who included 78 T2DM patients and 40 healthy and matched controls and used 3D-STE to evaluate the risk factors and LV remodeling. They reported a significantly reduced GLS in T2DM cases with normal LV compared to controls. Patients with LV remodeling had significantly reduced GLS, GCS, GAS, and GRS than the T2DM cases with normal geometry. They also reported Fasting plasma glucose (FBG), hyperlipidemia, and high BMI to be independently related to LV remodeling.

Chen et al. (16) divided 72 patients based on HbA1C level into 2 groups (HbA1C < 7 and ≥7) and compared them to 45 controls. The GLS, GCS, and GAS were significantly reduced in the poor glycemic control group. the duration of diabetes was independently related to lower GCS and GAS. HbA1c levels were independently related to lower GLS. They concluded that RT-3DE can distinguish subclinical LV dysfunction in poor glycemic control of T2DM which is also related to the duration of diabetes and HbA1c level. These findings disagree with our analysis of the T2DM patients, which revealed no significant correlation between the 3D-STE parameters and duration of diabetes or HbA1C level.

In a prospective study published in 2013, **Luis et al. (17)** studied a cohort of 78 cases who underwent 3D-STE and 2D-STE assessment to identify LV systolic dysfunction (LVEF <50%). They reported 3D-GCS to be the best marker of LV function and 3D-STE parameters to be particularly useful in recognising LV dysfunction (LVEF < 50%).

Regarding the agreement of 2D and 3D STE parameters, **Plášek et al.(18)** agreed with our findings when they studied 90 cases with normal LV, impaired systolic function, and cardiac pacing. They reported a strong association among 2D and 3D GLS measurements. The association between 2D and 3D GLS was weaker in persons with ventricular pacing of >50% than <50%, and in patients with LVEF of <35% than >35%.

CONCLUSION

3D-STE is considered a reliable and reproducible method for the recognition of subclinical LV dysfunction in cases with T2DM. When compared to 2D-STE parameters, 3D-GLS was a better indicator of subclinical LV dysfunction, and a more reproducible parameter compared to 2D-GLS. In both methods, GLS showed more consistent and reproducible measurements compared to GCS and GRS. Both 3D-STE and 2D-STE were significantly better than conventional echocardiography for detection of subclinical LV dysfunction.

LIMITATIONS

This study was cross-sectional research including no monitoring period. No data regarding the future incidence of clinical LV dysfunction was available for the analysis.

RECOMMENDATION

Large-scale prospective cohorts are needed to evaluate the predictive value of the strain parameters regarding the development of overt clinical LV dysfunction. More researches are required to compare controlled T2DM patients to non-controlled patients regarding subclinical LV dysfunction. Further studies comparing 3D-STE parameters to more complex investigations as CMR for the recognition of subclinical LV dysfunction in T2DM cases are recommended.

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