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Impact of Type II Diabetes Mellitus on Left Ventricular Longitudinal Strain in Patients with Structurally Normal Heart

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Abstract

Background and objectives: Type-2 Diabetes Mellitus is a widespread metabolic disorder linked to multiple cardiovascular complications, particularly left ventricular dysfunction, even in preserved left ventricular ejection fraction. Speckle tracking echocardiography has become a sensitive means to evaluate myocardial mechanics, particularly global strain. This study aimed to examine the influence of type 2 Diabetes Mellitus on left ventricular global strain in individuals with structurally normal heart.

Methods: A comprehensive cross-sectional investigation was carried out on 118 diabetic patients who showed no symptoms of coronary artery disease and were admitted to Surgical specialty hospital, Erbil Cardiac Center, between January 1st to April 1st, 2023. The global longitudinal strain of the left ventricle that was present in the patient population selected was assessed using strain echocardiography.

Results: The study population was 55 (46.6%) male and 63 (53.4%) female, with a mean age of 54.8+-9.57 years, the mean HbA1c of all Diabetic participants were 8.08 +-1.6.
weak and statistically significant negative correlation was found between global longitudinal strain The number of patients with normal GLS and reduced GLS should be mentioned in results with the duration of diabetes mellitus and HbA1c values with a *p*-value of (r=-020, *P*=0.032) and (r=-0.20, *P*=0.048) respectively. Oppositely a weakly positive correlation was found between global longitudinal strain and mitral annual plane systolic excursion diameters with a significant *P* value (r=0.26, *P* =<0.004).

Conclusion: Left ventricular global longitudinal strain using speckle tracking echocardiography has a significant negative correlation with the duration of diabetes.

Keywords: Coronary artery disease, Diabetes mellitus, Global longitudinal strain, Silent myocardial ischemia, Speckle tracking echocardiography

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Introduction

Type 2 diabetes mellitus (T2DM) is a significant and separate risk factor for cardiovascular disease and subsequent mortality. It is a causative element in the emergence of left ventricular dysfunction and heart failure, irrespective of the existence of coronary artery disease. It plays a pivotal role in the development of coronary artery disease and the progression of Heart Failure with Preserved Ejection Fraction (HFpEF).[1] At present, HFpEF comprises approximately 50% of the total instances of heart failure. Unlike heart failure with a reduced ejection fraction, the prevalence of heart failure with a preserved ejection fraction is steadily increasing at an approximate annual rate of 1%, which is a worrisome trend. Echocardiography is an important investigative tool for detecting structural changes in the heart. Moreover, speckle-tracking echocardiography can identify initial alterations in the structure of the left ventricle (LV). Specifically, speckle-tracking echocardiography can accurately measure Global Longitudinal Strain (GLS), which is a highly sensitive indicator of even minor alterations in the myocardium.[2] Patients diagnosed with type 2 diabetes mellitus who have a normal left ventricle ejection fraction and no apparent coronary artery disease or heart failure may still exhibit reduced GLS, suggesting impaired longitudinal movement of the LV. The presence of a reduced GLS should be regarded as an initial indication of the preclinical phase of diabetic cardiomyopathy.[3] Nevertheless, it remains unclear whether there exists a distinction in LV systolic dysfunction between T2DM patients with well-controlled and poorly controlled blood glucose levels and whether elevated blood glucose levels contribute to the preclinical decline in LV systolic function.[4]

Aim of study: to investigate the impact of T2DM on the left ventricular global longitudinal strain, to assess the relationship between the control of T2DM and the left ventricular global longitudinal strain, to facilitate early detection of sub-clinical LV dysfunction in patients with T2DM in patients with a structurally normal heart.

Patients and methods

This was a cross-sectional study conducted in the Cardiac Center in Erbil, Iraq, from January 1st to April 1st, 2023. The sample size consisted of 118 cases collected from the outpatient department of the Cardiac Center. four cases were excluded due to inappropriate data or views from echocardiography to determine the parameters. A comprehensive questionnaire was designed that consisted of three parts: demographic data (age, gender, Body Mass Index, etc.), presence of co-morbidities (hypertension, hyperlipidemia, renal impairment, etc.), and echocardiographic data including 2D parameters and diastolic parameters, from which the speckle tracking value was calculated. The inclusion criteria included type 2 diabetic patients who had been diagnosed at least 2 years prior and were on anti-diabetic medications.The exclusion criteria encompassed people exhibiting clinical indications of structural heart disease, including a history or suspicion of coronary artery disease, LV systolic dysfunction, previous history of open-heart surgery and congenital heart disease, uncontrolled hypertension > 180/100 mmHg or more than moderate primary valvular heart disease other than functional mitral regurgitation as determined by CT coronary angiography or coronary angiography.The continuous variables were summarized by computing the mean value and using the standard deviation as a measure of dispersion. To assess the bivariate correlation between GLS and the continuous variables (including the age of patients, HbA1c, and duration of diabetes), Pearson's product-moment correlation coefficient was used. The statistical and

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analytical tests that were performed used a two-sided design, for which a p-value below 0.05 (or 5%) was deemed to be significant statistically. The Kurdistan Higher Council of Medical Specialties granted authorization and approval of this study (No. 1737 on December 20, 2021) after meeting ethical requirements.

Results

The baseline clinical, biochemical, and echocardiographic characteristics of the study population (118 diabetic patients) are all summarized in Table (1).

Table (1): Clinical and Biochemical baseline characteristics of the Study population.

DM patients (n= 118)		
Age	Mean ± SD	54.8 ± 9.57
Gender	Male n (%) Female n (%)	55 (46.6) 63 (53.4)
BMI	Mean ± SD	28.68 ±4
Smoking	n (%)	21 (17.8)
Hypertension	n (%)	77 (65.3)
HbA1c	Mean ± SD	8.08 ±1.6
Duration of T2DM	Mean ± SD	8.1 ± 5.5

In an observation of GLS categories for the sake of comparison, GLS was separated into two groups: abnormal (=<-18) and normal (>-17). Based on this analysis of the study population, an independent sample T-test showed greater levels of lateral e', septal e', and LVEF in patients with abnormal GLS ratios, with statistical significance and *P* values of 0.009, <0.001, and 0.009, respectively. On the other hand, the independent test showed lower levels of Left Atrium (LA) size, Left ventricular end systolic diameter (LVESD), and E/A ratio in patients with an abnormal GLS ratio, with statistical significance and *P* values of 0.029, 0.018, and 0.45, respectively. This information is summarized in Table (2).

Table (2): Comparison of echocardiographic parameter finding of T2DM patients relative to Global Longitudinal Strain values.

Variables	Preserved GLS n=(50)	Reduced GLS n=(68)	p value	Statistical test
Lateral e'	8.97 ±0.33	10.21±0.32	0.009	Independent t-test
Septal e'	6.78 ±0.26	8.26 ± 0.27	<0.001	Independent t-test
LA size	32.46 ± 0.54	31.04 ±0.34	0.029	Independent t-test
LVEF	66.18 ± 0.38	67.50 ±0.32	0.009	Independent t-test
E/A ratio	1.06 ± 0.06	0.92 ± 0.03	0.045	Independent t-test
LVESD	28.10 ± 0.42	26.90 ±0.26	0.018	Independent t-test

Stepwise multiple regression analysis was performed to determine the predictors of GLS with other co-variants. The results showed that LVEF, E/A ratio, and duration of DM are independent predictors of GLS. These were significant, with *P* values of <0.001 for LVEF, 0.011 for the E/A ratio, and 0.010 for the duration of T2DM. This is illustrated in Table (3).

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Table (3): Stepwise Multiple linear regression model analysis for predicting GLS by adjusting different co-variates

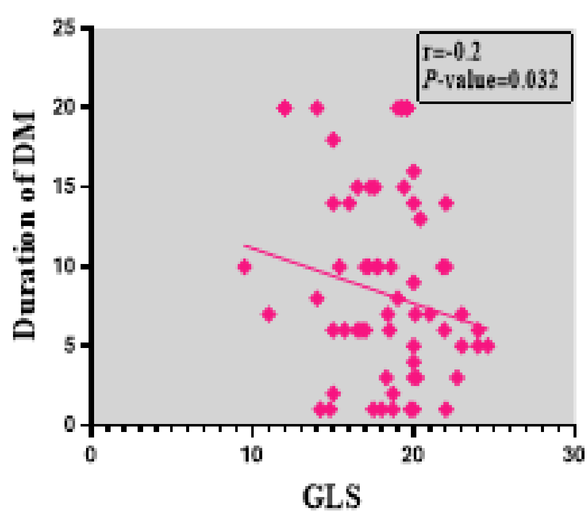
Model	Unstandardized B	Standardized Coefficient Beta	R^2	Adjusted R^2	p value
1					
LVEF (%)	0.276	0.986	97.3	0.973	<0.001
2					
LVEF (%)	0.306	1.095	0.975	0.974	<0.001
E/A ratio	-2.088	-0.115			0.01
3					
LVEF (%)	0.324	1,158	0.976	0.975	<0.001
E/A ratio	-2.191	-0.12			0.006
Duration of DM	-0.130	-0.069			0.010

*Data were analyzed by using the Pearson's correlation coefficient test.
** Data were analyzed by using the Spearman's correlation coefficient test.

The excluded variables are e/e' ratio, left ventricular end diastolic diameter (LVEDD), HbA1c, age, BMI, gender, and smoking. (B: The coefficient of regression without standardization, Beta, corresponds to the standardized coefficient in regression analysis. The coefficient of determination, represented by the symbol R2. Regarding the correlation analysis of GLS with other variables, a weak negative correlation and statistically significant relationship was found between GLS and duration of T2DM and HbA1c values with a p-value of (r = -020, P = 0.032) and (r = -0.20, P = 0.048), respectively. Oppositely, a weakly positive correlation was found between GLS and MAPSE diameters with a significant p value (r = 0.26, P =<0.004). A weak negative correlation was found between GLS and the E/A ratio of participants, with a significant P value of (r = -0.23, P = 0.015). This information is summarized in Table (4) and Figure (1).

Table (4). The correlation of GLS with clinical and echocardiographic parameters among T2DM patients

Parameters	Global longitudinal Strain	
	Diabetic patients (n=118)	
	r	*p*-value
Duration of DM (years)*	-0.20	0.032
HbA1c (%) *	-0.20	0.048
MAPSE (mm)*	0.26	0.004
E/A ratio (%) *	-0.23	0.015
e/e' ratio (%) *	0.05	0.529
BMI*	0.172	0.064
Smoking (Y/N) **	-0.062	0.507



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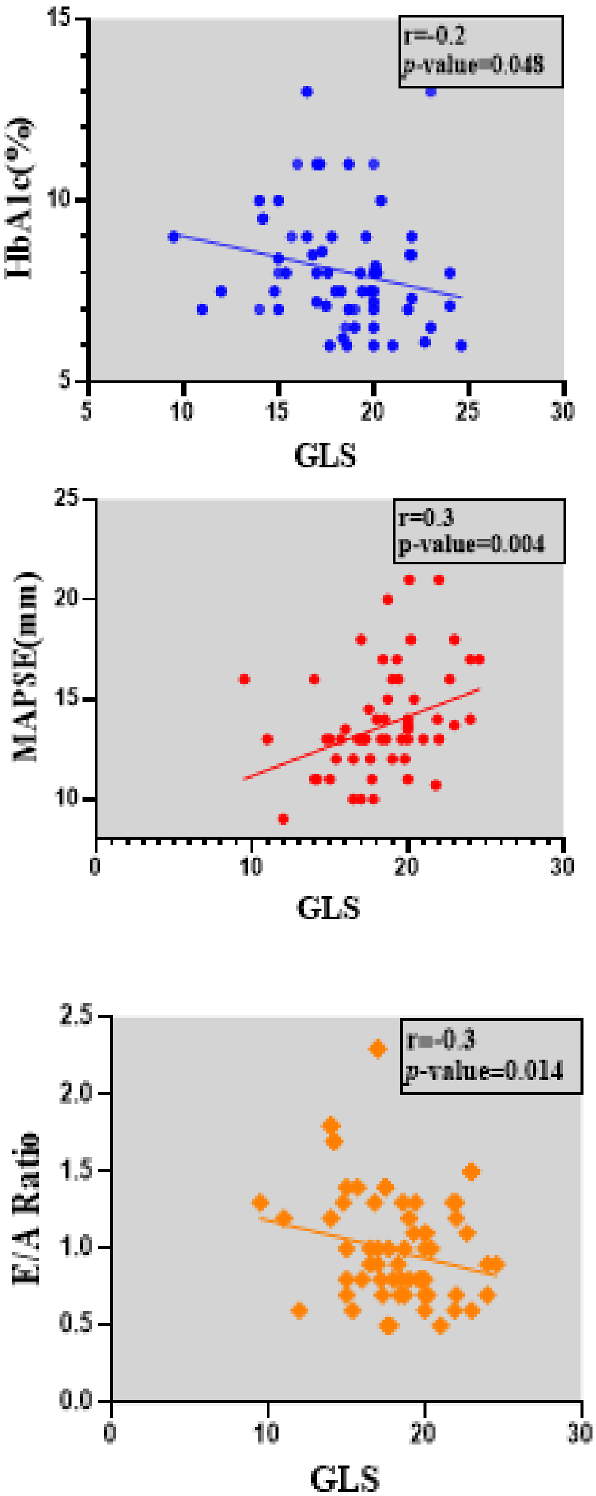

Figure (1): The correlation of Global Longitudinal Strain with clinical and echocardiographic parameters among DM patients.

Comparing the categorical groups of HbA1c among the study population with the mean of GLS of each group, we found that the mean of GLS is reducing as the glycemic control is worse among the study population. Furthermore, patients with good glycemic control had a GLS value of 19.22 ± 3.2, patients with fair glycemic control had a GLS of 18.78 ±2.8, and participants with poor glycemic control had a reduced GLS of 17.5 ±3.2, with a statistical significance of P value 0.5. This is plotted in Figure (2).

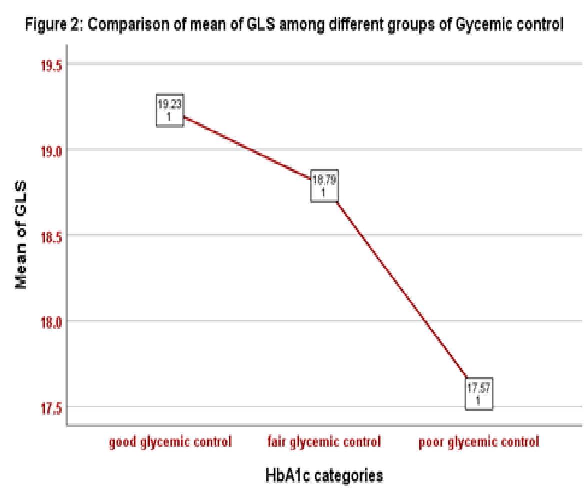

Figure (2): Comparison of GLS Means Among Different Groups of Glycemic Control.

Discussion

This research is the first of its kind conducted in Erbil city, the Kurdistan region of Iraq, employing a Speckle tackling echocardiography (STE) based GLS score to forecast left ventricular dysfunction in diabetic individuals who had no coronary angiographic or CT angiographic features for ischemic heart diseases. Left ventricular dysfunction represents one of the initial signs of diabetic cardiomyopathy in diabetic individuals, a condition that can only be

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identified in its early stages through sensitive techniques like longitudinal strain and myocardial tissue velocity.[3] The utilization of 2D echocardiography to measure GLS through STE is a straightforward and reliably repeatable process, as mentioned in previous studies.[5] GLS, specifically applied to the LV, serves as an indicator of myocardial deformation in the longitudinal direction during systole. This primarily mirrors the performance of subendocardial longitudinal fibers, which are particularly susceptible to ischemic injury and wall stress. Since the GLS ratio is a measure of LV function, it is only natural that there are associations between GLS and other echocardiographic parameters. Studies have shown associations between GLS and LVEF, especially among those with preserved EF.[6] Our study showed the following findings: There was a statistically significant difference (*P* value = 0.009) between the means of LVEF among those with preserved GLS (66.18 $\pm$ 0.38) and reduced GLS (67.50 $\pm$ 0.32). In other words, LVEF was slightly higher among those with a reduced GLS. Furthermore, our study also showed that LA size was slightly smaller in those with reduced GLS (*P* value = 0.029). However, it is evident that the differences in the means are very small in our study, and this might be since we had a small sample size of only 118 cases, in only a single center. In contrast, a study conducted by Biering-Sørensen, T et al. in Copenhagen showed reduced GLS to be associated with reduced LVEF and larger LA dimensions.[7] Our study also aimed to determine the predictors for a reduced GLS ratio. Using multiple linear regression analysis, LVEF, E/A ratio, and duration of DM were discovered to be independent predictors of GLS. This goes in line with the Shrestha SK study, which also showed the duration of DM to be a predictor for GLS.[8] This agrees with the knowledge that DM causes diabetic cardiomyopathy, left ventricular dysfunction, and subsequently reduced GLS.[9] DM causes microvascular damage to the heart, leading to ischemic changes that interfere with the contractile function of the heart and, consequently, cardiomyopathy.[10] GLS has been shown in many studies to be very effective in diagnosing subclinical LV dysfunction.[11] This explains the relationship we have discovered between GLS and LVEF. Furthermore, the E/A ratio has been demonstrated to be a strong indicator of diastolic dysfunction in diabetic patients.[12] Since our study was conducted among all diabetic patients it is consistent with our findings that the E/A ratio would be a predictor of the GLS ratio. In addition, we discovered a statistically significant, weak, negative correlation between HbA1c, duration of DM, and GLS value. This meant that as the duration of DM and HbA1c increased, the GLS value would decrease. This finding was in line with the study in Nepal (Shrestha SK et al.).[6] However, a study conducted by Sameh W et al. showed no statistically significant correlation between the duration of DM, HbA1c, and GLS values.[13] This may be since this study focused on T1DM while ours focused on T2DM.

Limitations

This was a cross-sectional study that is prone to incidence-prevalence bias. The study sample was also small due to the aggressive selection criteria.

In addition, the lack of diversity in the data pool and the single geographical location of its collection are also possible drawbacks of this study.

Conclusions

Findings included greater levels of lateral e', septal e', and LVEF in patients with abnormal GLS ratios, while LA size, LVESD, and E/A ratio had lower levels among those with reduced GLS. In addition, negative correlations were found between the duration of DM, HbA1c level, E/A ratio, and GLS

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ratio. Furthermore, the duration of DM, LVEF, and E/A ratio were found to be independent predictors of GLS value. These findings all highlight the structural and functional changes in the heart wrought by T2DM, signifying the importance of using STE and GLS in the follow-up of patients with T2DM to early detection of diabetic cardiomyopathy

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Conflict of Interest: The authors affirm that they do not have any conflicting interests.

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