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Original Article

The Association between Left Ventricular Myocardial Strains and Risk Factors of Cardiovascular Disease in a Population with Type 2 Diabetes Mellitus: A Primary Controlled Cross-Sectional Study

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ABSTRACT

Background: Cardiovascular complications are the primary reason for death in diabetic patients. Speckle tracking echocardiography is the method that can detect heart systolic dysfunction in the preclinical stage, even when the ejection fraction is normal range. This study aims to evaluate left ventricular myocardial strain parameters using the speckle tracking echocardiography method and to investigate the relationship between these parameters and cardiovascular risk factors in populations with type 2 diabetes mellitus.
Method: A controlled cross-sectional descriptive study was carried out on 75 people who have suffered type 2 diabetes mellitus and 75 controls. Participants in the study must satisfy the inclusion and exclusion criteria to be invited. They will be interviewed to take history, do clinical examinations, and do laboratory tests, and echocardiography. All data recorded on the data collection form was coded.
Results: The group of T2DM had a global longitudinal strain (-17.02±3.06%) and global circumferential strain (-29.04±6.39%) that were lower significantly than the controls. The global longitudinal strain had a positively significant correlation with values of blood pressure (r=0.3 for systolic and r=0.2 for diastolic), HbA1c (r=0.2), fasting plasma glucose (r=0.5), and total cholesterol (r=-0.25). The study also recorded there was a statistically significant correlation between global circumferential strain and values of blood pressure values (r=0.3 for systolic and r=0.2 for diastolic), and HDL (r=-0.3).
Conclusion: Both the global circumferential and global longitudinal strain have been reduced in individuals with type 2 diabetes mellitus. The reduction of global longitudinal strain and global circumferential strain has been correlated with cardiovascular risk factors (i.e. hypertension, poor glycemic control, increased BMI, and dyslipidemia).

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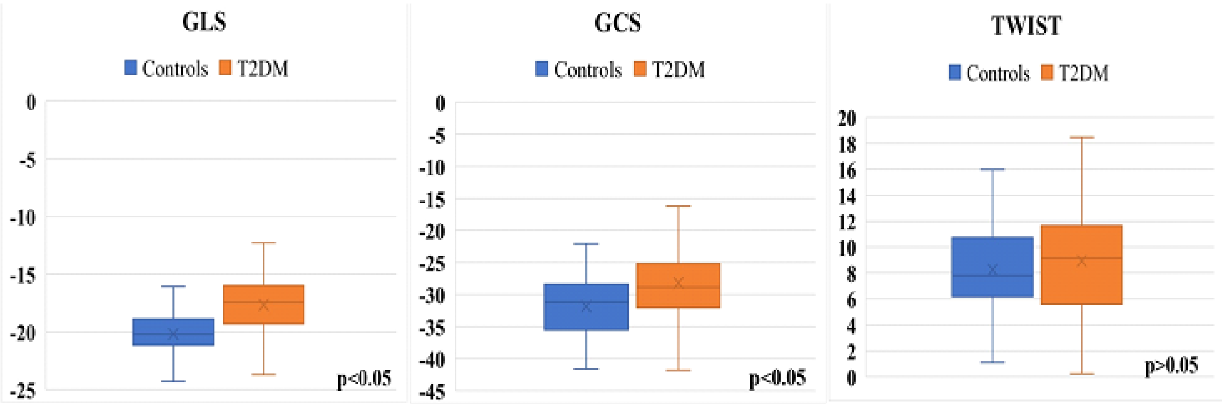
G R A P H I C A L A B S T R A C T



Introduction

Type 2 diabetes mellitus (T2DM) is a long-term illness that needs many medical treatments [1]. The prevalence of T2DM is quickly rising, making it a global epidemic. Diabetes affects 537 million adults (at the ages of 20 to 79) worldwide in 2021. By 2045, 783 million cases of diabetes are anticipated to exist, meaning the rate will increase by 46% [2]. To reduce and prevent either acute complications or long-term complications, besides glucose management, it is necessary to combinate multifactorial risk-reduction strategies, especially cardiovascular risk factors.

The momentous risk factor for cardiovascular diseases (CVD) is T2DM and individuals with T2DM have a higher prevalence of CVD mortality and morbidity than those who are not diabetic [3, 4]. In clinical practice, there are also some views that "diabetes is a cardiovascular disease" [5]. In a systematic literature review, 32.2% of type 2 diabetic patients had been affected by CVD, the leading reason for death for them [6].

Observational research has reported that people with T2DM have a higher risk of progressing heart failure (HF) 2-to-4-fold than non-diabetic subjects [7]. HF is also the main cause that makes type 2 diabetic patients have higher hospitalization prevalence than others [8, 9]. HF condition in individuals with T2DM has a pathophysiologic relationship between hypertension, atherosclerotic cardiovascular disease, and diabetic cardiomyopathy (DCM) [10, 11]. Although the DCM pathophysiology is more known, there are not any specific recommendations for diagnosis or treatment in clinical practice yet [12]. DCM is often asymptomatic in the early stage and its symptoms may overlap with other complications of diabetes, making the diagnosis difficult [12].

Ejection fraction (EF) of diabetic patients with HF may be preserved or reduced [13]. In the initial stages of HF, the diastolic function of the left ventricular (LV) may be distempered, whereas the left ventricular ejection fraction (LVEF) could be preserved [14]. Echocardiography can detect LV abnormalities associated with diabetes, such as increased mass, abnormal diastolic function, and reduced strain [15]. Especially, in 28% of individuals with T2DM who have had a normal diastolic function, LV longitudinal strain abnormalities have been found [16]. A sensible and practical parameter, global longitudinal strain (GLS) may detect LV dysfunctions and be a better predictor of CVD outcomes [17, 18]. Therefore, LV strain abnormalities should be considered as the first marker to detect heart dysfunctions in type 2 diabetic patients even when they are asymptomatic.

In Vietnam, especially in central Vietnam, there are currently not many studies on STE in people with T2DM. To confirm the great benefit of STE in the early detection of cardiac dysfunction, more published data are needed.

We conducted this study to provide more data on STE in diabetic patients so that health policymakers can provide the best possible medical care to people with T2DM.Initially, we identify LV strain parameters to detect LV dysfunctions at the initial stages of diabetes, and then we survey the relationship between LV strain parameters and CVD risk factors.

Materials and Methods

Study population

Our study collected 75 subjects with T2DM who came to the Hue University of Medicine and Pharmacy Hospital for treatment and examination between January 2021 and July 2023. T2DM was identified using the most recent clinical recommendations. Subjects who had these criteria were excluded: (1) pre-existing CVD that is not due to diabetes such as hypertrophic cardiomyopathy, dilated cardiomyopathy, valvular heart disease, stroke, and prior open-heart surgery; (2) LVEF < 50%; (3) poor echocardiography image quality; (4) atrial fibrillation (5) The patients did not consent to participate.

All participants' basic information was collected. Variables including age (years), gender (male/female), waist circumference (WC, cm), body mass index (BMI, kg/m^2), heart rate (HR, bpm), diastolic blood pressure (DBP, mmHg), systolic blood pressure (SBP, mmHg), T2DM duration (years), fasting blood glucose (G0, mmol/L), glycosylated hemoglobin (HbA1c, %), triglyceride (TG, mmol/L), total cholesterol (TC, mmol/L), high-density lipoprotein (HLD, mmol/L), and low-density lipoprotein (LDL, mmol/L). The 2020 recommendations of the American Diabetes Association (ADA) were used in evaluating glycemic control. We used glycemic goals: Preprandial capillary plasma glucose 4.4-7.2 mmol/L or HbA1c <7.0% [19]. Dyslipidemia assessment based on the recommendation of the National Cholesterol Education Program Coordinating Committee (NCEP) - ATP III. Criteria to diagnose dyslipidemia with: TG ≥1.7 mmol/L; TC ≥5.2 mmol/L; HDL ≤ 0.9 mmol/L; and LDL ≥2.6 mmol/L [20]. Hypertension was defined and assessed by the 2020 guidelines of the International Society of Hypertension. Diagnosis is determined when SBP is ≥140 mm Hg and/or DBP is ≥90 mm Hg in the office or clinic [21]. BMI is classified based on Asian standards of the World Health Organization (WHO) classification. The cut-off point for obese identify is 23 kg/m^2 [22]. Waist circumference is evaluated according to the WHO standards for Asians. People who have a waist circumference of males≥ 90 cm and females≥80 cm are diagnosed with central obesity [23]. T2DM duration was evaluated as one cardiovascular risk factor according to the American Diabetes Association's 2020 recommendations. T2DM duration ≥ 10 years is considered one cardiovascular risk factor [19].

We have also enrolled 75 control subjects to get normal parameters. The control group is those who have no history of special states such as hypertension, diabetes, and other cardiovascular diseases. They also have normal physical examination, electrocardiogram, and echocardiography.

Echocardiography

Echocardiography is performed in the Echocardiography room of Hue University of Medicine and Pharmacy Hospital, using Philips Affiniti 70 (Philips, American, 5S probe). After clearly explaining the examination, the subjects rest for 5-10 minutes, lie on the left side at an angle of about 45°, remove conductive jewelry, expose the chest, and apply ultrasound cream. Echocardiographic images were recorded at a speed of 100 mm/s, with simultaneous electrocardiogram measurement, measured at the end of expiration to limit the influence of respiration on the Doppler spectrum. Recording LV parameters by TM, 2D, and Doppler, include LVDs (LV diameter end-systolic); LVDd (LV diameter end-diastolic); LVPWd (LV posterior wall end-diastolic); LVPWs (LV posterior wall end-systolic); interventricular septum end-diastolic (IVSd); IVSs (interventricular septum end-systolic); LVEF; EF Simpson; LV mass (LVM); LV mass index (LVMI); the late and early peak velocity of the mitral annulus on the left ventricular sidewall (a and e, respectively); early diastolic mitral flow (E); late diastolic mitral flow (A); and left atrial volume (VLA). Parameters were recorded over 3 consecutive cardiac cycles, the final result being the average of these values. To assess the results of echocardiography, the American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) and ASE guidelines were used [24-26].

Strain images were offline analysed by QLAB software version 15.0 of Philips. Results of deformation have been recorded, including longitudinal strains in the 2-chamber plane (LS2), longitudinal strain in the 3-chamber plane (LS3), longitudinal strain in the 4-chamber plane (LS4), and global longitudinal strain (GLS). In each view, select 3 points (two points on either side of the annulus, 1 point at the apex) and the software automatically determines the endothelium margin and gives the myocardial deformation parameters of each segment of the myocardium in each section. The patients who had unclear endothelium were requiring manual correction. The strain value and strain velocity for each segment and the entire section are shown on the curve graph. Similarly, the apex, middle, and basal short-axis planes were employed to calculate circumferential strains (basal circumferential strain (CSb), apex circumferential strain (CSa), middle circumferential strain (CSm), and global circumferential strain (GCS)).

The local ethics committee of the Hue University of Medicine and Pharmacy has permissive this study.

Statistical analysis

The frequency (%) was used to express the categorical variables. To evaluate the differences in proportion, the Chi-square test was used. When presenting continuous variables, it is common to express them as standard deviations (SD). Standard deviations (SD) are a common way to present continuous variables, and we used the student t-test to compare them. Identify the correlation between the LV strain parameters and age, DM duration, heart rate, waist circumference, BMI, HbA1c, and lipid parameters by Pearson's correlation (normal distribution), or Spearman's correlation (non-normal distribution). A p-value of <0.05 or <0.01 was considered a significant statistic.

Results and Discussion

The following are our study's main conclusions: (1) in the subjects with T2DM, GLS and GCS were lower than the controls. These results suggest that STE should be used to detect early LV dysfunctions of patients with T2DM even though preserved LVEF; (2) There is a correlation between GLS, GCS, and some risk factors of CVD such as SBP, DBP, HbA1c, G_0, HDL, TC, LDL, and TG.

Baseline characteristics of the study population

Our study covered 150 people: 75 subjects with T2DM and 75 controls. The study population's basic characteristics are listed in Table 1. Gender, age, and BMI did not significantly differ between the two groups ($p > 0.05$), but the difference in SBP, DBP, and HR was recognized ($p < 0.05$). Besides, G_0, HbA1c, LDL, HDL, and TG, significantly differed between T2DM and others.

In these results of our study, either age or gender did not observe in difference ($p > 0.05$). This is an optimal feature for the study to exclude factors affecting cardiac morphology and function caused by gender and age. In addition, there was a significant difference between HR, SBP, DBP, G_0, HbA1c, TG, HDL, and LDL (Table 1). These results concur with those of a few other studies. In the research of Yang *et al.*, gender, age, BMI, and HR were not reported on significantly different between the groups, whereas HbA1c, G_0, LDH, and TG were significantly different [27]. In the Li W *et al.* (2022) research, there was a significant difference in BMI, DBP, and SBP, but there was no significant difference in HR and age [28]. In the same vein, Liao LL's study from 2022 found that while BMI, SBP, and DBP were significantly different, age was not significantly different between T2DM and others [29]. These findings of our study demonstrate once again that obesity and hypertension are popular co-morbidities and the primary risk factors to be worried about in people with T2DM.

Table 1: Baseline characteristics of the study population

	Controls group (n=75)	T2DM group (n=75)	P-value
Age (years)	59.85±8.40	62.56±11.01	0.093
Male (%)	51.7	48.3	0.739
BMI (kg/m^2)	21.92±2.32	21.86±3.72	0.899
HR (bpm)	73.68±10.29	80.04±7.64	<0.001
SBP (mm Hg)	118.20±7.69	141.73±20.95	<0.001
DBP (mm Hg)	71.07±8.94	79.20±10.99	<0.001
T2DM duration (years)	0	8.60±9.44	-
G_0 (mmol/L)	5.23±0.46	15.29±9.06	<0.001
HbA1c (%)	5.40±0.29	10.41±3.32	<0.001
HDL (mmol/L)	3.89±0.89	3.37±1.69	0.021
TC (mmol/)	5.77±0.95	5.33±2.54	0.164
TG (mmol/L)	1.48±0.90	2.64±4.29	0.025
LDL (mmol/L)	1.61±0.47	1.22±0.42	<0.001

BMI stands for body mass index; HR for heart rate; DBP for diastolic blood pressure; SBP for systolic blood pressure; T2DM for type 2 diabetes mellitus; G_0 for fasting glucose level; HbA1c for glycosylated haemoglobin; HDL for high-density lipoprotein; TC for total cholesterol; LDL for low-density lipoprotein; and TG for triglycerides.

Table 2: Parameters of traditional Doppler echocardiographic in the two groups

Parameters	Controls (n=75)	T2DM (n=75)	P-value
EF Simpson	63.59±5.24	59.88±5.91	<0.001
LVDs (cm)	2.79±0.31	2.74±0.47	0.475
LVDd (cm)	4.63±0.39	4.54±0.51	0.212
LVPWd (cm)	0.89±0.11	1.02±0.15	<0.001
LVPWs (cm)	1.37±0.14	1.43±0.15	0.018
IVSs (cm)	1.27±0.13	1.41±0.19	<0.001
IVSd (cm)	0.92±0.11	1.05±0.18	<0.001
LVFS (%)	39.83±3.97	38.97±4.80	0.230
LVEF (%)	70.26±4.84	67.72±9.99	0.050
LVM (g)	142.47±30.25	165.3±40.23	<0.001
LVMI (g/m^2)	92.3±21.44	107.75±24.47	<0.001
E (cm/s)	72.95±17.84	71.53±19.08	0.638
A (cm/s)	80.50±20.57	93.54±24.15	<0.001
Septal a (cm/s)	9.84±2.01	10.29±2.47	0.217
Septal e (cm/s)	8.15±2.05	6.50±1.81	<0.001
Septal S (cm/s)	8.29±1.47	8.13±1.84	0.551
Lateral S (cm/s)	9.95±1.96	9.14±1.92	0.012
Lateral e (cm/s)	10.61±2.38	8.51±2.34	<0.001
Lateral a (cm/s)	10.88±2.55	10.97±2.58	0.831
VLA (ml/m^2)	19.31±4.47	20.22±7.12	0.348

T2DM stands for type 2 diabetes mellitus; EF for ejection fraction; LVDs for LV diameter end-systolic; LVDd for LV diameter end-diastolic; LVPWd for LV posterior wall end-diastolic; LVPWs for LV posterior wall end-systolic; IVSs for interventricular septum end-systolic; IVSd for interventricular septum end-diastolic; LVFS for LV fractional shortening; LVEF for LV ejection fraction; LVM for LV mass; LVMI for LV mass index; VLA for volume of left atrial; E for early diastolic mitral flow; and A for late diastolic mitral flow.

Results of traditional doppler echocardiographic of the study population

Conventional Doppler echocardiographic parameters are presented in Table 2. The group of type 2 diabetic people has higher IVSd, LVPWd, IVSs, LVPWs, LVM, LVMI, and A than controls. Conversely, type 2 diabetic patients have lower EF Simpson, lateral S, lateral e, and septal e than controls. At $p < 0.01$ and $p < 0.05$, all difference is statistically significant. In the two groups, LVDd, LVDs, E, lateral a, septal S, septal a, and VLA were not statistically significant differences. Traditional Doppler echocardiography yielded results that were captured in the study: The group of people with T2DM had higher IVSd, LVPWd, IVSs, LVPWs, LVM, LVMI, A and lower EF Simpson, lateral S, lateral e, septal e than controls (Table 2). Our findings are similar to some other studies, there is no obvious distinction between the 2 groups [28, 29]; IVS was different [28]. According to the 2019 guidelines of the ESC, echocardiography is likely the preferred method for assessing the abnormal heart in individuals with DM [15]. Nowadays, the EF is still a useful parameter used to diagnose and classify HF [30, 31].

When compared to the controls, individuals with T2DM have lower EF and greater LVMI [32, 33]. Thus, hyperglycemia in individuals with T2DM had effects on morphology and function of left ventricular even when the LVEF is normal and the patients are asymptomatic.

Speckle tracking echocardiography results

Figure 1 describes the myocardial strains of patients with T2DM and controls. When compared to the controls, type 2 diabetic patients experienced a global longitudinal strain reduction (-17.02±3.06% vs. -20.32±2.04%, $p < 0.05$) and global circumferential strain reduction (-29.04±6.39% vs. -31.88±4.47%, $p < 0.05$). The patients with T2DM have no greater twist statistically significant than controls (9.23±6.75 vs. 8.23±3.38, $p > 0.05$).

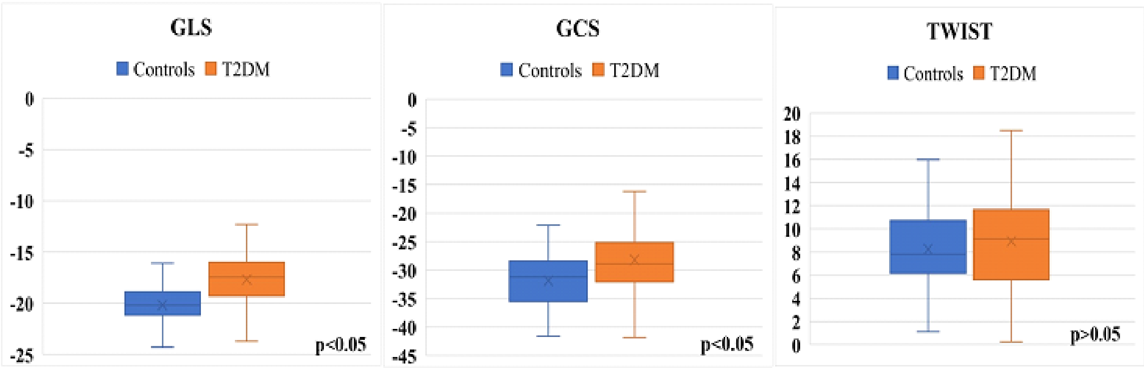


Figure 1: Myocardial strains in two groups

Table 3: Correlation between GLS, GCS, TWIST, and cardiovascular risk factors

Variables	GLS		GCS		TWIST	
	r	P-value	r	P-value	r	P-value
Age	0.085	0.302	-0.011	0.898	-0.032	0.702
T2DM duration	0.089	0.494	-0.145	0.260	0.134	0.098
BMI	0.087	0.288	0.038	0.648	0.035	0.673
Waist circumference	0.104	0.204	-0.010	0.902	-0.094	0.251
HR	0.171	0.036	0.137	0.094	0.015	0.854
DBP	0.202	0.012	0.248	0.002	-0.061	0.461
SBP	0.307	0.000	0.195	0.017	0.015	0.852
HDL	-0.194	0.071	-0.315	0.003	0.045	0.675
LDL	-0.184	0.123	-0.215	0.069	-0.021	0.862
TG	0.032	0.766	0.201	0.057	0.179	0.092
TC	-0.256	0.028	-0.169	0.149	0.463	0.000
HbA1c	0.218	0.007	0.032	0.760	0.038	0.718
G_0	0.519	0.000	0.083	0.311	0.097	0.239

T2DM stands for type 2 diabetes mellitus; GLS for global longitudinal strain; GCS for global circumferential strain; HR for heart rate; BMI for body mass index; DBP for diastolic blood pressure DBP; SBP for systolic blood pressure; G_0 for fasting glucose; HbA1c for glycosylated hemoglobin; TG for triglycerides; HDL for high-density lipoprotein; LDL for low-density lipoprotein; and TC for total cholesterol.

When compared with the controls, type 2 diabetic patients had reduced GLS and GCS than controls ($p<0.05$) (Figure 1). These findings were similar to some research on subjects with T2DM. In the research of Abd El Moneum MS *et al.* (2018), when conducting a study on 100 people with T2DM without cardiovascular symptoms and preserved ejection fraction, 43% of the patient group had GLS is abnormal and suggests that using STE to detect preclinical systolic dysfunction may offer helpful information for risk stratification [34]. In the study of Liao LL *et al.* (2022), the group of T2DM had lower GLS than the control group (-19.13±1.73% vs. -16.82 ±2.59%; $p < 0.001$). This means that damage to the myocardium has occurred even though the LVEF is still normal [29]. Another study by Li W *et al.* (2022) also noted that individuals with T2DM have lower GLS than the control group and concluded that 2D STE could detect muscle dysfunction [28]. In another systematic review by Silva *et al.*, when conducting data aggregation on 19 studies using 2D STE (1774 patients with diabetes) and 9 studies using 3D STE (488 patients with diabetes), concluded cardiac deformity abnormalities on STE 2D and STE 3D is valuable for early identification of preclinical systolic dysfunction, this difference becoming more apparent when combined with risk factors and status ventricular remodelling [35]. The GLS reduction occurred even though the patients had no symptoms. STE is the tool that helps to detect early asymptomatic regional myocardial dysfunction and its parameters were considered as a sensitivity index to evaluate left ventricular dysfunction [36-38].

Correlation between left ventricular strains and cardiovascular risk factors

GLS parameter was positively correlated with HR, SBP, DBP, HbA1c, G_0, TC, and HDL. However, we did not recognize a correlation between the GLS parameter and age, T2DM duration, BMI, WC, TG, and LDL (Table 3). GCS was correlated with SBP, DSP, and HDL. The correlation between GCS and age, T2DM duration, BMI, HR, waist circumference, HbA1c, G_0, TG, LDL, and TG were not recorded (Table 3).

There was no correlation between TWIST and age, T2DM duration, WC, BMI, HR, HbA1c, G_0, HDL, LDL, and TG, but also was correlated with TC (Table 3). Diabetes increases cardiovascular risks that also increase the rapid progression of complications in people with T2DM [15,19,39]. The correlation between GLS and some risk factors of CVD was indicated by some previous studies. In the research of Abd El Moneum MS *et al.* (2018), symptoms and duration of diabetes were only independent predictors of GLS reduction [34]. In another study by Lezama FS *et al.* (2021), the GLS reduction was linked to the stage of diastolic dysfunction, abnormalities in traditional Doppler echocardiography parameters, and the attendance of CVD risk factors [40]. In primary results, GLS was positively correlated with HR, SBP, DBP, HbA1c, G_0, TC, and HDL; GCS was correlated positively with HDL, SBP, and DBP; TWIST and TC were positively correlated (Table 3). Diabetic patients should undergo a systematic evaluation regularly for cardiovascular risk factors, including hypertension, obesity/overweight, not good glycemic control, and dyslipidemia. This is completely consistent with the guidelines and recommendations of the ADA, the ESC, and the European Society of Endocrinology [15,19].

Conclusion

Diabetes has certain effects on heart function even when patients have no clinical symptoms and the ejection fraction is still preserved. This study has shown that type 2 diabetic patients exhibit reduced strain parameters in speckle-tracking echocardiography. The abnormalities of global longitudinal strain or global circumferential strain had correlated with cardiovascular disease risk factors, such as increasing BMI, hypertension, poor glycemic control, and dyslipidemia.

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Authors' Contributions

The authors have the same contribution to the stage in editing the article and are responsible for all aspects of this work.

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