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Quantitative evaluation of subclinical left ventricular dysfunction in patients with type 2 diabetes mellitus by three-dimensional echocardiography

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Abstract

Left ventricular (LV) function undergoes subtle changes (subclinical left ventricular dysfunction) in a large proportion of patients with type 2 diabetes (T2DM) who develop diabetic cardiomyopathy. This study aimed to quantify LV myocardial strain and synchrony in T2DM by real-time three-dimensional echocardiography (RT-3DE), and to evaluate subclinical LV dysfunction in T2DM at different glycemic control levels. Seventy-two patients with T2DM with an LV ejection fraction (LVEF) ≥ 55% and 45 healthy individuals as controls who underwent RT-3DE were studied. Patients were also subdivided into the DMa group (glycosylated hemoglobin < 7%, n = 38) and the DMb group (glycosylated hemoglobin ≥ 7%, n = 34). Three-dimensional strain and synchronization parameters of the left ventricle were measured by RT-3DE and compared among the three groups. Despite a similar LVEF, global longitudinal strain (GLS), global circumferential strain (GCS), and global area strain (GAS) in the DMb group were lower, and the standard deviation of peak time (Tm-SD) and the maximum difference in peak time (Tm-Dif) in the DMb group higher, than those in the control and DMa groups (all $p < 0.05$). Multivariable linear regression analysis showed that the duration of diabetes was independently associated with GCS ($\beta = -0.516$, $p < 0.001$) and GAS ($\beta = -0.391$, $p = 0.005$). HbA1c levels were independently associated with GLS ($\beta = -0.675$, $p < 0.001$), Tm-SD ($\beta = 3.363$, $p < 0.001$), and Tm-Dif ($\beta = 3.895$, $p < 0.001$). RT-3DE can detect subclinical myocardial dysfunction in poor glycemic control of T2DM, and myocardial dysfunction is associated with the duration of diabetes and HbA1c.

Keywords Type 2 diabetes mellitus · Echocardiography · Real-time three-dimensional speckle-tracking imaging · Left ventricular dysfunction · Subclinical myocardial dysfunction

Introduction

Diabetes mellitus (DM) is a common risk factor for cardiovascular and cerebrovascular events [1]. The risk of cardiovascular disease in patients with DM is two to three times higher than that of healthy people, and nearly 80% of patients with DM die of cardiovascular complications [2]. Moreover, one of the main causes of increased mortality in DM is diabetic cardiomyopathy (DCM) [3, 4], which refers to cardiac dysfunction and heart failure in DM unrelated to coronary artery disease and hypertension [5]. A large proportion of patients with type 2 DM (T2DM) undergo subtle changes in cardiac function before the diagnosis of DCM. These changes include impaired left ventricular (LV) diastolic function and a reduction in myocardial perfusion, which is termed subclinical LV dysfunction (LVD) [6, 7]. Detection of T2DM subclinical LVD dysfunction at an early stage is important for preventing DCM.

Real-time three-dimensional echocardiography (RT-3DE) speckle-tracking imaging technology can track myocardial trajectory movement in 3D space and acquire 3D myocardial strain, which can be used to quantitatively analyze LV function [8, 9]. The sensitivity and specificity of this technique are significantly better than the traditional ejection fraction. Additionally, subclinical LVD (whereby myocardial strain has been reduced before the LV ejection fraction (LVEF) is preserved) can be determined by this technique [10, 11]. LV

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synchronous motion, which is an important mechanism, also affects LV function. The time for the systolic period of the left ventricle to reach minimum volume is consistent. When LV motion is not synchronized, the peak contraction time of each segment of the myocardium is different. The RT-3DE full-volume technique can comprehensively and quantitatively obtain the systolic peak time of the left ventricle. The standard deviation of the peak time (Tm-SD) and the maximum peak time difference (Tm-Dif) can then be used to evaluate LV systolic synchrony [12].

This study aimed to analyze LV myocardial strain and synchrony in T2DM patients with a normal LVEF by RT-3DE. We also aimed to apply these strain and synchrony parameters to assess subclinical LVD in T2DM with different degrees of glycemic control.

Methods

Subjects

In this prospective study we recruited 72 patients (age 30–64 years) with T2DM and an LVEF≥55%, which is in line with the 2010 American Diabetes Guidelines diagnostic criteria [13]. According to the control level of glycated hemoglobin (HbA1c), we divided the patients into the two following groups. The DMa group comprised 38 patients with HbA1c levels < 7% (good glycemic control) and the DMb group comprised 34 patients with HbA1c levels≥7% (poor glycemic control) [13]. The duration of diabetes was recorded as reported by the patient. For comparison, 45 age- and sex-matched healthy volunteers with no history of cardiac disease or DM were recruited from the local medical center (control group). The height and weight of all subjects were measured and body mass index was calculated as weight (kg) divided by the square of height (m). Blood pressure was measured in the right arm in a sitting position.

We excluded patients who had hypertension (systolic blood pressure≥140 mmHg), coronary heart disease, heart valve disease, myocardial infarction, cardiomyopathy, severe renal failure (estimated glomerular filtration rate < 30 ml/min), or poor echocardiographic image quality.

All subjects underwent echocardiography, electrocardiography, and biochemical examinations. Our Institutional Review Board approved the study. Informed consent was obtained from all patients.

Laboratory analysis

Biochemical analyses, including measurement of total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, and fasting plasma glucose levels, were performed using standard laboratory techniques in all subjects.

In patients with T2DM, HbA1c was measured < 2 weeks before the echocardiographic evaluation.

Echocardiography

Echocardiographic imaging was performed using the Vivid E9 GE Medical Systems commercial scanner (GE Vingmed Ultrasound, Norway), equipped with 5S probe (1–5 MHz) and 4 V probe (1.5–4.0 MHz). The subjects lay on their left side and breathed calmly, and electrocardiograms were recorded simultaneously during the examinations. Two-dimensional (2D) echocardiography with the 5S probe was used to determine the left ventricular mass index (LVMI), early and late mitral valvular blood flow velocity peak (E, A), and LV sidewall mitral annular early peak velocity (Em), then E/A and E/Em were calculated. The LVEF was measured by the Simpson biplane method. We obtained the cardiac isovolumic contraction time (ICT), isovolumic relaxation time (IRT), and ejection time (ET). We then calculated the Tei index as follows:

$$Tei = (ICT + IRT)/ET.$$

RT-3DE with the 4 V probe was used to obtain the apical four-chamber view and then entered 4D mode to record the subject's six consecutive cardiac cycles during a breath-hold. The "store" button was then used to store 3D dynamics. It was necessary to avoid occasional premature beats when collecting images with the six consecutive cardiac cycles in sinus rhythm. The images required a heart rate with a frame rate > 40%. The range of the imaging frame rate in this study was 25–49.

Echocardiographic image analysis

Echo PAC analysis software (version: 201) was used for analysis of echocardiographic images. We selected the midpoint of the mitral annulus and the apical endocardium at the end of diastole and end-systole, respectively. The system automatically delineates the endocardium and epicardium and is manually adjusted to correctly track the myocardium. The software automatically calculates 3D myocardial strain and 16-segment peak contraction time of the left ventricle. If ≤2 segments of the left ventricle cannot be analyzed, we click the "approve" button in the software, accept the analysis results, and obtain the strain value. If the image quality is too poor for analysis, we do not accept it as valid.

Data from a total of 80 patients were initially collected for this study, 3 of whom were significantly obese and could not hold their breath and 2 of whom had atrial fibrillation, which resulted in failure to acquire 3D full-volume images. In addition, no data were available from 3 patients because of poor image quality. Finally, 72 patients were enrolled.

After this analysis, we obtained 3D general longitudinal strain (GLS), general circumferential strain (GCS), general radial strain (GRS), and general area strain (GAS) (Fig. 1). After standardization of the RR interval of the cardiac cycle, the Tm-SD and Tm-Dif were used as parameters for synchrony of LV wall contraction. Image storage and analysis were performed by experienced physicians.

Intra-observer and inter-observer reproducibility

Echocardiographic image analysis was repeated in 10 selected subjects. Intra-observer reliability assessment was performed 1 week apart by the same observer on the same echocardiographic images in a random order. Assessment of inter-observer reproducibility was carried out by another independent observer.

Statistical analysis

All statistical analyses were performed with SPSS 17.0 (SPSS, Chicago, IL, USA). Continuous data are presented as mean $\pm$ SD. Frequencies are expressed as percentages. The Student's t-test or one-way analysis of variance with the post hoc least significant difference test was used as appropriate for comparison of continuous data among the three groups. The chi-square test was used for comparing the variable of sex. Pearson's correlation was chosen for test correlations among parameters of the three groups. Independent determinants of subclinical LV dysfunction in T2DM were examined using multivariate stepwise linear regression. p values of < 0.05 were considered statistically significant.

The intraclass correlation coefficient (ICC) was used to evaluate inter- and intra-observer variability. Clinical significance was categorized as follows: good, ICC ≥ 0.75; moderate, ICC ≥ 0.4 and < 0.75; poor, ICC < 0.4.

## Results

Participants' characteristics

The characteristics of the three groups of participants are shown in Table 1. There were no differences in sex, age, body mass index, heart rate, and blood pressure among the three groups (all p values > 0.05). Total cholesterol and high-density lipoprotein levels were greater in patients with T2DM than in those in the control group. However, low-density lipoprotein levels were lower in patients with T2DM than in those in the control group. The duration of diabetes and HbA1c levels were higher in the DMb group than in the DMa group.

General echocardiographic parameters

General parameters of echocardiography among the three groups are shown in Table 2. The LVMI in the DMa and DMb groups was higher than that in the control group (both p values < 0.05). The LVMI was not different between the DMb and DMa groups. The E peak in the DMb group was lower than that in the DMa and control groups (both p values < 0.05). The A peak, E/A ratio, and E/Em ratio in the DMb group were higher than those in the DMa and control groups (all p values < 0.05). There were no differences in the E peak, LVEF, and Tei index among the three groups.

Three-dimensional strain and synchronization parameters

The DMb group had decreased peak systolic strains in GLS, GCS, and GAS compared with DMa and control groups (-16.67 ± 2.44 vs -19.31 ± 3.91 vs -20.19 ± 3.23, -14.80 ± 6.10 vs -19.76 ± 4.95 vs -19.30 ± 6.34, and -26.49 ± 5.42 vs -30.26 ± 5.50 vs -32.99 ± 6.60; all p values < 0.05). Nevertheless, Tm-SD and Tm-Dif in the DMb group were higher than those in DMa and control groups (36.98 ± 6.36 vs 26.23 ± 7.87 vs 27.00 ± 6.93, and
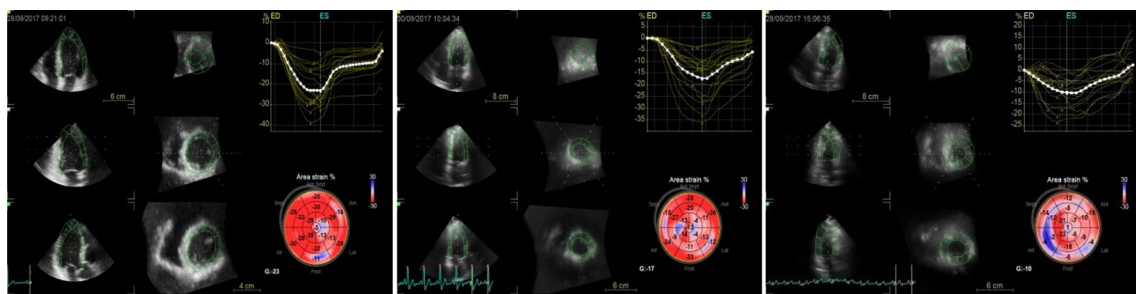
Fig. 1 3D strain parameter analysis showing that the color of the bull's eye in the controls, DGa, and DMb groups gradually faded

Table 1 Baseline characteristics of the three groups

Parameter	Normal n = 45	DMa group n = 38	DMb group n = 34	F/t	p Value
Male gender, n (%)	23 (51%)	19 (50%)	19 (56%)	–	
Age (years)	50.08 ± 6.01	52.35 ± 8.25	53.15 ± 7.50	1.968	0.144
Body mass index (kg/m^2)	24.30 ± 1.90	25.08 ± 1.55	24.60 ± 2.38	1.656	0.195
Heart rate (beats/min)	67.10 ± 7.21	66.34 ± 8.01	69.07 ± 6.63	1.325	0.270
Systolic BP (mm Hg)	119.00 ± 10.46	121.89 ± 10.78	121.02 ± 9.57	0.865	0.424
Diastolic BP (mmHg)	77.37 ± 6.27	79.48 ± 8.41	78.53 ± 8.04	0.701	0.566
Diabetes duration (years)	–	2.26 ± 1.76	10.36 ± 3.45#	12.724	< 0.001
Fasting plasma glucose (mmol/l)	4.73 ± 1.20	8.14 ± 1.09*	8.31 ± 0.69*	157.099	< 0.001
HbA1c (%)	–	6.08 ± 0.36	9.22 ± 0.92#	19.402	< 0.001
Plasma triglycerides (mmol/l)	1.19 ± 0.27	1.89 ± 0.44*	1.81 ± 0.57*	33.210	< 0.001
Total cholesterol (mmol/l)	4.13 ± 0.58	4.41 ± 0.52*	4.47 ± 0.38*	5.037	< 0.001
LDL (mmol/l)	2.78 ± 0.30	2.25 ± 0.60*	2.34 ± 0.51*	14.675	< 0.001
HDL (mmol/l)	1.21 ± 0.83	1.30 ± 0.64	1.33 ± 0.75	0.700	0.502

Data given as the mean ± SD

HDL high-density lipoprotein cholesterol, *LDL* low-density lipoprotein cholesterol

*$p < 0.05$ versus normal group; #$p < 0.05$ versus DMa group

Table 2 Echocardiographic findings of the three groups

	Normal n = 45	DMa n = 38	DMb n = 34	F	p value
LV mass index (g/m^2)	107.49 ± 17.88	131.85 ± 19.16*	137.49 ± 12.00*	36.581	< 0.001
E (cm/s)	86.04 ± 15.11	85.49 ± 20.40	58.12 ± 12.54*	34.374	< 0.001
A (cm/s)	68.98 ± 9.98	91.33 ± 15.63**	88.36 ± 18.46**	28.434	< 0.001
E/A ratio	1.28 ± 0.31	0.91 ± 0.27*	0.70 ± 0.25*	43.038	< 0.001
E/Em ratio	6.66 ± 1.44	7.27 ± 2.95	5.16 ± 1.64*#	9.567	< 0.001
LVEF (%)	66.86 ± 3.83	65.08 ± 7.62	68.30 ± 6.85	2.472	0.089
Tei	0.49 ± 0.10	0.42 ± 0.09	0.46 ± 0.24	2.318	0.103
GLS (%)	− 20.19 ± 3.23	− 19.31 ± 3.91	− 16.67 ± 2.44*#	11.687	< 0.001
GCS (%)	− 19.30 ± 6.34	− 19.76 ± 4.95	− 14.80 ± 6.10*#	7.890	0.001
GRS (%)	45.67 ± 7.51	45.45 ± 6.98	44.50 ± 4.85	0.322	0.726
GAS (%)	− 32.99 ± 6.60	− 30.26 ± 5.50	− 26.49 ± 5.42*#	11.623	< 0.001
Tm-SD (ms)	27.00 ± 6.93	26.23 ± 7.87	36.98 ± 6.36*#	25.695	< 0.001
Tm-Dif (ms)	26.82 ± 8.87	30.63 ± 7.02	45.31 ± 10.67*#	44.523	< 0.001

Data given as the mean ± SD. *GLS* global longitudinal strain, *GCS* global circumferential strain, *GRS* general radial strain, *GAS* global area strain, *Tm-SD* standard deviation of peak time, *Tm-Dif* maximum difference in peak time

*$p < 0.05$ versus normal group; #$p < 0.05$ versus DMa group

45.31 ± 10.67 vs 30.63 ± 7.02 vs 26.82 ± 8.87 l; both p values < 0.05) (Table 2 and Fig. 2).

Associations between general parameters and 3D parameters in T2DM

Duration of diabetes was inversely correlated with 3D strain parameters (GLS, GCS, GAS) and positively associated with 3D synchrony parameters (Tm-SD, Tm-Dif) ($r = − 0.229$, $p = 0.043$; $r = − 0.412$, $p < 0.001$; $r = − 0.327$, $p = 0.005$; $r = 0.529$, $p < 0.001$; $r = 0.523$, $p < 0.001$, respectively).

Similarly, HbA1c values were negatively correlated with 3D strain parameters (GLS, GCS, GAS) and positively correlated with 3D synchrony parameters (Tm-SD, Tm-Dif) ($r = − 0.329$, $p = 0.005$; $r = − 0.376$, $p = 0.001$; $r = − 0.313$, $p = 0.007$; $r = 0.646$, $p < 0.001$; $r = 0.581$, $p < 0.001$, respectively). Additionally, fasting plasma glucose levels were negatively correlated with 3D strain parameters (GLS, GAS) and the E/A ratio was positively correlated with 3D strain parameters (GLS, GAS) ($r = − 0.266$, $p = 0.004$; $r = − 0.341$, $p < 0.001$; $r = 0.250$, $p = 0.008$; $r = 0.236$, $p = 0.011$, respectively) (Table 3).
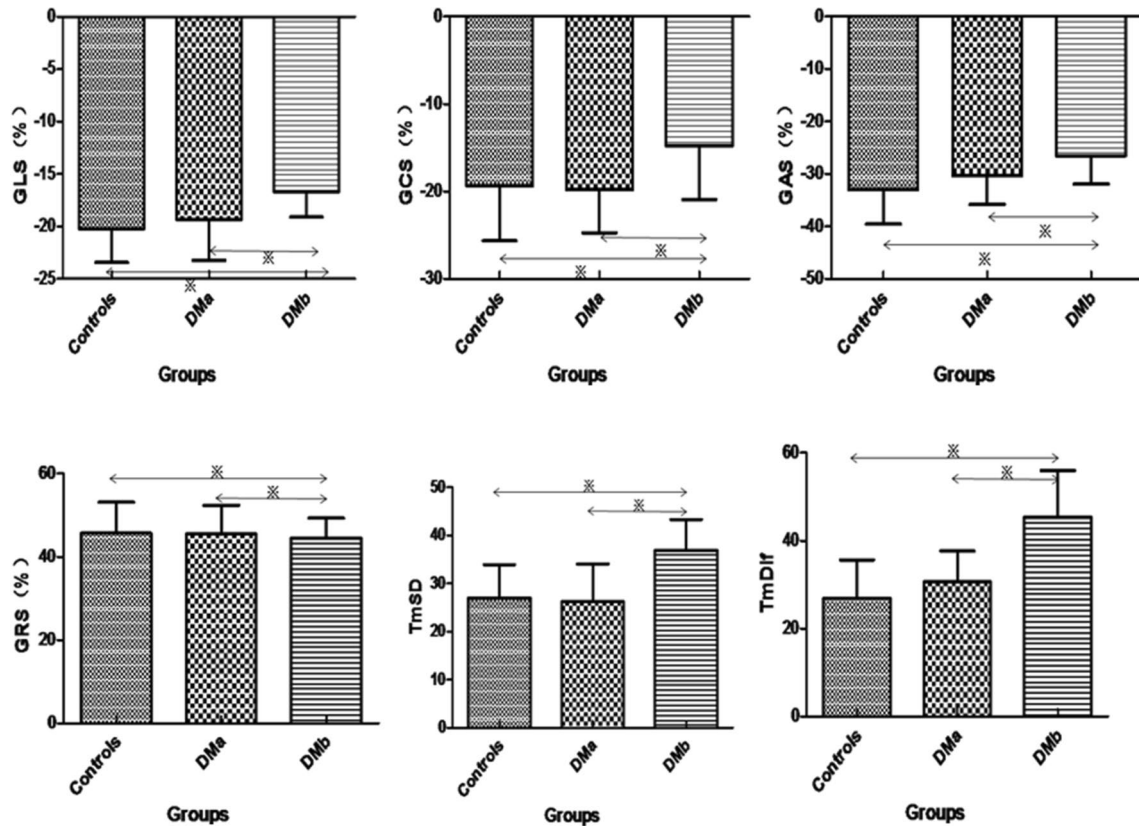
Fig. 2 Comparison of 3D strain and synchronization parameters among the three groups. *GLS* global longitudinal strain, *GCS* global circumferential strain, *GRS* general radial strain, *GAS* global area strain, *Tm-SD* standard deviation of peak time, *Tm-Dif* maximum difference in peak time. *$p < 0.05$

Table 3 Correlation analysis of general parameters with myocardial 3D parameters in T2DM

	GLS (*r*)	*p* value	GCS (*r*)	*p* value	GAS (*r*)	*p* value	Tm-SD (*r*)	*p* value	Tm-Dif (*r*)	*p* value
Diabetes duration (years)	−0.229	0.043	−0.412	<0.001	−0.327	0.005	0.529	<0.001	0.523	<0.001
Fasting plasma glucose (mmol/l)	−0.266	0.004	−0.204	0.057	−0.341	<0.001	0.202	0.059	0.420	0.082
HbA1c (%)	−0.329	0.005	−0.376	0.001	−0.313	0.007	0.646	<0.001	0.581	<0.001
Plasma triglycerides (mmol/l)	−0.209	0.102	−0.367	0.059	−0.259	0.083	0.458	0.061	0.582	0.057
Total cholesterol (mmol/l)	−0.094	0.193	−0.356	0.073	−0.087	0.064	0.237	0.074	0.304	0.075
LDL (mmol/l)	0.672	0.062	−0.143	0.482	0.041	0.326	−0.319	0.071	−0.385	0.086
LV mass index (g/m²)	−0.228	0.073	−0.142	0.127	−0.257	0.065	0.297	0.051	0.430	0.064
E/A ratio	0.250	0.008	0.098	0.294	0.236	0.011	−0.192	0.069	−0.428	0.071
E/Em ratio	−0.252	0.066	−0.077	0.411	−0.053	0.569	−0.218	0.068	−0.241	0.079

GLS global longitudinal strain, *GCS* global circumferential strain, *GAS* global area strain, *Tm-SD* standard deviation of peak time, *Tm-Dif* maximum difference in peak time, *LDL* low-density lipoprotein cholesterol

Analysis of risk factors for preclinical LV myocardial dysfunction

Clinical and echocardiographic parameters were analyzed using multiple stepwise linear regression, and we assessed risk factors for subclinical LV dysfunction. Confounding factors included the duration of diabetes, levels of HbA1c, fasting blood glucose, triglycerides, total cholesterol, and low-density lipoprotein, the LVMI, E/A ratio, and E/Em ratio. Inclusion of these parameters was based on physiological rationality and the results of the aforementioned data. We found that the duration of diabetes was independently

associated with GCS ($\beta = -0.516$, $p < 0.001$) and GAS ($\beta = -0.391$, $p = 0.005$) (Table 4). Moreover, HbA1c levels were independently associated with GLS ($\beta = -0.675$, $p < 0.001$), Tm-SD ($\beta = 3.363$, $p < 0.001$), and Tm-Dif ($\beta = 3.895$, $p < 0.001$).

Inter-observer and intra-observer variability

Table 5 shows inter-observer and intra-observer variability for echocardiographic image analysis. The ICCs for inter- and intra-observer variability were 0.835–0.993 and 0.802–0.978, respectively, which suggested that echocardiographic image analysis was consistent.

Discussion

The main findings of our study were as follows. 3D myocardial strain parameters in the DMb group were lower, and 3D synchronization parameters higher, compared with the DMa and control groups. The duration of diabetes and HbA1c levels were independently associated with GLS, GCS, GAS, Tm-SD, and Tm-Dif.

Analysis of 3D myocardial strain and synchrony parameters among the three groups

In the present study, there was no significant difference in the LVEF between controls and patients with T2DM. Determination of the ejection fraction has been shown to be insufficient for detecting minor myocardial abnormalities [11]. Speckle-tracking echocardiography can measure subtle alterations of an impaired myocardium in patients with preclinical T2DM. Subclinical LVD is considered to be an early sign of DCM [14, 15].

Most previous studies measured LV strain by speckle-tracking echocardiography in patients with T2DM for detection of LV systolic and diastolic dysfunction, and consequent impairment of LV function [16–18]. For decades, 2D strain was generally used to analyze cardiac function. However, since 2D strain image acquisition is affected by plane motion and perspective, this may misunderstand the true anatomy of the left ventricle [19]. Therefore, 2D speckle-tracking echocardiography (2DSTE) may seriously misunderstand strain data under various pathological conditions. 3D full-volume images contain all-round information of the left ventricular 3D structure, have the potential to overcome the inherent limitations of 2DSTE, and are more accurate and effective than 2DSTE in evaluating LV myocardial function [20, 21]. 3D speckle-tracking echocardiography (3DSTE) promises to simplify the assessment of tissue deformation by replacing the traditional parameters of multidirectional strain assessments [19]. Studies have shown that real-time 3DSTE can

Table 4 Multivariable linear regression analysis of all patients

	GLS			GCS			GAS			Tm-SD			Tm-Dif		
	β	95% CI	p value	β	95% CI	p value	β	95% CI	p value	β	95% CI	p value	β	95% CI	p value
Diabetes duration (years)	−0.033	–	0.846	−0.516	0.244–0.788	<0.001	−0.391	0.122–0.660	0.005	0.110	–	0.424	0.203	–	0.164
HbA1c (%)	−0.675	0.212–1.137	0.005	−0.157	–	0.339	−0.155	–	0.361	3.363	2.416–4.311	<0.001	3.895	2.595–5.195	<0.001

CI confidence interval, *GLS* global longitudinal strain, *GCS* global circumferential strain, *GAS* global area strain, *Tm-SD* standard deviation of peak time, *Tm-Dif* maximum difference in peak time

Table 5 Inter-observer and intra-observer variability of 3D strain and synchronization parameters (n = 20)

	Inter-observer (n = 10) ICC	95% CI	Intra-observer (n = 10) ICC	95% CI
GLS	0.835	0.669–0.956	0.802	0.688–0.947
GCS	0.906	0.667–0.976	0.968	0.879–0.992
GAS	0.980	0.924–0.995	0.855	0.552–0.963
GRS	0.992	0.968–0.998	0.907	0.671–0.976
Tm-SD	0.993	0.974–0.998	0.945	0.796–0.986
Tm-Dif	0.992	0.967–0.998	0.978	0.913–0.994

ICC interclass coefficient, *CI* confidence interval, *GLS* global longitudinal strain, *GCS* global circumferential strain, *GAS* global area strain, *GRS* general radial strain, *Tm-SD* standard deviation of peak time, *Tm-Dif* maximum difference in peak time

comprehensively and rapidly quantitatively evaluate LV systolic function in 3D space [8, 9], and real-time 3D full volume can quantitatively evaluate the synchrony of LV contraction [12]. In our study, these two techniques were used to obtain myocardial strain and synchrony parameters (GLS, GCS, GAS, GRS, Tm-SD, and Tm-Dif). Various studies have shown that these 3D parameters are reproducible and that they can be used to evaluate subtle LV systolic dysfunction with a preserved LVEF [9].

HbA1c reflects the level of terminal glycosylation products in the body. HbA1c can be used to monitor the level of glycemic control in patients with diabetes to determine long-term glycemic control level and stability of patients with T2DM [13]. HbA1c values < 7% reflect good blood sugar control [13]. Our study showed that patients with good blood glucose control (HbA1c values < 7%) showed no difference in 3D myocardial strain parameters and synchronization parameters compared with the control group, which is consistent with previous studies [10, 22]. We also found lower 3D strain parameters (GLS, GCS, and GAS) and higher synchronization parameters (Tm-SD and Tm-Dif) in patients with poor glucose control (HbA1c values ≥ 7%) compared with those with good blood glucose control. These findings suggest that myocardial function is slightly impaired in T2DM patients with poor glucose control, manifesting as subclinical LVD [10, 22].

Correlation and regression analysis

Impaired islet cell function contributes to the pathophysiology of T2DM. Most previous studies have shown that, with a prolonged duration of T2DM, islet cell function gradually declines, leading to worsening of glycemic control [23]. Our study showed that HbA1c values were positively correlated with the duration of T2DM, in accordance with this previous finding. Simultaneously, myocardial strain parameters were negatively correlated with HbA1c values and the duration of diabetes, and synchronous parameters were positively correlated with HbA1c values and the duration of diabetes. Multiple regression analysis showed that HbA1c values and the duration of T2DM were independently associated with GLS, GCS, GAS, Tm-SD, and Tm-Dif. These findings suggest that T2DM with a shorter duration has better control of blood glucose levels [24] and myocardial function, and patients with a longer duration have poor control of blood glucose levels [24] and subclinical myocardial dysfunction. Conversely, observational studies indicated that HbA1c was associated with the risk of heart failure in T2DM patients, independent of blood pressure, obesity, age, and the presence of coronary heart disease [25, 26]. These data support the notion that glycemic control in individuals with T2DM is a critical mechanism in the prevention of LV cardiac dysfunction [27].

Elevated HbA1c levels indicate poor glycemic control in DM. Persistent hyperglycemia can lead to resistance to insulin metabolism in the cardiac tissue, which occurs independently of other cardiac risk factors [27]. The mechanism of myocardial damage caused by diabetes is not fully understood. Possible causes include cardiac insulin resistance, glucotoxicity, mitochondrial dysfunction, oxidative stress, endoplasmic reticulum stress, impaired calcium treatment, systemic and tissue renin–angiotensin–aldosterone system activation, impaired mitochondria and autophagy, coronary microvascular dysfunction, and dysregulation of exosomes [27–32]. These factors continuously damage the myocardium, leading to lipid accumulation and disturbance of autonomic nerve and humoral regulation, and may eventually lead to myocardial cell hypertrophy, necrosis, myocardial fibrosis, and increased myocardial weight [33]. We considered that myocardial stiffness is characterized by decreased myocardial strain and poor myocardial synchrony, which is reflected in subclinical LVD.

Conclusions

RT-3DE can detect subclinical LV myocardial dysfunction in poor glycemic control of T2DM. LV myocardial dysfunction is associated with the duration of diabetes and HbA1c levels of T2DM.

Limitations

The main limitation of this trial is that no follow-up studies have been conducted. When glycemic reduction in the poor glycemic control of T2DM (HbA1c values ≥ 7%), whether their LV function is improved has not been studied. Second, the population comprised patients with uncomplicated

T2DM without any other significant comorbidities. Therefore, there is limited applicability of our results. The real-world population has a high incidence of comorbidities. Consequently, we could not perform receiver-operating characteristic curve analysis to identify an appropriate level of myocardial strain and synchrony parameters for subclinical myocardial dysfunction. This might have weakened the clinical implications of our study. Future research needs to address this issue.

Compliance with ethical standards

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