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Cut-Off Point Value to Evaluate Abnormality of Systolic Deformation Parameters in Patients with Type 2 Diabetes

ABSTRACT

Objective: The goal of this study is to determine the cut-off value that can be used to evaluate systolic deformation parameters and the prevalence of abnormalities in left ventricular function in patients with type 2 diabetes (T2D).

Materials and methods: The study used a cross-sectional descriptive method. The study's sample size was 311 people (including 192 subjects with T2D and 119 subjects as the controls). The subjects who participated had to meet both the exclusion criteria and inclusion criteria. Besides clinical examinations, they underwent an echocardiography and laboratory tests. Statistical analyses included frequency, mean, unpaired t-test or Mann-Whitney U test, and receiver operating characteristic curve.

Results: The average age of the T2D group was 66.5 ± ± 10.2 years, and the control group were aged 64.7 ± 6.0 years; the groups comprised 37% men and 63% women. The cut-off value to evaluate the abnormality of global longitudinal strain (GLS) was –19%, the global longitudinal strain rate (GLSR) was –1.9 1/s, the global circumferential strain (GCS) was –27.4%, the global circumferential strain rate (GCSR) was –3.2 1/s, and the longitudinal — circumferential index was –22.4%. The proportion of T2D patients with abnormal GLS was 78.6%, GLSR was 65.1%, GCS was 45.8%, GCSR was 60.9%, and longitudinal-circumferential index was 50%.

Conclusions: Speckle tracking echocardiography was more sensitive in identifying subclinical myocardial dysfunction than conventional echocardiography. A large proportion of patients with T2D had abnormal left ventricular systolic deformation, even though the ejection fraction was still normal. (Clin Diabetol 2024; 13, 5: 291–298)

Keywords: type 2 diabetes, speckle tracking echocardiography, global longitudinal strain, global circumferential strain

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Introduction

With its rapidly increasing rate, type 2 diabetes (T2D) is becoming a major problem of health that has attracted the attention of endocrinologists. The International Diabetes Federation reports that the number of cases of individuals with diabetes mellitus globally (aged 20 to 79 years) is currently 537 million, and by

2030 it is predicted to rise to 643 million. Half of this number (45%) have undiagnosed diabetes [1].

In individuals with T2D, heart failure (HF) is a major cardiovascular event that is related to mortality and morbidity [2]. T2D and HF are closely related: patients with T2D are 2-4 times more likely to progress to congestive HF than people without T2D [3, 4]. HF also increases the risk of hospitalization for patients with T2D by 33% [5].

In addition to the macrovascular cause of hypertension and atherosclerotic cardiovascular disease, the development of HF in patients with T2D is also greatly influenced by the microvascular cause of diabetic cardiomyopathy [6, 7]. HF in patients with diabetes may have reduced or preserved ejection fraction (EF) [2]. In the early stages, most patients have no symptoms and are also affected by other complications of diabetes. Therefore, there is a large percentage of people with T2D who have HF but in whom it is not recognized [8].

Early determination of abnormal left ventricular (LV) function will help clinicians to formulate a better treatment strategy to prevent and slow down adverse events for patients with T2D. To evaluate LV function, many methods can be used such as electrocardiogram, echocardiography, cardiac catheterization, angiography, magnetic resonance, and nuclear medicine [9–11]. Echocardiography is a non-invasive imaging technique that can be performed many times, is not very expensive, and is valuable in the early identification of cardiac dysfunction [12]. Hence, echocardiography is still considered the first choice to detect abnormalities in LV function early [6]. In particular, abnormal LV deformation that can be detected by speckle tracking echocardiography (STE) is an early disorder that appears in patients with T2D even when the patient has no clinical symptoms [6, 13].

Also, there is evidence that the global longitudinal strain (GLS) parameter on STE is a parameter with greater sensitivity than ejection fraction (EF) for assessing LV dysfunction, and it provides additional information for prognosis [12, 14, 15]. In Vietnam, there is currently little research using STE to identify cardiac function abnormalities early in patients with T2D. We researched the topic to detect the cut-off point to evaluate abnormal systolic deformation parameters and the prevalence of abnormalities in LV function in patients with T2D.

Materials and methods

Study design

A cross-sectional descriptive study was carried out after receiving the permission of the local ethics committee of the Hue University of Medicine and Pharmacy.

Study population

We conducted the study on 192 patients with T2D who received treatment and a health examination at the Hue University of Medicine and Pharmacy Hospital from January 2021 to August 2023. We used the guidelines of the American Diabetes Association (ADA) in 2020 to identify T2D [16]. Subjects who met the following criteria were not included: (1) EF < 50%; (2) having cardiovascular diseases not caused by T2D; (3) cancer patients undergoing chemotherapy and radiotherapy; (4) poor echocardiography image quality; and (5) patients who refused to participate.

We also enrolled 119 subjects as the control, who are similar to the patient group in age and gender, but with no history of diabetes or cardiovascular disease. Also, the controls did not reveal any abnormalities on physical examination, blood tests, electrocardiogram, and echocardiography. In addition, poor image quality and refusal to participate in the study were other exclusion criteria for the control group.

Data collection

First, we use approved questionnaires to interview patients about medical history and related factors. Second, we performed a clinical examination to find signs of heart failure, and to measure and record weight, height, and heart rate. After that, the patients underwent laboratory tests, including fasting blood glucose, glycosylated hemoglobin, electrocardiogram, and echocardiography. Variables included age, gender, body mass index (BMI), heart rate, T2D duration, fasting blood glucose, and glycosylated hemoglobin. We evaluated glycemic control based on the 2020 recommendations of the ADA. The glycemic targets included fasting blood glucose 4.4–7.2 mmol/L and HbA1c < 7.0% [16]. BMI is classified based on Asian standards of the World Health Organization classification. The cut-off point for obesity was 23 kg/m^2 [17]. Patients with T2D were considered to be at high risk when the T2D duration was ≥10 years [6].

The Philips Affiniti 70 (Philips, American, 5S probe) device was used to perform echocardiography. Echocardiographic images were recorded at a speed of 100 mm/s, with simultaneous electrocardiogram measurements, measured at the end of expiration to limit the influence of respiration on the Doppler spectrum. All echocardiographic parameters (TM, 2D, and Doppler) were recorded over 3 consecutive cardiac cycles, and the final result was the average of these values. To evaluate the results of echocardiography, we used the guidelines of the American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) [11, 18, 19]. The images of strain were

Table 1. The Baseline Characteristics of the Study Population

Characteristics	T2D (n = 192)	Controls (n = 119)
Age [years]	66.5 ± 10.2	64.7 ± 6.00
Sex, F [%]	63.0	63.0
BMI [kg/m2]	22.9 ± 3.7	21.6 ± 2.3
Heart rate [bpm]	81.9 ± 15.7	74.5 ± 11.9
SBP [mmHg]	145.7±17.8	117.0 ± 6.7
DBP [mmHg]	81.6 ± 9.4	72.0 ± 9.3
T2D duration (years)	8.00 ± 6.5	
Hypertension [%]	82.3	
Coronary artery disease [%]	25.5	
Irregular treatment [%]	15.1	

Data presented as mean ± SD or %
BMI — body mass index; DBP — diastolic blood pressure; F — female; SBP — systolic blood pressure; SD — standard deviation; T2D — type 2 diabetes

analyzed offline with the support of QLAB software version 15.0 from Philips. We recorded the images in 3 views for long-axis planes (4-chamber, 2-chamber, and 3-chamber,) and 3 views for short-axis planes (middle, apex, and basal short-axis planes). In each view, we selected 3 points (one point at the apex and 2 points on the annulus' side), and the endothelium margin was automatically determined by the software. After analysis, the results of the strain value and strain velocity parameters were shown on the curve graph and the bull's eye image. We had to manually correct the images of the patients with endothelium, which were unclear. The manual editing process was performed under the guidance and support of technicians in clinical applications of echocardiography from Philips and doctors from the echocardiography room of the Hue University of Medicine and Pharmacy Hospital. We recorded strain parameters, including longitudinal strain (LS) and longitudinal strain rate (LSR) in the 3-chamber plane (LS3, LSR3), LS and LSR in the 4-chamber plane (LS4, LSR4), LS and LSR in the 2-chamber plane (LS2, LSR2), GLS and GLS rate (GLSR), circumferential strain (CS) and circumferential strain rate (CSR) in the apex plane (CSa, CSRa), CS and CSR in the middle plane (CSm, CSRm), CS and CSR in the basal plane (CSb, CSRb), global circumferential strain (GCS), GCS rate (GCSR), and the longitudinal-circumferential index (L-C index) [20].

Statistical analysis

Data were analyzed using SPSS version 26.0. Frequency (percentage) is used to display the qualitative variables. Quantitative variables are expressed as the mean value ± standard deviation (SD) if they belong to a normal distribution, or median and interquartile range of the value in position (25th percentile — 75th percentile) if non-normally distributed. We compared the difference between 2 averages using the unpaired t-test (if the averages had normal distribution), and the Mann-Whitney U test (if the averages did not have normal distribution). We used the receiver operating characteristic (ROC) curve and the area under the ROC curve (AUC) to determine the cut-off point to classify abnormal systolic deformation parameters. Significance was defined as when the value of p was less than 0.05.

Results

The baseline characteristics of the study population

The study was performed on 311 subjects: 192 people with T2D and 119 people as the controls. Table 1 displays the study population's basic characteristics. The average age of the T2D group was 66.5 ± 10.2 years, comprising 37% men and 63% women.

The group of individuals with T2D had higher BMI, heart rate, systolic blood pressure, and diastolic blood pressure than the controls. Also, there was a significant prevalence of patients with T2D having complications such as hypertension (82.3%) or coronary artery disease (25.5%).

Value of deformation parameters of the study population

When compared to the controls, the GLS, GLSR, GCS, GCSR, and L-C index of the patients with T2D were significantly decreased ($p < 0.001$) (Fig. 1).

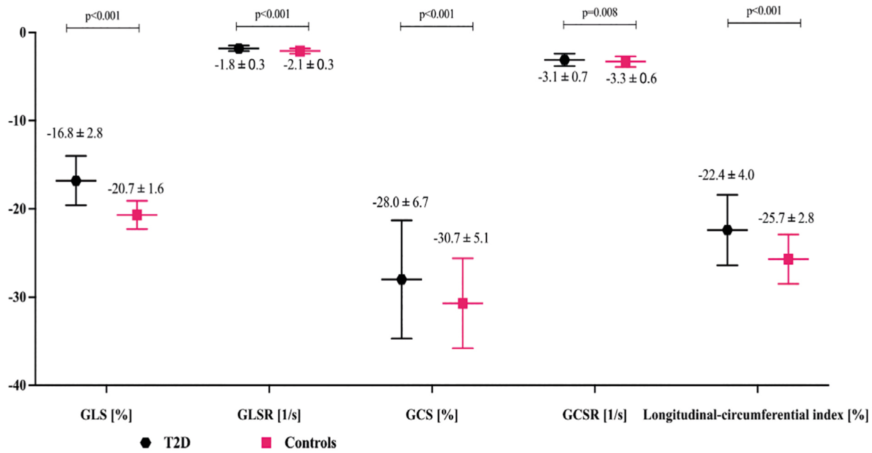

Figure 1. Value of Left Ventricular Systolic Deformation Parameters of the Study Population
GCS — global circumferential strain; GCSR — global circumferential strain rate; GLS — global longitudinal strain; GLSR — global longitudinal strain rate; T2D — type 2 diabetes

Table 2. The Cut-off Point Value to Evaluate Abnormal Systolic Deformation Parameters Based on the Receiver Operating Characteristic Curve

Parameters	The cut-off point	Sensitivity [%]	Specificity [%]	AUC [%]	p
GLS [%]	> –19.0	78.7	93.2	88.5	< 0.001
GLSR [1/s]	> –1.9	65.1	84.9	78.8	< 0.001
GCS [%]	> –27.4	45.8	74.8	62.2	< 0.001
GCSR [1/s]	> –3.2	60.5	62.2	60.0	0.002
Longitudinal-circumferential index [%]	> –22.4	50.0	88.2	74.2	< 0.001

AUC — area under the curve; GCS — global circumferential strain; GCSR — global circumferential strain rate; GLS — global longitudinal strain; GLSR — global longitudinal strain rate

The cut-off point to evaluate abnormal systolic deformation parameters in patients with T2D

Our study recorded that the cut-off value to evaluate the abnormality of GLS was -19% (sensitivity 78.7%; specificity 93.3%), GLSR was –1.9 1/s (sensitivity 65.1%; specificity 84.9%), GCS was –27.4% (sensitivity 45.8%; specificity 74.8%), GCSR was –3.2 1/s (sensitivity 60.5%; specificity 62.2%), and the longitudinal-circumferential index was –22.4% (sensitivity 50%; specificity 88.2%) (Tab. 2).

Prevalence of normal and abnormal systolic deformation parameters of patients with T2D

The proportion of people with T2D who had abnormal GLS was 78.6%, GLSR was 65.1%, GCS was 45.8%, GCSR was 60.9%, and the longitudinal-circumferential index was 50% (Tab. 3).

Discussion

The baseline characteristics of the population

Our results show no significant difference in age and gender between the group with T2D and the controls. Compared to other studies, the age of the group of T2D patients in our study was higher than that of other authors' studies, such as Nakai et al. (2009), Hatani et al. (2020), Ng et al. (2019), and Yamauchi et al. (2021) [21–24]. Although there is a difference with other studies, the difference is not great, and the average age is also at an intermediate level when compared to the above studies. To eliminate the effect of gender and age on heart function, in this study design, we selected a control group that was similar in age and gender to the group of patients with T2D.

The BMI and heart rate of T2D patients was higher than that of the controls. This result also reflects a com-

Table 3. Prevalence of Normal and Abnormal Systolic Deformation Parameters in the T2D Group

Parameters	Normal N (%)	Abnormal N (%)
GLS (> –19.0%)	41 (21.4)	151 (78.6)
GLSR (> –1.87 1/s)	67 (34.9)	125 (65.1)
GCS (> –27.4%)	104 (54.2)	88 (45.8)
GCSR (> –3.239 1/s)	75 (39.1)	117 (60.9)
Longitudinal-circumferential index (%) (> –22.4)	96 (50.0)	96 (50.0)

GCS — global circumferential strain; GCSR — global circumferential strain rate; GLS — global longitudinal strain; GLSR — global longitudinal strain rate; T2D — type 2 diabetes

mon characteristic of T2D patients, which is obesity. Increased heart rate is considered a marker that is related to cardiovascular risk and cardiovascular outcomes [24]. In routine clinical practice, diabetes is also considered a cardiovascular disease [25]. Also, the hyperglycemia status in subjects with T2D will have certain effects on the autonomic nervous system and consequently cause changes in heart rate [26].

The T2D duration of the patient group was 8.00 ± ± 6.5 years. According to 2019 ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases, developed in collaboration with the EASD, T2D duration is also a major cardiovascular risk factor. The longer the duration of T2D, the higher the cardiovascular risk [6].

Value of left ventricular systolic deformation parameters of the study population

Nowadays, STE is widely applied in cardiovascular clinical practice. The ASE/EACVI uses STE to assess cardiac function. With the advantage of not only helping to assess the entire left ventricular function, the bull's eye image of STE also shows the reduced contractility of the myocardium in each region, thereby helping to evaluate the left ventricular function of each of those regions, and thus helping to guide the identification of damaged coronary arteries. Myocardial deformation can be assessed along the longitudinal, circumferential, and radial axis. However, GLS is a parameter that is widely studied in routine clinical practice [11]. In individuals with T2D, there is evidence that GLS is disturbed while EF is still within normal range [20, 22].

We noted a significant difference in statistics ($p < 0.001$) in deformation parameter values of patients with T2D compared to the controls. Specifically, patients with T2D have reduced GLS, GLSR, GCS, and GCSR compared to the control group (Fig. 1). Our study results are similar to those from studies on T2D patients by many other authors, such as Nakai et al. (2009), in which the GLS of T2D was –17.6 ± 2.6% and GCS was –22.6 ± 3.7% (lower than GLS and GCS of the controls, with GLS of –20.8 ± 1.8% and GCS of –24.4 ± 4.1%) [22]; Ng et al. (2019), in which the GLS of the patients was –17.3 ± 2.3%, which was lower than the controls (–20.5 ± 1.8%) [23]; and Yamauchi et al. (2021), in which the GLS of the patients was –17.6 ± 3.1%, which was lower than the controls (–20.3 ± 1.9%) [24].

The GLS results of patients with T2D in this study were very similar to those found in the study of Li et al. (2023) when evaluating left ventricular deformation by magnetic resonance imaging, in which the GLS of T2D patients was –16.51 ± 2.53%, which was lower than for the control group (–19.66 ± 3.21%) [27]. Although our study was performed using echocardiography, the result was highly similar to that of the study using magnetic resonance imaging, which is considered the gold standard in evaluating abnormal deformation of the heart muscle.

The cut-off point to evaluate abnormal systolic deformation parameters in patients with T2D

When drawing the ROC curve and calculating the AUC, using the Delong method to calculate the standard error, the Youden index (Youden index) J was used to determine the cut-off point to establish the abnormal left ventricular deformation parameters, and we found that GLS, GLSR, GCS, GCSR, and the longitudinal-circumferential index were the parameters that have value in diagnosing abnormal left ventricular deformation. However, with the AUC results, our study noted that the GLS has good diagnostic value (with cut-off point –19%; AUC = 88.5%; sensitivity 78.7%; specificity 93.3%; $p < 0.001$). GLSR (–1.9 1/s; AUC = 78.8%; sensitivity 65.1%; specificity 84.9%; $p < 0.001$) and longitudinal-circumferential index (with cut-off –22.4%; AUC = 74.2%; sensitivity 50%; specificity 88.2%; $p < 0.001$) were 2 parameters that have quite good diagnostic value. Because the AUC of the 2 parameters

(GCS and GCSR) is 62.2% and 60.0%, respectively, the cut-off point of –27.4% for GCS and the cut-off point of –3.2 1/s for GCSR does not have an unusually good diagnostic value for GCS and CSR (Tab. 2).

Prevalence of normal and abnormal systolic deformation parameters in the T2D group

When using the found cut-off point to evaluate the abnormal systolic deformation parameters, we recorded that in 192 patients with T2D, 78.6% had abnormal GLS, 65.1% had abnormal GLSR, 45.8% had abnormal GCS, 60.9% had abnormal GCSR, and 50% had abnormal longitudinal-circumferential index (Tab. 3). The results obtained show that the parameter with the highest disorder rate is GLS, followed by GCS, and the longitudinal-circumferential index has the lowest rate among the 3 parameters. The abnormal GLS prevalence of T2D patients has been described by some authors, such as Nakai et al. (43%) [22], Ng et al. (44.8%) [23], Hatani et al. (55%) [21], Halabi et al. (17%) [28], Li et al. (66%) [29], and Liu et al. (44%) [30]. By comparing the results of studies on patients with T2D, we found that the prevalence of GLS disorders in people with T2D was different. This difference in prevalence is caused by many factors. Besides the machine and its software, the group of T2D patients had different ages, the patient group could be single T2D, T2D with comorbidities, or with cardiovascular risk factors. Another reason that may also cause differences in the rate of GLS abnormalities is that the cut-off points of the authors are different depending on their study.

Until now, there has been no recommendation on the cut-off point of left ventricular deformation parameters on STE. In addition, due to specific limitations in media and processing support software, each study must have a control group, and the cut-off value used is based on the results from the control group. Therefore, the current rate of disorders of left ventricular deformation parameters is still not consistent. There have not been many publications related to the rate of disorders of other parameters such as GCS, and GRS in patients with T2D. Currently, most current publications focus on the rate of GLS disorders. Therefore, the GLS parameter is still the main parameter commonly used in clinical practice. Although the LV function of patients with T2D is normal on conventional echocardiography, using STE techniques has detected a large proportion of patients with preclinical LV functional abnormalities. Thus, with the results obtained from the study, we have contributed more scientific evidence about the role of STE in the early detection of LV dysfunction. Therefore, in clinical practice, this technique should be widely used to detect LV dysfunction early in patients with T2D.

Our study has some limitations, including the fact that no long-term follow-up was done; cardiac magnetic resonance, the gold standard for diagnosing cardiomyopathy, was not performed; and the number of patients and controls was small. Therefore, further studies with a larger cohort of patients are needed.

Conclusions

STE is a more sensitive method than conventional echocardiography in the detection of subclinical left ventricular dysfunction. Our study recorded that the cut-off value to evaluate the abnormality of GLS is –19%, GCS is –27.4%, and GCSR is –3.2 1/s. These are 3 parameters that have a diagnostic value of abnormal left ventricular systolic deformation. Even though EF is still within the normal range, a large proportion of subjects with T2D have abnormal left ventricular systolic deformation.

Article information

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval

The study was approved by the Ethics Committee of the Hue University of Medicine and Pharmacy.

Written informed consent was obtained from all individual participants included in the study.

Author contribution

The authors are responsible for all aspects of this work and made an equal contribution to every stage in writing the article.

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Conflict of interest

The authors declare no conflict of interest.

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