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LEFT VENTRICULAR SYSTOLIC FUNCTION BY SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH TYPE 2 DIABETES

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The dissertation can be found at:

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INTRODUCTION

1. RATIONALE FOR THE STUDY

With a rapid increase, diabetes has become an urgent health problem globally. In particular, type 2 diabetes is considered a major risk factor for cardiovascular diseases, and cardiovascular diseases are also the most common cause of death in people with type 2 diabetes. In the early stages, most patients have no symptoms and are also overlapped by other complications of diabetes. Hypertension, atherosclerotic and diabetic cardiomyopathy are factors leading to cardiac function abnormalities in patients with type 2 diabetes.

Recently, speckle tracking echocardiography has emerged. This is a new technique, independent from the angle of insonation and partly from cardiac translational movements. Speckle tracking echocardiography can help detect preclinical left ventricular systolic dysfunction early, identifying subtle deterioration of cardiac function, even when the ejection fraction is still within normal limits. Besides, based to the principle of marking and tracking myocardial tissue throughout the cycle of the myocardium, speckle tracking echocardiography helps detect myocardial deformation. This is also one of the disorders that appear in the early stages in patients with type 2 diabetes.

We conducted the study "***Left ventricular systolic function by speckle tracking echocardiography in patients with type 2 diabetes***" with the two following objectives:

1. To evaluate left ventricular systolic function by 2D speckle tracking echocardiography in patients with type 2 diabetes.
2. To investigate the relationship between left ventricular systolic deformation parameters and related factors in patients with type 2 diabetes.

2. SCIENTIFIC CONTRIBUTIONS AND PRACTICAL IMPLICATIONS

This study aims to evaluate left ventricular systolic function using 2D speckle tracking echocardiography and investigate the relationship between left ventricular deformation parameters and related factors in patients with type 2 diabetes. From the research results, we should use left ventricular deformation parameters by 2D speckle tracking echocardiography, which can help early detect left ventricular dysfunction in patients with type 2 diabetes. Besides, the good control of factors related to left ventricular deformation parameters to reduce left ventricular dysfunction in patients with type 2 diabetes.

3. CONTRIBUTIONS OF THE DISSERTATION

Applying 2D speckle tracking echocardiography helps early detect left ventricular systolic dysfunction in patients with type 2 diabetes, even when the ejection fraction is still within normal value. Disorders of left ventricular deformation parameters are related to cardiovascular risk factors in patients with type 2 diabetes. Therefore, in addition to good control of blood glucose, it is also necessary to pay attention to controlling cardiovascular risk factors, which will help to reduce the rate of left ventricular deformation disorders in patients with type 2 diabetes.

Chapter 1
LITERATURE REVIEW

1.1. OVERVIEW OF TYPE 2 DIABETES

Type 2 diabetes mellitus (T2DM) is characterized by progressive loss of pancreatic beta cell function on a background of insulin resistance. Most patients with T2DM are obese or overweight and/or have abdominal obesity. Due to insulin resistance, in the early stages, beta cells compensate and increase insulin secretion in the blood. If insulin resistance persists or worsens, beta cells will not secrete enough insulin, and clinical T2DM will occur. T2DM accounts for over 90% of all diabetes cases and this rate is increasing in all regions globally. Patients with T2DM are at high risk of morbidity, hospitalization, and mortality.

1.2. LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

1.2.1. Epidemiology of left ventricular systolic dysfunction in patients with type 2 diabetes

T2DM is associated with left ventricular systolic dysfunction, and left ventricular systolic dysfunction also increases the risk of morbidity and mortality for patients with T2DM. Left ventricular systolic function in patients with T2DM may be disturbed even when the patient has no clinical symptoms (at a rate of 17-37.5%).

1.2.2. Causes and pathogenesis of left ventricular systolic dysfunction in patients with type 2 diabetes

The cause of left ventricular systolic dysfunction as well as heart failure in patients with T2DM is due to the influence of many factors. Hypertension and coronary artery disease are considered the main causes. In addition, the main risk factors for heart failure such as obesity, dyslipidemia, microangiopathy, and macrovascular disease are common in patients with T2DM. In addition, diabetic cardiomyopathy (related to microangiopathy, metabolic factors, or myocardial fibrosis) is also an important contributing factor in the pathogenesis of left ventricular dysfunction and heart failure in patients with T2DM.

1.3. FACTORS ASSOCIATED WITH LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Left ventricular systolic dysfunction in patients with T2DM is associated with cardiovascular risk factors such as obesity, hypertension, dyslipidemia, abdominal obesity, smoking, and physical inactivity. Good control of these metabolic risk factors will help reduce the rate of left ventricular systolic and diastolic dysfunction in patients with T2DM.

1.4. SOME METHODS FOR ASSESSING LEFT VENTRICULAR SYSTOLIC FUNCTION

Evaluation of left ventricular function is a basic requirement in cardiovascular clinical practice, helping to provide important information for diagnosis, treatment strategies, and prognosis for cardiovascular patients. Nowadays, there are many techniques used to evaluate left ventricular function such as echocardiography, cardiac magnetic resonance, and nuclear cardiology. Although new cardiovascular imaging techniques such as magnetic resonance and nuclear cardiovascular imaging have made great progress, however, in practical conditions in Vietnam, these techniques are still not popular. Until now, transthoracic echocardiography is still the most commonly used technique to evaluate left ventricular function in daily clinical practice because of meeting the following criteria: availability, low cost as well as acceptable accuracy.

1.5. MYOCARDIAL DEFORMATIONS AND THE ROLE OF SPECKLE TRACKING ECHOCARDIOGRAPHY IN ASSESSING LEFT VENTRICULAR SYSTOLIC FUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

1.5.1. Myocardial deformation

The term “strain” is considered myocardial deformation and is used to evaluate myocardial function. The term myocardial deformation was first used in cardiology by authors Mirsky I. and Parmley W.W. in 1973. When the heart contracts, it deforms in many different directions, including longitudinal strain, radial strain, circumferential strain, and twist.

1.5.2. 2D speckle tracking echocardiography

Two-dimensional speckle tracking echocardiography is a new echocardiography technique, using a typical B-mode image to analyze tracer tissue. Each marked tissue sample corresponds to each myocardial region and is relatively stable throughout the myocardial cycle. When there is a shift in the marked tissue position, it indicates myocardial deformation. When selecting a region of interest (ROI), the software will calculate the geometric transformation of the selected area image by image and record the displacement, velocity, strain, and strain rate of each myocardial location.

- Advantage:

+ Independent of the angle and allows to recording of the movement of speckles in 2D in any direction. Besides, it only reflects active muscle contraction, so it is not disturbed by the passive contraction of dead myocardium by adjacent myocardial tissue.

+ Non-invasive, safe for patients, and its results are highly correlated with cardiac magnetic resonance, so it is more economically beneficial than cardiac magnetic resonance and myocardial scintigraphy.

+ High reproducibility and can be analyzed offline.

- Limits:

+ Depends on image quality.

+ Depends on frame rate. The optimal frame rate for speckle tracking is 50 - 70 frames/s.

+ Different machines and software give different values, even depending on the version of the machine.

1.5.3. The role of speckle tracking echocardiography in assessing left ventricular systolic function in patients with type 2 diabetes

In patients with T2DM, when evaluated by speckle tracking echocardiography, recorded: that increased twist suggests preclinical microangiopathy.

Speckle tracking echocardiography techniques can detect early preclinical left ventricular systolic dysfunction in patients with T2DM, who are without cardiovascular symptoms. The disorder of the global longitudinal strain parameter has been demonstrated through many studies on asymptomatic T2DM patients.

In addition to the value of early detection of preclinical left ventricular systolic dysfunction, disorders of these myocardial deformation parameters have also been shown to correlate with cardiovascular risk factors in patients with T2DM, such as duration of diabetes, blood glucose control, blood pressure, waist circumference, body mass index, heart rate, HbA1c, blood lipids, the occurrence of microvascular complications.

1.6. RESEARCH OF LEFT VENTRICULAR SYSTOLIC FUNCTION BY SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH TYPE 2 DIABETES

In the world, there have been studies using speckle tracking echocardiography to early detect left ventricular systolic dysfunction in patients with T2DM. In Vietnam, the evaluation of left ventricular dysfunction has also been researched by domestic authors. However, most of the current studies are on patients with cardiovascular diseases such as hypertension, ischemic heart disease, and valvular heart disease. For patients with T2DM, there are not many independent research projects, but type 2 diabetes is mostly a comorbid condition.

Chapter 2
STUDY SUBJECTS AND METHODOLOGY

2.1. STUDY SUBJECTS

The study was conducted at the Department of General Internal Medicine - Endocrinology, Internal Medicine Clinic, Department of Cardiology and Echocardiography room, Hue University of Medicine and Pharmacy Hospital, from 1/2021 to 9/2023.

2.1.1. Study group: including 192 patients with T2DM who must satisfy the inclusion and exclusion criteria.

2.1.2. Control group: including 119 people undergoing echocardiography at the Echocardiography room of Hue University of Medicine and Pharmacy Hospital, similar in age and gender, meeting the inclusion and exclusion criteria.

2.2. RESEARCH METHODOLOGY

2.2.1. Study design

A controlled cross-sectional descriptive study.

2.2.2. Sample size: We used sample size calculation formula in cross-sectional descriptive research

$$n = Z^2_{1-\alpha/2}\frac{p(1-p)}{d^2}$$

2.2.3. Data collection

Patients who met the inclusion and exclusion criteria were included in the study.

- First, we use approved questionnaires to interview patients about medical history and related factors.

- Do clinical examination to find signs of heart failure, measure and record systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), waist circumference, and heart rate.

- After that, the patient will be given laboratory tests, including fasting blood glucose, HbA1c, lipids, NT-proBNP, electrocardiogram, and echocardiography.

2.2.4. Echocardiography

- Traditional Doppler echocardiography:

+ Measure and record LVEF, LVFS, LVIDd, LVIDs, IVSd, IVSs, LVPWd, LVPWs, LVM, LVMI.

+ Assess left ventricular morphology based on left ventricular mass index. Patients are left ventricular hypertrophy when left ventricular mass index (LVMI) >95 g/m^2 (female) hoặc >115 g/m^2 (male).

+ Diagnose diastolic dysfunction according to the guidelines of ASE/EACVI 2016, based on 4 parameters:

1. Septal e’ velocity <7 cm/s or lateral e’ velocity <10 cm/s;
2. Average E/e' >14;
3. Left atrial volume index >34 ml/m^2;
4. Tricuspid regurgitation velocity >2,8 m/s.

- 2D speckle tracking echocardiography:

+ First, take images in longitudinal planes of the 4 chambers, 2-chambers, and 3-chambers plane. Then, take the image in the apex, middle, and basal short-axis planes. The data is backed up and transferred to the computer hard drive and analyzed by the QLAB 15.0 software of Philips.

+ After analyzing 3 longitudinal planes and 3 short-axis planes, the software synthesizes and displays GLS and GCS with bull's eye chart.

+ Record the strain values and strain rates of the longitudinal planes and circumferential planes: LS2, LSR2, LS3, LSR3, LS4, LSR4, GLS, GLSR, basal CS, basal CSR, middle CS, middle CSR, apex CS, apex CSR, GCS, GCSR.

+ Calculate and record longitudinal-circumferential index.

2.2.5. Laboratory tests

Blood samples for tests for fasting blood glucose, HbA1c, blood lipids, and NT-proBNP were conducted at the department of Laboratory Hue University of Medicine and Pharmacy Hospital, based on the guideline of the Ministry of Health, using Cobas© 6000 machine.

2.2.6. Data analysis: All analyses were employed using statistical software SPSS version 26.0. Draw graphs using PRISM software and Microsoft Excel 365. Statistical methods:

- Descriptive statistics:

+ Quantitative variables: Check for normal distribution using the Kolmogorow - Smirnov test. If the data has a normal distribution when the p value is ≥ 0.05, then present it as the mean value ± standard deviation; In case the variable belongs to a non-normal distribution ($p < 0.05$), the median and interquartile range of values are presented in the position (25th percentile - 75th percentile).

+ Qualitative variables: presented frequency (n) and percentage (%).

- Statistical analysis:

+ Compare the difference between two average numbers using the unpaired t-test (in case of normally distributed variables), Mann-Whitney U test (in case of non-normally distributed variables); Compare the difference on 2 mean values (≥ 3) using 1-factor analysis of variance ANOVA if the variable is normally distributed and Kruskal- Wallis non-parametric test if the variable is not normally distributed.

+ Linear correlation analysis between two quantitative variables is expressed by coefficient r and tested by p-value (Pearson correlation if normal distribution and Spearman rho correlation if non-normal distribution).

- Linear regression analysis to find the relationship between left ventricular deformation parameters on 2D speckle tracking echocardiography (GLS, GLSR, GCS, GCSR, longitudinal-circumferential index) with related factors.

- Classification of left ventricular systolic function based on the area under the ROC curve (AUC) of the ROC curve.

- A p-value of <0.05 is considered statistically significant.

2.2.7. Research ethics

The local ethics committee of the Hue University of Medicine and Pharmacy has permissive this study. All participants' information was kept confidential and used for research purposes only. Study subjects had done echocardiography on a modern echocardiography machine, evaluating more parameters of cardiac morphology and function. The cost of NT-pro BNP testing is paid by the researcher, study subjects do not have to pay any fees.

Chapter 3
RESULTS

3.1. GENERAL CHARACTERISTICS OF THE STUDY POPULATION

3.1.1. Characteristics of age and gender

Table 3.1. *Characteristics of age and gender of the study population*

Characteristics		T2DM (n=192)		Controls (n=119)		Total (n=311)		p
Age	X±SD	66.52±10.15		64.73±5.96		65.84±8.12		0.058*
Gender	Male	71	37.0 %	44	37.0%	115	37.0%	0.999
	Female	121	63.0%	75	63.0%	196	63.0%	

**Mann-Whitney U*

Comment: The average age of the study population was 65.84 ± 8.12 years old, 37% of men and 63% of women. There were no differences in age and gender between the 2 groups (p>0.05).

3.1.2. Some clinical and pre-clinical characteristics and related factors of study subjects

- The group of patients with T2DM had body mass index (22.92 ± 3.73 kg/m^2), waist circumference (84.13 ± 11.67 cm), heart rate (81.93 ±

15, 70 bpm), systolic blood pressure (145.68 ± 17.82 mmHg) and diastolic blood pressure (81.61 ± 9.38 mmHg) were statistically significantly higher when compared with the controls ($p < 0.05$).

- The proportion of patients with T2DM with abdominal obesity is 59.4%, hypertension is 82.3%, and physical inactivity is 56.3%. Other cardiovascular risk factors such as obesity, smoking, dyslipidemia, and coronary artery disease also account for a relatively high proportion. Most patients had a previous history of diabetes, and only 15.1% of patients did not receive regular treatment.

- The proportion of patients with T2DM with diastolic dysfunction was 1.6%, indeterminate was 13.5%, and heart failure with preserved ejection fraction was 6.8%.

3.2. ASSESSMENT OF LEFT VENTRICULAR SYSTOLIC FUNCTION BY SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH T2DM

3.2.1. Values of left ventricular systolic deformation parameters in patients with T2DM were compared with the controls

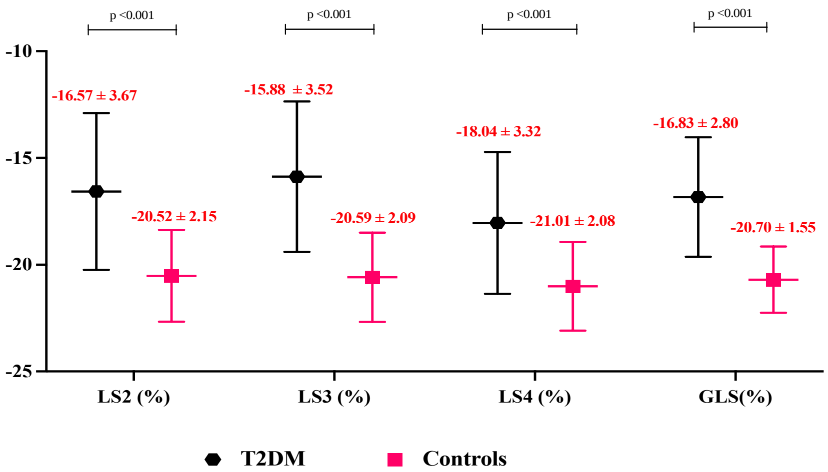

Figure 3.4. *Values of longitudinal strain parameters in 2-chamber, 3-chamber, and 4-chamber planes and GLS of the study population*

Comment: Patients with T2DM have decreased values of longitudinal strain parameters in 2-chamber, 3-chamber, and 4-chamber planes and GLS when compared with the controls ($p<0.001$).

Table 3.8. *Values of longitudinal strain rate in 2-chamber, 3-chamber, and 4-chamber planes and GLS of the study population*

Parameters	**T2DM (X ± SD)**	**Controls (X ± SD)**	**p**
LSR4 (1/s)	-1.86 ± 0.40	-2.06 ± 0.27	**<0.001**
LSR2 (1/s)	-1.80 ± 0.44	-2.10 ± 0.38	**<0.001**
LSR3 (1/s)	-1.72 ± 0.45	-2.11 ± 0.36	**<0.001**
GLSR (1/s)	-1.79 ± 0.33	-2.09 ± 0.25	**<0.001***

**Mann Whitney*

Comment: Patients with T2DM have decreased values of longitudinal strain rate in 2-chamber, 3-chamber, and 4-chamber planes and GLS when compared with the controls (p<0.001).

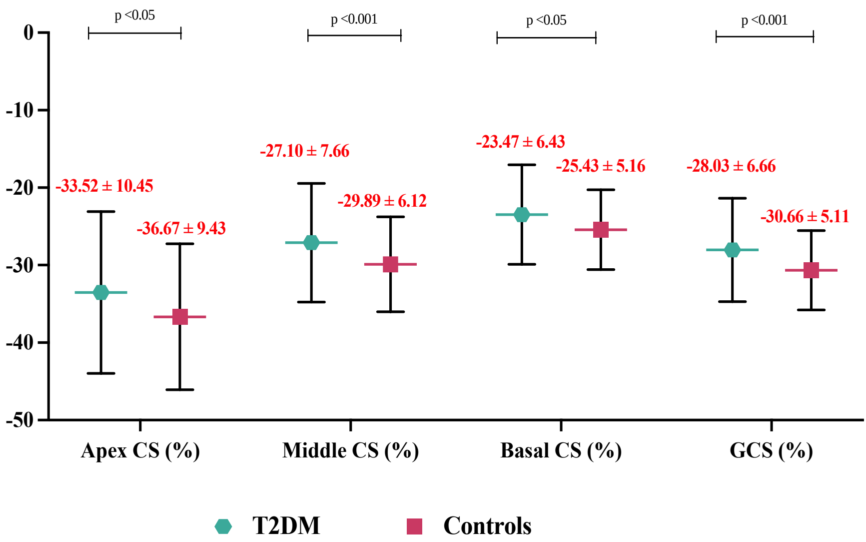

Figure 3.5. *Values of circumferential strain in the apex, middle, basal planes, and GCS of the study population*

Comment: Patients with T2DM have decreased values of circumferential strain in the apex, middle, basal planes, and GCS when compared with the controls (p<0.05).

Table 3.9. *Values of circumferential strain rate in the apex, middle, basal planes, and GCSR of the study population*

Parameters	**T2DM (X ± SD)**	**Controls (X ± SD)**	**p**
Basal CSR (1/s)	-2.78 ± 0.77	-3.02 ± 0.65	**0.006**
Middle CSR (1/s)	-3.02 ± 0.80	-3.13 ± 0.64	0.166
Apex CSR (1/s)	-3.61 ± 1.11	-3.84 ± 0.96	**0.014***
GCSR (1/s)	-3.14 ± 0.70	-3.33 ± 0.57	**0.008**
Longitudinal-circumferential index (%)	-22.43 ± 3.99	-25.68 ± 2.83	**<0.001**

**Mann Whitney*

Comment: Patients with T2DM have decreased values of circumferential strain rate in the apex and basal planes, GCSR, and longitudinal-circumferential index when compared with the controls ($p<0.05$).

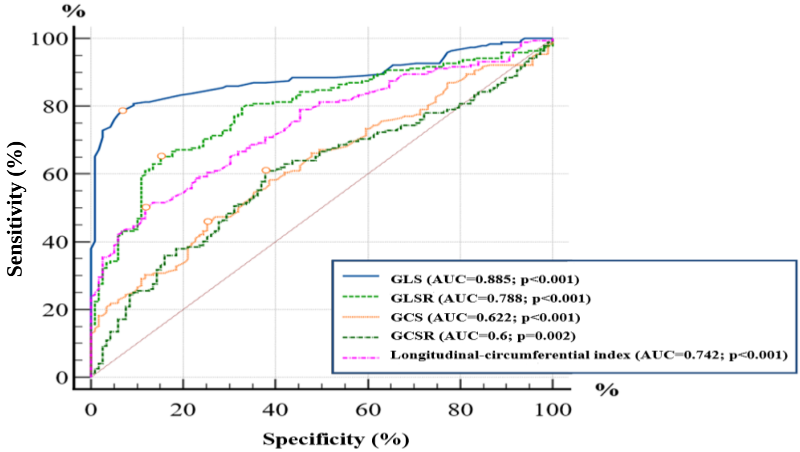

Figure 3.6. *ROC curve of parameters related to systolic function in evaluating the ability to classify between T2DM and controls*

Comment: GLS and GLSR related to left ventricular systolic function have good classification ability between T2DM and controls with AUC=0.885; $p<0.001$ and AUC=0.788; $p<0.001$. The longitudinal-circumferential index has a quite good classification value with AUC=0.742; $p<0.001$.

Table 3.10. *The cutoff point, sensitivity, and specificity of some parameters related to systolic function in the ability to classify between T2DM and controls*

Parameters	The cutoff point	Sensitivity (%)	Specificity (%)	p
GLS (%)	>-19.0	78.65	93.28	**<0.001**
GLSR (1/s)	>-1.87	65.10	84.87	**<0.001**
GCS (%)	>-27.4	45.83	74.79	**<0.001**
GCSR (1/s)	>-3.239	60.49	62.18	**0.002**
Longitudinal-circumferential index (%)	>-22.4	50.0	88.24	**<0.001**

Comment: The cutoff points were -19% (for GLS), -1.87 1/s (for GLSR), -27.4% (for GCS), -3.239 1/s (for GCSR), -22.4% (for longitudinal-circumferential index) are values related to left ventricular systolic dysfunction in the ability to classify between disease groups T2DM and controls (p<0.05).

3.2.2. Left ventricular systolic function of patients with T2DM

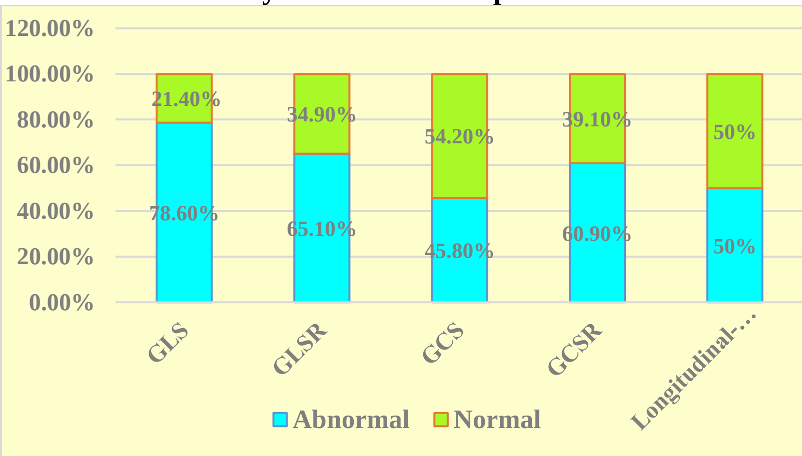

Figure 3.7. *Proportions of disorders in systolic deformation parameters in patients with T2DM*

Comment: The proportion of T2DM patients with abnormal GLS is 78.6%, GLSR is 65.1%, GCS is 45.8%, GCSR is 60.9%, and longitudinal-circumferential index is 50%.

3.3. RELATIONSHIP BETWEEN LEFT VENTRICULAR SYSTOLIC DEFORMATION PARAMETERS AND RELATED FACTORS IN PATIENTS WITH T2DM

3.3.1. Comparison of average values of left ventricular systolic deformation parameters according to related factors in patients with T2DM

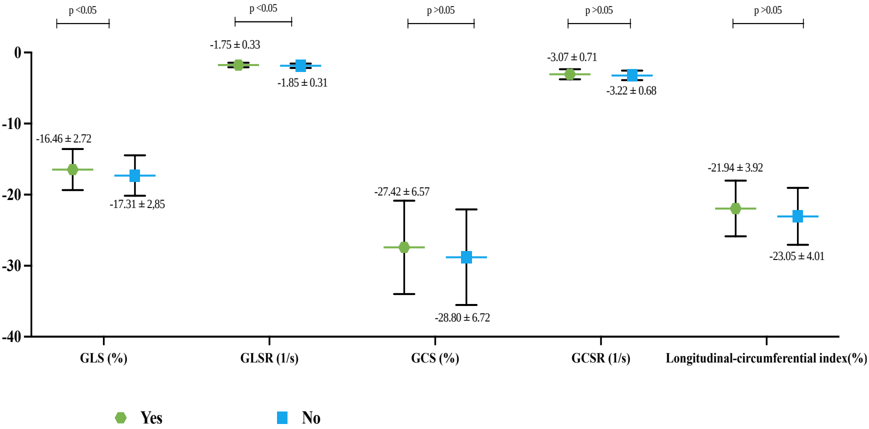

Figure 3.9. *Comparison of average values of left ventricular systolic deformation parameters according to physical inactivity*

Comment: T2DM patients with physical inactivity have decreased GLS and GLSR when compared with T2DM patients without physical inactivity (p < 0.05).

Table 3.18. *Comparison of average values of left ventricular systolic deformation parameters according to T2DM duration*

Parameters	**T2DM duration**		**p**
	≥10 years (n=69)	**<10 years (n=123)**	
GLS (%)	-16.07 ± 2.56	-17.26 ± 2.86	0.005
GLSR (1/s)	-1.72 ± 0.31	-1.84 ± 0.33	0.025*
GCS (%)	-27.86 ± 6.86	-28.12 ± 6.57	0.792
GCSR (1/s)	-3.05 ± 0.64	-3.18 ± 0.73	0.205
Longitudinal-circumferential index (%)	-21.96 ± 4.10	-22.69 ± 3.92	0.227

**Mann-Whitney U*

Comment: T2DM patients with T2DM duration ≥10 years have decreased values of GLS and GLSR when compared with others (p<0.05).

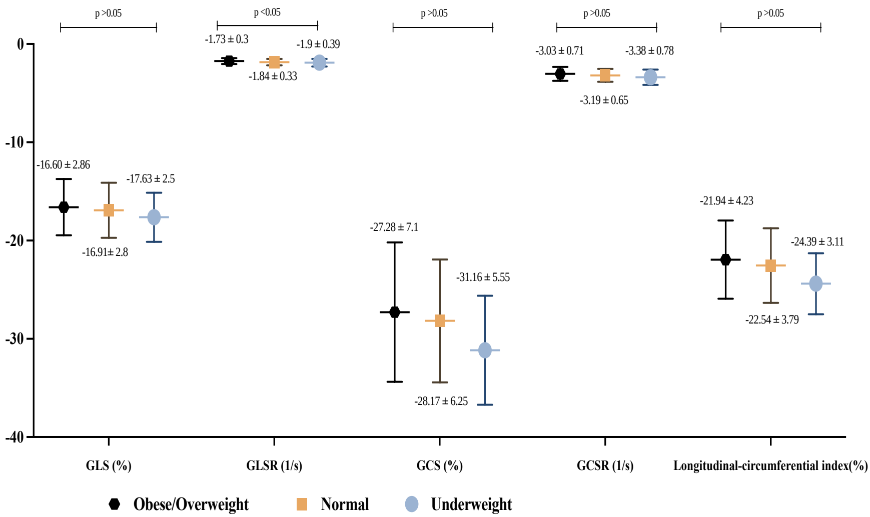

Figure 3.12. *Comparison of average values of left ventricular systolic deformation parameters according to body mass index*

Comment: T2DM patients with obesity/overweight have decreased GLSR when compared to T2DM patients with lean and normal body mass index ($p<0.05$).

Table 3.22. *Comparison of average values of left ventricular systolic deformation parameters according to HbA1c control*

Parameters	**HbA1c control**		**p**
	Not good (n=134)	**Good (n=47)**	
GLS (%)	-16.55 ± 2.78	-17.54 ± 2.79	**0.040**
GLSR (1/s)	-1.75 ± 0.29	-1.92 ± 0.41	**0.024***
GCS (%)	-28.51 ± 6.81	-27.68 ± 6.38	0.469
GCSR (1/s)	-3.17 ± 0.72	-3.13 ± 0.61	0.716
Longitudinal-circumferential index (%)	-22.53 ± 4.08	-22.61 ± 3.85	0.906

**Mann-Whitney U*

Comment: T2DM patients with not good HbA1c control have decreased GLS and GLSR when compared with T2DM patients with good HbA1c control ($p < 0.05$).

Table 3.24. *Comparison of average values of left ventricular systolic deformation parameters according to LVMI*

Parameters	**LVMI**		**p**
	Increase (n=102)	**Not increase (n=90)**	
GLS (%)	-16.24 ± 2.77	-17.50 ± 2.70	0.002
GLSR (1/s)	-1.73 ± 0.31	-1.86 ± 0.34	0.004*
GCS (%)	-27.28 ± 6.84	-28.87 ± 6.38	0.098
GCSR (1/s)	-3.05 ± 0.71	-3.23 ± 0.67	0.082
Longitudinal-circumferential index (%)	-21.76 ± 4.11	-23.19 ± 3.73	0.013

**Mann-Whitney U*

Comment: T2DM patients with increased LVMI have decreased GLS, GLSR, GCSR, and longitudinal-circumferential index when compared with T2DM patients without increased LVMI ($p < 0.05$).

3.3.2. Correlation between left ventricular systolic deformation parameters with related factors

Table 3.25. *Correlation between GLS, GLSR with related factors*

Parameters	**GLS**		**GLSR**	
	r	**p**	**r**	**p**
Age	0.13	**0.019**	0.13	**0.024**
T2DM duration	0.19	**0.008**	0.18	**0.015**
Body mass index	0.22	**<0.001**	0.23	**<0.001**
Waist circumference	0.32	**<0.001**	0.26	**<0.001**
Heart rate	0.27	**<0.001**	-0.19	**0.001**
SBP	0.51	**<0.001**	0.44	**<0.001**
DBP	0.31	**<0.001**	0.26	**<0.001**
Fasting blood glucose	0.51	**<0.001**	0.39	**<0.001**
HbA1c	0.28	**<0.001**	0.23	**0.001**
Triglycerid	0.30	**<0.001**	0.21	**0.002**
LDL-C	-0.07	0.345	-0.16	**0.021**
LVMI	0.27	**<0.001**	0.24	**<0.001**
NT-proBNP	0.03	0.686	0.23	**0.001**

Comment: GLS is highly correlated with SBP and fasting blood glucose; moderate correlation with waist circumference and DBP; Low correlation with age, T2DM duration, body mass index, heart rate, HbA1c, triglyceride, LVMI ($p<0.05$); GLSR was moderately correlated with SBP and fasting blood glucose; Low correlation with age, T2DM duration, waist circumference, body mass index, heart rate, DBP, HbA1c, triglyceride, LDL-C, LVMI, NT-proBNP ($p<0.05$).

3.3.3. Linear regression model (univariate, multivariate) between left ventricular systolic deformation parameters and related factors in patients with T2DM

Table 3.28. *Linear regression model (univariate, multivariate) between related factors in T2DM patients and GLS (%)*

Related factors	Beta	95%CI	p	Adjusted B	95%CI	p
T2DM duration *(years)*	0.07	0.01-1.13	**0.023**	0.02	-0.04-0.08	0.444
BMI (kg/m^2)	0.15	0.04-0.25	**0.007**	0.09	-0.02-0.19	0.098
Waist circumference (cm)	0.03	-0.003- 0.07	0.075			
SBP (mmHg)	0.01	-0.01- 0.03	0.369			
DBP (mmHg)	0.01	-0.03-0.05	0.647			
G_0 *(ref: good control)*	-0.93	-1.85 - -0.01	**0.047**	-0.42	-1.50 -0.67	0.453
HbA1c *(ref: good control)*	-0.99	-1.19 - -0.05	**0.038**	-0.27	-1.29-0.77	0.613
Triglycerid *(ref: disorder)*	1.36	0.54- 2.17	**0.001**	**1.16**	**0.33-1.99**	**0.006**
LDL-C *(ref: disorder)*	0.54	-0.32- 1.41	0.218			
Smoking *(ref: yes)*	-0.01	-0.90-0.89	0.979			
Physical inactivity (*ref: yes)*	0.85	0.05-1.64	**0.038**	0.61	-0.22– 1.43	0.150
LVMI (g/m^2)	0.02	0.002-0.03	**0.027**	0.01	-0.004-0.03	0.138
NT-proBNP *(ref: increased)*	0.60	-0.26-1.46	0.168			
Coronary artery disease *(ref: yes)*	0.52	-0.40-1.44	0.264			
Treatment adherence *(ref: no)*	-0.45	-1.56-0.67	0.432			

Variables with p<0.05 in the univariate analysis will be included in the multivariate regression model.

Comment: After adjustment in the multivariable linear model, triglyceride disorders were statistically significantly associated with the GLS index ($p<0.05$) in T2DM patients.

Table 3.29. *Linear regression model (univariate, multivariate) between related factors in T2DM patients and GLSR (1/s)*

	Beta	**95%CI**	**p**	**Adjusted B**	**95%CI**	**p**
T2DM duration *(years)*	0.08	0.001-0.02	**0.028**	0.01	-0.002-0.01	0.143
BMI (kg/m^2)	0.02	0.004-0.03	**0.008**	**0.01**	**0.001-0.024**	**0.036**
Waist circumference (cm)	0.003	-0.000491- 0.007	0.085			
SBP (mmHg)	0.002	-0.000493-0.005	0.111			
DBP (mmHg)	0.03	-0.002-0.008	0.270			
G_0 *(ref: good control)*	-0.08	-0.19-0.03	0.144			
HbA1c *(ref: good control)*	**-0.17**	**-0.28- -0.06**	**0.002**	**-0.15**	**-0.26 - -0.04**	**0.007**
Triglycerid *(ref: disorder)*	**0.16**	**0.06-0.25**	**0.001**	**0.14**	**0.04-0.23**	**0.004**
LDL-C *(ref: disorder)*	-0.08	-0.18- 0.02	0.133			
Smoking (ref: yes)	-0.01	-0.12 -0.09	0.799			
Physical inactivity (ref: yes)	**0.11**	**0.01-0.20**	**0.027**	0.04	-0.06-0.14	0.456
LVMI (g/m^2)	0.001	-0.002-0.003	0.107			
NT-proBNP *(ref: increased)*	**0.16**	**0.06-0.26**	**0.002**	**0.15**	**0.05 - 0.25**	**0.004**
Coronary artery disease *(ref: yes)*	**0.15**	**0.04 - 0.25**	**0.005**	0.07	-0.06-0.19	0.296
Treatment adherence (ref: no)	-0.09	-0.21 - 0.05	0.200			

Variables with p<0.05 in the univariate analysis will be included in the multivariate regression model.

Comment: After adjustment in the multivariable linear model, body mass index, HbA1c control, triglyceride disorders, and increased NT-proBNP were statistically significantly associated with GLSR index in patients with type 2 diabetes (p< 0.05).

Chapter 4
DISCUSSION

4.1. GENERAL CHARACTERISTICS OF THE STUDY POPULATION

4.1.1. Characteristics of age and gender

The average age of the study population was 65.84 ± 8.12 years old. The average age of T2DM patients is 66.52 ± 10.15 years old and the age of controls is 64.73 ± 5.96 years old. Men account for 37% and women account for 63%. There was no statistically significant difference in age and gender between the 2 groups ($p>0.05$). To eliminate the impact of age and gender on the heart, in the study design, we selected a control group that was similar in age and gender to the group of patients with type 2 diabetes.

4.1.2. Some clinical and pre-clinical characteristics and related factors of study subjects

Our research results recorded: the group of T2DM patients has higher BMI, waist circumference, heart rate, systolic blood pressure, and blood pressure than the controls ($p<0.05$). The proportion of T2DM patients with associated cardiovascular risk factors is high, especially: abdominal obesity (59.4%), hypertension (82.3%), and physical inactivity (56. 3%). This result reflects the characteristics of T2DM, which is common in patients with metabolic syndrome, in which abdominal obesity and hypertension are key factors. Our research results are similar to several studies such as Le Thi Tham, Nakai H., Ng A. C. T. Besides, the rate of left ventricular dysfunction in conventional Doppler echocardiography of T2DM patients in our study was low (diastolic dysfunction was 1.6% and 6.8% of patients with heart failure with preserved ejection fraction). It may be the study subjects selected in the study were patients without clinical symptoms and with preserved ejection fraction to demonstrate the role of early detection of left ventricular dysfunction by speckle tracking echocardiography.

4.2. ASSESSMENT OF LEFT VENTRICULAR SYSTOLIC FUNCTION BY SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH T2DM

4.2.1. Values of left ventricular systolic deformation parameters in patients with T2DM were compared with the controls

In this study, we found that patients with T2DM had GLS (-16.83±2.80%), GLSR (-1.79±0.33 1/s), GCS (-28.03±6.66%%), GCSR (-3.14 ±0.70 1/s) and longitudinal - circumferential index (-22.43±3.99%). There was a statistically significant difference in the values of longitudinal strain and circumferential strain of type 2 diabetes patients compared to the control group. Specifically, T2DM patients have reduced GLS, GLSR, GCS, and GCSR compared to the control group. Our research results are similar to many others: Nakai H. (2009), GLS of T2DM patients is -17.6±2.6%, GCS is -22.6±3.7% (lower than GLS and GCS of the control group); Ng A. C. T. (2019), the GLS of the T2DM group is -17.3±2.3%, that was lower than the control group (-20.5±1.8%); Yamauchi Y. (2021), T2DM patients had GLS (-17.6±3.1%), that is lower when compared with controls (-20.3±1.9%); Liao L. (2022), T2DM patients have GLS is -16.82±2.59%, statistically significantly lower when compared to the controls (-19.13±1, 72%).

Drawing the ROC curve and calculating AUC, determine the cutoff point of parameters related to left ventricular systolic function (including GLS, GLSR, GCS, GCSR, and longitudinal-circumferential index). We recorded: that GLS (AUC=0.885; $p<0.001$) and GLSR (AUC=0.788; $p<0.001$) could classify left ventricular systolic function well between the group of patients with T2DM and the control group; The longitudinal-circumferential index (AUC=0.742; $p<0.001$) can classify left ventricular systolic function quite well between the group of patients with T2DM and the controls.

The cutoff point that helps to classify left ventricular systolic function between the group of patients with T2DM and the controls of GLS is -19%, GLSR is -1.87 1/s, GCS is -27.4 %, GCSR is -3.239 1/s, the longitudinal-circumferential index is -22.4%. Until now, there is still no consensus and recommendation of professional associations on the cutoff point of left ventricular deformation parameters on speckle tracking echocardiography. Therefore, our study was conducted on patients with T2DM and still had a control group of similar age and gender to find the cutoff point to classify all parameters GLS, GLSR, GCS, GCSR, longitudinal-circumferential index, without using the average GLS value of previous studies.

4.2.2. Left ventricular systolic function of patients with T2DM

Results recorded: 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.

Especially, analyzing the proportion of abnormal deformation parameters in the group of T2DM patients with normal left ventricular function on conventional Doppler echocardiography, we found that: there is a large proportion of patients with disorders in deformation parameters, (the highest rate is GLS, with 78.5%). This proves that myocardial deformation disorders have already appeared even when T2DM patients do not show signs of left ventricular dysfunction on conventional Doppler echocardiography.

4.3. RELATIONSHIP BETWEEN LEFT VENTRICULAR SYSTOLIC DEFORMATION PARAMETERS AND RELATED FACTORS IN PATIENTS WITH T2DM

3.3.1. Comparison of average values of left ventricular systolic deformation parameters according to related factors in patients with T2DM

In clinical practice, most T2DM patients have had certain cardiovascular events. Besides, when patients are admitted to the hospital, they often have many comorbidities and risk factors.

When classification of cardiovascular risk for patients with T2DM, those who had T2DM duration ≥10 years are considered to be at high risk. Our study noted that the group of T2DM patients with T2DM duration ≥10 years had lower average values of the parameters GLS and GLSR than the group of patients with T2DM duration <10 years ($p<0.05$). This result is similar to the results of Nakai H., and Halabi A.: the longer T2DM duration, the greater the risk of developing complications. Even, the impact of T2DM duration on microvascular complications is stronger than age.

Our results show that the group of T2DM patients overweight and obese had the average value of the GLSR (-1.73 ± 0.3 1/s) lower when compared with other groups ($p<0.05$). This means that overweight/obesity is associated with reduced GLSR in patients with T2DM.

Poor blood glucose control increases the risk of microvascular and macrovascular complications in patients with T2DM. We found a statistically significant difference in longitudinal strain with the glucose control. Most studies in T2DM patients have noted an association between good HbA1c control and preclinical left ventricular dysfunction. This shows that either the group of patients with preclinical left ventricular dysfunction has a higher average HbA1c level than others.

In addition, T2DM patients with increased LVMI had lower values of GLS, GLSR, GCSR, and longitudinal-circumferential index than others ($p <0.05$). With our findings, we have also provided additional scientific evidence to confirm the early effects that occur on the heart in patients with T2DM, including left ventricular hypertrophy and abnormal myocardial deformation.

4.3.2. Correlation between left ventricular systolic deformation parameters with related factors

There are some studies on the correlation between left ventricular deformation parameters and cardiovascular risk factors in T2DM patients. However, most of the existing research mainly focuses on GLS without paying attention to the other parameters. Our study results show that there is a correlation between left ventricular deformation parameters and age, T2DM duration, body mass index, waist circumference, heart rate, systolic blood pressure, diastolic blood pressure, fasting blood glucose, HbA1c, triglyceride, left ventricular mass index and NT-proBNP concentration ($p<0.05$). In the research of Tadic M., Li Z., Pishgahi M., and Chen Y., correlations between GLS parameters and some related factors similar to our study were also recorded.

4.3.3. Linear regression model (univariate, multivariate) between left ventricular systolic deformation parameters and related factors in patients with T2DM

When conducting univariate linear regression analysis between left ventricular deformation parameters on 2D speckle tracking echocardiography with independent variables, we recorded that GLS is related to factors such as T2DM duration, body mass index, blood glucose control, HbA1c control, triglyceride disorder, and physical inactivity and LVMI; GLSR is related to the T2DM duration, body mass index, HbA1c control, triglyceride disorders, physical inactivity, coronary disease, and LVMI; GCS is associated with body mass index; GCSR is related to systolic blood pressure and diastolic blood pressure. These results once again confirm the effects on left ventricular systolic function that appear in T2DM patients at the early stages, even when ejection fraction is still within the normal range.

Multivariate regression analysis noted that triglyceride disorder is a factor independently associated with GLS; Body mass index, HbA1c control, triglyceride disorders, and increased NT-proBNP levels are factors independently associated with GLSR; Thus, we found that the related factors examined mainly affect the left ventricular longitudinal axis deformation parameters (GLS and GSLR). In summary, cardiovascular events, with preclinical left ventricular systolic dysfunction (assessed through left ventricular systolic deformation), are increased in T2DM patients because of a combination of many different factors. Obesity, poor blood glucose control, and triglyceride disorders are factors that have been shown by many studies to have a statistically significant relationship.

CONCLUSION

After studying 192 patients with type 2 diabetes and 119 people in the controls, from January 2021 to August 2023, at Hue University of Medicine and Pharmacy Hospital, we concluded that:

1. Left ventricular systolic function by 2D speckle tracking echocardiography in patients with type 2 diabetes

- Patients with type 2 diabetes have decreased values of global longitudinal strain and global circumferential strain than the control group (-16.83 ± 2.80% vs -20.70 ±1.55% and -28.03 ±6.66% vs. -30.66 ±5.10%; $p<0.001$).

- The proportion of abnormal global longitudinal strain is 78.6, and abnormal global circumferential strain is 45.8%.

2. Relationship between left ventricular systolic deformation parameters and related factors in patients with type 2 diabetes

- There are decreased global longitudinal strain value situations in patients with type 2 diabetes are physical inactivity (-16.46±2.72%), commodity condition (-16.7 ±2.8%), type 2 diabetes duration ≥10 years (-16.07±2.56%), poor fasting blood glucose and HbA1c control (-16.58±2.75% and -16.55±2.78%), increased triglycerides (-16.06±2.74%), irregular treatment, increased left ventricular mass index (-16.24±2.77%) than type 2 diabetic patients without these factors (p<0.05);.

- There are decreased global circumferential strain value situations in patients with type 2 diabetes commodity condition (-27.55±6.55%), and hypertension (-27.56±6.66%) than type 2 diabetic patients without these factors (p<0.05).

- Global longitudinal strain parameter is correlated with age (r=0.13; p=0.019), diabetes duration đường (r=0.19; p=0.008), body mass index (r=0.22; p <0.001), waist circumference (r=0.32; p <0.001), heart rate (r=0.27; p <0.001), systolic blood pressure (r=0.51; p <0.001), diastolic blood pressure (r=0.31; p <0.001), fasting blood glucose (r=0.51; p <0.001), HbA1c (r=0.28; p <0.001), triglyceride (r=0.30; p <0.001), left ventricular mass index (r=0.27; p <0.001).

- Global circumferential strain parameter is correlated with body mass index (r=0.12; p=0.034), heart rate (r=0.24; p <0.001), systolic blood pressure (r=0.20; p <0.001), diastolic blood pressure (r=0.15; p=0.007) and left ventricular mass index (r=0.14; p=0.014).

- Univariate regression analysis showed diabetes duration, body mass index, systolic blood pressure, diastolic blood pressure, control of fasting blood glucose and HbA1c, triglyceride disorders, physical inactivity, increased left ventricular mass index and N-terminal pro-B-type natriuretic peptide concentration were factors related to left ventricular systolic deformation parameters (p<0.05).

- Multivariate regression analysis showed that body mass index, HbA1c control, triglyceride disorders, and increased N-terminal pro-B-type natriuretic peptide levels were factors independently associated with longitudinal strain parameters (p<0.05).

RECOMMENDATION

Based on the findings of this study, we propose the following recommendations:

1. It is necessary to assess left ventricular systolic deformation even when patients with type 2 diabetes have normal left ventricular diastolic function and preserved ejection fraction. Using parameters of left ventricular global longitudinal strain, left ventricular global longitudinal strain rate and longitudinal-circumferential index have good values in classifying left ventricular systolic function.

2. It is necessary to have good related factors control to left ventricular function in patients with type 2 diabetes such as comorbidities, early detection of type 2 diabetes, and good control of blood glucose as well as other cardiovascular risk factors to reduce abnormal myocardial deformation parameters in patients with type 2 diabetes.

LISTED OF RELATED SCIENTIFIC WORKS THAT HAD BEEN PUBLISHED

1. Nguyen Nguyen Trang, Nguyen Anh Vu, Le Van Chi (2023), Evaluation of left ventricular systolic function by speckle tracking echocardiography in type 2 diabetic patients, Journal of Medicine and Pharmacy, 13 (5), pp. 132-139.
2. Nguyen Trang Nguyen, Anh Vu Nguyen, Van Chi Le (2024), 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, Journal of Medicinal and Chemical Sciences, 7 (1), pp. 166-175. DOI:10.26655/JMCHEMSCI.2024.1.16.