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Association Between Left Ventricular Strains and Cardiovascular Risk Factors in Type 2 Diabetic Patients: a Controlled Cross-sectional Study

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ABSTRACT

Background: Cardiovascular complications are the leading cause of death in diabetic patients. Speckle tracking echocardiography can early detect left ventricular systolic dysfunction even when normal ejection fraction. **Objective:** The study aims to evaluate left ventricular systolic function by Speckle tracking echocardiography and its relation with cardiovascular risk factors in type 2 diabetic patients. **Methods**: A controlled cross-sectional descriptive study was conducted on 150 patients (75 type 2 diabetic patients and 75 controls). **Results**: Type 2 diabetic patients had global longitudinal strain (-17.02±3.06%), global circumferential strain (-29.04±6.39%) were lower than the control group (p<0.05). Global longitudinal strain was correlated with systolic blood pressure (r=0.3), diastolic blood pressure (r=0.2), fasting plasma glucose (r=0.5), HbA1c (r=0.2), total cholesterol (r=-0.25), (p<0.05). Global circumferential strain was correlated with systolic blood pressure (r=0.2), diastolic blood pressure (r=0.2), HDL (r=-0.3), (p<0.05). **Conclusion**: Type 2 diabetic patients have reduced global longitudinal strain and global circumferential strain. The reduction of global longitudinal strain, global circumferential strain was correlated with cardiovascular risk factors (hypertension, not good glycemia control, increasing BMI, dyslipidemia).

Keywords: type 2 diabetes mellitus, speckle tracking echocardiography, global longitudinal strain, global circumferential strain, cardiovascular risk factors.

1. BACKGROUND

Diabetes mellitus (DM) is a chronic disease, that requires multiple medical care. In order to prevent acute complications and reduce the risk of long-term complications, a combination of glucose management and multifactorial risk-reduction strategies is necessary (1). With rapidly increasing, type 2 diabetes mellitus (T2DM) is becoming a global epidemic. According to the International Diabetes Federation (IDF) 2021, there are 537 million people worldwide who have diabetes, and it is estimated to reach 643 million by 2030, and 783 million by 2045 (2).

Diabetes is a major risk factor for cardiovascular diseases (CVD) and people with T2DM have higher cardiovascular morbidity and mortality than non-diabetic subjects (3,4). In clinical practice, there are also some views that "diabetes is a cardiovascular disease" (5). In a systematic literature review, CVD affects approximately 32.2% of type 2 diabetic patients and CVD is a major cause of mortality among people with T2DM (6).

Observational studies have reported that diabetic patients have a 2-to-4-fold increased risk of heart failure than non-diabetic subjects (7). The rate of heart failure hospitalization is higher in type 2 diabetic patients than in others (8, 9). Heart failure in type 2 diabetic patients has a pathophysiologic relationship between hypertension, atherosclerotic cardiovascular disease and diabetic cardiomyopathy (10,11). Although the pathophysiology of diabetic cardiomyopathy is more and more known, there are currently no specific guidelines for diagnosing or treatment strategies in clinical practice (12). In the early stage, diabetic cardiomyopathy is often asymptomatic and its symptoms may overlap with other complications of diabetes, making the diagnose difficulty (12).

Diabetic patients may have heart failure with preserved ejection fraction (HFpEF) or with reduced ejection fraction (HFrEF) (13). In the early stages, left ventricular ejection fraction (EF) could be preserved, whereas diastolic dysfunction could be dysfunctional (14). Structural and functional abnormalities associated with diabetes, such as increased left ventricular mass (LVM), diastolic dysfunction, and impaired LV deformation may be discovered by echocardiography (15). Especially, left ventricular longitudinal strain abnormalities have occurred in 28% of type 2 diabetic patients with normal diastolic function (16). Besides, global longitudinal strain (GLS) by speckle tracking echocardiography (STE) is a sensitive and feasible parameter that may detect LV dysfunctions and be a superior predictor of CVD outcomes (17,18). So, left ventricular strain abnormalities should be considered the first marker to detect heart dysfunctions in type 2 diabetic patients even when they are asymptomatic.

In Vietnam, especially in central Vietnam, there are currently not many studies on STE in type 2 diabetic patients.

2. OBJECTIVE

This study aimed to recognize LV dysfunctions in the early stage of diabetes and the relationship between GLS and cardiovascular risk factors, then supply the most optimal medical care to diabetic patients.

3. MATERIALS AND METHODS

Study population

Our study included 75 patients with T2DM who came to get the examination and treatment at Hue University of Medicine and Pharmacy Hospital between January 2021 and July 2023. T2DM was diagnosed according to current clinical guidelines. We excluded patients if they met any of the following criteria: (1) history of pre-existing cardiovascular disease that is not due to diabetes such as valvular heart disease, hypertrophic cardiomyopathy, dilated cardiomyopathy, stroke, previous history of open-heart surgery; (2) LVEF < 50%; (3) poor echocardiography image quality; (4) atrial fibrillation (5) The patients did not consent to participate in the study.

Basic data were collected from all participants including sex, age, height, weight, body mass index (BMI), waist circumference (cm), systolic blood pressure (SBP–mmHg), diastolic blood pressure (DBP–mmHg), T2DM duration (years), fasting blood glucose (mmol/L), triglyceride (mmol/L), high-density lipoprotein (HDL, mmol/L), LDL (mmol/L), total cholesterol (mmol/L), and HbA1c (%). Assessment of glycemic control was based on the 2020 guidelines of American Diabetes Association (19). Dyslipidemia was evaluated by the report of National cholesterol education program coordinating committee – ATP III (20). Hypertension was defined and assessed by the 2020 guidelines of International Society of Hypertension (21). Evaluation of BMI according to the World Health Organization classification and Asian standards for adults (22). Waist circumference is evaluated according to World Health Organization standards for Asians (23). T2DM duration was evaluated as a cardiovascular risk factor according to the 2020 guidelines of American Diabetes Association (19).

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

Echocardiography

Echocardiography is performed at the Echocardiography room of Hue University of Medicine and Pharmacy Hospital, using Philips Affiniti 70 (5S probe). After clearly explaining the examination, the subjects rest for 5-10 minutes, lie on the left side at an angle of about 45°, remove conductive jewelry, expose the chest, applies ultrasound cream. Echocardiographic images were recorded at a speed of 100mm/s, with simultaneous electrocardiogram measurement, measured at the end of expiration to limit the influence of respiration on the Doppler spectrum. Recording left ventricular structural and functional parameters by TM, 2D and Doppler, include: interventricular septum end-diastolic (IVSs), LVDd (left ventricular diameter end-diastolic), LVPWd (left ventricular posterior wall end-diastolic), IVSs (interventricular septum end-systolic), LVDs (left ventricular diameter end-systolic), LVPWs (left ventricular posterior wall end-systolic), LVEF (using the Simpson biplane method), left ventricular mass (LVM) and left ventricular mass index (LVMI) were calculated, E (early diastolic mitral flow–pulse Doppler), A (late diastolic mitral flow–pulse Doppler), left ventricular sidewall mitral annulus early and late peak velocity (e and a, respectively) were obtained, and E/A, e/a, and E/e were calculated, volume of left atrial (VLA is average of VLA 4 chamber and VLA 2 chamber). Parameters were recorded over 3 consecutive cardiac cycles, the final result being the average of these values. Planes and parameters used to evaluate left ventricular morphology and function according to the 2015 guidelines of the American Society of Echocardiography/European Association of Cardiovascular Imaging (24), the 2016 guidelines of the American Society of Echocardiography/European Association of Cardiovascular Imaging (25) and the 2019 recommendations of the American Society of Echocardiography (26).

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

This study was approved by the local ethics committee of our institution.

Statistical Analysis

Continuous variables were expressed as mean±standard deviation (SD) and compared by the student t-test. The categorical variables were expressed as a frequency (percentage–%). Proportional differences were evaluated with Chi-square test and Fisher's exact-test. Independent association of GLS with clinical and echocardiographic parameters in T2DM patients was evaluated with multiple regression analysis. Sequential logistic regression models were used to determine the utility of GLS over that of clinical variables including age, DM duration, HbA1c, and BMI, heart rate. Pearson's correlation was chosen to test correlations between the parameters of the two groups. A value of p <0.05 was considered statistically significant.

4. RESULTS

Baseline characteristics

This study population consisted of 150 individuals: 75 patients with T2DM (mean age: 62.56±11.01 years; 48.3% male) and 75 controls (mean age: 59.85±8.40 years; 51.7% male). Table 1 shows the clinical characteristics of the study population. There was no significant difference in age, sex and BMI between the two groups, but there was a significant difference in SBP, DBP and heart rate (p < 0.05). In some laboratory tests, there were significant differences in fasting blood glucose, HbA1c, triglycerides, HDL, LDL between the groups; the differences in fasting blood glucose, HbA1c, triglycerides, HDL, LDL were all significant with p <0.05.

	Controls (n=75)	T2DM (n=75)	p value
Age (years)	59.85±8.40	62.56±11.01	0.093
Male (%)	51.7	48.3	0.739
BMI (kg/m²)	21.92±2.32	21.86±3.72	0.899
SBP (mmHg)	118.20±7.69	141.73±20.95	<0.001
DBP (mmHg)	71.07±8.94	79.20±10.99	<0.001
Heart rate (bpm)	73.68±10.29	80.04±7.64	<0.001
Diabetes duration (years)	0	8.60±9.44	-
Fasting glucose level (mmol/L)	5.23±0.46	15.29±9.06	<0.001
HbA1c (%)	5.40±0.29	10.41±3.32	<0.001
Total Cholesterol (mmol/)	5.77±0.95	5.33±2.54	0.164
Triglycerides (mmol/L)	1.48±0.90	2.64±4.29	0.025
HDL (mmol/L)	3.89±0.89	3.37±1.69	0.021
LDL (mmol/L)	1.61±0.47	1.22±0.42	<0.001

Table 1. Baseline characteristics of the study population. . T2DM, type 2 diabetes mellitus; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycosylated hemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein

Traditional doppler echocardiographic parameters of left ventricular structure and function in the study population is shown in Table 2. IVSd, LVPWd, IVSs, LVPWs, LVM, LVMI, A parameters in type 2 diabetic patients are greater than controls (1.05±0.18 vs. 0.92±0.11, 1.02±0.15 vs. 0.89±0.11, 1.41±0.19 vs. 1.27±0.13, 1.43±0.15 vs. 1.37±0.14, 165.3±40.23 vs.142.47±30.25, 107.75±24.47 vs. 92.3±21.44, 93.54±24.15 vs. 80.50±20.57). Conversely, type 2 diabetic patients have lower EF simpson, lateral S, lateral e, septal e (59.88±5.91% vs. 63.59±5.24%, 9.14±1.92 vs. 9.95±1.96, 8.51±2.34 vs. 10.61±2.38, 6.50±1.81 vs. 8.15±2.05) than controls. All difference is statistically significant with p <0.05. There was no statistically significant difference in LVDd, LVDs, E, lateral a, S septal, a septal, VLA between 2 groups (p >0.05).

	Controls (n=75)	T2DM (n=75)	P value
IVSd (cm)	0.92±0.11	1.05±0.18	<0.001
LVDd (cm)	4.63±0.39	4.54±0.51	0.212
LVPWd (cm)	0.89±0.11	1.02±0.15	<0.001
IVSs (cm)	1.27±0.13	1.41±0.19	<0.001
LVDs (cm)	2.79±0.31	2.74±0.47	0.475
LVPWs (cm)	1.37±0.14	1.43±0.15	0.018
LVEF (%)	70.26±4.84	67.72±9.99	0.050
LVFS (%)	39.83±3.97	38.97±4.80	0.230
EF simpson	63.59±5.24	59.88±5.91	<0.001
LVM (g)	142.47±30.25	165.3±40.23	<0.001
LVMI (g/m²)	92.3±21.44	107.75±24.47	<0.001
E (cm/s)	72.95±17.84	71.53±19.08	0.638
A (cm/s)	80.50±20.57	93.54±24.15	<0.001
Lateral S (cm/s)	9.95±1.96	9.14±1.92	0.012
Lateral e (cm/s)	10.61±2.38	8.51±2.34	<0.001
Lateral a (cm/s)	10.88±2.55	10.97±2.58	0.831
Septal S (cm/s)	8.29±1.47	8.13±1.84	0.551
Septal e (cm/s)	8.15±2.05	6.50±1.81	<0.001
Septal a (cm/s)	9.84±2.01	10.29±2.47	0.217
VLA (ml/m²)	19.31±4.47	20.22±7.12	0.348

Table 2. Traditional doppler echocardiographic parameters of left ventricular structure and function in the study population. T2DM, type2 diabetes mellitus; IVSd, interventricular septum end-diastolic; LVDd, left ventricular diameter end-diastolic; LVPWd, left ventricular posterior wall end-diastolic; IVSs, interventricular septum end-systolic; LVDs, left ventricular diameter end-systolic; LVPWs, left ventricular posterior wall end-systolic; LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; LVM, left ventricular mass; LVMI, left ventricular mass index; E, early diastolic mitral flow (pulse Doppler); A, late diastolic mitral flow (pulse Doppler); VLA, volume of left atrial

Results of speckle tracking echocardiography

Figure 1 describes myocardial strains of type 2 diabetic patients and controls. When compared with the controls, type 2 diabetic patients had global longitudinal strain reduction (-17.02±3.06% vs -20.32±2.04%) and global circumferential strain reduction (-29.04±6.39% vs -31.88±4.47%) than the control group (p<0.05). Twist in type 2 diabetic patients was no greater statistically significant than controls (9.23±6.75 vs. 8.23±3.38; p >0.05).

Correlation between left ventricular strains and cardiovascular risk factors

The GLS was positively correlated with heart rate, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, HbA1c, total cholesterol and HDL (p <0.05); GLS was not correlated with age, diabetes duration, BMI, waist circumference, triglycerides, LDL (p>0.05) (Table 3).

GCS was positively correlated with systolic blood pressure, diastolic blood pressure and HDL (p <0.05); GLS was not correlated with age, diabetes duration, BMI, waist circumference, heart rate, fasting plasma glucose, HbA1c, total cholesterol, triglycerides, LDL (p>0.05) (Table 3).

TWIST was positively correlated with total cholesterol (p <0.05) and was not correlated with age, diabetes duration, BMI, waist circumference, heart rate, fasting plasma glucose, HbA1c, triglycerides, HDL, LDL (p >0.05) (Table 3).

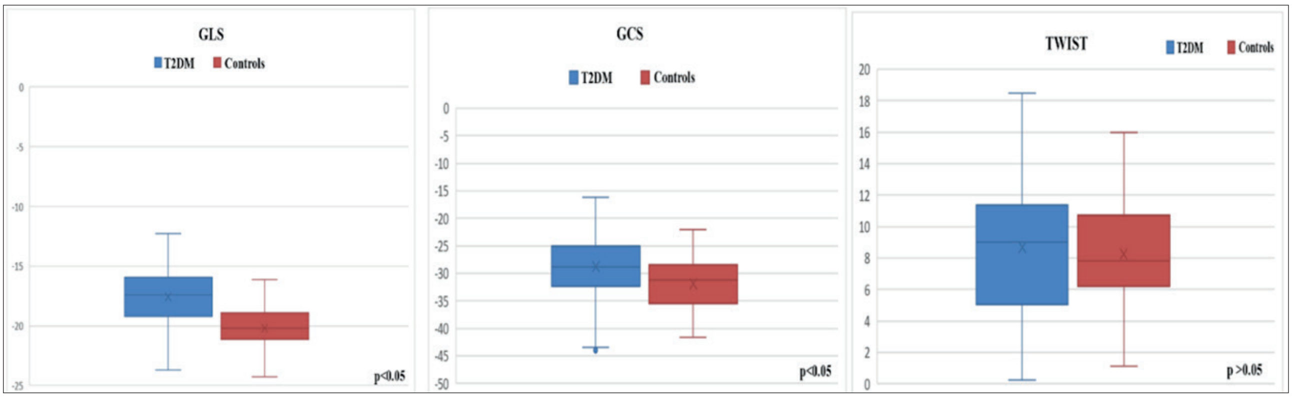

Figure 1. Myocardial strains of type 2 diabetic patients and controls

Variables	GLS		GCS		TWIST	
	r	p	r	p	r	p
Age	0.085	0.302	-0.011	0.898	-0.032	0.702
Diabetes duration (years)	0.089	0.494	-0.145	0.260	0.134	0.098
BMI (kg/m2)	0.087	0.288	0.038	0.648	0.035	0.673
Waist circumference (cm)	0.104	0.204	-0.010	0.902	-0.094	0.251
Heart rate (bpm)	0.171	0.036	0.137	0.094	0.015	0.854
SBP (mmHg)	0.307	0.000	0.195	0.017	0.015	0.852
DBP (mmHg)	0.202	0.012	0.248	0.002	-0.061	0.461
Fasting glucose level (mmol/L)	0.519	0.000	0.083	0.311	0.097	0.239
HbA1c (%)	0.218	0.007	0.032	0.760	0.038	0.718
Total Cholesterol (mmol/)	-0.256	0.028	-0.169	0.149	0.463	0.000
Triglycerides (mmol/L)	0.032	0.766	0.201	0.057	0.179	0.092
HDL (mmol/L)	-0.194	0.071	-0.315	0.003	0.045	0.675
LDL (mmol/L)	-0.184	0.123	-0.215	0.069	-0.021	0.862

Table 3. Correlation between GLS, GCS, TWIST and cardiovascular risk factors. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycosylated hemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein; GLS, global longitudinal strain; GCS, global circumferential strain

5. DISCUSSION

The main findings of this study are as follows: (1) Type 2 diabetic patients had lower GLS and GCS than controls. These results suggest that STE should be used to detect early LV dysfunctions of patients with T2DM even though preserved LVEF; (2) There is a correlation between GLS, GCS and some cardiovascular risk factors, such as SBP, DBP, heart rate, fasting blood glucose, HbA1c, total cholesterol, triglycerides, HDL, LDL.

General characteristics of study population

In this study, there was no significant difference in age or gender. This is an optimal feature for the study to exclude factors affecting cardiac morphology and function caused by age and gender. Besides, there was a significant difference in SBP, DBP and heart rate, fasting blood glucose, HbA1c, triglycerides, HDL, LDL between the two groups (Table 1). The results of this study are similar to the results of some other studies. In the study of Yang et al, there was no significant difference in age, gender, heart rate, BMI and there was a significant difference in fasting blood glucose, HbA1c, triglycerides, LDL (27). In the study of Li W et al (2022), there was a difference in BMI, SBP, and DBP and there was no difference in age, or heart rate (28). Similarly, in the study of Liao LL (2022), there was no significant difference in age between the two groups, but there was a significant difference in BMI, SBP and SBP ($p < 0.05$) (29). The results of this study once again prove that hypertension and obesity are common co-morbidities, and are also the major risk factors to be concerned with in patients with type 2 diabetes.

In the results of traditional Doppler echocardiography, our study recorded: the group of type 2 diabetics patients had higher IVSd, LVPWd, IVSs, LVPWs, LVM, LVMI, A and lower EF simpson, lateral S, lateral e, septal e than controls (Table 2). This result is similar to the results of some other studies, there is no significant difference in LVIDd, LVIDs between the two groups (28,29); and there was a difference in IVS between the 2 groups (28).

According to the 2019 recommendations of the European Society of Cardiology (ESC), echocardiography is the first choice to evaluate structural and functional disorders of the heart for patients with diabetes (15). Until nowadays, ejection fraction is still a useful parameter used to diagnose and classify heart failure (30,31). When compared to the controls, type 2 diabetic patients have lower EF and greater LVMI (32,33). Thus, hyperglycemia in patients with T2DM had effects on left ventricular morphology and function even when normal left ventricular ejection fraction and no clinical symptoms.

Speckle tracking echocardiography results

When compared with the controls, type 2 diabetic patients had reduced GLS and GCS than the control group ($p<0.05$) (Figure 1). These results were similar to some research on type 2 diabetic patients. In the research of Abd El Moneum MS et al (2018), when conducting a study on 100 patients with type 2 diabetes without cardiovascular symptoms and with preserved ejection fraction, 43% of patients with type 2 diabetes had GLS is abnormal and suggests that using STE to detect preclinical systolic dysfunction may provide useful information for risk stratification in the non-diabetic population (34). In the study of Liao LL et al (2022), the GLS in the patients with type 2 diabetes was significantly lower than that in the control group (-19.13±1.73% vs -16.82) ±2.59%; $p < 0.001$), indicating damage to the left ventricular myocardium, although the LV ejection fraction (LVEF) remains normal (29). Another study by Li W. et al (2022) also noted that GLS in diabetic patients was lower than that in the control group (p<0.001) and concluded that 2D STE could detect muscle dysfunction. preclinical echocardiography, which is more sensitive than conventional echocardiography (28). In another systematic review by Silva et al, when conducting data aggregation on 19 studies using 2D STE (1774 patients with diabetes) and 9 studies using 3D STE (488 patients with diabetes), concluded Cardiac deformity imaging by STE 2D and STE 3D is valuable for early identification of preclinical systolic dysfunction, this difference becoming more apparent when combined with risk factors and status ventricular remodeling (35).

The reduction of GLS occurred even though the patients had no symptoms. STE is the tool that helps to detect early asymptomatic regional myocardial dysfunction and its parameters were considered sensitivity index to evaluate left ventricular dysfunction (36-38).

Correlation between left ventricular strains and cardiovascular risk factors

Diabetes is a cardiovascular risk factor, and cardiovascular risk factors are also a risk factor for the rapid progression of the occurrence of complications in patients with T2DM (15,19,39). The correlation between GLS and some cardiovascular risk factors was indicated by some previous studies. In the research of Abd El Moneum MS et al (2018), symptoms and duration of diabetes were only independent predictors of GLS reduction (34). In another study by Lezama FS et al (2021), the reduction of GLS was correlated with the degree of diastolic dysfunction, abnormalities of parameters in conventional Doppler echocardiography, as well as the presence of cardiovascular risk factors (40).

In this study, GLS was positively correlated with heart rate, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, HbA1c, total cholesterol and HDL; GCS was positively correlated with systolic blood pressure, diastolic blood pressure and HDL; TWIST was positively correlated with total cholesterol (Table 3). For management and delay of the occurrence of heart failure, diabetic patients should be systematically assessed at least annually for cardiovascular risk factors. These cardiovascular risk factors include obesity/overweight, hypertension, not good glycemia control, dyslipidemia. This is completely consistent with the recommendations of the American Diabetes Association, the European Society of Cardiology, and the European Society of Endocrinology (15, 19).

6. CONCLUSION

Type 2 diabetic patients have reduced global longitudinal strain and global circumferential strain in speckle-tracking echocardiography. The reduction of global longitudinal strain, global circumferential strain was correlated with cardiovascular risk factors (hypertension, not good glycemia control, increasing BMI, dyslipidemia).

- **Authors' contributions:** All authors have equally contributed to the concept and design of the study, analysis and interpretation of the data, literature search and writing the manuscript. All authors have revised the manuscript critically for important intellectual content, and all authors have read and agreed to the published final version of the article.
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