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Association between Newly Diagnosed Type 2 Diabetes Mellitus and Left Ventricular Global Longitudinal Strain: A Single Center, Cross-sectional Study

ABSTRACT

Objective: Diabetes mellitus is a major cardiovascular risk factor. Diabetic complications in the cardiovascular system randomly appear following long standing diabetes. However, newly diagnosed diabetes can also be associated with cardiac problems. The aim of this study was to compare patients with newly diagnosed type 2 diabetes mellitus (T2DM) to healthy controls in regard to echocardiography features, specifically left ventricular global longitudinal strain (LV GLS).

Materials and methods: This was a prospective cross-sectional study conducted on 94 patients, 52 patients with newly diagnosed T2DM that formed the first group and 42 healthy subjects, without history of diabetes mellitus and/or cardiovascular disease, which formed the second group.

Results: Patients with newly diagnosed T2DM had mean glucose level of 16.37 ± 7.43 mmol/L and HbA1c of 8.57 ± 2.31 %. The groups did not differ in regard to age, gender, smoking, arterial hypertension or heart rate at the time of examination. The ratio between early mitral inflow velocity and mitral annular early diastolic velocity (E/e’) of the septal wall was significantly lower in patients with newly diagnosed T2DM (6.21 ± 3.14 vs. 7.8 ± 2.45, p = 0.009). The LV GLS resulted lower in patients with newly diagnosed T2DM compared to the healthy subjects (|–19.36|% ± 2.98 vs. |–20.43|% ± 1.99. p = 0.049). Of note, the LV GLS values are expressed as absolute numbers. The ratio of patients with LV GLS strain <|–18.8|% was significantly higher in patients with newly diagnosed T2DM (42.31% vs. 21.43%, p = 0.03).

Conclusions: LV GLS may serve as an important echocardiographic parameter to detect early myocardial changes in asymptomatic patients with newly diagnosed T2DM. (Clin Diabetol 2022, 11; 4: 245–250)

Keywords: newly diagnosed type 2 diabetes mellitus, global longitudinal strain, speckle tracking echocardiography, diastolic dysfunction

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Introduction

Coronary artery disease (CAD) is one of the main causes of morbidity and mortality in patients with type 2 diabetes mellitus (T2DM). On the other hand, diabetes mellitus is a major cardiovascular risk factor which frequently leads to severe cardiovascular complications. Diabetic complications in the cardiovascular system randomly appear following long standing diabetes mellitus. However, newly diagnosed diabetes can also be associated with cardiac problems. In a multinational cohort of younger adults, < 55 years of age, presenting to hospital with acute myocardial infarction, 14.5% had newly diagnosed diabetes [1]. Early diagnosis and treatment of diabetes can reduce the risk of long-term complications, especially for ischemic heart disease [2].

The degree of myocardial strain, more precisely Global Longitudinal Strain (GLS) measures the systolic function of the left ventricle (LV) and it allows early detection of systolic dysfunction. GLS has also a growing prognostic role in coronary artery disease [3]. Subendocardial muscular fibers of the LV are mainly oriented longitudinally and since this layer is more susceptible towards ischemia, GLS will detect these alterations earlier than other echocardiography methods.

The aim of this study was to compare patients with newly diagnosed T2DM to healthy controls matched for age and gender, in regard to echocardiography features, specifically GLS.

Materials and methods

This was a prospective cross-sectional study that included 94 patients, 52 patients with newly diagnosed diabetes that formed the first group and 42 healthy subjects, without a history of diabetes mellitus and/or cardiovascular disease, which formed the second group. Diabetes mellitus was diagnosed according to American Diabetes Association (ADA) criteria, including the following: fasting plasma glucose level ≥ 7mmol/L, or a two hour plasma glucose ≥ 11.1 mmol/L or higher during a 75 g oral glucose tolerance test, or random plasma glucose ≥ 11.1 mmol/L in patients with classic symptoms, or hemoglobin A1c (HbA1c) level ≥ 6.5%. Exclusion criteria included patients with known coronary artery disease, severe anemia, < 18 years of age, with a history of stroke or transient ischemic attack and those who refused to enter the study. Demographic and history data, physical examination, laboratory tests, ECG, transthoracic echocardiography were obtained for each patient.

The study was approved by the Ethical Board of our institution and written informed consent was taken from every patient.

Echocardiography

Echocardiography (Phillips EPIQ 7C, X5-1 probe) examinations and measurements were performed according to the recommendations of the American Society of Echocardiography [4]. Left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), septal wall and posterior wall thickness were measured from parasternal M-mode view according to standard criteria. Left ventricular ejection fraction (LVEF) and left ventricular end diastolic volume (LVEDV) were derived from LV longitudinal strain rate measurements. Left atrial (LA) diameter was measured in 2D projection at end-ventricular systole in parasternal long axis view. Pulsed wave Doppler was used to record trans-mitral flow from the apical four-chamber view. Peak velocity of early (E), late (A) atrial diastolic filling of the Doppler mitral flow and E/A ratio were calculated. Tissue Doppler imaging was applied in the apical four-chamber view, where pulsed wave tissue Doppler imaging across the septal annulus was used. From the obtained negative deflection, maximal e' and a' velocities were measured as well as maximal s wave from the positive deflection. The average ratio between early mitral inflow velocity and mitral annular early diastolic velocity (E/e´) was derived from the above measurements.

For Speckle Tracking Echocardiography, images from the apical four-chamber, three-chamber and two-chamber views with ECG gating were attained. The endocardial border was manually adjusted at end-systole. The software system automatically generated the strain values for each segment and the average LV GLS.

Statistical analysis

Data were expressed as mean ± standard deviation (SD) and percentages. Comparison between parametric variables was performed using the two-tailed unpaired t-test, and for categorical variables the chi-square test was used. For all tests, a p value < 0.05 was considered significant. MedCalc Software Ltd. Version 20.007 and 20.008 were used to compare the two groups.

Results

Fifty-two patients with newly diagnosed T2DM entered our study, with mean glucose level 16.37 ± 7.43 mmol/L and HbA1c of 8.57 ±2.31 %. In the control group we included 42 healthy subjects. Table 1 demonstrates that the mean patient age was almost identical between groups (55.5 years of age) and there were no statistical differences between the groups in regard to gender, smoking, arterial hypertension or heart rate at the time of examination. However, there was a significant difference in terms of associated dyslipidemia and body mass index (BMI) in patients with T2DM.

As concerns echocardiography parameters, several measurements showed significant differences between the two groups, including aortic bulb diameter, interventricular and posterior left ventricular wall thickness, left ventricular end diastolic and end systolic diameter, peak E wave of the mitral flow. However, though sta-

Table 1. Baseline Patient Characteristics of the Two Groups

	Patients with diabetes mellitus (n = 52)	Control group (n = 42)	P value
Age	55.5 ± 12.25	55.5 ± 10.66	n.s.
Gender, females	22/52 (42.31%)	26/42 (61.9%)	0.06
Smokers	22/52 (42.31%)	18/42 (42.86%)	0.96
Arterial hypertension	30/52 (57.69%)	10/42 (23.81%)	0.09
Dyslipidemias	25/52 (48.01%)	4/42 (9.52%)	0.0001
Family history for CAD	16/52 (30.77%)	10/42 (23.81%)	0.46
BMI [kg/m^2]	31.64 ± 5.74	28.07 ± 4.11	0.001
Heart rate	74.56 ± 10.79	72.19 ± 11.41	0.3

BMI — body mass index; CAD — coronary artery disease

Table 2. Comparison of Echocardiographic Parameters Between the Two Groups

	Patients with diabetes mellitus (n = 52)	Control group (n = 42)	P value
Aorta [mm]	32.38 ± 2.84	30.57 ± 3.04	0.0037
LA diameter [mm]	35.36 ± 2.36	34.21 ± 3.92	0.08
IVS [mm]	11.13 ± 1.44	10.15 ± 1.63	0.003
PW [mm]	10.88 ± 1.37	9.8 ± 1.25	0.0002
LVEDD [mm]	51.79 ± 4.01	47.76 ± 4.5	< 0.0001
LVESD [mm]	33.46 ± 3.94	31.5 ± 3.79	0.017
FS [%]	33.85 ± 4.7	33.57 ± 3.99	0.76
RA [mm]	31.33 ± 3.69	30.59 ± 3.96	0.35
RV [mm]	27.52 ± 2.97	27.25 ± 3.01	0.66
Peak E wave [cm/s]	50.43 ± 17.56	66.25 ± 17.42	< 0.0001
E/A	1.03 ± 0.49	0.98 ± 0.35	0.58
e' [cm/s]	8.24 ± 2.95	8.66 ± 2.35	0.45
E/e'	6.21 ± 3.14	7.8 ± 2.45	0.009
MR (gr. I)	15/52 (28.85%)	14.42 (30.95%)	0.83
AR (gr. I)	0/52 (0%)	5/42 (11.9%)	0.01
TR (gr. I, II)	6/52 (11.54%)	11/42 (26.19%)	0.07

AR — aortic regurgitation; FS — fractional shortening; IVS — interventricular septum; LA — left atrium; PW — posterior wall; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter; MR — mitral regurgitation; RA — right atrium; RV — right ventricle; TR — tricuspid regurgitation

tistically significant, the mean values for both groups in above mentioned parameters were within reference range, as demonstrated in Table 2. On the other hand, the E/e' ratio of the septal wall was significantly lower in patients with newly diagnosed T2DM (6.21 ± 3.14 vs. 7.8 ± 2.45, p = 0.009) and its mean value did not belong to normal reference range values.

Referring to the main aim of our study, the speckle tracking parameters, specifically the left ventricular longitudinal strain, several features derived from these measurements resulted with statistical significance, as presented in Table 3. Most notably LV GLS resulted to be lower in patients with newly diagnosed T2DM compared to the healthy subjects (|–19.36|% ± 2.98 vs. |–20.43| % ± 1.99. p = 0.049). Of note, we analyzed the LV GLS values as absolute numbers in order to avoid confusion. Furthermore, the ratio of patients with LV GLS strain < |–18.8| % was significantly higher in patients with newly diagnosed T2DM (42.31% vs. 21.43%, p = 0.03). Likewise, end diastolic volume and left ventricular ejection fraction that were derived from left ventricular longitudinal strain measurements resulted in significant statistical differences, as displayed in Table 3.

Table 3. Comparison of Strain Rate Parameters Between the Two Groups

	Patients with diabetes (n = 52)	Control group (n = 42)	P value
LV 2 chamber LS	–19.46 ± 4.38	–20.6 ± 2.76	0.15
LV 2 chamber LS < |–18.8|%	21/52 (40.38%)	10/42 (23.81)	0.09
LV 3 chamber LS	–19.08 ± 3.17	–20.63 ± 2.15	0.008
LV 3 chamber LS <|–18.8|%	21/52 (40.38%)	7/52 (13.46%)	0.004
LV 4 chamber LS	–19.61 ± 2.87	–20.04 ± 2.44	0.44
LV 4 chamber LS <|–18.8|%	14/52 (26.92%)	9/42 (21.43%)	0.5
LV Global LS	–19.36 ± 2.98	–20.43 ± 1.99	0.049
LV Global LS <|–18.8|%	22/52 (42.31%)	9/42 (21.43%)	0.03
EDV [mL]	94.7 ± 23.57	81.44 ± 18.19	0.0035
EF [%]	59.92 ± 5.62	63.13 ± 6.89	0.015

EDV — end diastolic volume; EF — ejection fraction; LS — longitudinal strain; LV — left ventricle

Discussion

It is considered that around one third of patients presenting with newly diagnosed T2DM develop clinical complications within 10 years [5]. The VALIANT (VALsartan In Acute myocardial iNfarcTion) trial showed that 3400 patients with previously known diabetes had similar risk of mortality and cardiovascular events as 580 patients with newly diagnosed diabetes [6]. Therefore, a watchful strategy concerning cardiovascular complica-tions should be applied without delay.

BMI was significantly higher in our patients with newly diagnosed T2DM as opposed to the controls (31.64 ± 5.74 vs. 28.07 ± 4.11, p = 0.001). Mean BMI of our patients newly diagnosed T2DM belonged to the obesity class 1 category, whereas patients from the control group belonged to the overweight classification. It is generally accepted that an increased BMI is associated with an increased risk of T2DM and cardiovascular disease. Bodegard et al. in their study, where they analyzed the influence of BMI change on cardiovascular mortality risk, they showed that the baseline BMI in newly diagnosed patients with diabetes was 30.2 kg/m^2, which is comparable to our results [7]. Dyslipidemia was also significantly more frequent in our newly diagnosed diabetes patients (48% vs. 9.5%, p = 0.0001). Likewise, Soebardi et al. found that the prevalence of dyslipidemia in subjects with newly diagnosed diabetes was higher among all age groups than that in subjects without diabetes [8]. Moreover, Krishnamurthy el al. reported a very high prevalence (89.2%) of dyslipidemia in newly diagnosed patients with T2DM [9].

Among echocardiography features, several measurements resulted in significant differences between the groups, including left ventricular diastolic dysfunction characteristics, such as E/e'. Left ventricular diastolic dysfunction is considered the earliest preclinical manifestation of diabetic cardiomyopathy, which can advance to symptomatic heart failure [10]. Ultrasound techniques can detect diabetic cardiomyopathy far earlier than symptom emergence. Early diastolic abnormalities have repeatedly been demonstrated using Doppler ultrasound techniques. However, Tissue Doppler appears advantageous as it represents a less pre-load dependent and more linear expression of diastolic dysfunction [11]. Therefore, the Tissue Doppler technique demonstrated altered diastolic dysfunction features in our asymptomatic patients with newly diagnosed T2DM. Likewise, Boyer et al. with conventional Doppler techniques found left ventricular diastolic dysfunction in 46% of their asymptomatic normotensive patients with T2DM, whereas following application of newer ultrasound techniques diastolic dysfunction was found in 75% of them [12]. Ayman et al. found that diastolic dysfunction is highly present in patients with newly diagnosed diabetes and it also correlates with HbA1c level, obesity, dyslipidemia and the duration of diabetes [13]. Similarly, Chaudhary et al. showed that left ventricular diastolic dysfunction is very common in newly diagnosed T2DM patients (41% of patients), while HbA1c and age are strong indicators associated with left ventricle diastolic dysfunction in these patients [14]. Table 2 shows additional echocardiography parameters (aortic root, septal and posterior wall thickness, LVEDD, LVESD) that were significantly higher in the diabetes group; however, the mean values were within reference range. Very similar results were presented by Zhao et al. in their study regarding echocardiography changes in newly diagnosed T2DM patients [15].

LV GLS was significantly lower in our patients with newly diagnosed T2DM. The mean value in both groups was around the reported normal range, although the guidelines do not precise yet the normal values of LV GLS, but –20% (± 2) may be considered normal [4]. LV GLS is more sensitive than LV ejection fraction to depict LV systolic dysfunction, either due to longitudinal orientation of the subendocardial fibers, which are more predisposed to ischemia, or compensatory function of the circumferential fibers, which achieve to maintain the normal LV ejection fraction [4]. LV GLS has enabled detection of subclinical LV dysfunction in almost half (45%) of patients with type 2 diabetes mellitus with LV ejection fraction > 50% [16].

Longitudinal strain is a speckle tracking analysis that is able to detect early ischemic changes. The European Society of Cardiology guidelines for the diagnosis and management of non-ST-elevation acute coronary syndrome and chronic coronary syndrome recommend the use of speckle tracking to support diagnosis in cases with clinical suspicion of ischemic disease [17, 18]. A cutoff value of LV GLS < |–18.8|% is suggested for detection of coronary stenosis in patients with angina [19]. Therefore, we used this value as a reference in our data and around 42% of our patients with T2DM had LV GLS under this value with significant difference from the control group. Other studies that correlated longitudinal strain with coronary stenosis found that values < |–18|% and < |–19|% could reflect significant coronary stenosis [20, 21].

The relationship between speckle tracking parameters and diabetes mellitus has been evaluated by several authors. However, patients with complications due to diabetes were often included in these studies [22, 23]. On the other hand, Ng et al. found that asymptomatic patients with diabetes with a mean duration of 4 years, despite the normal LV mass and LVEF, had impaired LV GLS [24]. Liu et al. showed that in patients with diabetes without cardiovascular complications, impaired LV GLS is associated with cardiovascular events. Moreover, GLS provides incremental prognostic value compared to clinical demographics, HbA1c and LV diastolic function [25].

There are no studies to date, to our best knowledge, that analyze the LV GLS as a possible LV dysfunction and/or ischemic indicator in asymptomatic patients with newly diagnosed T2DM. A limitation of this study is that it is a single-center, cross-sectional study with a relatively small sample size; therefore, these findings must be considered with caution. Additional limitation is that potential coronary artery disease has not been documented by well-established methods, such as coronary angiography or CT coronary angiography.

Conclusions

Echocardiography is an effective tool to reveal diastolic dysfunction in patients with newly diagnosed type 2 diabetes mellitus. Furthermore, LV GLS may serve as an appropriate echocardiographic parameter to detect early myocardial changes in asymptomatic patients with newly diagnosed T2DM.

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Conflict of interest

None declared.

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