



## Original Article

# Impairment of left and right ventricular longitudinal strain in asymptomatic children with type 1 diabetes



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## ABSTRACT

**Aim:** The relationship between type 1 diabetes (T1DM) and cardiac function in children is not well established. The purpose of this study was to investigate whether children and adolescents with T1DM present early asymptomatic abnormalities of left ventricular (LV) and right ventricular (RV) function. In addition, we evaluated the relationship of any such abnormalities with glycemic control and diabetes duration.

**Methods:** This was a prospective study. Standard echocardiography, tissue Doppler imaging, and two-dimensional strain analysis were performed prospectively in 52 children with T1DM. The results were compared with those from 52 healthy children matched for age and sex.

**Results:** There were no significant differences between the two groups in LV ejection fraction or RV systolic function. There was a difference between the two study groups in transtricuspid flow: the E-wave and A-wave velocities were significantly higher in the diabetic group. Left ventricular global longitudinal strain (LV GLS) was significantly lower in children with T1DM ( $-20.01 \pm 1.86\%$  vs.  $-22.99 \pm 0.98\%$ , respectively;  $P < .001$ ), as was RV free-wall longitudinal strain (RV FWLS) ( $-29.13 \pm 1.85\%$  vs.  $-30.22 \pm 1.53\%$ , respectively;  $P = .002$ ). LV GLS was correlated with diabetes duration ( $r = 0.444$ ,  $P < .001$ ) and glycated hemoglobin (HbA1c) ( $r = 0.683$ ,  $P < .001$ ); however, no correlation was found between RV FWLS and HbA1c or diabetes duration.

**Conclusions:** Our findings suggest that LV GLS and RV FWLS are impaired in children with T1DM and that the decrease in LV GLS is correlated with diabetes duration and HbA1c levels.

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## 1. Introduction

Type 1 diabetes mellitus (T1DM) is a major cardiovascular risk factor in young adults that is associated with increased mortality due to premature cardiovascular events,<sup>1</sup> including heart failure.<sup>2</sup>

**Abbreviations:** 2D, Two-dimensional; LV GLS, Left ventricular global longitudinal strain; HbA1c, Glycated hemoglobin; LV, Left ventricular; LVEF, Left ventricular ejection fraction; ROC, Receiver operating Characteristic; RV FWLS, right ventricular free-wall global longitudinal strain; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

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The relationship between T1DM and cardiac structure and function in children and adolescents is not well established.<sup>3</sup> All proposed mechanisms leading to left ventricular (LV) impairment in T1DM are systemic changes and therefore might affect right ventricular (RV) function,<sup>4</sup> causing both systolic and diastolic abnormalities.<sup>5</sup>

In clinical practice, RV dysfunction is relevant in a variety of disease states affecting both the course and prognosis, and therefore, one may assume that RV performance is also an important issue in patients with diabetes.<sup>5</sup>

Only a few echocardiographic studies in the literature discuss the right ventricle in diabetes in children.<sup>6–9</sup>

In fact, echocardiography is an important diagnostic tool for representation of cardiomyopathy and cardiac functional abnormalities.

The two-dimensional (2D) strain analysis technique is the most sensitive echocardiographic tool for the detection of the subclinical impairment of myocardial function observed in many conditions causing predisposition to heart failure.<sup>10</sup>

The present study used 2D strain analysis to investigate whether children and adolescents with T1DM present early asymptomatic abnormalities in LV and RV function. In addition, we evaluated the relationship of any such abnormalities with glycemic control and diabetes duration.

## 2. Research design and methods

### 2.1. Study design

This was a prospective study.

### 2.2. Study population

The study prospectively recruited 52 patients with diabetes aged 5–15 years (diabetic group), who were prospectively enrolled between January 2014 and January 2016 and followed up at the pediatric department. The control group included asymptomatic healthy children matched by age and sex from our outpatient department of pediatric cardiology, selected from children who were being investigated for physiological cardiac murmur and whose echocardiography was normal.

### 2.3. Inclusion criteria for the diabetic group

T1DM was diagnosed according to the World Health Organization criteria<sup>11</sup> together with a permanent need for insulin therapy. The inclusion criteria were diabetes duration >1 year, LV ejection fraction (LVEF) >55%, normal resting electrocardiogram (ECG), and no congenital heart disease.

### 2.4. Inclusion criteria for the control group

The children in the control group had to have no congenital heart disease, personal antecedents, or a family history of high blood pressure, hypercholesterolemia, or diabetes.

### 2.5. Exclusion criteria

Information of whether and when there was cardiopathy or any significant concomitant disease from all three apical views was not available; thus, 11 patients were excluded.

### 2.6. Clinical evaluation

All patients underwent history taking for demographic data. For patients with diabetes, diabetes duration (expressed in years) was considered for each individual based on the full-attained age on the first day of insulin therapy, use of medication, and average dose of insulin. Children with diabetes and healthy children also underwent clinical examination and anthropometric measurements, including heart rate and cardiac auscultation. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after 10 min at rest, using a calibrated automatic blood pressure monitor. Standard 12-lead electrocardiogram (ECG) data were recorded in children with and without diabetes.

The body mass index (BMI) was calculated according to the formula of weight (kg) divided by height squared (m<sup>2</sup>).

### 2.7. Laboratory investigations

Glycated hemoglobin (HbA1c), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and serum triglyceride were recorded. This study used the mean quarterly HbA1c (%) for the year before the study (four samples).

### 2.8. Echocardiography

All patients and controls underwent an echocardiographic examination. Echocardiography with a simultaneous ECG was performed with a General Electric Vivid E9 imaging system device (GE Vingmed Ultrasound AS) using a 3.5-MHz transducer in accordance with the recommendations of the American Society of Echocardiography.<sup>12</sup>

Echocardiographic examinations were read and analyzed offline using a dedicated software program General Electric EchoPac software (EchoPAC PC, version 112; GE Vingmed) by two independent observers blinded to patient history. Three consecutive heart cycles were recorded.

LVEF was assessed using the biplane Simpson's method in apical view. LV end-diastolic dimension and end-systolic

**Table 1**  
Physical and biological characteristics in children with type 1 diabetes mellitus and children without diabetes.

| Physical and biological characteristics | Children with diabetes (n = 52) | Children without diabetes (n = 52) | P   |
|-----------------------------------------|---------------------------------|------------------------------------|-----|
| Male                                    | 29                              | 29                                 |     |
| Age (years)                             | 11.2 ± 2.4                      | 11.2 ± 2.4                         | 1   |
| Weight (kg)                             | 28.6 ± 5.5                      | 27.3 ± 5.2                         | .21 |
| Height (m)                              | 1.4 ± 0.2                       | 1.3 ± 0.14                         | .06 |
| BMI (kg/m <sup>2</sup> )                | 16.6 ± 3.5                      | 15.9 ± 2                           | .22 |
| Heart rate (bpm)                        | 91 ± 13                         | 94 ± 17                            | .2  |
| SBP (mmHg)                              | 111 ± 2                         | 111 ± 1                            | .61 |
| DBP (mmHg)                              | 63 ± 4                          | 63 ± 3                             | .90 |
| Diabetes duration (years)               | 5.9 ± 3.2                       | —                                  |     |
| HbA1c (%)                               | 9.9 ± 1.9                       | —                                  |     |
| Total cholesterol (mmol/L)              | 3.5 ± 0.3                       |                                    |     |
| LDL (mmol/L)                            | 1.9 ± 0.4                       |                                    |     |
| HDL (mmol/L)                            | 1.2 ± 0.2                       |                                    |     |
| Triglycerides (mmol/L)                  | 0.9 ± 0.2                       |                                    |     |
| Daily dose of insulin (units)/24 h      | 35.9 ± 9.7                      | —                                  |     |

Values are presented as means ± standard deviations.

BMI: body mass index; bpm: beats per minute; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol.

**Table 2**

Standard two-dimensional echocardiographic characteristics in children with and without diabetes.

| Standard two-dimensional echocardiographic | Children with diabetes (n = 52) | Children without diabetes (n = 52) | P   |
|--------------------------------------------|---------------------------------|------------------------------------|-----|
| LV-EDD (mm)                                | 40.9 ± 5                        | 42.9 ± 1.4                         | .01 |
| LV-ESD (mm)                                | 24.7 ± 4.5                      | 25.5 ± 2.3                         | .31 |
| IVS-EDD (mm)                               | 6.1 ± 2.9                       | 5.6 ± 0.5                          | .90 |
| LVPW-EDD (mm)                              | 5.5 ± 2.4                       | 5.4 ± 0.5                          | .40 |
| LVEF (%)                                   | 67 ± 8                          | 67 ± 3                             | .93 |
| LVM (g)                                    | 61.4 ± 20.8                     | 65.4 ± 9.6                         | .15 |
| LVMI (g/m <sup>2</sup> )                   | 62.7 ± 14.7                     | 66.9 ± 11.3                        | .13 |
| LAV (mL)                                   | 22.9 ± 6.6                      | 24.3 ± 6.1                         | .89 |
| RV-EDD (cm)                                | 12.3 ± 2.3                      | 11.9 ± 2.4                         | .30 |
| RV free-wall thickness (cm)                | 2.9 ± 0.8                       | 3 ± 0.7                            | .80 |
| FAC                                        | 42.8 ± 3.8                      | 44.4 ± 3.6                         | .09 |
| RAV (mL)                                   | 20.2 ± 6.7                      | 21.3 ± 5.5                         | .35 |
| TAPSE (cm)                                 | 20.7 ± 1.6                      | 20.8 ± 1.8                         | .99 |

Values are presented as means ± standard deviations.

LV-EDD: left ventricular end-diastolic dimension; LV-ESD: left ventricular end-systolic dimension; IVS-EDD: interventricular septal end-diastolic dimension; LVPW-EDD: left ventricular posterior wall end-diastolic dimension; LVM: left ventricular mass; LVMI: left ventricular mass indexed to estimated body surface area; LVEF: left ventricular ejection fraction; LAV: left atrial volume; RV-EDD: right ventricular end-diastolic diameter; RV free wall: right ventricular free wall; FAC: fractional area change (two-dimensional); RAV: right atrial volume; TAPSE: tricuspid annular plane systolic excursion.

dimension, interventricular septal end-diastolic dimension, and LV posterior wall end-diastolic dimension were measured in time motion mode in the parasternal long-axis view. LV mass was calculated.<sup>13</sup>

The RV free-wall thickness was measured from the subcostal view at end diastole by 2D echocardiography. RV end-diastolic diameter was measured in the modified low parasternal view. RV systolic function was evaluated by 2D fractional area change and tricuspid annular plane systolic excursion (TAPSE).

Conventional Doppler echocardiography was used to measure LV and RV diastolic functional parameters.

Acquisitions in pulse tissue Doppler imaging were made in the apical four-chamber view. The sample volume was placed at the level of the septal mitral annulus to measure the peak systolic myocardial velocity (Sa), peak early diastolic myocardial velocity (e'), and late diastolic myocardial velocity (a') at the time of atrial contraction. The sample volume was placed at the basal level of the RV lateral tricuspid annulus to measure the peak systolic myocardial velocity, peak early diastolic myocardial

velocity, and late diastolic myocardial velocity at the time of atrial contraction.

### 2.9. 2D strain analysis

The left ventricular global longitudinal strain (LV GLS) was measured by 2D speckle-tracking echocardiography, in which deformation of the LV is determined by tracking speckles from frame to frame. Apical images of the two-, three-, and four-chamber views of the LV are divided into 6 segments (basal, mid, and apical segments in opposing walls). For the present analysis, LV GLS was determined as the average of 17 segments, thereby providing a LV GLS measure for the entire LV.<sup>14</sup>

The peak systolic RV free-wall global longitudinal strain (RV FWLS) was measured in the four-chamber view by speckle-tracking analysis. All images were recorded with a frame rate ranging from 40 to 80 frames/s.

The RVGLS was calculated as a mean value of three segments of the RV free wall (basal, mid, and apical).

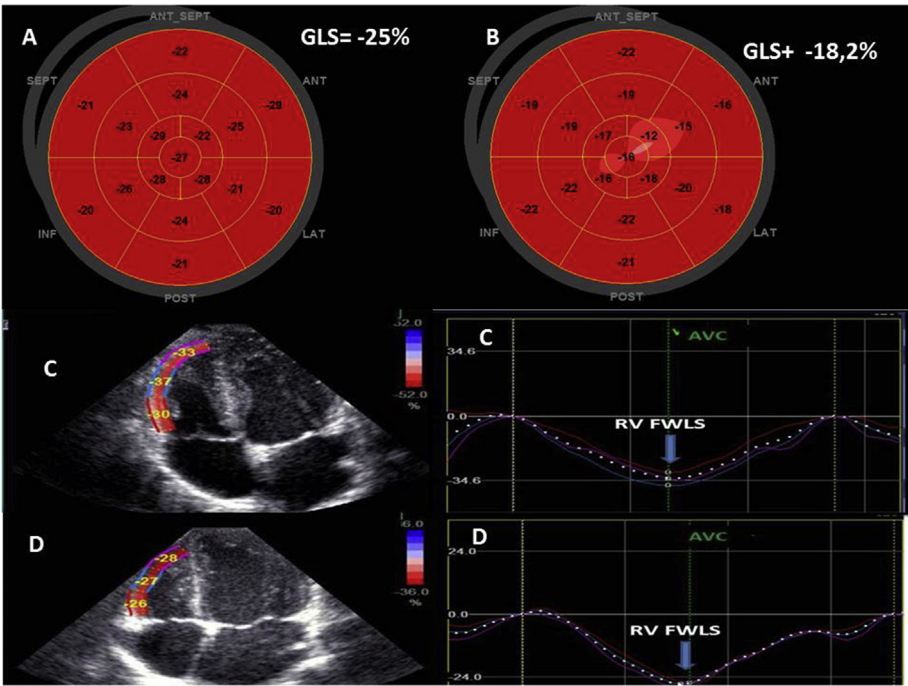
**Table 3**

Conventional and pulse tissue Doppler indexes for left and right ventricle in patients with diabetes and children without diabetes.

| Conventional and pulse tissue Doppler indexes | Children with diabetes (n = 52) | Children without diabetes (n = 52) | P   |
|-----------------------------------------------|---------------------------------|------------------------------------|-----|
| <b>Transmitral flow</b>                       |                                 |                                    |     |
| E (cm/s)                                      | 109.8 ± 16.5                    | 105.2 ± 5.05                       | .12 |
| A (cm/s)                                      | 60.7 ± 12.5                     | 59.7 ± 5.7                         | .22 |
| E/A                                           | 1.92 ± 0.7                      | 1.77 ± 0.2                         | .97 |
| MDT (ms)                                      | 140.3 ± 24.3                    | 134.8 ± 19.6                       | .20 |
| <b>Mitral annular velocities</b>              |                                 |                                    |     |
| Sa (cm/s)                                     | 9.5 ± 1.8                       | 9.6 ± 1.7                          | .82 |
| e' (cm/s)                                     | 20.6 ± 2.6                      | 19.6 ± 2.6                         | .17 |
| a' (cm/s)                                     | 7.3 ± 1.39                      | 8 ± 1.3                            | .00 |
| E/e'                                          | 5.4 ± 1.1                       | 5.5 ± 1.4                          | .60 |
| <b>Tricuspid annular velocities</b>           |                                 |                                    |     |
| Sa (cm/s)                                     | 14 ± 2.5                        | 13.9 ± 0.8                         | .42 |
| Ea (cm/s)                                     | 15.4 ± 4.2                      | 15.7 ± 2.8                         | .11 |
| Aa (cm/s)                                     | 9.6 ± 2.5                       | 10.6 ± 0.9                         | .01 |
| <b>Transticuspid flow</b>                     |                                 |                                    |     |
| E-peak filling rate (cm/s)                    | 35.4 ± 3.9                      | 32.1 ± 1.6                         | .00 |
| E deceleration peak (ms)                      | 132.4 ± 4.5                     | 133.8 ± 4.6                        | .11 |
| A-peak filling rate (cm/s)                    | 24 ± 2.7                        | 22.2 ± 1.9                         | .00 |
| E/A                                           | 1.5 ± 0.1                       | 1.4 ± 0.1                          | .47 |
| LV GLS (%)                                    | −20.01 ± 1.8                    | −22.99 ± 0.9                       | .00 |
| RV FWLS (%)                                   | −29.13 ± 1.8                    | −30.22 ± 1.5                       | .00 |

Values are presented as means ± standard deviations.

E: mitral early peak velocity; A: mitral late peak velocity; MDT: mitral deceleration time; Sa: peak systolic velocity; Ea: early diastolic velocity, Aa: late diastolic velocity; a': late diastolic velocity; e': diastolic velocity; LV GLS: left ventricular global longitudinal strain; RV FWLS: right ventricular free-wall global longitudinal strain.



**Fig. 1.** Bull's-eye plot of LV GLS from a normal control (A) and patient with diabetes (B). Right ventricular free-wall global longitudinal strain (RV FWLS) from a normal control (C) and patient with diabetes (D). LV GLS: left ventricular global longitudinal strain.

2.10. Statistical methods

Normality distribution was tested using the Kolmogorov–Smirnov test for all continuous data. Categorical variables were presented as percentages of occurrence. Continuous variables were presented as means and standard deviations. Comparison of categorical data was performed using chi-square test or Fisher's exact test, where appropriate. The correlations between continuous variables were assessed with the Pearson correlation coefficient (*r*). A *P* value of 0.05 was considered statistically significant. A receiver operating characteristic (ROC) analysis was applied to assess the probability that echographic parameters correctly identified patients with diabetes. The intraobserver and interobserver variabilities for GLS and RVGLS parameters were analyzed in 20 randomly selected subjects. The reproducibility analysis for the GLS and RVGLS measurements was based on a combination of coefficient of variation (CV) and intraclass correlation coefficient (ICC).

2.11. Ethical considerations

The study protocol was approved by the hospital ethics review board. Patients provided informed consent through their legal representatives.

3. Results

3.1. Study population

Between January 2014 and January 2016, 52 children and adolescents with T1DM were enrolled (age:  $11.2 \pm 2.4$  years, 29 male). Their diabetes duration ranged from 2 to 15 years ( $5.9 \pm 3.2$  years). Results of the patients with diabetes were compared with those of 52 healthy children recruited during the same time period. The children with and without diabetes were matched according to age and sex and were comparable with regard to SBP and DBP. The physical and biological characteristics of our study population are shown in Table 1.

**Table 4**  
Receiver operating characteristic (ROC) analysis to identify diabetic group.

|                                     | AUC (mean $\pm$ SD) | <i>P</i> | Cutoff value | Sensitivity (%) | Specificity (%) |
|-------------------------------------|---------------------|----------|--------------|-----------------|-----------------|
| LV GLS (%)                          | 0.91 $\pm$ 0.028    | <.001    | −22.15       | 86.5            | 84.6            |
| RV FWLS (%)                         | 0.68 $\pm$ 0.053    | .002     | −29.9        | 59.6            | 67.3            |
| LV-EDD (mm)                         | 0.63 $\pm$ 0.060    | .001     | 41           | 48.1            | 92.3            |
| <b>Mitral annular velocities</b>    |                     |          |              |                 |                 |
| Aa (cm/s)                           | 0.74 $\pm$ 0.049    | <.001    | 7.5          | 57.7            | 80.8            |
| <b>Tricuspid annular velocities</b> |                     |          |              |                 |                 |
| Aa (cm/s)                           | 0.63 $\pm$ 0.057    | .02      | 9.5          | 36.5            | 92.3            |
| <b>Transticuspid flow</b>           |                     |          |              |                 |                 |
| E-peak filling rate (cm/s)          | 0.76 $\pm$ 0.048    | .001     | 34.5         | 53.8            | 92.3            |
| A-peak filling rate (cm/s)          | 0.69 $\pm$ 0.052    | .001     | 23.5         | 55.8            | 75              |

LV GLS: left ventricular global longitudinal strain; RV FWLS: right ventricular free-wall longitudinal strain; LV-EDD: left ventricular end-diastolic dimension; Aa: late diastolic velocity; AUC: area under the curve.

### 3.2. Echocardiographic measurements

#### 3.2.1. Conventional M-mode and 2D echocardiography

The LV and RV echocardiographic findings in the two groups are summarized in Table 2. There were no significant differences between the two study groups in LVEF, LV end-systolic diameter, and LV mass.

The LV end-diastolic diameter was significantly lower in the diabetes than in the nondiabetes group ( $40.87 \pm 5$  vs.  $42.94 \pm 1.43$ , respectively;  $P = .01$ ). There were also no significant differences in RV end-diastolic diameter, 2D fractional area change, TAPSE, or RV free-wall thickness.

#### 3.2.2. Conventional Doppler and pulse tissue Doppler findings

There were no significant differences between the two study groups in transmitral flow (Table 3). In transtricuspid flow, E-wave and A-wave velocities were significantly higher in the diabetic group ( $P < .005$ ), whereas there was no difference between the two study groups in tricuspid deceleration time, tricuspid E/A ratio, or E/e' ratio.

Pulse tissue Doppler imaging (TDI) at the level of the septal mitral annulus showed significantly lower late diastolic myocardial velocity ( $a'$ ) in the diabetes than in the nondiabetes group ( $7.29 \pm 1.39$  vs.  $8.02 \pm 1.33$ , respectively;  $P < .005$ ).

The parameters derived from pulse tissue Doppler imaging TDI at the level of the tricuspid annulus are listed in Table 3. Late diastolic velocity was significantly lower in the diabetic group ( $P < .005$ ), whereas there were no significant differences between the two study groups in peak systolic and early diastolic velocity.

### 3.3. 2D strain analysis

An example of LV GLS and RV FWLS analysis is shown in Fig. 1.

LV GLS was significantly lower in the diabetes than in the nondiabetes group ( $-20.01 \pm 1.86\%$  vs.  $-22.99 \pm 0.98\%$ , respectively;  $P < .001$ ), as was RV FWLS ( $-29.13 \pm 1.85\%$  vs.  $-30.22 \pm 1.53\%$ , respectively;  $P = .002$ ) (Table 3).

### 3.4. ROC curves to identify the diabetic group

The diagnostic performances of LV GLS, RV FWLS, LV end-diastolic diameter, tricuspid E-wave and A-wave velocities, late diastolic myocardial velocity (Aa) of mitral annular velocities, late diastolic velocity of tricuspid annular velocities, and proposed

cutoff values are presented as receiver operating characteristic (ROC) curves (Table 4). GLS was able to better identify the diabetic group than RV FWLS.

### 3.5. Correlations between HbA1c and clinical, biological, and echocardiographic parameters

No correlation was found between HbA1c and clinical and biological parameters, whereas GLS was significantly correlated with HbA1c ( $r = 0.683$ ,  $P < .001$ ; Fig. 2). No correlation was found between HbA1c and RV FWLS ( $r = 0.137$ ,  $P = .33$ ).

### 3.6. Correlations between diabetes duration and clinical, biological, and echocardiographic parameters

Diabetes duration was correlated with age ( $r = 0.384$ ,  $P < .005$ ) and GLS ( $r = 0.444$ ,  $P < .001$ ; Fig. 3). No correlation was found between diabetes duration and RV FWLS ( $r = 0.05$ ,  $P = .69$ ).

### 3.7. Intraobserver reproducibility

The CVs of LV GLS and RV FWLS were 4.5% and 2.7%, respectively. The ICCs for LV GLS and RV FWLS were 0.98 (0.96–0.99,  $P < .005$ ) and 0.94 (0.86–0.97,  $P < .005$ ), respectively. There was an excellent linear agreement between the two measurements ( $r = 0.95$ ,  $P < .001$  and  $r = 0.84$ ,  $P < .001$ , respectively).

### 3.8. Interobserver reproducibility

The CVs of LV GLS and RV FWLS were 7.4% and 5%, respectively. The ICCs for LV GLS and RV FWLS were 0.90 (0.96–0.99,  $P < .005$ ) and 0.97 (0.92–0.98,  $P < .005$ ), respectively. There was an excellent linear agreement between the two measurements ( $r = 0.94$ ,  $P < .001$  and  $r = 0.90$ ,  $P < .001$ , respectively).

## 4. Discussion

Our study suggests that impairment of longitudinal LV deformation, assessed by 2D strain analysis, and RV FWLS are associated with diabetes in childhood; that the decrease in LV GLS is correlated with diabetes duration and HbA1c level; and that LV GLS was independently associated with HbA1c level.

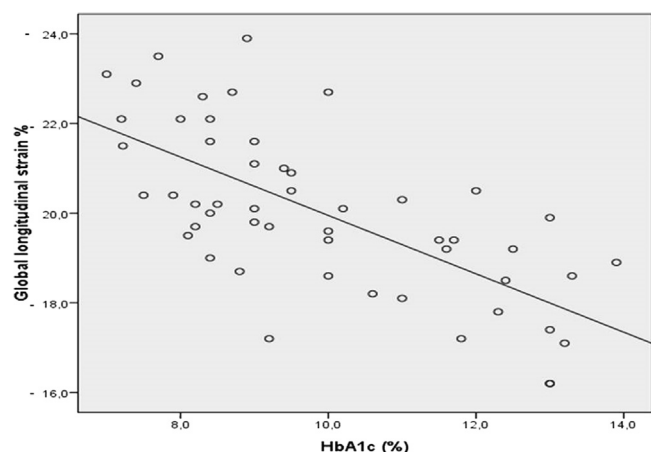


Fig. 2. Relationship between global longitudinal strain (%; GLS) and mean hemoglobin (%; HbA1c).

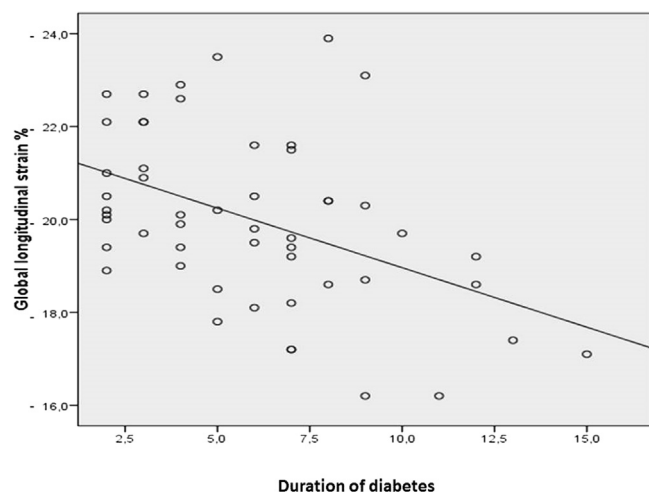


Fig. 3. Relationship between global longitudinal strain (%; GLS) and duration of diabetes.



Diabetes generates asymptomatic myocardial impairment during childhood, via endothelial dysfunction and increased arterial stiffness, both of which are established markers of coronary artery atherosclerosis.<sup>15,16</sup> Previous echocardiographic studies in children with diabetes focused on LV diastolic function and suggested a reduction in early diastolic filling based on transmitral flow analysis.<sup>17–20</sup>

All previous studies conducted in children with diabetes concluded that there was no LV systolic dysfunction assessed using LVEF. However, because systolic function is the result of a complex 3D myocardial deformation, LVEF alone cannot be used to assess ventricular function, and myocardial deformations cannot be reduced to a simple variation in volume.

Recently, more sensitive methods have been applied for the assessment of systolic function and the detection of cardiac abnormalities before symptoms appear. Two-dimensional speckle-tracking echocardiography is a novel method for the assessment of global and regional LV myocardial function. LV longitudinal strain is extremely important for cardiac function, and an impairment of LV GLS was proven to be the first anomaly observed in many conditions.<sup>21</sup> This is because longitudinal strain is primarily controlled by subendocardial longitudinal myofibers that are more susceptible to ischemia.<sup>22</sup>

Previous studies have also shown that diabetics and non-diabetics have comparable cardiac dimensions and LVEF.<sup>18,23,24</sup> Our results with regard to LVEF, LV end-systolic diameter, LV mass, or LV wall thickness are in line with these reports. However, LV end-diastolic diameter was significantly lower in the diabetic group in our study.

In our study, LV GLS measurements were lower in the diabetic group. Our findings are in agreement with those of a pediatric study by Labombarda et al,<sup>3</sup> who evaluated GLS in 100 T1DM children compared with 79 controls. Longitudinal deformation was significantly lower in the T1DM group ( $-17.6 \pm 1.6\%$  vs.  $-20.5 \pm 1.4\%$ ,  $P < .001$ ).

Our study confirms previous reports describing subclinical LV longitudinal systolic dysfunction in patients with diabetes.<sup>25–27</sup>

In addition, recent investigations have found that LV longitudinal myocardial systolic dysfunction, rather than LV diastolic dysfunction, should be considered the first marker of a preclinical form of diabetic cardiomyopathy in patients with type 2 diabetes mellitus (T2DM) with preserved LVEF.<sup>28,29</sup>

In the present study, we found a correlation between HbA1c and decreased GLS. Our results agree with those of several studies that demonstrated a relationship between glycemic control and cardiac function or heart failure in children,<sup>3,30</sup> adults,<sup>31</sup> and animals with diabetes.<sup>32</sup> However, other studies have not found any correlation between HbA1c and GLS.<sup>24,30,33</sup>

In the present study, we found a correlation between diabetes duration and decreased GLS. However, we should emphasize that this relation was weak. This is consistent with other studies using TDI, which showed the lack of correlation of left systolic function<sup>24,30,33</sup> with diabetes duration. According to current data based on the Diabetes Control and Complications Trial, the risk of microvascular complications is related to hyperglycemia and the time length in which vascular system is exposed to hyperglycemic state. The risk increases with longer duration of hyperglycemia and decreases with intensive hyperglycemic treatment.<sup>34,35</sup>

Nevertheless, no evidence of deleterious effects of diabetes duration on myocardial function has been found in children,<sup>3,17,24</sup> adults,<sup>8</sup> or experimental rats with diabetes.<sup>32</sup>

The cardiac effect is not confined to the left ventricle but also involves the right ventricle, the functional impairment of which encompasses both systolic and diastolic abnormalities.<sup>36,37</sup> Our study shows that diabetics and nondiabetics have comparable RV

dimensions and systolic function, which is in agreement with previous studies.<sup>8,9,38,39</sup> However, other studies have found reduced RV systolic function.<sup>6,40</sup>

In the present study, the parameters of RV diastolic function were impaired in patients with diabetes compared with healthy subjects. Our study confirms previous reports describing RV diastolic dysfunction in patients with diabetes.<sup>6,40</sup>

In transtricuspid flow, E-wave and A-wave velocities were significantly higher in the diabetic group ( $P < .005$ ). We found that the tricuspid E-wave velocity was significantly higher in the diabetic group. Our results agree with those of some studies,<sup>8</sup> whereas they differ from those of others studies.<sup>9,37</sup> Our study also found that the tricuspid A-wave velocity was significantly higher in the diabetic group control. Some studies have reported similar results,<sup>8,37</sup> but others have not found this difference.<sup>9</sup>

In our study, there was no difference in the tricuspid E/A ratio between the two groups.

This finding is in concordance with some studies<sup>9,34</sup> but in disagreement with others.<sup>8,37,39</sup>

Two-dimensional strain software created for the LV assessment is used for RV assessment. RV chamber shape is more complex, and a thin RV wall makes it difficult to limit the width of the region of interest to the myocardium. The image quality is the major limitation. Furthermore, software originally designed for analysis of LV strain must be “tricked” to calculate RV strain because the images are inverted compared with LV assessment.

Our study shows that RV FWLS measurements, although in the normal range,<sup>41</sup> were lower in the diabetic group. Our findings are in agreement with those of the studies by Kosmala et al<sup>6</sup> and Tadic et al,<sup>39</sup> who revealed decreased RV global strain in patients with diabetes compared with controls. In the present study, we did not find any significant correlations between the duration of diabetes and HbA1c and RV FWLS nor other systolic or diastolic parameters. Our findings are in agreement with those of Kosmala et al,<sup>6</sup> whereas Tadic et al<sup>39</sup> found correlations between HbA1c level and RV global strain.

#### 4.1. Limitations

Our study was limited by its sample size. HbA1c was only for the year before the study. Therefore, glycemic control of the whole diabetic duration in our patients was unknown.

## 5. Conclusion

Our findings suggest that LV longitudinal function is impaired in children with T1DM and that the decrease in ventricular longitudinal strain is correlated with HbA1c and duration of diabetes. Diabetic cardiomyopathy affects the right ventricle, as demonstrated by RV FWLS strain in children with T1DM. However, a prospective follow-up of these children with diabetes might clarify the mechanism and allow identifying the parameters predictive of the development of diabetes.

## Conflicts of interest

The authors declare that they have no competing interest.

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All authors read and approved the final manuscript.

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