ORIGINAL PAPER

Longitudinal strain bull's eye plot patterns in young women with type 1 diabetes – association of regional cardiac systolic function with thyroid autoimmunity and iron status

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ABSTRACT

INTRODUCTION: Although heart failure in diabetes develops insidiously and affects even young people, especially those with type 1 diabetes mellitus (T1DM), there is still lack of non-invasive methods to facilitate its early diagnosis. The main aims of this pilot study were to evaluate early left ventricular segmental changes in young women with T1DM and to determine if they correlate with Hashimoto's thyroiditis (HT) and iron or ferritin serum levels.

MATERIAL AND METHODS: Thirty women with T1DM (20 of whom had HT) and 30 age-matched controls included in the study underwent medical interview, laboratory tests (serum iron and ferritin levels, glycated haemoglobin, lipid, and thyroid profile) and echocardiography using 2-dimensional speckle tracking imaging.

RESULTS: Women with T1DM had significantly reduced longitudinal strain (LS) in the basal and medial anterior and anterolateral segments ($p = 0.022$ and $p = 0.010$, respectively) and basal inferior and inferolateral segments than controls ($p = 0.035$). Significant correlation was found between global and medial anterior and anterolateral LS and HT duration ($r = -0.366$, $p = 0.046$ and $r = -0.411$, $p = 0.024$, respectively), basal inferolateral LS and iron levels ($r = 0.404$, $p = 0.027$), and medial anteroseptal and inferoseptal LS and ferritin levels ($r = -0.498$, $p = 0.005$).

CONCLUSIONS: The longitudinal strain bull's eye plot pattern appears to be a non-invasive method for identifying early changes in contractile function, which in women with T1DM are characterized by lesions in basal and medial parts of anterior and anterolateral segments and basal inferior and inferolateral segments. Moreover, part of these changes may be correlated with longer duration of HT and lower serum iron levels.

KEY WORD: iron, speckle tracking echocardiography, ferritin, type 1 diabetes, thyroid autoimmunity.

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Introduction

Heart failure (HF) developing in people with diabetes is characterized by worse course and more severe prognosis than in people without diabetes. Moreover, it develops insidiously and appears at a young age, especially in patients with type 1 diabetes mellitus (T1DM). The presence of another autoimmune disease such as Hashimoto's disease in young women with T1DM is likely to be related to a preceding impairment of myocardial contractile function, which is probably due to an autoimmune factor [1]. Despite increasing knowledge of pathogenetic background and new therapeutic options for heart failure, there is still a lack of specific laboratory markers or echocardiographic features that would facilitate its early diagnosis, especially in T1DM patients.

It has recently been reported that iron deficiency, irrespective of anaemia, is an independent predictor of poor prognosis in both chronic [2] and acute HF [3]. However, the exact mechanism of how iron affects myocardial function is not clear. This is probably due to mitochondrial damage and impairment of oxidoreductive processes that determine myocardial contractility [4]. Recently, lower serum iron levels have been shown to be associated with subclinical systemic inflammation induced by immune factors, leading to the development of HF with reduced ejection fraction [5]. Interestingly, iron status was reported to be abnormal in the myocardium of patients with severe diabetic cardiac damage, which correlated with cardiac lipid deposition [6]. In fact, oxidative stress, inflammation, lipotoxicity, and other abnormalities resulting from hyperglycaemia are well known pathogenic factors of diabetic cardiomyopathy [7]. Nevertheless, the role of iron status in the development of HF in diabetic patients has not been sufficiently evaluated. Notably, previous studies have shown that both iron deficiency and iron overload may increase cardiovascular risk [8]. In fact, serum ferritin levels on the one hand indicate iron stores while on the other may signal an inflammatory process. A large cohort study found that increased serum ferritin levels independently increased the risk of HF, but only in women [9]. On the other hand, a recent systematic review and meta-analysis showed that iron deficiency affects thyroid autoimmunity in pregnant and reproductive-aged women [10], suggesting its association with autoimmune processes that have been shown to play an important role in cardiovascular complications in T1DM [11]. All this together indicates that studies evaluating the relationship between iron status, thyroid autoimmunity, and cardiac function in women with T1DM are needed, which could be especially useful in evaluating subclinical changes.

Given the high cardiovascular risk in women with T1DM, which is still not fully explained [12], we performed a thorough echocardiographic evaluation in this group of patients using the most sensitive echocardiographic techniques, such as speckle tracking imaging. We evaluated global and regional left ventricular (LV) systolic function presented as a single graph called a bull's eye plot, which is now attracting attention by providing valuable insight into the characteristics of various cardiomyopathies [13]. What is important is that to date the literature has not presented comprehensive data on the typical bull's eye plot in patients with diabetes. Therefore, the present pilot study had 2 main objectives: the first was to evaluate LV segmental changes in young, asymptomatic women with T1DM to determine the bull's eye plot patterns characteristic of this group, and the second was to investigate whether any early segmental changes in myocardial contractility correlate with iron, ferritin, anti-thyroid peroxidase antibodies (aTPO), anti-thyroglobulin antibodies (aTg) titre, or Hashimoto's thyroiditis (HT) duration in the study population.

Material and methods

Thirty women with T1DM aged 18–37 years and 30 age- and sex-matched healthy controls were recruited for this study. The participants were enrolled from the outpatient diabetes clinic of the Central Clinical Hospital of the Ministry of Internal Affairs and Administration in Warsaw. The control group comprised hospital employees and their relatives. Informed consent was obtained from all patients included in the study. The study was designed in accordance with the Declaration of Helsinki and was approved by the Human and Animal Research Supervision and Ethics Commission of the Central Clinical Hospital of the Ministry of Internal Affairs and Administration (9 May 2018, IRB number: 22/2018). All study participants completed a questionnaire including demographic data, comorbidities, medications taken, duration of diabetes, and presence of diabetes complications. Data were verified from past medical records. We also conducted a physical examination and calculated body mass index (BMI, kg/m^2). Laboratory tests, systolic and diastolic blood pressure measurements, 12-lead standard resting electrocardiog-

raphy (ECG) in a supine position during rest, and conventional, tissue Doppler, and speckle tracking echocardiography were performed on the same day in all participating patients.

The inclusion criteria for the study group were as follows: female sex, diagnosis of T1DM, HbA_{1c} < 10%, age 20–35 years, and euthyroid state confirmed by laboratory tests. The control group consisted of age-matched women without any severe co-morbid states and not taking medication on a regular basis.

Exclusion criteria for both groups included a medical history for current or past liver, kidney, bowel disease, anaemia, heart failure, hypertension, history of any other cardiovascular disease (stroke, myocardial infarction, thrombosis, embolism), smoking behaviour, or taking any medications that affect the cardiovascular system. Exclusion criteria for all patients were also abnormal systolic and diastolic cardiac function parameters assessed by conventional transthoracic echocardiography or abnormal blood pressure or heart rate assessed by 12-lead ECG. Patients in the control group additionally had normal thyroid function parameters without any laboratory or ultrasound features of autoimmunity.

In all patients, serum levels of glycated haemoglobin (HbA_{1c}), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) level, low-density lipoprotein (LDL) level, thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4), aTPO, and aTG titres were assessed in the morning. The range of normal values for iron was 33–193 (µg/dl), and for ferritin it was 15–150 (ng/ml). The diagnosis of HT among the T1DM group was based on the presence of circulating aTPO and/or aTG antibodies and a typical ultrasound. Thyroid imaging was performed with a 5–12 MHz linear transducer using a high-resolution echograph (Aplio a, Canon Medical System) according to the guidelines of the Polish Ultrasound Society [14].

One experienced echocardiographer, blinded to the study group, performed a complete echocardiographic examination in each subject using the EPIQ system (version 7C/CVx, Philips Medical Systems, Best, Netherlands). All measurements were performed according to the recommendations of the European Association of Cardiovascular Imaging and the American Society of Echocardiography [15]. Two-dimensional (2-D) speckle tracking analyses were performed on standard images from apical 4-, 3-, and 2-chamber projections to quantify LV longitudinal strain (LS). Automatic global longitudinal strain (GLS) evaluation software AutoStrain was used to provide rapid, reproducible 2-D quantification of LV strain, which eliminated manual errors. Left ventricular strain values were automatically assessed in 18 segments, and the mean value of each strain was calculated as GLS. We presented the obtained strain values divided into the anterior and anterolateral, anteroseptal and inferoseptal, and inferior and inferolateral segments with basal, mid, and apical regions.

Statistica 13 software was used for statistical analysis. Data were presented as mean and standard deviation (SD) using descriptive statistical methods. The distribution of the data was assessed visually and using the Shapiro-Wilk test. Continuous variables with normal distribution were analysed by Student's t-test, while continuous variables with non-normal distribution were analysed by Mann-Whitney *U* test. The degree of correlation between echocardiographic measurements and selected parameters was assessed by Spearman's test. Statistical significance was set at p-value ≤ 0.05.

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Results

This study included 30 women with T1DM with a mean age of 26.9 years and 30 age-matched healthy controls. The study and control groups were similar in age, BMI, lipid profile, TSH, fT3, fT4, serum iron, and ferritin levels. In Table 1 we presented comparative characteristics of study and control group.

In women with T1DM, the mean ±SD disease duration was 14.4 ±6.8 years and the daily dose of insulin per day was 35.5 units with an HbA_{1c} of 7.3 ±1.1 at the time of examination. Out of the total number (N = 30) of women with T1DM, 20 (66.7%) were diagnosed with HT, while the other 10 (33.3%) had no additional disease. Medical history of diabetic retinopathy was present in 2 women (in one with T1DM and HT and in one with exclusively T1DM) and neuropathy was present in 2 women with T1DM (in one with T1DM and HT and in one with exclusively T1DM). None of the participants had diabetic nephropathy. The type 1 diabetes mellitus HT+ and T1DM HT– group were similar in age, BMI, HbA_{1c}, diabetes duration, thyroid hormones (TSH, fT3, fT4), and serum iron and ferri-

Table 1. Comparative characteristics of groups of patients with type 1 diabetes (T1DM) and healthy controls

Parameters	T1DM (*n* = 30)	Controls (*n* = 30)	*p*
Age (years)	26.9 ±4.7	26.7 ±3.7	0.97
BMI [kg/m^2]	22.2 ±3.1	22.5 ±3.0	0.72
SBP [mm Hg]	115.4 ±6.4	114.3 ±6.0	0.48
DBP [mm Hg]	71.6 ±7.5	71.5 ±2.8	0.98
HR	72.4 ±10.8	72.5 ±12.4	0.98
HbA_{1c} (%)	7.3 ±0.6	5.2 ±0.3	< 0.001
Total cholesterol [mg/dl]	175.6 ±25.3	172.8 ±29.0	0.62
LDL [mg/dl]	86.9 ±25.4	83.9 ±28.4	0.76
HDL[mg/dl]	74.4 ±17.4	72.6 ±21.1	0.66
Triglyceride [mg/dl]	71.1 ±23.9	82.7 ±30.4	0.13
TSH [μIU/ml]	2.3 ±2.4	2.4 ±1.1	0.09
fT4 [ng/dl]	1.3 ±0.2	1.3 ±0.4	0.99
fT3 [pg/ml]	3.1 ±0.4	3.2 ±0.7	0.49
aTPO [IU/ml]	111.4 ±217.9	10.1 ±7.3	0.01
aTg [IU/ml]	176.7 ±182.2	17.2 ±15.0	< 0.001
Iron [mcg/dl]	98.9 ±45.5	111.8 ±62.0	0.36
Ferritin [ng/ml	48.9 ±33.9	53.7 ±45.2	0.64

aTg – anti-thyroglobulin antibodies, aTPO – anti-thyroid peroxidase antibodies, BMI – body mass index, DBP – diastolic blood pressure, fT3 – triiodothyronine, fT4 – free thyroxine, HDL – high-density lipoproteins, HR – hazard ratios, LDL – low-density lipoproteins, SBP – systolic blood pressure, TSH – thyroid-stimulating hormone

Table 2. Comparative characteristics of women with type 1 diabetes and Hashimoto's thyroiditis (T1DM HT+) and T1DM without additional diseases (T1DM HT–)

Parameters	T1DM HT+ (*n* = 20)	T1DM HT– (*n* = 10)	*p*
Age (years)	26.8 ± 4.6	27.3 ± 5.2	0.89
Diabetes duration (years)	15.5 ± 7.0	12.3 ± 6.2	0.24
HT duration (years)	7.75 ± 6.7	0 ± 0	0.001
BMI [kg/m^2]	22.7 ± 3.3	21.2 ± 2.7	0.32
SBP [mm Hg]	116.4 ± 6.5	113.5 ± 6.3	0.25
DBP [mm Hg]	71.1 ± 7.1	72.5 ± 8.5	0.64
HR	71.6 ± 10.8	74.1 ± 11.1	0.56
HbA_{1c} (%)	7.4 ± 0.6	6.9 ± 0.6	0.08
Total cholesterol [mg/dl]	183.7 ± 23.7	159.5 ± 21.1	0.02
LDL [mg/dl]	93.7 ± 26.8	73.4 ± 15.9	0.06
HDL[mg/dl]	75.5 ± 19.6	72.4 ± 12.5	0.86
Triglyceride [mg/dl]	72.7 ± 26.7	67.7 ± 17.7	0.72
TSH [μIU/ml]	2.5 ± 2.8	2.0 ± 0.9	0.38
ft4 [ng/dl]	1.4 ± 0.2	1.2 ± 0.1	0.09
ft3 [pg/ml]	3.0 ± 0.3	3.3 ± 0.5	0.17
aTPO [IU/ml]	162.6 ± 253.4	9.1 ± 8.3	0.002
aTG [IU/ml]	230.7 ± 181.2	68.8 ± 135.0	0.005
Iron [mcg/dl]	96.8 ± 46.1	103.1 ± 46.4	0.69
Ferritin [ng/ml]	52.5 ± 39.5	41.8 ± 18.00	0.64

aTg – anti-thyroglobulin antibodies, aTPO – anti-thyroid peroxidase antibodies, BMI – body mass index, DBP – diastolic blood pressure, fT3 – triiodothyronine, fT4 – free thyroxine, HDL – high-density lipoproteins, HR – hazard ratios, HT – Hashimoto's thyroiditis, LDL – low-density lipoproteins, SBP – systolic blood pressure, T1DM – type 1 diabetes mellitus, TSH – thyroid-stimulating hormone

tin levels. The type 1 diabetes mellitus HT+ had slightly higher LDL levels and significantly higher TC levels than T1DM HT– group. The comparative characteristics of T1DM HT+ and T1DM HT– women is presented in Table 2.

Using conventional echocardiography and tissue Doppler imaging there were no significant differences between systolic and diastolic cardiac function parameters, except for the isovolumetric relaxation time (IVRT) between the T1DM and the control group. Longer IVRT in the T1DM group compared to the control group (92.6 ±16.9 vs. 79.9 ±8.9, $p = 0.001$) may suggest a trend toward diastolic dysfunction (Table 3).

Using speckle tracking imaging in women with T1DM, we found that although GLS was not significantly different from the control group, LS in the basal and medial anterior and anterolateral and basal inferior and inferolateral segments was significantly lower compared with healthy subjects (Table 4).

Figure 1 shows the patients with the best GLS among women with T1DM, to demonstrate that, despite normal GLS, the first affected segments are likely to be those located in the basal regions of the anterior, anterolateral, inferior, and inferolateral walls.

To check if the concomitant of HT with T1DM make worse segmental strains we also performed comparative analysis between T1DM HT+ and T1DM HT– group, and we showed that in T1DM HT+ patients, GLS and medial parts of the anterior and anterolateral segments are significantly lower than in the T1DM HT– group (Table 5).

The association of GLS and segmental LS with aTG, aTPO, Hashimoto's thyroiditis duration, serum iron, and serum ferritin levels was checked using correlation analysis in all T1DM women and the control group. There were no significant correlations between aTPO or aTG titres and GLS or regional LS in the study groups. However, when checking the correlation with HT duration, there

Table 3. Baseline echocardiographic parameters obtained by conventional echocardiography and tissue Doppler imaging measurements divided into study and control groups

Parameters	T1DM ($n = 30$)	Controls ($n = 30$)	p
BSA	1.67 ±0.11	1.69 ±0.13	0.33
LAVI	22.95 ±5.6	24.9 ±5.9	0.41
LVMI	42.4 ±12.4	44.6 ±10.2	0.05
LVEDd	11.4 ±4.7	9.0 ±2.4	0.06
IVSDd	8.7 ±1.7	9.0 ±1.3	0.49
E/A	1.6 ±0.4	1.7 ±0.6	0.97
DT	224.1 ±48.2	220.6 ±67.2	0.62
Emed'	12.2 ±2.1	13.2 ±3.2	0.14
E/Emed'	7.58 ±1.21	7.56 ±3.29	0.11
E/Elat'	5.5 ±0.9	5.2 ±1.4	0.17
IVRT	92.6 ±16.9	79.9 ±8.9	0.001
EF	63.3 ±4.2	64.5 ±2.0	0.15

BSA – body surface area, DT – dual-task, EF – ejection fraction, IVRT – isovolumetric relaxation time, IVSDd – interventricular septum enddiastolic diameter, LAVI – left atrial volume indexed, LVEDd – left ventricular enddiastolic dimension diameter, LVMI – left ventricular mass indexed, T1DM – type 1 diabetes mellitus

Table 4. Characteristics of longitudinal strain in type 1 diabetes mellitus and healthy controls

Parameters		T1DM ($n = 30$)	Controls ($n = 30$)	p
GLS		–18.0 ±1.7	–19.0 ±2.5	0.079
Anterior and anterior lateral segments	Basal	–16.8 ±2.8	–20.8 ±6.2	0.022
	Mid	–17.0 ±3.1	–19.4 ±3.7	0.010
	Apical	–16.8 ±3.9	–18.2 ±5.6	0.300
Anterior septal and inferior septal segments	Basal	–16.7 ±2.1	–16.1 ±2.8	0.395
	Mid	–19.1 ±2.1	–19.6 ±2.8	0.652
	Apical	–19.2 ±3.4	–19.2 ±4.6	0.790
Inferior and inferior lateral segments	Basal	–17.6 ±2.8	–19.9 ±4.4	0.035
	Mid	–18.7 ±2.2	–19.1 ±3.2	0.113
	Apical	–19.1 ±2.9	–19.8 ±5.4	0.311

GLS – global longitudinal strain, T1DM – type 1 diabetes mellitus

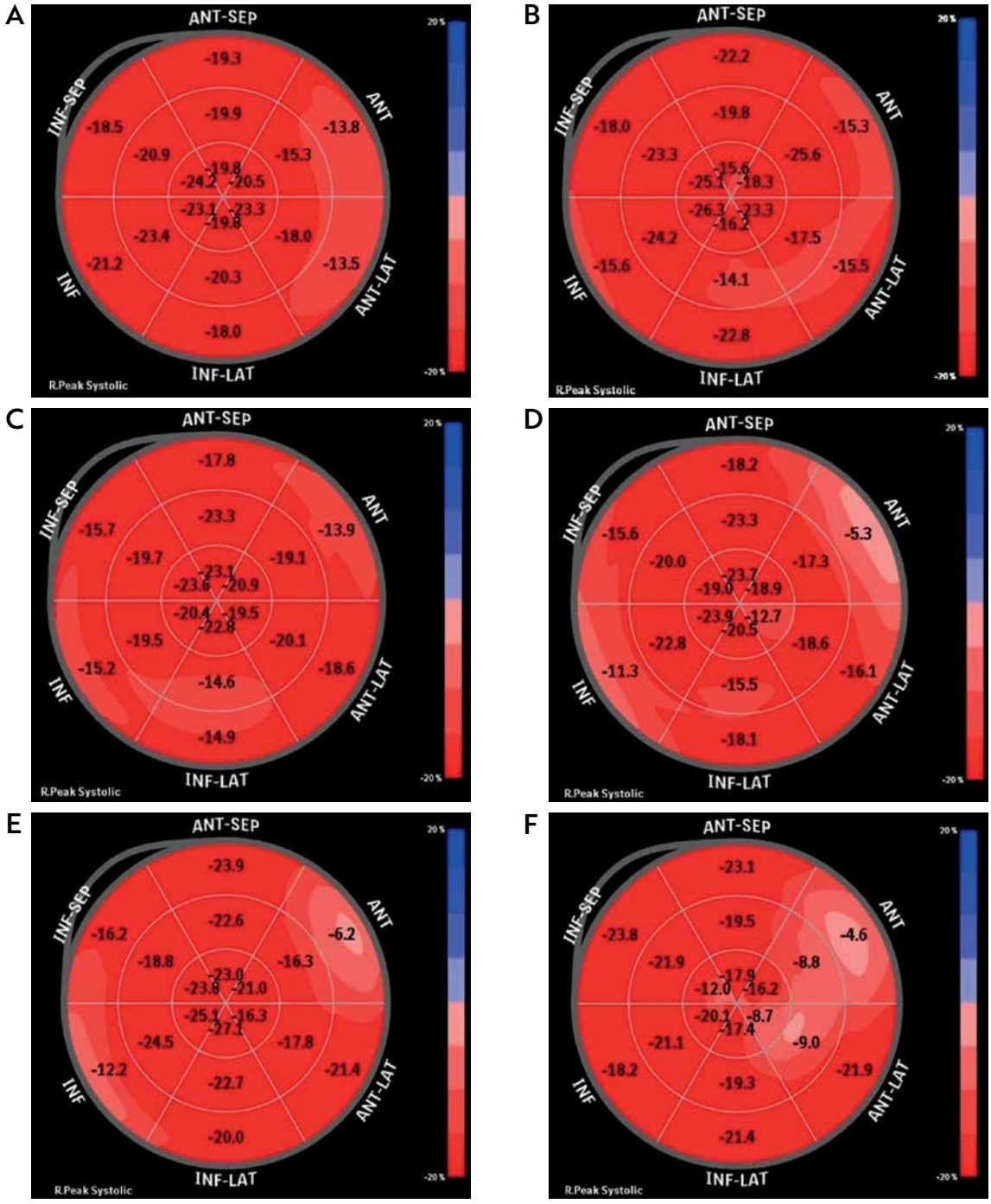

Fig. 1. The bull's eye plot of global longitudinal strain (GLS) with segmentation on the left and the matching image from 2- (anterior and inferior wall – **A**, **C**) or 4- (anterolateral and inferoseptal wall – **B**) chamber view on the right in the following patients. **A** – a 21-year-old woman with an 11-year history of type 1 diabetes mellitus (T1DM) and HbA_{1c} at the examination 6.3% without diabetic microvascular complication, without Hashimoto's thyroiditis, iron level 59, ferritin level 42, GLS – 20.0%, left ventricular end diastolic dimension diameter (LVEDd) 44 mm, intraventricular septum diastolic diameter (IVSDd) 9 mm, left ventricular mass indexed (LVMI) 77 g/m^2; **B** – a 27-year-old woman with a 14 -year history of T1DM and HbA_{1c} at the examination 7.4% without diabetic microvascular complication, without Hashimoto's thyroiditis, iron level 72, ferritin level 23, GLS – 20.2%, LVEDd 45 mm, IVSDd 7 mm, LVMI 62.3 g/m^2; **C** – a 34-year-old woman with a 20-year history of T1DM and HbA_{1c} at the examination 7.3% with the history of diabetic retinopathy, without Hashimoto's thyroiditis, iron level 179, ferritin level 22, GLS – 20.1%, LVEDd 38 mm, IVSDd 9 mm, LVMI 61 g/m^2, **D** – a 20-year-old woman with a 15-year history of T1DM and HbA_{1c} at the examination 7.9% without diabetic microvascular complication, with a 10 year history of Hashimoto's thyroiditis, iron level 83, ferritin level 26, GLS – 17.6%, LVEDd 45 mm, IVSDd 8 mm, LVMI 67.9 g/m^2; **E** – a 24-year-old woman with a 9-year history of T1DM and HbA_{1c} at the examination 7.4% without diabetic microvascular complication, with a 4-year history of Hashimoto's thyroiditis, iron level 157, ferritin level 75, GLS – 19.6%, LVEDd 45 mm, IVSDd 11 mm, LVMI 83.6 g/m^2; **F** – a 29-year-old woman with a 15-year history of T1DM and HbA_{1c} at the examination 7.3% without diabetic microvascular complication, with a 15-year history of Hashimoto's thyroiditis, iron level 66, ferritin level 11, GLS – 17.0%, LVEDd 47 mm, IVSDd 8 mm, LVMI 81.5 g/m^2

Table 5. Characteristics of longitudinal strains in type 1 diabetes mellitus with Hashimoto's thyroiditis and without

Parameters		T1DM HT+ (*n* = 20)	T1DM HT– (*n* = 10)	*p*
GLS		–17.4 ±1.5	–19.0 ±1.3	0.010
Anterior and anterior lateral segments	Basal Mid Apical	–16.3 ±2.8 –16.1 ±3.2 –16.0 ±4.2	–17.7 ±2.7 –18.8 ±1.8 –18.4 ±3.0	0.218 0.027 0.090
Anterior septal and inferior septal segments	Basal Mid Apical	–16.2 ±2.3 –18.8 ±2.1 –18.3 ±3.7	–17.5 ±1.8 –19.7 ±2.2 –20.9 ±2.2	0.139 0.187 0.090
Inferior and inferior lateral segments	Basal Mid Apical	–17.3 ±2.7 –18.6 ±2.2 –18.5 ±3.2	–18.3 ±3.0 –19.1 ±2.2 –20.2 ±1.7	0.416 0.612 0.118

GLS – global longitudinal strain, HT – Hashimoto's thyroiditis, T1DM – type 1 diabetes mellitus

was a significant association with GLS (r = –0.366, *p* = 0.046) and with LS in the medial anterior and anterolateral segments (r = –0.411, *p* = 0.024) in diabetic women (Fig. 2 A, B). In women with T1DM, there was also a significant positive correlation between serum iron levels and LS in the basal inferolateral segments (r = 0.404, *p* = 0.027) and a significant negative correlation between ferritin levels and the medial anteroseptal and inferoseptal segments (r = –0.498, *p* = 0.005), which was not observed in the control group (Fig. 2 C, D).

Correlation analysis between serum iron and ferritin levels and aTPO and aTG and HT duration showed no significant associations.

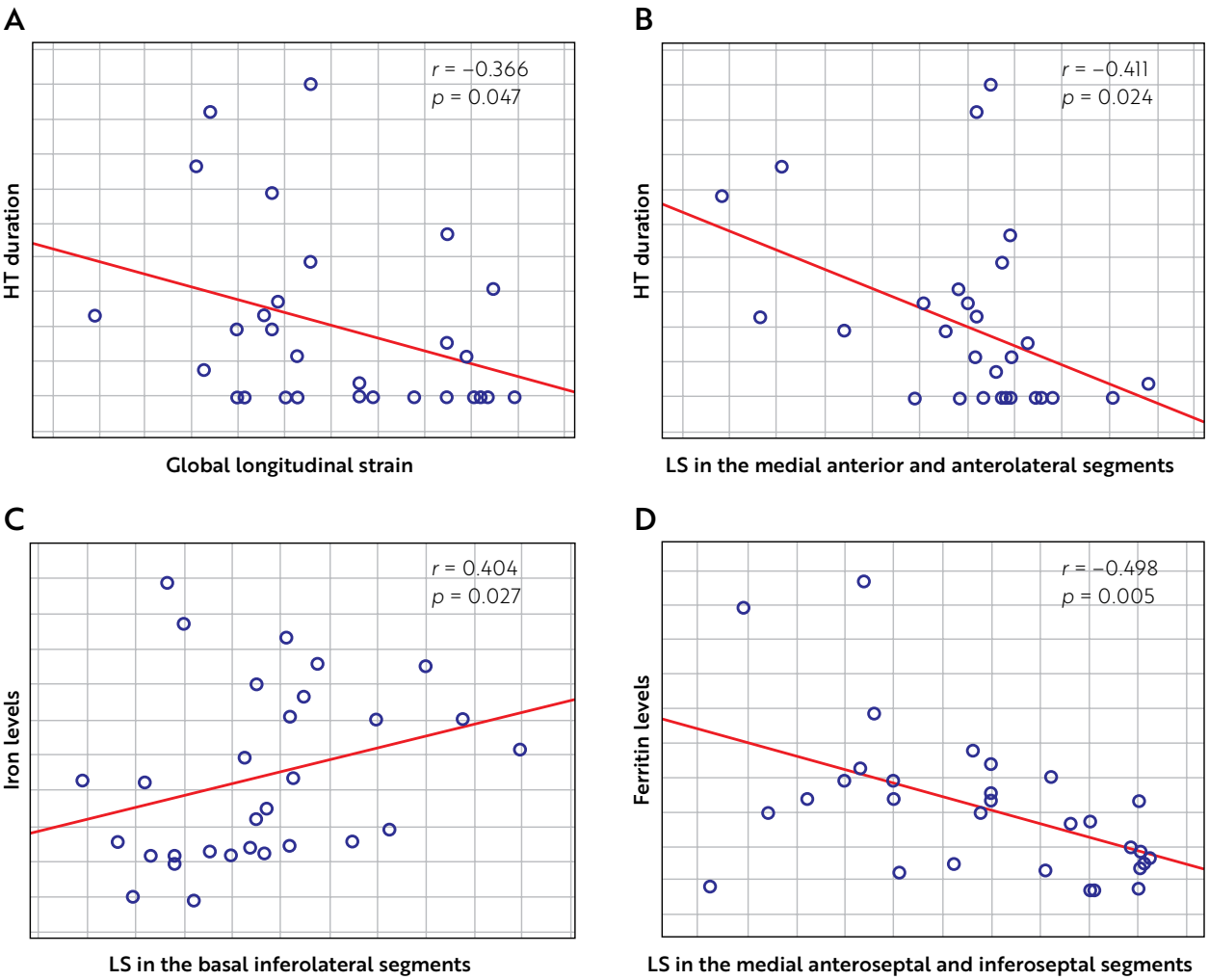

Fig. 2. Analysis of selected longitudinal strain correlation with Hashimoto's thyroiditis duration (**A**, **B**), iron levels (**C**) and ferritin levels (**D**) in T1DM women (*N* = 30)

HT – Hashimoto's thyroiditis, LS – longitudinal strain

Discussion

Our results showed that although GLS in women with T1DM was not significantly different from healthy controls, contractility in the basal and medial anterior and anterolateral and basal inferior and inferolateral regions was significantly lower compared with controls. These findings suggest that the longitudinal bull's eye plot pattern in young women with T1DM is characterized by a slightly reduced LS at the basal parts of the anterior, anterolateral, inferior, and inferolateral segments, which are likely to be the first affected in the course of cardiac dysfunction in this group of patients.

The longitudinal bull's eye plot pattern found in our patients seem to be very similar to that found in athletes or hypertensive individuals without LV hypertrophy [16, 17], displaying a slightly reduced LS at the basal segments. Given that the basal segments have greater regional LV wall stress than the LV apical segments, its contractility may be the first to be damaged by cardiotoxicity due to hyperglycaemia. By analogy, in stress cardiomyopathy (Takotsubo), more often observed in women, also basal segments are affected the most, which is associated with neurohormonal factors [18]. In turn, in Fabry disease, associated with myocardial glycolipid storage, reduced LS was present in the basal posterior and lateral segments of the LV, probably resulting from fibrosis processes most advanced in these regions [19]. Similar mechanisms to those mentioned above, such as oxidative stress, excessive sympathetic nervous system activity associated with diabetic neuropathy, and hyperglycaemia-induced fibrosis play important roles in the development of HF in diabetic patients [20], which may explain the presence of the first lesions precisely in the basal parts of myocardium.

Interestingly, our findings showed that HT coexistence in women with T1DM was associated with significantly lower global and regional (the medial anterior and anterolateral segments) LV contractility compared with women with T1DM alone. These results are consistent with previous observations showing that GLS is reduced in euthyroid HT patients compared with healthy controls [21]. Although our study did not show that aTPO and aTG antibody titres correlate with the global or regional myocardial contractility studied, we found a significant correlation between HT duration and GLS and LS in the medial anterior and anterolateral segments. Such results suggest that only a longer duration of thyroid autoimmunity may be related to regional contractile dysfunction of the myocardium, whereas short-term exposure to antithyroid antibodies alone does not have such deleterious effects on cardiac function. Presumably, this is related to systemic inflammation and oxidative stress resulting from thyroid autoimmunity, which also affects the cardiovascular system [22] and a higher tendency of atherosclerosis observed in women with 2 autoimmune diseases [23]. In addition, it may depend on epigenetic factors and immune imbalance, as shown by the recently proven association between sirtuin 1 and IL-27 levels and poorer cardiac function parameters in young women with T1DM and HT [24].

In our study, we showed that lower serum iron levels correlate with lower LS in the basal regions of the inferolateral segments. Possible reasons for this may be low-grade chronic inflammation occurring in autoimmune diseases, which may also affect iron utilization in the body [25], as well as digestive malabsorption resulting from diabetic enteropathy. The adverse effects on the myocardium are probably due to reduced iron content, which leads to reduced activity of enzymes that protect against oxidative stress [26]. In turn, excessive formation of oxygen free radicals is associated with activation of proinflammatory cytokines and fibrotic processes that underlie diabetic cardiomyopathy [27]. Conversely, not only iron deficiency but also iron overload in the myocardium can exert toxic effects and lead to cardiomyopathy, which has been confirmed in patients with thalassemia [28] and in patients with hereditary haemochromatosis [29]. Our results showed a significant correlation between higher ferritin concentration and lower LS in the medial anteroseptal and inferoseptal segments. These results are consistent with previous ones showing that iron deposition is very common in the septal LV wall, leading to lower strains in these regions [28]. In agreement with our results are recent reports suggesting that non-enzymatic glycation of transferrin, a major iron transport protein, leads to excessive iron accumulation in the body and is closely associated with the development of diabetic complications [30]. It is not clear whether disturbances in iron status contribute to myocardial contractile dysfunction or whether they are merely a result of hyperglycaemia and immune imbalance in patients with T1DM. Our study did not provide evidence of an association between thyroid autoimmunity and iron disturbances in T1DM women. Nevertheless, given the relatively

small group of patients, this relationship needs to be clarified in further studies.

The limitation of our study was the lack of evaluation all parameters of iron metabolism, which would give a more complete insight into the association with cardiac dysfunction and the relatively small number of patients. Therefore, the relationship between thyroid autoimmunity, iron status, and cardiac dysfunction requires clarification in studies conducted on a larger group of patients.

Conclusions

Our pilot study suggests that the LS bull's eye plot pattern is a non-invasive method for identifying early changes in systolic function in diabetic patients, which has potential use in early diagnosis. In young women with T1DM, they have been shown to occur in the basal anterior, anterolateral, inferior and inferolateral, and medial anterior and anterolateral segments. Furthermore, these changes may be correlated with longer HT duration and lower serum iron levels, which requires further investigation.

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Conflict of interest

The authors declare no conflict of interest.

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