Aim. Early left ventricle (LV) abnormalities are hardly detectable by means of standard echocardiography in patients with hypertension (HTN) and glucose metabolism disorders. The objective of this study was to assess changes in LV function with speckle tracking echocardiography in hypertensive males with different types of glucose metabolism abnormalities.

Methods and results. We recruited 158 hypertensive males with different glycemic status. The multidirectional LV strain was assessed by two-dimensional speckle tracking echocardiography. The patients with HTN and type 2 diabetes mellitus demonstrated significant reduction of LV global longitudinal strain and early diastolic strain rate despite preserved LV ejection fraction.

Conclusion. Speckle tracking echocardiography can identify subclinical myocardial alterations in hypertensive males with glucose metabolism abnormalities.

Key words: Hypertension, Type 2 Diabetes Mellitus, Glucose Metabolism Disorders, Echocardiography.

Type 2 diabetes mellitus (DM) and arterial hypertension (HTN) are major medical and public health problems worldwide. The total number of people with DM will rise from 171 million in 2000 to 552 million by 2030 [1]. The number of adults with HTN is predicted to increase by 60% to a total of 1.56 billion people by 2025 [2]. HTN is present in approximately 60% of patients with type 2 DM [3]. 80% of diabetic patients die from cardiovascular complications. Both diseases affect the same major target organs. Myocardial involvement is characterized by microvascular disease, altered metabolism and increased fibrosis that lead to gradual decline in left ventricular (LV) function. Early alterations of myocardium should be diagnosed early and treated aggressively to prevent microvascular and macrovascular morbidity and mortality.

Insulin resistance (IR) is a key pathogenic mechanism of type 2 DM and exists for many years even in normoglycemic patients. Impaired fasting glucose (IFG), or ‘pre-diabetes’, reflect the natural history of progression from normoglycaemia to type 2 DM. The hypertensive patients with IR and pre-diabetes may have long-standing subclinical myocardial dysfunction before onset of DM [4]. Speckle-tracking echocardiography is a modern ultrasound technique which allows to investigate early myocardial changes in patients even without LV hypertrophy and diastolic dysfunction. Compared to standard echocardiography parameters, myocardial strain and strain rate (SR) analyses are more sensitive indices of LV function. At present, there is a lack of studies concerning the development of structural and functional myocardial abnormalities in patients with different glucose abnormalities like IR, pre-diabetes and type 2 DM.

The aim of our study was to assess changes in LV function with speckle tracking echocardiography in hypertensive patients with different types of glucose metabolism abnormalities.

Materials and methods

Study cohort. We enrolled 158 untreated hypertensive males (mean age 51±8 years). The inclusion criteria were: arterial HTN, sinus rhythm, insulin resistance, IFG or newly diagnosed
increased LV mass index (LVMI) was determined. LV mass was calculated according to Devereux’s formula. The LV ejection fraction (EF), end-systolic diameters, and left atrial (LA) dimension were determined from M-mode echocardiography. LV wall thicknesses, end-diastolic and end-systolic diameters, and two-chamber (2C) views with subjects in the left lateral decubitus position. The LV wall thicknesses, end-diastolic and end-systolic diameters, and LA dimension were determined from M-mode echocardiography. LV ejection fraction was calculated using the biplane modified Simpson’s method. LV mass was calculated according to Devereux’s formula. The increased LV mass index (LVMI) was defined as 125 g/m². Transmitral peaks of early diastolic mitral inflow velocity (E), and late diastolic mitral inflow velocity (A) were recorded at the tips of the mitral valve leaflets. Early (’e’) diastolic myocardial velocity was measured in the apical 4-chamber view, placing the sample volume at the junction of LV interventricular septum with mitral annulus. The E/e’ ratio was calculated.

Speckle tracking echocardiography. 2D harmonic image cine-loops recordings were acquired and stored with good quality ECG signal and a frame rate between 60–70 fps. Strain analysis was performed offline by use of a software package XStrain (Esaote, Florence, Italy). Segmental evaluation of strain was conducted from clips of basal, apical parasternal short axis and apical 4C, 3C and 2C views. The initial frame was chosen, when endocardial border was better visible, and border tracking of the LV was manually traced by operator in the recorded clips. Endocardial border was traced as a sequence of 13 equidistant points and frame-by-frame displacement of these points was automatically evaluated. Global longitudinal strain (LS) was calculated as the mean strain of all 18 segments, derived from three apical views. Peak global longitudinal strain rate (LSR) was measured at peak of systole, early and late diastole. The global strain rate values were averaged from the 3 apical views and used for final analysis. Two short-axis planes were acquired at basal and apical levels to evaluate LV rotation, twist, circumferential and radial strain. The average circumferential and radial strain and strain rate were calculated for the six basal LV segments and for the six apical LV segments. Twist was calculated as the net difference of LV mean rotation between basal and apical short-axis plane.

Laboratory tests. Venous blood samples were taken in the morning between 7 and 9 into plasma vacuum tubes containing 7.2 mg di-potassium EDTA. Creatinine, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, glucose and glycated hemoglobin (HbA1c) were measured by standard kits and using an auto analyzer Prestige 24i (Tokyo-Boehi, Japan). Insulin was measured using ELISA kits (DRG Diagnostics, Germany). Insulin resistance was assessed from fasting insulin and glucose levels using homeostasis model assessment (HOMA-IR), thus: HOMA-IR=fasting glucose (mmol/L) x fasting insulin (μU/mL)/22.5. The value above 2.77 was considered to be pathological. IFG was defined as level from 6.1 to 6.9 mmol/l. Undiagnosed diabetes was defined by the 2014 ADA criteria (fasting glucose >7.0 mmol/l and/or HbA1c >6.5%). Renal function was expressed as estimated glomerular filtration rate (eGFR, ml/min/1.73 m²) calculated from the Modification in Diet and renal Disease equation.

Statistical tests. Statistical analysis was performed using standard commercial software Statistica 7.0 (Statsoft, Tulsa, USA). Continuous variables are presented as mean±standard deviation. Categorical variables are presented as counts and proportions. All normally distributed parameters were compared using a one-way ANOVA, followed, in case of significance, by a two-side Neuman-Keuls test for multiple comparisons. Categorical variables were compared using Fisher’s exact test or χ² test whenever appropriate. Correlation analysis was performed using Spearman rank correlation. A p-value of <0.05 was considered significant.

Results and discussion
We divided the patients into 4 groups according to glycemic status. The first group included the normoglycemic hypertensive patients without IR (n=43). The second group included the normoglycemic hypertensive males with IR (n=70). The third group contained patients with HTN and IFG (n=25). The fourth group consisted of patients with HTN and newly diagnosed type 2 DM (n=20). The clinical characteristics of the patients are summarized in Table 1. The age, smoking status, of body mass index, of waist circumference compared with other groups. The patients of the 4th group had higher LV ejection fraction with IFG had raised triglycerides.

Table 2 shows comparisons of echocardiographic parameters. The patients with HTN and IR had higher LV ejection fraction compared with hypertensives with DM. The participants of the 4th group demonstrated reduced e’ velocity and increased E/e’ ratio.
Global LS was significantly reduced in diabetic patients compared with other patients (Table 3). Circumferential and radial strain at the basal and the apical LV levels didn’t differ between groups. Diabetic patients had also significantly lower global longitudinal strain rate at early diastole (LSR E) compared with insulin resistant hypertensives (Figure 1, A, B, C, D). Global LS correlated positively with LV ejection fraction (r=0.36; p<0.00002), E/A ratio (r=0.2; p=0.01), e’ septum (r=0.34; p=0.00001) and negatively with 24-hour SBP (r=-0.19; p=0.02), 24-hour DBP (r=-0.27; p=0.00006), LVMI (r=-0.26; p=0.0008) and E/e’ ratio (r=-0.19; p=0.01). Global LSRs demonstrated positive correlation with LV ejection fraction (r=0.22; p=0.006), E/A ratio (r=0.41; p=0.0001), e’ septum (r=0.44; p<0.0001) and negative correlation with age (r=-0.26; p=0.001), 24-hour SBP (r=-0.29; p=0.02), 24-hour DBP (r=-0.32; p=0.00005), LVMI (r=-0.22; p=0.004) and E/e’ ratio (r=-0.18; p=0.02). Global LSRs correlated also negatively with glucose (r=-0.17; p=0.03) and HBA1c (r=-0.28; p=0.0005).

The present study confirmed that hypertensive patients with glucose abnormalities have subclinical alterations of myocardium. Early manifestation of myocardial disorders is characterized by impaired longitudinal function. The subendocardial fibers, which are very sensitive to myocardial damage, have mainly longitudinal direction. The presence of impaired longitudinal function in diabetic patients has been reported previously using tissue Doppler imaging [5]. However, this ultrasound technique has many limitations (angle dependency, one-dimensional imaging). The tissue Doppler imaging reflects predominantly...
Figure 1 (A, B). Examples of left ventricular segmental longitudinal strain analysis from 4-chamber apical view in a hypertensive patient without IR [A, global LS= -17.3%] in a patient with HTN and IR [B, global LS= -17%].
Figure 1 (C, D). Examples of left ventricular segmental longitudinal strain analysis from 4-chamber apical view in a hypertensive patient with IFG [C, global LS=-14.2%] and in a patient with HTN and type 2 DM [D, global LS=-11.6%].
diastolic rather than systolic disorders in early stage of disease. We have found that LV ejection fraction is inadequate to identify early myocardial impairment in hypertensive patients with glucose metabolism disorders. The values of this parameter were in normal ranges like in healthy individuals. Opposite, the global LS was below normal range in all patients (less than -18%). The progressive decline of this marker was found in hypertensive patients with pre-diabetes and type 2 DM in our study.

Glucose metabolism disorders adversely affect heart function, as evidenced by the decreased left ventricular longitudinal function.

Table 3

<table>
<thead>
<tr>
<th></th>
<th>1st group (n=43)</th>
<th>2nd group (n=70)</th>
<th>3rd group (n=25)</th>
<th>4th group (n=20)</th>
<th>P</th>
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<tbody>
<tr>
<td>Global LS (%)</td>
<td>-15.9±1.96</td>
<td>-16.3±1.28</td>
<td>-16.2±2.3</td>
<td>-14.3±2.9</td>
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<tr>
<td>Global LSR (s⁻¹)</td>
<td>0.92±0.13</td>
<td>0.96±0.14</td>
<td>0.99±0.14</td>
<td>0.95±0.15</td>
<td>0.22</td>
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<tr>
<td>Global LSRs (s⁻¹)</td>
<td>0.91±0.29</td>
<td>0.99±0.32</td>
<td>0.9±0.21</td>
<td>0.79±0.21</td>
<td>0.03</td>
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<tr>
<td>Global LSRs (s⁻¹)</td>
<td>0.66±0.18</td>
<td>0.69±0.18</td>
<td>0.72±0.2</td>
<td>0.68±0.18</td>
<td>0.49</td>
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<tr>
<td>Basal CS (%)</td>
<td>-18.5±5.03</td>
<td>-19.2±3.58</td>
<td>-18.9±4.88</td>
<td>-17.4±6.72</td>
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</tr>
<tr>
<td>Basal CSR (s⁻¹)</td>
<td>1.25±0.3</td>
<td>1.38±0.32</td>
<td>1.34±0.33</td>
<td>1.24±0.32</td>
<td>0.14</td>
</tr>
<tr>
<td>Basal RS (%)</td>
<td>27.5±10.86</td>
<td>25.8±10.54</td>
<td>24±8.92</td>
<td>21.7±8.8</td>
<td>0.18</td>
</tr>
<tr>
<td>Basal RSR (s⁻¹)</td>
<td>1.94±0.5</td>
<td>2±0.58</td>
<td>1.94±0.37</td>
<td>1.86±0.48</td>
<td>0.68</td>
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<tr>
<td>Basal rotation (*)</td>
<td>4.7±1.72</td>
<td>4.9±2.17</td>
<td>4.4±2.48</td>
<td>5.1±2.13</td>
<td>0.72</td>
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<tr>
<td>Apical CS (%)</td>
<td>-28.7±7.1</td>
<td>-28.7±6.3</td>
<td>-29±7.03</td>
<td>-26.5±7.72</td>
<td>0.58</td>
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<tr>
<td>Apical CSR (s⁻¹)</td>
<td>1.79±0.6</td>
<td>1.81±0.44</td>
<td>1.9±0.53</td>
<td>1.76±0.55</td>
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<tr>
<td>Apical RS (%)</td>
<td>23.8±11.6</td>
<td>25.6±11</td>
<td>24.8±12.32</td>
<td>25.6±8.08</td>
<td>0.87</td>
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<tr>
<td>Apical RSR (s⁻¹)</td>
<td>1.54±0.51</td>
<td>1.57±0.45</td>
<td>1.6±0.48</td>
<td>1.58±0.42</td>
<td>0.97</td>
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<tr>
<td>Apical rotation (*)</td>
<td>6.1±2.9</td>
<td>6.3±3.65</td>
<td>6.9±3.3</td>
<td>5.7±2.44</td>
<td>0.64</td>
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<tr>
<td>Twist (*)</td>
<td>10.8±3.02</td>
<td>11.2±4.59</td>
<td>11.3±4.16</td>
<td>5.7±2.44</td>
<td>0.89</td>
</tr>
</tbody>
</table>

NB: LS, longitudinal strain; LSR, longitudinal strain rate; CS, circular strain; CSR, circular strain rate; RS, radial strain; RSR, radial strain rate; * p<0.05 4th group vs. 1st group; § p<0.05 4th group vs. 2nd group; # p<0.05 4th group vs. 3rd group.

**References**


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Поступила в редакцию 05.11.2014 г.