UDC 616.12-073.432.19:616-008.9]-055.1

M.Yu. Kolesnyk

Speckle tracking echocardiography in hypertensive males with glucose metabolism disorders

Zaporizhzhia State Medical University

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

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.

Спекл-трекінг ехокардіографія в чоловіків з артеріальною гіпертензією та порушеннями метаболізму глюкози

М.Ю. Колесник

Стандартна ехокардіографія не має достатньої чутливості для оцінювання впливу порушень метаболізму глюкози на стан міокарда лівого шлуночка (ЛШ) у хворих з артеріальною гіпертензією. З метою оцінювання можливості ранньої діагностики субклінічного ураження міокарда ЛШ залучили до обстеження 158 чоловіків з артеріальною гіпертензією та різним глікемічним статусом, яким виконали спекл-трекінг ехокардіографію. Встановили, що у хворих на гіпертензію та цукровий діабет 2 типу реєструється вірогідне зменшення глобального поздовжнього стрейну та раннього діастолічного стрейн рейту ЛШ, незважаючи на збережену фракцію викиду ЛШ. Це свідчить про доцільність використання спекл-трекінг ехокардіографії у хворих з артеріальною гіпертензією та порушеннями метаболізму глюкози.

Ключові слова: *артеріальна гіпертензія, цукровий діабет 2 типу, порушення метаболізму глюкози, спекл-трекінг ехокардіографія.*

Запорізький медичний журнал. – 2014. – №6 (87). – С. 4–10

Спекл-трекинг эхокардиография у мужчин с артериальной гипертензией и нарушениями метаболизма глюкозы

М.Ю. Колесник

Стандартная эхокардиография не обладает достаточной чувствительностью для оценки влияния нарушений метаболизма глюкозы на состояние миокарда левого желудочка (ЛЖ) у больных с артериальной гипертензией. С целью ранней диагностики субклинического поражения миокарда ЛЖ обследовано 158 мужчин с артериальной гипертензией и различным гликемическим статусом, которым выполнили спекл-трекинг эхокардиографию. Установили, что у больных с гипертензией и сахарным диабетом 2 типа регистрируется достоверное уменьшение глобального продольного стрейна и раннего диастолического стрейн рейта ЛЖ, несмотря на сохраненную фракцию выброса ЛЖ. Это свидетельствует о целесообразности использования спекл-трекинг эхокардиографии у больных с артериальной гипертензией и нарушениями метаболизма глюкозы.

Ключевые слова: *артериальная гипертензия, сахарный диабет 2 типа, нарушение метаболизма глюкозы, спекл-трекинг эхокардиография.*

Запорожский медицинский журнал. – 2014. – №6 (87). – С. 4–10

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 envolvement 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 pathogenetic 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

type 2 DM. The exclusion criteria were: white-coat hypertension, secondary hypertension, cardiomyopathy, documented coronary artery disease, moderate to severe valvular heart disease, reduced LV ejection fraction (<45%), atrial fibrillation, type 1 DM, type 2 DM on insulin therapy, chronic kidney disease (defined in case of creatinine clearance less than 60 ml/min/1.73 m^2) and significant pulmonary disease. All patients gave written informed consent to our study protocol that was supported by local Ethical Committee. The study was conducted in accordance to Helsinki Declaration.

24-hour ambulatory blood pressure monitoring. The HTN was confirmed by office measurement and 24–hour ambulatory blood pressure monitoring (ABPM) using ABPM-04 device (Meditech, Hungary). The measurements were carried out every 15 minutes during the active period and every 30 minutes during the passive period. The periods were set according to the diary of patient. The cuff was placed on the non-dominant arm and the patients were instructed to maintain their usual level of activity. HTN was defined as office blood pressure exceeding 140/90 mm Hg and average 24-hour blood pressure above 125/80 mm Hg.

Echocardiographic study. Conventional echocardiography was performed with My Lab 50 echocardiographic machine (Esaote, Italy), equipped with a 2.5-MHz phased array transducer. Standard echocardiographic views were obtained in two-dimensional (2D) modes, including parasternal long- and short-axis views, apical four-chamber (4C), three-chamber (3C), and two-chamber (2C) views with subjects in the left lateral decubitus position. The LV wall thicknesses, end-diastolic and end-systolic diameters, and left atrial (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/m^2. 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 ($HbA1_c$) 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 $HbA1_c$ >6.5%). Renal function was expressed as estimated glomerular filtration rate (eGFR, mL/min/1.73 m^2) 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 χ^2 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, office systolic (SBP) and diastolic blood pressure (DBP), heart rate, glomerular filtration rate, cholesterol level were comparable in all groups. The patients with HTN and type 2 DM had significantly higher body mass index. The participants of the 1st group had lower waist circumference compared with other groups. The patients of the 4th group had higher 24-hour SBP level, despite similar office SBP and DBP values in all groups. The hypertensives 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.

Table 1

Baseline characteristics of the patients

	1st group (n=43)	2nd group (n=70)	3rd group (n=25)	4th group (n=20)	p
Age (years)	51.2±8.73	50.2±7.64	50.3±8.35	53.1±7.66	0.53
Smoking, n (%)	23 (53%)	31 (44%)	13 (52%)	6 (30%)	0.32
BMI (kg·m^{-2}; median and range)	26.7±3.23	28.5±3.5	29±3.65	29.8±2.51*	0.003
Waist circumference (cm)	94.3±9.64	100.2±8.47^{x}	100.4±10.89$^{‰}$	103.9±9.22*	0.0005
Office SBP (mm Hg)	153±22	150±20	152±21	150±17	0.9
Office DBP (mm Hg)	100±13	97±10	98±12	99±13	0.68
24-hour SBP (mm Hg)	145±14	141±12	144±14	154±19*§$^{\#}$	0.008
24-hour DBP (mm Hg)	92±9	88±8	90±10	92±14	0.123
Heart rate (beats/min)	74±11	73±9	75±9	75±10	0.84
Total cholesterol (mmol/l)	5.8±1.23	5.7±1.23	6.3±1.26	6±1.15	0.11
Low-density lipoprotein cholesterol (mmol/l)	3.9±1.15	3.9±1.19	4.5±1.13	4.3±0.9	0.11
High-density lipoprotein cholesterol (mmol/l)	1.4±0.5	1.2±0.27	1.2±0.26	1.2±0.32	0.06
Triglycerides (mmol/l)	1.5±0.78	1.9±0.28	2.6±1.46$^{‰}$	2.2±1.08	0.003
Glomerular filtration rate (mL/min/1.73 m^2)	97±19	100±16	91±19	91±19	0.11
Fasting venous plasma glucose (mmol/l)	5±0.48	5.2±0.51	6.3±0.21$^{‰√}$	8.2±3.05*§$^{\#}$	<0.0001
HbA_{1c} (%)	4.7±0.67	5.1±0.67	5.7±0.8$^{‰√}$	7.3±1.3*§$^{\#}$	<0.0001
Insulin (mU/mL)	8.7±2.8	20.2±7.6^{x}	17.3±10.46$^{‰}$	22.1±8.67*	<0.0001
HOMA-IR (median and range)	1.9±0.58	4.6±1.76^{x}	4.9±3.06$^{‰}$	8.3±5.03*§$^{\#}$	<0.0001

NB: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA, homeostasis model assessment; IR, insulin resistance; HbA_{1c}, glycated hemoglobin; * p<0.05 4th group vs. 1st group; ^{x} p<0.05 2nd group vs. 1st group; § p<0.05 4th group vs. 2nd group; $^{‰}$ p<0.05 3rd group vs. 1st group; $^{√}$ p<0.05 3rd group vs. 2nd group; $^{\#}$ p<0.05 4th group vs. 3rd group.

Table 2

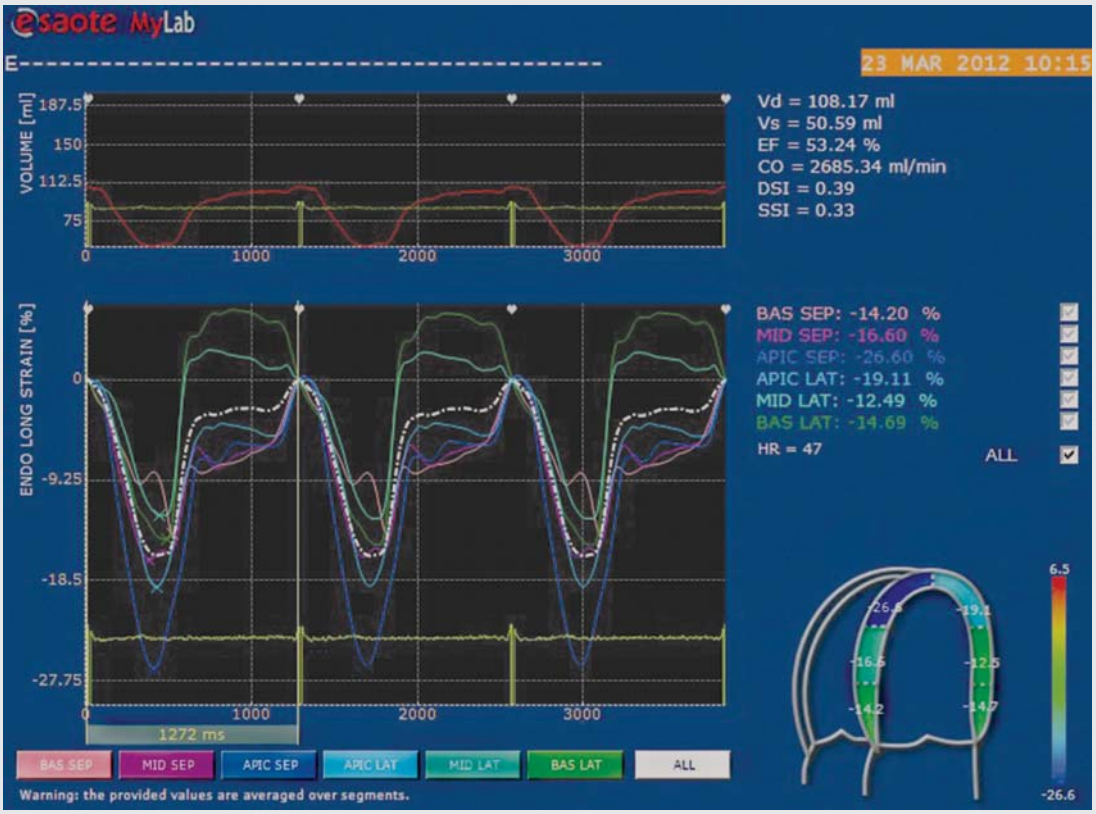
Conventional echocardiographic characteristics of the patients

	1st group (n=43)	2nd group (n=70)	3rd group (n=25)	4th group (n=20)	p
LV end-diastolic diameter (cm)	5.3±0.6	5.2±0.49	5.1±0.36	5.2±0.36	0.68
Interventricular septum thickness (cm)	1.17±0.21	1.17±0.21	1.19±0.21	1.27±0.17	0.24
Posterior wall thickness (cm)	1.05±0.18	1.06±0.21	1.05±0.19	1.16±0.2	0.17
LV mass index (g/m^2)	139.2±41.82	129.4±30.17	126.8±30.8	147.3±28.2	0.11
LA volume index (mL/m^2)	27.1±6.59	27.2±7.46	28.4±9.17	28.6±7.46	0.81
LV ejection fraction (%)	67.8±7.4	71.8±6.14	69.2±7.05	66.1±9.52§	0.004
E (m/s)	0.57±0.15	0.59±0.14	0.59±0.13	0.55±0.15	0.54
A (m/s)	0.63±0.1	0.59±0.1	0.64±0.09	0.63±0.11	0.18
E/A ratio	0.92±0.28	1.03±0.28	0.94±0.25	0.91±0.2	0.13
e' (cm/s)	7.8±2.5	8.3±2.01	7.4±2.29	6.4±1.88§	0.007
E/e' ratio	7.6±1.92	7.3±1.96	8.5±2.26$^{√}$	8.8±1.9*§	0.004

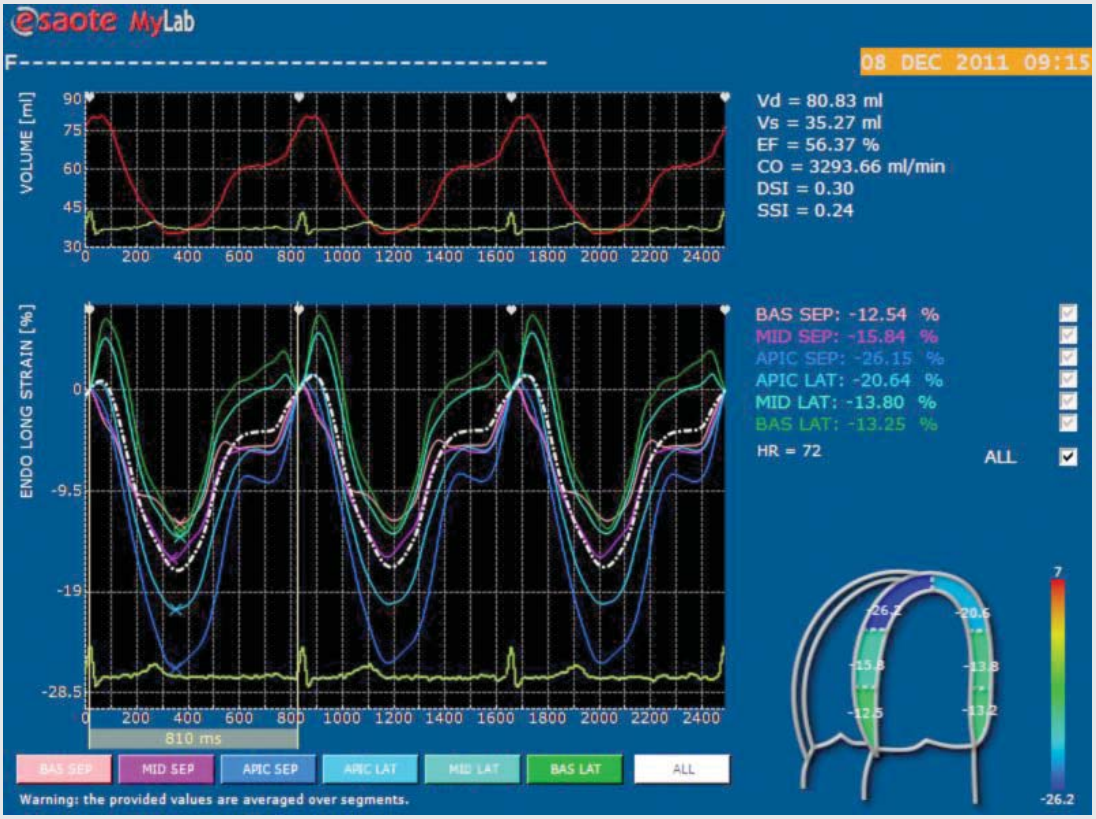
NB: LV, left ventricle; LA, left atrium; E, early diastolic velocity; A, atrial systole velocity; e', early diastolic myocardial velocity; * p<0.05 4th group vs. 1st group; § p<0.05 4th group vs. 2nd group; $^{√}$ p<0.05 3rd group vs. 2nd group.

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=0.000002), 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=0.0006), LVMI (r=-0.26; p=0.0008) and E/e' ratio (r=-0.19; p=0.01). Global LSR_E 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 LSR_E correlated also negatively with glucose (r=-0.17; p=0.03) and HBA_{1c} (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

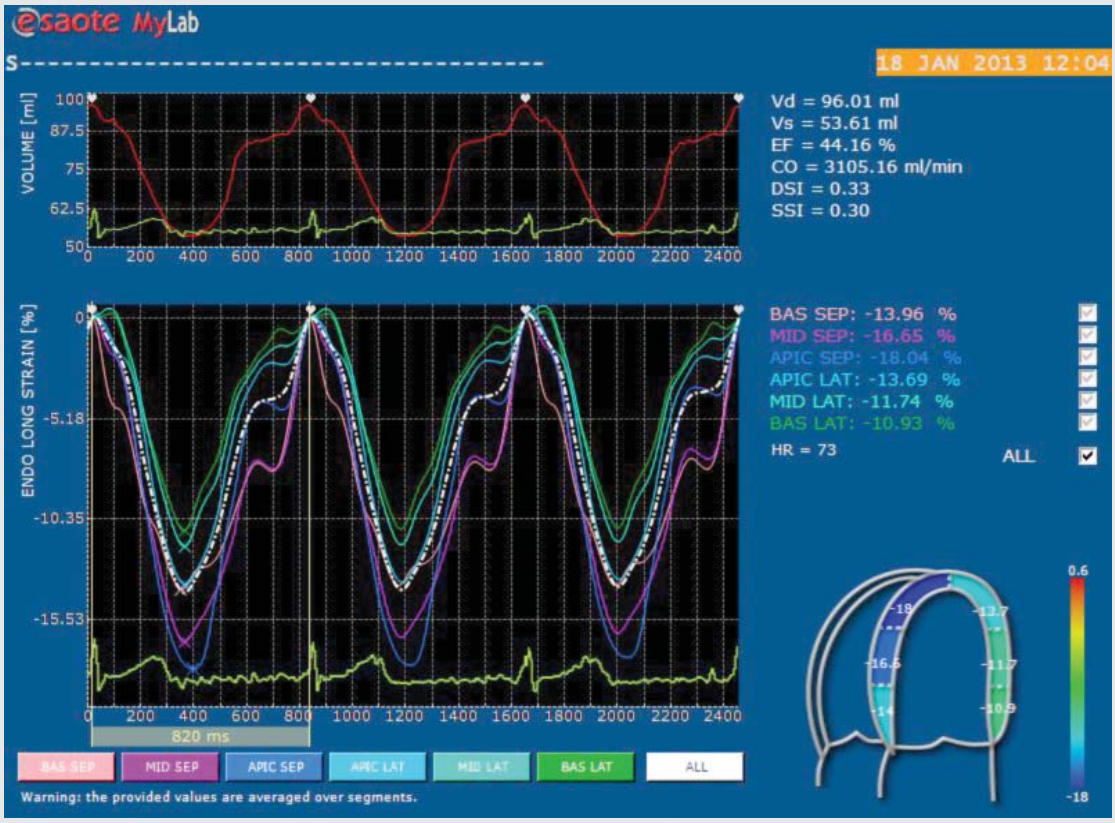


A

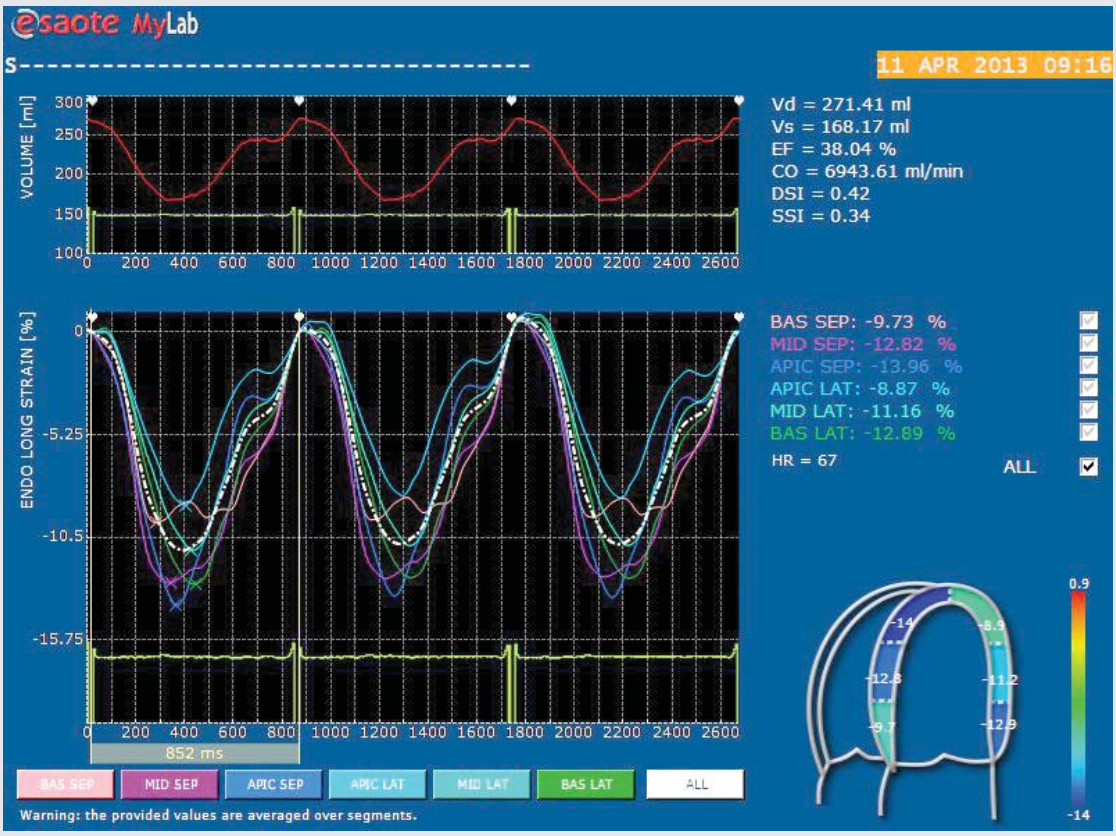


B

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%].



C



D

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%].

Table 3

Speckle tracking echocardiography

	1st group (n=43)	2nd group (n=70)	3rd group (n=25)	4th group (n=20)	p
Global LS (%)	-15.9±1.96	-16.3±1.28	-16±2.3	-14.3±2.3#§*	0.009
Global LSR (s^{-1})	0.93±0.13	0.96±0.14	0.98±0.14	0.9±0.15	0.22
Globa LSR_E (s^{-1})	0.91±0.29	0.99±0.32	0.91±0.21	0.78±0.2§	0.03
Global LSR_A (s^{-1})	0.66±0.18	0.69±0.18	0.72±0.2	0.66±0.18	0.49
Basal CS (%)	-18.5±5.03	-19.2±3.58	-18.9±4.88	-17.4±4.72	0.41
Basal CSR (s^{-1})	1.25±0.3	1.38±0.32	1.34±0.33	1.24±0.32	0.14
Basal RS (%)	27.5±10.86	25.8±10.54	24±8.92	21.7±8.8	0.18
Basal RSR (s^{-1})	1.94±0.5	2±0.58	1.94±0.37	1.86±0.48	0.68
Basal rotation (°)	4.7±1.72	4.9±2.17	4.4±2.48	5.1±2.13	0.72
Apical CS (%)	-28.7±7.1	-28.7±6.3	-29±7.03	-26.5±7.72	0.58
Apical CSR (s^{-1})	1.79±0.6	1.81±0.44	1.9±0.53	1.76±0.55	0.8
Apical RS (%)	23.8±11.6	25.6±11	24.8±12.32	25.6±9.08	0.87
Apical RSR (s^{-1})	1.54±0.51	1.57±0.45	1.6±0.48	1.58±0.42	0.97
Apical rotation (°)	6.1±2.9	6.3±3.65	6.9±3.3	5.7±2.44	0.64
Twist (°)	10.8±3.02	11.2±4.59	11.3±4.16	5.7±2.44	0.89

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.

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. The global LS was significantly reduced in patients with HTN and type 2 DM compared with other participants. Surprisingly, the presence of isolated IR wasn't associated with worsening of standard echocardiographic and speckle tracking imaging parameters in hypertensives. The role of IR in cardiac remodeling remains complex and controversial. Some experimental studies found that IR may be part of the antioxidant defense mechanism [6]. Hyperinsulinemia exerts cardioprotective effects via glucose-dependent and independent mechanisms, including aversion of glucose toxicity, positive inotropy, modulation of apoptosis, inflammation and coronary flow [7]. W. Dinh et al. registrated that ranges of global LS didn't differ between IR and non-IR patients in a cross-sectional study [8]. According to Framingham Heart Study, IR was associated with increased LVMI and wall thickness in women but not in men [9]. From another point of view, long standing IR may have deleterious effect on LV diastolic function. C. Cadeddu et al demonstrated that even isolated IR may adversely affect cardiac function, as evidenced by reduced global LSR at peak of dobutamine stress test [10]. The manifestation of type 2 DM in HTN is associated with significant decrease of both systolic and diastolic speckle tracking markers (global LS and global LSR_E). It was estimated in the study of Nakai H. et al. and confirmed by the results of our study [11]. Recently, it was shown that speckle tracking echocardiography may have advantages in follow-up of diabetic patients. Asymptomatic patients with type 2 DM and normal LVEF showed mild deterioration of subclinical LV function assessed with speckle tracking echocardiography during 2.5-year follow-up period [12].

Conclusions

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

Speckle tracking echocardiography can identify subclinical alterations of left ventricle systolic and diastolic function in patients with arterial hypertension and glucose metabolism disorders.

The presence of insulin resistance isn't associated with worsening of systolic and diastolic function in hypertensive patients, assessed by conventional and speckle tracking echocardiography.

Worsening of glycemic status (from insulin resistance to type 2 diabetes mellitus) is characterized by deterioration of left ventricle global longitudinal strain and early diastolic strain rate with significant reduction of these markers in diabetic patients.

The perspectives for future research. There is a lack of longitudinal evaluations concerning the changes of structural and functional myocardial abnormalities in patients with HTN and type 2 DM assessed with two-dimensional speckle tracking analysis.

References

1. Danaei G., Finucane M., Lu Y., Singh G., Cowan M., Paciorek C., Lin J., et al. (2011). National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2·7 million participants. *Lancet,* 378 (9785), 31-40. doi: 10.1016/S0140-6736(11)60679-X.
2. Kearney P., Whelton M., Reynolds K., Muntner P., Whelton P., He J. (2005). Global burden of hypertension: analysis of worldwide data. *Lancet,* 365 (9455), 217-223. doi:10.1016/S0140-6736(05)17741-1.
3. Lopez-Jaramillo P., Lopez-Lopez J., Lopez-Lopez C., Rodriguez-

Alvarez M. (2014). The goal of blood pressure in the hypertensive patient with diabetes is defined: now the challenge is go from recommendations to practice. *Diabetol Metab Syndr.* 6 (1), 31. doi: 10.1186/1758-5996-6-31.
4. Li R.J., Yang J., Yang Y., Ma N., Jiang B., Sun Q.W., et al. (2014). Speckle tracking echocardiography in the diagnosis of early left ventricular systolic dysfunction in type II diabetic mice. *BMC Cardiovasc Disord.* 8 (14), 141. doi: 10.1186/1471-2261-14-141.
5. Di Bonito P., Moio N., Cavuto L., Covino G., Murena E., Scilla C., et al. (2005). Early detection of diabetic cardiomyopathy: usefulness of tissue Doppler imaging. *Diabet Med.* 22 (12), 1720-1725. doi: 10.1111/j.1464-5491.2005.01685.x.
6. Hoehn K., Salmon A., Hohnen-Behrens C., Turner N., Hoy A., Maghzal G.J, et al. (2009). Insulin resistance is a cellular antioxidant defense mechanism. *Proc Natl Acad Sci USA.* 106 (42), 17787-17892. doi: 10.1073/pnas.0902380106.
7. Ng K., Allen M., Desai A., Macrae D., Pathan N. (2012). Cardioprotective effects of insulin: how intensive insulin therapy may benefit cardiac surgery patients. *Circulation.* 125 (5), 721-728. doi:10.1161/CIRCULATIONAHA.111.063784.
8. Dinh W., Lankisch M., Nickl W., Scheyer D., Scheffold T., Kramer F., et al. (2010). Insulin resistance and glycemic abnormalities are associated with deterioration of left ventricular diastolic function: a cross-sectional study. *Cardiovasc Diabetol* 9, 63. doi: 10.1186/1475-2840-9-63.
9. Rutter M., Parise H., Benjamin E., Levy D., Larson M., Meigs J., et al. (2003). Impact of glucose intolerance and insulin resistance on cardiac structure and function: sex-related differences in the Framingham Heart Study. *Circulation,* 107(3), 448-454. doi: 10.1161/01.CIR.0000045671.62860.98.
10. Cadeddu C., Nocco S., Piano D., Deidda M., Cossu E., Baroni M., et al. (2013). Early impairment of contractility reserve in patients with insulin resistance in comparison with healthy subjects. *Cardiovasc Diabetol*, 12, 66. doi: 10.1186/1475-2840-12-66.
11. Nakai H., Takeuchi M., Nishikage T., Lang R., Otsuji Y. (2009). Subclinical left ventricular dysfunction in asymptomatic diabetic patients assessed by two-dimensional speckle tracking echocardiography: correlation with diabetic duration. *Eur J Echocardiogr,* 10 (8), 926-932. doi: 10.1093/ejechocard/jep097.
12. Roos C., Scholte A., Kharagjitsingh A., Bax J., Delgado V. (2014). Changes in multidirectional LV strain in asymptomatic patients with type 2 diabetes mellitus: a 2-year follow-up study. *Eur Heart J Cardiovasc Imaging*, 15(1), 41-47. doi: 10.1093/ehjci/jet075.

Information about author:
Kolesnyk M.Yu., Ph. D., Department of Family Medicine and Internal Medicine, Associate Professor, Zaporizhzhia State Medical University, E-mail: zsmumk@gmail.com.

Поступила в редакцию 05.11.2014 г.