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"ISOLATED" DIASTOLIC MYOCARDIAL DYSFUNCTION IN DIABETES MELLITUS

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ABSTRACT
Usually, the presence of a low ejection fraction (LV) of the left ventricle (LV) clearly explains the clinical picture of chronic heart failure (CHF). However, recently there has been an increase in the number of patients with CHF clinic against the background of normal LV LV (>50%). Most often, these are elderly women with arterial hypertension (AH), prone to the sudden development of acute left ventricular failure with a clinical picture of pulmonary edema. In such patients, diastolic dysfunction (DD) of the myocardium is especially often found against the background of preserved LV LV. It is proved that the myocardium in the diastole is more sensitive to ischemia and the presence of DD earlier and more accurately indicates the pathology of the myocardium.
According to 10 large population studies based on the results of EchoCG, from 39 to 71% of patients with CHF have preserved LV LV. This variation may be related to the characteristics of the criteria and methods of DD diagnosis. However, even in the absence of a clinical picture of CHF, already at the initial stage of DD, the risk of mortality increases by 5 times.

Keywords: diabetes mellitus, arterial hypertension, chronic heart failure, diastolic dysfunction.

Introduction

In diabetes mellitus (DM), LV myocardial DD is considered to be the earliest sign of heart damage. The prevalence of "isolated" DD in DM, according to the literature, ranges from 23 to 75%. In 70-80% of patients with type 2 diabetes ((DM2), concomitant hypertension is detected, but even in the absence of hypertension and coronary heart disease ((CHD), almost 60% of patients with DM2 have a violation of diastolic function (DF). It is known that in patients with cardiovascular prognosis is much more severe than in patients without diabetes.
The search for the causes of a more severe prognosis in DM in patients with preserved PV led to a detailed study of the role of LV myocardial DF. The capabilities of modern ultrasound diagnostics technologies allow us to detect the initial signs of DD, assess its degree, the magnitude of the increase in LV filling pressure, identify violations of coronary microcirculation and systolic function (SF) of the LV.
Hypertension is one of main risk factors for the development of cardiovascular diseases and mortality. In this regard, proper management, monitoring and treatment of patients primarily in the primary care is of great importance. Systematic monitoring of morbidity, in particular awareness of the presence of blood pressure among the population, timely and constant, rather

than episodic use of antihypertensive drugs, is the key to effective treatment, and hence to improving the quality of life of patients. In connection with the above, we conducted a study among primary care patients with hypertension. The transition from prehypertension to overt hypertension reflects, at least in part, changes such as hypertrophy of the muscular layer of the arteriole wall and endothelial dysfunction. Against the background of such structural and functional changes in persons with prehypertension, an increase in vasoconstriction and a decrease in vasodilation were described. It should be noted that according to literature data, an increase in blood pressure is most often observed in women during puberty, pregnancy, during childbirth and in the postpartum period, which is associated with hormonal restructuring and is especially dangerous for both women and fetal development. The big problem is that many women do not even suspect that they have arterial hypertension, and therefore do not receive timely treatment, and many are not treated because of ignorance about the need for treatment and the consequences that await them.

The aim of the study was to compare the features of myocardial DD under the condition of maintaining global EF LV in patients with DM2 with hypertension and in patients with stage 2 hypertension (AH) without DM.

MATERIALS AND METHODS

The study involved 87 patients with Myocardial DD and preserved EF LV, who complained of shortness of breath, fatigue and restriction of physical activity. They were diagnosed with CHF from I to III FC by NYHA (2009). The diagnosis of DM2 was established in 53 patients with hypertension based on criteria recommended by WHO. The control group consisted of 34 patients with stage 2 AH without DM.

The exclusion criteria from the study were: myocardial infarction, coronary artery intervention, non-sinus rhythm, heart defects, endocarditis, myocarditis, pericarditis, lung diseases, anemia, thyroid pathology, liver failure, GFR <60 ml/min/1.73 m^2. When comparing the clinical characteristics, the groups did not differ in age, gender, body mass index, SAD and DAD levels, the number of patients with coronary artery disease (stable angina pectoris I— III FC), levels of liver enzymes and creatinine. In the group of patients with DM2, the average level of glycated hemoglobin (Table. 2) was 8.2%. The patients suffered from diabetes for an average of about 14 years (from 5 to 23 years). Complications of DM in the form of diabetic retinopathy were observed in 41.5% of patients, diabetic nephropathy — in 22.6% of patients. Distal diabetic polyneuropathy was diagnosed in 67.9% of patients. All patients (with the exception of one who is on diet therapy) received hypoglycemic therapy. Oral hypoglycemic drugs were received by 50.9% of patients, insulin — 47.2%. Patients of both groups received antihypertensive therapy (beta-blockers, ACE inhibitors and statins).

Standard transthoracic echocardiography was performed on a Philips iE 33 ultrasound machine (USA) using a volumetric phased matrix sensor xMATRIX X5-1. To assess the state of the left atrium (LP) in the parasternal position along the long axis, the maximum anterior-posterior size (MPR) of the LP (the upper limit of the norm is up to 40 mm) was measured in B-mode. From the apical position, the LP area (norm criterion up to 20 cm^2) and the volume of the LP cavity were calculated. LV thicknesses were measured in all patients in the B-mode in the

diastole: TMJPd and TZSd (norm criteria up to 11 mm); (CDR) LV (norm up to 57 mm). MMLJ is calculated according to the formula R. Devereux:
MMLJ=1.04=[(TMJPd+CDR+Tss)3– CDR)]3×0.8+0.6 (g).
To calculate the IMLJ, the formula was used:
IMLJ= MMLJ /BPT of the body (g/m^2), where BPT is the surface area of the body according to the Du bois formula. The criteria for the norm of LVL for men — less than or equal to 115, for women — less than or equal to 95 g / m^2. LV OTC was determined by the formula: OTS=(Tmzhp+Tss)/LV CDR (the norm criterion is less than 0.42).
The diastolic function of the LV myocardium was evaluated by the following method.
1. First of all, the assessment was carried out by types
LV myocardial DD (rigid, pseudonormal and restrictive), which were determined comprehensively by the following parameters:
— by the size of the left atrium in B-mode;
— according to the E/A ratio, where: peak E is the velocity
of the transmittal flow in the early diastole, peak A
is the velocity in the late diastole (cm/s) in the pulse—wave mode;
— by the ratio Ė/Ȧ, where: peak Ė is the speed
of movement of the medial part of the mitral ring in
the early diastole; peak Ȧ is the speed of movement in
late diastole in the mode of tissue dopplerography (these speeds depend on the shortening and elongation of longitudinally oriented myocardial fibers; the norm criterion for Ė >8 cm/s).
2. In the second place, the severity of the violation of DFLJ was
quantified by two indicators:
— integral echocardiographic E/e ratio. This noninvasive indicator is the most sensitive marker of LV filling pressure and closely correlates with cardiac catheterization data (norm criterion E/e`≤8). The value of 9<E/e`<15 allows us to assume (but does not prove) increased filling pressure in the LV.
The value E/e`>15 is highly specific for
increasing the filling pressure in the LV;
— the pressure of jamming in the pulmonary capillaries (DLC), which was calculated according to the formula: DLC = 2 + 1/3 × E/e` (norm criteria from 8 to 10 mm Hg).
Assessment of the contractile function of the LV myocardium was carried out in two ways.
1. Traditionally, according to the Simpson method, in four and two-chamber apical positions in B-mode (the norm criterion is 50% or more).
2. On myocardial deformation using Speckle tracking echocardiography (Echocg). Seroscale images of the heart were obtained in B-mode for three cardiac cycles with ECG registration during respiratory retention. To assess the global longitudinal deformation (GPA) of the LV, images were analyzed from three apical positions along the long axis of the LV (two-, three- and four-chamber) semi-automatically: initially, the analyzed endocardial surface was determined manually at three points (at the apex and bases of the LV). Then, using the Q-lab 3.0 Advanced Ultrasound Quantification software, a computer analysis was performed by the tracking system for each of the 17 segments, followed by a final calculation of the LV

myocardial GPA. For the average LV efficiency value for healthy individuals, 18.9±2.5 was taken%.

To study radial (towards the center of the cavity) and circular (circumferentially) deformations, LV images were studied along the short axis at the basal and middle levels. Global radial and circular LV deformations were calculated.

RESULTS

In all examined patients, the presence of normal LV LV according to the Simpson method was confirmed (>50%). The groups did not statistically differ in the size of BWW, CSR and LVF. All patients visually lacked areas of violation of local LV myocardial contractility. When comparing groups by the main standard LV EchoCG parameters no statistically significant differences were found. Considering that the LV myocardial contractility assessed by the Simpson method did not differ between the groups, it can be assumed that the difference in the prognosis of CHF in patients with and without DM 2 may be determined by the different prevalence of certain types or the severity of DD. When using the method of tissue Dopplerography, really important information was obtained about the more pronounced severity of DD in DM. It was found that the speed of movement of the medial part of the mitral ring ė in DM was significantly lower than in patients without DM ($p<0.05$), and its average value was below the normal criteria. Compared with the parameters of the transmittal flow (E and A), the velocity Ė is a more sensitive marker of LV relaxation disorders. In both groups, the average values of E/Ė and ZLK were higher than the norm criteria, but with DM, more severe violations of DF were noted: the values of E/ė ($p=0.000$) and DLC ($p=0.001$) were significantly higher (14±15.5 units and 15.3±4.7 mmHg) than in patients without DM (9.7±2.3 units and 11.9±1.3 mmHg).

When analyzing the spectrum of occurrence of various

types of LV myocardial DD, a rigid type was most often found in both groups (in the group with DM in 56%, in the group without DM in 47% of patients), and then a pseudonormal type of DD (with DM in 38%, without DM in 41% of patients). Restrictive type D is more rare (with DM in 6%, without DM in 12% of patients). However, there were no significant differences in the occurrence of different types of DD between the groups.

Thus, despite the similarity of the clinical picture and the spectrum of occurrence of various types of DD under the condition of normal LVF according to Simpson, patients with DM2 and AH had a more pronounced violation of LV DF than patients with stage 2 AH.

DISCUSSION

Cognized, which is associated with several points. Firstly, a violation of DF can also occur with normal LP sizes, since its volume is a cumulative indicator and increases with the chronic course of DD. Secondly, the DF analysis needs a comprehensive assessment of the E/A or E/A parameters. This is due to the fact that during the progression of DD, the E/A ratio can change deceptively. As is known, at the stage of the rigid type (E<A), there is a decrease in the early velocity (E) and an increase in the late velocity (A) of the transmittal flow, and the LV filling pressure is still normal. However, with the progression of DD, pseudonormalization of the

transmittal flow occurs. The ratio of flow rates becomes correct (E>A or E/A=1.0-1.5), but the filling pressure in the LP and LV will already be increased. To overcome the difficulties of diagnosing the pseudonormal type of DD, the tissue Dopplerography mode helps, which is relatively easy to perform in everyday clinical practice (compared to studying the flow in the pulmonary veins) and does not depend on cooperation with the patient (sample Valsalva). In the mode of tissue Dopplerography with pseudonormal type DD, the ratio of peaks Ė <Ȧ is violated (as in rigid), and E / Ė is higher than normal, but less than 15 mm Hg. Pseudonormal type DD occupies an intermediate position between initial and severe violations of DF and is accompanied by a more pronounced increase in end-diastolic pressure in the LV than in persons with normal DF. It is in this group of patients that DD often remains unrecognized and DF is mistakenly regarded as normal. In this study, there was a significant percentage identification of a pseudonormal type of DD (41% in stage 2 GB without DM and 38% in patients with DM2 with AH), which could be mistaken for the absence of a violation of DF. At the next stage of DF violation (restrictive type of DD reversible/irreversible), there is a further deterioration in the elasticity and extensibility of the LV myocardium (E/A>1.5; Ė<8 mm/s) and the filling pressure of LP and LV increases significantly (E/Ė>15).

In this regard, the ratio of E/Ė and DLC can be used to objectively determine the severity of LV DD and follow-up of patients as the progression of DF disorders in DM progresses. As clinical observations show, it is the severity of DD, and not LVEF, that correlates with the severity of CHF. Being an important part of the pathophysiology of CHF, DD is associated with the worst survival of patients for 2 years.

Assessment of the contractility of the LV myocardium according to Simpson is carried out visually by the movement of the walls of the heart, depends on the experience of the researcher and the quality of the equipment. But even in this case, it can be difficult to identify minor violations of myocardial contractility. In addition, it is noted that the LVF according to Simpson depends mainly on the radial, and not on the longitudinal contractility of the LV.

The method is based on tracking the specks that make up the structure of the myocardial wall during the cardiac cycle. During systole, muscle fibers of different directions undergo the following changes: in the longitudinal direction there is a shortening of the fibers (–), in the radial (transverse) — thickening (+), and in the circular (circular) — shortening (–). The change in the length of the section relative to its initial value is called deformation (or with a train) and expressed in %.

The triggering mechanisms of the development of systolic-diastolic CHF in DM are hyperglycemia and a violation of cardiac metabolism. When the oxidative phosphorylation of glucose is turned off, fatty acids begin to be used as the main energy source.This induces oxidative stress, activates a number of secondary pathological mechanisms leading to hypertrophy, fibrosis and cell death. The addition of AH to DM is accompanied by an increase in myocyte necrosis by 1.4 times. The risk of irreversible myocardial damage in patients with DM without coronary blood flow disorders corresponds to the risk of patients without DM with a pronounced obliterating lesion of the trunks of the main coronary arteries.

Violation of intracellular calcium metabolism and changes in contractile proteins damage contractile processes, lead to rigidity of diabetic myocardium. Remodeling of the heart,

violation of coronary microcirculation against the background of generalized endothelial dysfunction, autonomous neuropathy have detrimental consequences in DM. Due to metabolic disorders in DM, both systolic and diastolic myocardial dysfunction develops, which begins subclinically, and then progresses, forming a complete picture of congestive CHF.

CONCLUSION

Despite the similarity of clinical manifestations and the data of traditional methods of assessing function LP and LV according to EchoCG data, patients with DM2 and AH have more pronounced DF disorders than patients with stage 2 GB without DM. Speckle tracking EchoCG makes it possible to detect an "invisible" violation of the global longitudinal contractility of the LV myocardium in patients with traditional methods DM2. The continuity of the combination of deterioration of systolic and diastolic LV functions in DM is associated with metabolic disorders in the heart muscle in conditions of chronic hyperglycemia. Early the development of combined systolic-diastolic dysfunction in DM2 is prognostically more unfavorable than in patients without DM. Patients with DM requires increased attention and alertness in terms of early development of life-threatening rhythm disturbances, sudden death and faster progression and decompensation of CHF.

Currently, LV myocardial DF indicators to a greater extent than a decrease in myocardial contractility can be used to determine the severity of CHF and evaluate the effectiveness of therapeutic measures in daily clinical practice.

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