[1]Belovol A.N., [2]Shalimova A.S., [3]Kochueva M.N.
[1]Professor, MD, Kharkiv National Medical University
[2]Associate Professor, PhD, Kharkiv Medical Academy of Postgraduate Education
[3]Professor, MD, Kharkiv Medical Academy of Postgraduate Education
E-mail: annashalimova@yandex.ru

CARDIOVASCULAR REMODELING IN PATIENTS WITH ESSENTIAL HYPERTENSION AND TYPE 2 DIABETES

Type 2 diabetes has adopted worldwide scale infectious epidemic. Type 2 diabetes along with arterial hypertension (AH) and obesity among the top three most common diseases in the world [1]. Presence of type 2 diabetes potentiates the development of cardiovascular disease (CVD), including atherosclerosis, coronary heart disease (CHD), as well as their complications [2]. The combination of AH and type 2 diabetes is the most aggressive in the context of CVD and mortality. Elevated blood pressure (BP) is detected in 65-80% of patients with type 2 diabetes [3, 4]. 50-70% patients with type 2 diabetes violation of carbohydrate metabolism have developing on the background of already existing hypertension. Metabolic determinants of type 2 diabetes potentially can run pathophysiological cascade leading to endothelial dysfunction, cardiac remodeling and vascular immunoinflammatory activation and apoptotic processes [5].

According to the literature, AH may be both as consequence, as perhaps, the cause of type 2 diabetes [6, 7]. The main link in the pathogenesis of AH in type 2 diabetes is the insulin resistance (IR) and the hyperinsulinemia is resulting by this state [8].

Recent years, it has been believed that IR is the independent risk factor of dyslipidemia, systemic inflammation, oxidative stress [8]. Cardiac dysfunction in type 2 diabetes occurs in the form of heart failure (HF), as well as violations of subclinical contractile capacity and filling of the left ventricle (LV). According to some authors, in type 2 diabetes morphologically marked diffuse myocardial

damage, left ventricular hypertrophy (LVH) and impaired myocardial contractility [9]. Other authors consider a major pathophysiological feature of myocardial injury in diabetic patients with is cardiomyopathy development with reducing the rate of myocardial diastolic relaxation [10, 11]. Chronic heart failure (CHF) is combined with type 2 diabetes in 33% of patients [7]. The association of these two pathologies significantly aggravates the course of each of them.

Aim of the study was to assess the contribution to the development of type 2 diabetes cardiovascular remodeling in patients with EH.

Clinical characteristics of patients and research methods. 205 patients who gave written informed consent to participate in the study and met the inclusion criteria were examined at the Department of therapy and nephrology of Kharkiv Medical Academy of Postgraduate Education. The first group consisted of 116 patients with EH in combination with type 2 diabetes, the second consisted of 89 patients with EH without type 2 diabetes. Both groups were matched for age, sex, EH stage, AH grade, functional class (FC) CHF. The control group consisted of 20 healthy individuals who EH and type 2 diabetes was excluded on the basis of the complex clinical and instrumental examinations.

Standard biochemical methods determined glucose concentration of venous blood, glycosylated hemoglobin (HbA1c), lipid profile. Ultrasound examinations were performed on cardiac ultrasound scanner («ULTIMA RA» firm "RADMIR", Ukraine) in one-, two-dimensional and Doppler modes with color mapping by conventional methods. Volumes of the left atrium (LA) and right atrium (RA), end-systolic diameter (ESD) and end-diastolic diameter (EDD) of left ventricular end-diastolic pressure in the LV (EDP), left ventricular ejection fraction (EF), index of relative wall thickness (IRWT), myocardial mass index of LV (MMI) were estimated. LVH was defined as MMI 115 g/m^2 or more in men and 95 g/m^2 or more in women. LV geometry was considered unchanged at IRWT $\leq$ 0,42 and normal MMI. At IRWT > 0,42 and normal LV geometry MMI change was seen as concentric remodeling, at IRWT > 0,42 and an increase in MMI – concentric hypertrophy, at IRWT $\leq$ 0,42 and increase MMI – eccentric hypertrophy [ESH,

2013]. LV diastolic function was assessed by the study of blood flow in the pulmonary artery and transmitral diastolic flow in the pulsed Doppler mode with the definition of the following parameters: maximum rate of early LV filling (E) , the maximum speed of late (atrial) LV filling (A), the ratio of the maximum velocity of early and late LV filling (E/A), left ventricular isovolumic relaxation time (IVRT), deceleration time of early diastolic flow velocity (DT), the average pressure in the artery pulmonary to Kitabatake (PAP) , the ratio of peak e and E on the mitral valve in the spectral and tissue Doppler (E/e). For the study of endothelial function determination of the degree EDVD in reactive hyperemia was conducted in all patients. Investigations were carried out broadband linear transducer 5–12 MHz Doppler color mapping with three on the left and right brachial artery in 15-minute intervals between samples by the method of Celermajer D.S. in modification Ivanova O.V. Normally, the maximum vasodilation of the brachial artery have to exceed 10% of the original diameter. Simultaneously, we measured the of the intima-media thickness (IMT) of the carotid artery (CA 2 cm proximal to the bifurcation of the common carotid artery. Pulse wave velocity (PWV) by the CA was determined W-Track- method (method of phase tracking, patented scanner manufacturers). Determination of PWV by the abdominal aortic (AA) (on the left subclavian artery to the femoral artery) was performed using a phased transducer with a frequency of 2–4 MHz.

Statistical data processing was performed using the software package «Statistics for Windows» 6.0.

Results and discussion

The study found that both groups of patients characterized by preserved LV systolic function, as evidenced by the values of EF LV in the normal range. IRWT values and IMM significantly in both groups ($p<0,05$) higher than the levels of these indicators in the control group. The level of MMI in patients with type 2 diabetes was higher than in nondiabetic patients 2m ($p<0,05$).

All patients with type 2 diabetes and the vast majority of patients with EH without type 2 diabetes (94,4%) occurred LVH. In patients with EH without type 2

diabetes almost equally met hypertrophic (concentric and eccentric hypertrophy) and nonhypertrophic (concentric remodeling) LV remodeling options. Predominant types of remodeling in patients with EH without type 2 diabetes were concentric remodeling (43,8%) and concentric hypertrophy (41,6%). At the same time, the absolute majority of patients with EH and type 2 diabetes dominated hypertrophic LV remodeling options – concentric (67,2%) and eccentric (17,2%) hypertrophy, which are prognostically unfavorable types of remodeling [12, 13].

Analysis of the diastolic function of the heart demonstrated that both groups of patients were different from the control group from the values of A, E/A, IVRT and DT ($p<0,05$). With mean pulmonary artery pressure in patients with EH and type 2 diabetes was significantly higher than in patients with EH without type 2 diabetes ($p<0,05$) and the control group ($p<0,01$). By a combined indicator of diastolic function, both groups of patients were significantly different from the control, but this value of E/e were higher in patients with EH and type 2 diabetes ($p<0,05$), than in patients with EH without type 2 diabetes.

In all patients with EH without type 2 diabetes diastolic dysfunction of the heart was represented type of impaired relaxation, where as in patients with EH and type 2 diabetes severity of diastolic dysfunction was greater. So in 85,3% of patients with EH and type 2 diabetes initial changes in diastolic function in the form of impaired relaxation were observed, whereas 12,9% patients had pseudonormalization flow.

Evaluation of structural and functional state of the great vessels in patients of both groups showed changes in the vascular wall, which were apparent increase in IMT, PWV CA and PWV AA, as well as lower power EDVD, which was significantly ($p<0,05$), these groups differed from the control. The setting changes can be attributed to the activation of mediators of sympathetic nervous and renin-angiotensin-aldosterone system, which leads to endothelial damage, thickening of the intima-media makeover architectonics media and adventitia, increased rigidity of the vascular wall, and in the end – to the acceleration pulse wave [14].

A distinctive feature of the group of patients with EH and type 2 diabetes compared with hypertensive patients without diabetes were significantly larger IMT values PWV CA and PWV AA at significantly lower magnitude EDVD ($p<0,05$). These changes observed in patients with EH and type 2 diabetes, can be explained by more pronounced in these atherosclerotic processes that are affected by impaired carbohydrate metabolism.

Thus, this study has allowed to establish the effect of type 2 diabetes on the development of structural and functional changes in the heart and blood vessels in patients with EH.

Conclusions

1. Patients with essential hypertension and type 2 diabetes are characterized by preserved LV systolic function of the heart and more pronounced compared to hypertensive patients without type 2 diabetes prevalence concentric (67,2%) and eccentric (17,2%) LVH – worst case remodeling.

2. In patients with EH and concomitant type 2 diabetes degree of LV diastolic dysfunction more pronounced than in nondiabetic patients. In the presence of 100% of hypertensive patients without type 2 diabetes diastolic dysfunction type violations LV relaxation, in 12,9% of patients diagnosed with type 2 diabetes heavier pseudonormal type of LV diastolic dysfunction.

3. Changes in the vascular wall in patients with EH with and without type 2 diabetes manifested increase PWV and IMT in the carotid arteries and abdominal aorta, lower power EDVD. The distinctive feature of the group of patients with a combination of EH and type 2 diabetes compared with a group of hypertensive patients without type 2 diabetes were significantly larger IMT values, PWV CA, PWV AA and a significantly lower value EDVD.

References

1. American Diabetes Association: Standards of Medical Care in Diabetes 2011. Diabetes Care. 2011; 34(1): 11–61.

2. Бутрова С.А. Метаболический синдром: патогенез, клиника, диагностика, подходы к лечению / С.А. Бутрова // Русский медицинский журнал. – 2012. – Т.20. – №3. – С.56–58

3. Colwell J.A. Type 2 Diabetes, Pre-Diabetes, and the Metabolic Syndrome JAMA. 2011; 306(2): 215.

4. Dandona P., Aljada A., Chaudhuri A. et al. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. Circulation. 2005; 111: 1448–1454.

5. Демидова Т.Ю. Атеросклероз и сахарный диабет 2: механизмы и управление / Т.Ю. Демидова // Кардиосоматика. – 2011. – Т.2. – №2. – С.22–30.

6. Кобалава Ж.Д. Эхокардиографическая оценка фиброза миокарда у молодых мужчин с артериальной гипертонией и разными типами ремоделирования левого желудочка / Ж.Д. Кобалава, Ю.В. Котовская, А.Ф. Сафарова, В.С. Моисеев // Кардиология. – 2011. – № 2. – С. 34–39.

7. Коваленко В.М. Регіональні медико-соціальні проблеми хвороб системи кровообігу. Димаміка та аналіз. Аналітично-статистичний посібник / В.М. Коваленко, В.М. Карнацький. – Київ, 2013. – 239 с.

8. Маньковский Б.Н. Новое руководство по лечению сахарного диабета 2 типа – что изменилось, в чем значение для клинической практики? / Б.Н. Маньковский // Диабет. Ожирение. Метаболический синдром. – 2012. – №1 . – С.31–36.

9. Майоров А.Ю. Инсулинорезистентность в патогенезе сахарного диабета 2 типа / А.Ю. Майоров // Сахарный диабет. – 2011. – №1. – С.35–43.

10. Nicholls S.J., Tuzcu E.M., Kalidindi S. et al. Effect of diabetes on progression of coronary atherosclerosis and arterial remodeling: a pooled analysis of 5 intravascular ultrasound trials. J. Am. Coll. Cardiol. 2008; 52(4): 255–262.

11. Ryden L., Standl E., Bartnik M. et al. Guidelines on diabetes, prediabetes, and cardiovascular diseases: executive summary. The task force on diabetes and cardiovascular diseases of the European Society of Cardiology (ESC) and of the

European Association for the Study of Diabetes (EASD). European Heart J. 2007; 28(1): 88–137.

12. Shimamoto K., Miura T. Metabolic syndrome. Nippon Rinso. 2009; 67(4): 771–776.

13. Shoelson S.E., Lee J., Goldfine A.B. Inflammation and insulin resistance. J. Clin. Invest. 2006; 116(7): 1793–1801.

14. Syed Abdus Saboor Aftab. Thickness of the intima media as a new correlate for atherosclerosis risk factors in Indian type 2 diabetes patients. International Journal of Diabetes Mellitus. 2009;1: P.7–10.