MYOCARDIAL REMODELING IN PATIENTS WITH CORONARY ARTERY DISEASE AND TYPE 2 DIABETES MELLITUS

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Abstract

The aim of the work was a comparative study of the structural and geometric remodeling of the myocardium in patients with coronary heart disease with and without concomitant type 2 diabetes. 110 patients with coronary artery disease who had previously undergone myocardial revascularization were examined, with an average age of 58.3 ± 4.9 years. The patients were divided into two groups. The first main group consisted of 56 patients with coronary artery disease. Stable angina pectoris FC 2 with concomitant type 2 diabetes, the second comparison group included 54 patients with coronary heart disease, without diabetes. The control group consisted of 20 practically healthy individuals. All examined patients underwent medical history collection, ECG, EchoCG, and blood determination of glycated hemoglobin. There was a tendency to decrease LVEF, an increase in cavity dilation and an increase in LV myocardial mass in the group of coronary heart disease with type 2 diabetes compared with the group of coronary heart disease without diabetes. Concentric LVH was found in 14 (25%) patients, concentric LV remodeling in 24 (42.8%) patients, eccentric LVH in 14 (25%) patients, and normal left ventricular geometry in 4 (7.1%) patients. The relationship between the level of glycated hemoglobin and the presence of left ventricular hypertrophy was revealed: in the main group in 14 patients, 80% of them had HbA1c levels of more than 6.5%, including HbA1c levels of more than 7.5% to 45.4% of patients ($p<0.05$). Thus, the study of the features of the structural and functional restructuring of the left heart in patients with coronary artery disease with type 2 diabetes should be taken into account in predicting cardiovascular risk.

Keywords: remodeling, coronary heart disease, type 2 diabetes mellitus, left ventricular hypertrophy

Introduction. Coronary heart disease remains an important medical and social problem leading to high mortality [1,2]. Concomitant diabetes mellitus plays an important role [3,4]. At the same time, numerous evidences of a close relationship between diabetes and cardiovascular diseases (CVD) have been accumulated, it is coronary heart disease that is the most common cause of death in patients with diabetes. One of the first studies where this relationship was convincingly demonstrated was the Framingham study, according to which the absolute risk of coronary death in diabetes was twice as high in men and 4.7 times in women, compared with people without diabetes [5,6].

Remodeling of the heart is a process of complex disruption of its structure and function and includes an increase in myocardial mass, dilation of cavities and a change in the geometric characteristics of the ventricles [16]. There is evidence of the effect of cardiac remodeling on the prognosis of arrhythmias, the development and progression of chronic heart failure and cardiovascular mortality [7].

In type 2 diabetes (DM2), it is the heart that is recognized as the most important target of damage. The combination of insulin resistance, hyperinsulinemia, and hyperglycemia accelerates the development and progression of atherosclerosis-related diseases, increasing the risk of cardiovascular complications [10]. LV diastolic dysfunction (DD) is considered an early marker of myocardial damage in DM2. A pathogenetic relationship between DD and LV hypertrophy during the development and progression of CHF has been noted [8,9]. Despite the availability of clinical data on the pathogenesis of remodeling, there is no complete data reflecting the holistic picture of the formation of structural and functional disorders of the heart in patients with T2DM with coronary artery disease. The question of the severity of heart changes and risk factors for LV remodeling in DM2 remains unresolved [11,12].

In this regard, the aim of our study was to compare the parameters of structural and geometric remodeling of the heart in patients with coronary heart disease with and without concomitant type 2 diabetes**.**

Materials and methods. 110 patients with coronary artery disease (65 men and 45 women) with an average age of 58.3 ± 4.9 years, who had previously undergone myocardial revascularization, were examined. Depending on the glycemic status, the patients were divided into two groups. The first main group consisted of 56 patients diagnosed with coronary heart disease. Stable angina pectoris FC 2 with concomitant type 2

diabetes. The second group (the comparison group) included 54 patients with coronary artery disease, angina pectoris without diabetes. The control group consisted of 20 practically healthy individuals. The diagnosis of T2DM was established based on criteria recommended by WHO [9].

The exclusion criteria were: type 1 diabetes, bronchial asthma and obstructive pulmonary diseases with respiratory insufficiency of grades II-III, diseases of the systemic hematopoiesis, oncological diseases, non-sinus rhythm, heart defects, endocarditis, myocarditis, pericarditis, liver failure and participation in any other study within 30 days before selection.

Research methods. Glycated hemoglobin levels were examined in all patients, and a 12-lead ECG was recorded using a Schiller device.

The EchoCG study was performed on a Samsung medison ultrasound device "Accuvix.V20" (Korea) using a sector sensor with color mode and pulse-wave, continuous-wave mode with a frequency of 2-4 MHz in standard echocardiographic positions in M- and B-modes according to the recommendations of the American Echocardiographic Society (ASE) (Schiller N.B. et al., 1989).

Based on relative wall thickness (OTC) and The LV myocardial mass index (IMMI) was evaluated by the geometric model of LV and the types of its remodeling were distinguished.

Statistical processing. The materials used in this study were statistically processed using parametric and nonparametric methods. Statistical processing and analysis of the obtained results were carried out in the statistical analysis system MS Excel 2010. When estimating the linear relationship between the values, the Pearson pair correlation coefficient was calculated. Spearman's rank correlation coefficient was used to study the relationship between quantitative features. The differences were considered statistically significant at $p<0.05$.

Results. As part of the study, structural and functional changes in the myocardium were studied using EchoCG. When analyzing the left ventricular ejection fraction (LVEF), there was a tendency to decrease this indicator in the main group to 50.8±3.2% compared with patients in the comparison group, where LVEF was 54.2±2.4%, $p<0.05$ (Table 1).

Table 1

The state of central hemodynamics in the groups of studied IHD patients with and without type 2 diabetes

Index	Control group (n-20)	Main group (n-56)	Group comparison (n-54)
EDV, ml	120,7±4,1 *	170,3±5, 8*/***	149,7±4,1 ***
ESV, ml	36,4±2,9**	77,5±3,7***	61,4±2,9**/***
EF,%	65,6±4,8	50,8±3,2***	54,2±2,4***
ΔS, %	37,4±0,6	28,1±0,6	29,9±0,7
LV PWT, cm	9,0±0,9	12,3±0,32	11,4±0,24
IVS, cm	9,0±0,7	12,5±0,32	11,0±0,25
Total thickness LV, cm	0,37±0,03	0,52±0,03	0,47±0,05
LVM, g	99,5±3,5**	302,4±9,5	268,9±9,2**
LVMI, g/m^2	106,7±12,6*	144,6±6,8*/***	117,8±4,5***

Note: * - $p<0.05$ differences are significant between the values of the control group and the main group, ** - $p<0.05$ differences are significant between the values of the control group and the comparison group, *** - $p<0.05$ differences are significant between the values of the main group and the comparison group.

An analysis of the structural and geometric parameters of the left chambers of the heart showed that in the main group, in comparison with the comparison group, there was an increase in cavity dilation (final diastolic and systolic volume) and an increase in LV myocardial mass.

A similar trend was obtained when quantifying the fraction of systolic shortening of the anteroposterior size of the left ventricle – in the main group, the indicator was 28.1± 0.6%, in the comparison group – 29.9±0.7%. The analysis of individual data on OTC and LV IMM made it possible to determine the presence of structural and geometric remodeling of the left ventricle in 52 (92.8%) patients of the main group and 45 (83.3%) patients in the comparison group.

Significant differences in the nature of LV remodeling were found between the groups of patients. In combination with coronary heart disease and DM2 (the main group), the following variants of structural and geometric remodeling of the heart were identified: concentric LVH in 14 (25%) patients, concentric LV remodeling in 24 (42.8%) patients, eccentric LVH in 14 (25%) patients, and normal geometry in 4 (7.1%) patients. left ventricle (Table 2).

Table 2

Features of structural and geometric LV remodeling in the group of CHD patients with and without type 2 diabetes

Remodeling indicators	Main group (n-56)	Comparison group (n-54)
Eccentric hypertrophy, %	14 (25%)	9 (16,6%)
Concentric remodeling, %	24 (42,8%)	22 (40,7%)
Concentric hypertrophy,%	14 (25%)	5 (9,2%)
Normal geometry, %	4 (7,1%)	18 (33,3%)

In the comparison group, the normal type of geometry was noted in 18 (33.3%) of the observed, concentric remodeling prevailed in 22 (40.7%), concentric LV hypertrophy and eccentric LV hypertrophy were registered in 5 (n=9.2%) and in 9 (n=16.6%) cases. The analysis suggests that groups with and without DM2 are comparable in terms of the frequency of concentric remodeling. In patients with impaired carbohydrate metabolism, the option of left ventricular remodeling according to the type of concentric LVH significantly prevailed (25%). It should be noted that patients with eccentric (n = 14) and concentric (n = 14) hypertrophy had a higher incidence of myocardial infarction (9, 10, and 11 patients, respectively) and clinical manifestations of CHF (94.3%, respectively) compared with patients with concentric LV remodeling (n = 24). 98.4% and 64.2%). It was interesting to study the features of left ventricular remodeling at different levels of glycated hemoglobin in a group of CHD patients with type 2 diabetes (Table 3).

Table 3

Parameters of structural and geometric remodeling of the left ventricle at different values of glycated hemoglobin in groups of patients with CHD with and without type 2 diabetes

Remodeling indicators	**<6,5%**	**6,5-7,5%**	**>7,5%**
Eccentric hypertrophy, %	2	5	7
Concentric remodeling, %	5	7	12
Concentric hypertrophy,%	3	5	6
Normal geometry, %	1	1	2

A study of the results of quantifying the parameters of LV structural and geometric remodeling and the level of glycated hemoglobin (HbA1c) between groups of CHD patients with and without type 2 diabetes revealed a relationship between the level of glycated hemoglobin and the presence of left ventricular hypertrophy: LVH was detected in 14 patients in the main group, 80% of them with HbA1c levels higher than 6.5%, including with an HbA1c level of more than 7.5% to 45.4% of patients ($p<0.05$).

It is known that a high risk of developing cardiovascular complications in carbohydrate metabolism disorders is associated with the development of LV remodeling. The predominance of the concentric type of LV remodeling in patients of both groups (24 (42.8%) and 22 (40.7%), respectively, is explained by the compensatory nature of LV hypertrophy. On the other hand, an increase in the frequency of concentric and eccentric LV hypertrophy in patients with T2DM in combination with coronary heart disease (37.0%) may indicate an increase in structural and geometric changes in the heart, contributing not only to a violation of the geometric shape of the ventricle and an increase in the tension of its walls, but also to a further increase in myocardial stress, which is accompanied by the progression of heart failure.

LV remodeling in coronary heart disease in combination with T2DM is based on hormonal, neurohumoral and metabolic processes, the triggering factors of which are insulin resistance and hyperinsulinemia. Apparently, activation of the sympathoadrenal system, stimulation of renin and angiotensin II production, followed by an increase in aldosterone formation, contributes to the transformation of the hyperkinetic variant of hypertension into a volume-dependent one, while hypertrophic and proliferative processes leading to concentric LVH are complemented by processes of cardiac volume overload, which may contribute to eccentric LV remodeling, which also prevails in DM patients (in in the main group – 25%), in contrast to patients without impaired carbohydrate metabolism (in the comparison group – 16.6%). All this indicates the presence of additional metabolic and hormonal factors in the pathogenesis of disorders of the structure and function of the heart muscle in patients with type 2 diabetes mellitus. The study of the features of the structural and functional restructuring of the left heart in patients with coronary artery disease with type 2 diabetes should be taken into account in predicting cardiovascular risk.

References:

1. Кондратьева Д.С., Афанасьев С.А., Будникова О.В., Ворожцова И.Н., Ахмедов Ш.Д., Козлов Б.Н. Структурно-функциональные показатели сердца пациентов с ишемической болезнью сердца и сахарным диабетом 2 типа. Ритмоинотропная реакция изолированного миокарда при разном уровне гликированного гемоглобина. Сахарный диабет. 2021;24(1):45-54. https://doi.org/10.14341/DM12484

2. Щукина Е.В., Приколота О.А., Багрий В.А., Андрусяк А.Ю., Рыбалко Г.С., Шестерина Ю.Б., Стефано Е.А. Лечение пациентов с хронической ишемической болезнью сердца и сахарным диабетом 2 типа. Архивъ внутренней медицины. 2023;13(2):97-109. https://doi.org/10.20514/2226-6704-2023-13-2-97-109

3. Fu, Q., Zhou, L., Fan, Y. Et al. Effect of SGLT-2 inhibitor, dapagliflozin, on left ventricular remodeling in patients with type 2 diabetes and HFrEF. BMC Cardiovasc Disord 23, 544 (2023). https://doi.org/10.1186/s12872-023-03591-3

4. Yap J, Tay WT, Teng TK, Anand I, Richards AM, Ling LH, MacDonald MR, Chandramouli C, Tromp J, Siswanto BB; ASIAN-HF (Asian Sudden Cardiac Death in Heart Failure) Registry Investigators; Zile M, McMurray J, Lam CSP. Association of Diabetes Mellitus on Cardiac Remodeling, Quality of Life, and Clinical Outcomes in Heart Failure With Reduced and Preserved Ejection Fraction. J Am Heart Assoc. 2019 Sep 3;8(17):e013114. Doi: 10.1161/JAHA.119.013114. Epub 2019 Aug 21. PMID: 31431116; PMCID: PMC6755825.

5. Jensen, M. T., Risum, N., Rossing, P. & Jensen, J. S. Self-reported dyspnea is associated with impaired global longitudinal strain in ambulatory type 1

diabetes patients with normal ejection fraction and without known heart disease – The Thousand & 1 Study. J. Diabetes Complicat. 30, 928–934. https://doi.org/10.1016/j.jdiacomp.2016.02.005 (2016).

6. Hossein Pour, A. H., Gholami, M., Saki, M. & Birjandi, M. The effect of inspiratory muscle training on fatigue and dyspnea in patients with heart failure: A randomized, controlled trial. Japan J. Nurs. Science: JJNS. 17, e12290. https://doi.org/10.1111/jjns.12290 (2020).

7. Shaver, A. Et al. Role of Serum Biomarkers in Early Detection of Diabetic Cardiomyopathy in the West Virginian Population. Int. J. Med. Sci. 13, 161–168. https://doi.org/10.7150/ijms.14141 (2016).

8. Pan, L., Wang, T. Features of cardiac remodeling in Patients with Acute Coronary Syndrome Complicated with Rheumatoid Arthritis. Sci Rep 7, 10268 (2017). https://doi.org/10.1038/s41598-017-11123-1

9. Hassan, A., Samaan, K., Asfour, A. Et al. Ventricular remodeling and hemodynamic changes in heart failure patients with non-ischemic dilated cardiomyopathy following dapagliflozin initiation. Egypt Heart J 76, 76 (2024). https://doi.org/10.1186/s43044-024-00508-z

10. Chandu Siripuram, K. Balu Mahendran, Shreelaxmi V Hegde, Sanjana Murali Krishna, Shruti Suresh Suvarna, Ramesh Kandimalla Cureus.Role of Echocardiography in Detecting Left Ventricular Dysfunction Among Diabetic Patients: A Clinical and Biochemical Perspective2025;[Epub]

11. Zhang, DP., Xu, L., Wang, LF. Et al. Effects of antidiabetic drugs on left ventricular function/dysfunction: a systematic review and network meta-analysis. Cardiovasc Diabetol 19, 10 (2020). https://doi.org/10.1186/s12933-020-0987-x

12. Wan J, Xu F, Zuo H, et al. Impact of SGLT2 Inhibitors on Left Ventricular Remodeling in Diabetic Patients with Acute Myocardial Infarction. Journal of Cardiovascular Pharmacology and Therapeutics. 2024;29. Doi:10.1177/10742484241301191