Magna Scientia Advanced Research and Reviews

eISSN: 2582-9394

Cross Ref DOI: 10.30574/msarr

Journal homepage: https://magnascientiapub.com/journals/msarr/

(RESEARCH ARTICLE)

Central hemodynamic parameters and endothelial function in patients with coronary artery disease with diabetes mellitus who underwent COVID-19

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Magna Scientia Advanced Research and Reviews, 2023, 07(01), 129–133

Publication history: Received on 11 January 2023; revised on 20 February 2023; accepted on 23 February 2023

Article DOI: https://doi.org/10.30574/msarr.2023.7.1.0032

Abstract

Coronary heart disease is a common pathological process among population and is one of the main causes of disability and death worldwide. According to the latest studies, the incidence rate of this pathological process is increasing among the population. This is due to the number of factors, including the increase in the age range of the population, economic, social and nutritional factors, the lack of proper control of risk factors, and the improvement of diagnostic possibilities due to the development of medicine. In this article central hemodynamic parameters and endothelial function were studied in patients with coronary artery disease with diabetes mellitus who underwent COVID-19. Patients who underwent COVID-19 tended to have more severe impaired endothelial properties and impaired hemodynamic parameters.

Keywords: COVID-19; Coronary artery disease; Diabetes mellitus; Endothelial function

1. Introduction

The term "coronary heart disease" (CHD) was proposed by the WHO Expert Committee in 1962 to refer to acute and chronic heart disease caused by insufficient blood supply to the myocardium, a mismatch between myocardial oxygen demand and coronary blood flow [1]. IHD is a disease, the main pathogenetic mechanism of which is: organic narrowing of the coronary arteries due to damage to them by atherosclerosis and other causes (coronary spasm, impaired microcirculation, coronary thrombosis) [2]. Damage to the coronary arteries of the heart, followed by insufficient supply of oxygen-enriched blood to the myocardium, leads to the development of metabolic (exchange) disorders and inactive connective tissue in it [3]. The replacement of actively functioning myocardial cells (myocardiocytes) and the conduction system of the heart by this tissue leads to the development of heart failure, heart rhythm and conduction disturbances [4]. The prevalence of coronary artery disease among the adult population of developed countries is approximately 10%, among the elderly and the elderly - about 20%. Only 40–50% of patients are aware of their disease; in the remaining 50–60%, it remains unrecognized. In Russia, almost 10 million of the working population suffer from coronary artery disease and more than 1/3 of them have stable angina. IHD adversely affects the quality of life, is the main cause of disability and mortality in people. In the population over 65 years of age, this disease is the cause of 75% of all deaths.

Recent years have been characterized by a steady increase in the number of patients with type 2 diabetes mellitus (DM). According to experts from the International Diabetes Association (IDF), by 2035 the number of patients with diabetes in the world will reach 592 million people, almost every tenth inhabitant of the planet [5]. In the Russian Federation, according to the State Register as of January 1, 2015, the number of patients with DM was 4.094 million people [6]. Type 2 diabetes is characterized by a high risk of developing coronary heart disease (CHD), myocardial infarction, stroke, heart failure, in addition, it is known that diabetes and cardiovascular disease (CVD) mutually aggravate each other. In

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type 2 DM, the risk of developing coronary artery disease increases by 2–5 times [7]. Numerous studies show that more than half of patients are unaware of the presence of type 2 diabetes, and diagnosis often occurs against the background of already existing cardiovascular complications [8]. Almost 50% of patients with an established diagnosis of coronary artery disease are diagnosed with newly diagnosed type 2 diabetes, impaired glucose tolerance, or fasting hyperglycemia [9]. In this regard, the American Heart Association (AHA) has determined that patients with type 2 diabetes have the equivalent of a high risk of vascular complications, comparable to that in overt CVD [10].

During the pandemic of a new coronavirus infection, patients with cardiovascular diseases (CVD) were a special risk group [11]. This is largely due to the fact that the pathology of the cardiovascular system is the most common comorbid condition in COVID19. According to statistics, CVDs are registered in every third patient who is hospitalized with a diagnosis of a new coronavirus infection [12]. The relevance of the problem of cardiac comorbidity in COVID-19 is due to the following factors: concomitant cardiovascular pathology affects the course of a new viral infection, increases the risk of death, certain difficulties create potential side effects of a number of drugs used to treat CVD [13] . At the same time, with COVID-19, additional damage to the cardiovascular system is possible, which contributes to the development of complications and worsening of the course of CVD. In addition, the combination of COVID-19 with the pathology of the cardiovascular system (CVS) causes a number of difficulties in terms of diagnosis, choice of priority tactics, and determining the order of routing of persons with emergency conditions. The danger of such a large-scale spread of coronavirus infection lies in the decompensation of the existing cardiovascular pathology, especially in severe cases of COVID-19 [14, 15]. The new strain of coronavirus, SARS-CoV-2, is a single-stranded RNA virus with phylogenetic similarities to another coronavirus, SARS-CoV, which caused an outbreak of SARS in 2003 with a 10% mortality rate in patients with a confirmed diagnosis of SARS (severe acute respiratory syndrome) [16, 17]. For a short time it was believed that the new coronavirus infection mainly affects the respiratory tract with the development of pneumonia and ARDS (acute respiratory distress syndrome) in severe cases, but now it is established that COVID-19 also affects the cardiovascular system, causing a specific myocardial damage. The cardiovascular tropism of SARS-CoV-2 is not yet fully understood, but several possible mechanisms are being discussed. An important role is played by ACE type II signaling pathways involved in the cascade of pathological reactions of heart damage. Angiotensin converting enzyme II (ACE II) is a type I transmembrane protein, the expression level of which is especially high on the surface of type II alveolar cells, in cardiomyocytes, vascular endothelium, gastrointestinal tract, kidneys, liver and ovaries. In addition, ACE II can be contained in the free form in the blood. The physiological role of this enzyme is to cleave angiotensin I (AT) to inactive AT1-9, which is then transformed into AT1-7 with the participation of ACE, as well as to degrade AT II to AT1-7, which binds to Mas receptors. AT1-7 has vaso- and cardioprotective effects, as well as anti-inflammatory, anti-proliferative and natriuretic effects. In turn, ACE II type, due to cleavage, reduces the negative properties of AT II, such as vasoconstriction, cytokine-like activity, sodium retention, and the development of fibrosis. The initial step in the penetration of SARS-CoV-2 into target cells is the binding of the virus to ACE II receptors using a peplomer (S-protein, spike protein), which is structurally similar to ACE II. Then SARS-CoV-2 and the transmembrane domain of ACE II enter the cell by endocytosis. As a result, an imbalance occurs, manifested by a drop in the level of AT1-7 against the background of an increase in AT II and activation of the ACE-ATII-AT1-receptor signaling pathway. Therefore, the primary damage of COVID-19 to the lungs, myocardium, blood vessels, and other organs may increase [18, 19, 20].

Aim

Aim of the study was to evaluate central hemodynamic parameters and endothelial function in patients with coronary artery disease with diabetes mellitus who underwent COVID-19.

2. Material and methods

The results of clinical and functional features of coronary heart disease and type 2 diabetes mellitus after COVID-19 in 120 patients aged 45 to 72 years were studied. Depending on the presence of COVID-19 all patients were divided into 2 groups: I - 90 patients with CAD and T2DM after COVID-19 (mean age - 59.1±12.6 years); II — 30 patients with CAD and T2DM without COVID-19 (mean age 62.6±14.6 years). An echocardiographic study was carried out on the basis of the Department of Functional Diagnostics of the RCCC using the TOSHIBA - COREVISION model SSA-350 A using a sensor with a frequency of 3 MHz, 2.5 MHz in B- and M-modes according to the generally accepted method. Determination of end-diastolic size (EDS), interventricular septal thickness (IVSD) and left ventricular posterior wall thickness (PVSLV) was performed in M-mode at the level of mitral valve chords from parasternal access along the long axis of the heart. Only records with a clear visualization of the internal surfaces were allowed for analysis, giving a clear picture of the interventricular septum, the internal diameter of the left ventricle, and the posterior wall of the left ventricle. Left ventricular myocardial mass (LVML) was calculated using the formula proposed by Devereux et al. (1986). To correct the effect of excess body weight, the mass index of the left ventricular myocardium (IMM) was determined according to the formula de Simone G. Et al. 1992). The body surface area was calculated using the Dubois formula, taking into

account height (cm) and weight (kg). The presence of LVH was recognized if the thickness of the posterior wall of the left ventricle and / or the thickness of the interventricular septum was 12 mm or more, and the value of the mass index of the left ventricular myocardium, correlated to the body surface area, was equal to or exceeded 110 g/m2. Whereas the concentric or eccentric types of left ventricular hypertrophy were assessed by the previously calculated relative thickness of the walls of the left ventricle in %. Endothelial function were performed using immune enzyme method with Humanizer. All statistical analysis were performed using STATA software.

3. Results and Discussion

The revealed features of the anamnesis and clinical course of CAD with diabetes mellitus who underwent COVID-19 in the examined patients suggested ambiguity in the change in the structural and functional characteristics of the myocardium in 1 group. When conducting a comparative assessment of the indicators of the structural and functional state of the heart according to echocardiography, we obtained the data reflected in the table. As can be seen from the data presented in the table, the sizes of the aorta and the left atrium in the compared groups did not differ significantly, while the average sizes of the left ventricle in women of the 1st group as a whole in diastole were smaller compared to the 2nd group of women. At the same time, the smallest parameters of the diameter of the cavity of the left ventricle in both phases of the cardiac cycle were detected in group 1 of patients.

Table 1 EchoCG parameters in the examined patients

Parameter	Group 1	Group 2	P
Aortic diameter. mm	3.57±0.28	3.195±0.38	< 0.01
Left atrium diameter. mm	3.43±0.25	2.64 ± 0.62	< 0.01
LV EDD. mm	4.96±0.28	4.59±1.0	< 0.01
LV ESD. mm	5.96±0.16	4.08±0.85	< 0.01
Thickness of the posterior wall of the left ventricle (ZSLZh). mm	1.395±0.38	1.10±0.1	< 0.01
Thickness of the interventricular septum (IVS). mm	1.837±0.16	1.03±0.12	< 0.01
LVML. g	328.2± 24	123.3±11	< 0.01
LVMI. g / m2	275.16±15.9	95.3±63	< 0.01
UTS	0.490±0.04	0.37±0.8	< 0.01
Ejection fraction. %	38.35±3.7	59.02±5	< 0.001

The thickness of the walls of the left ventricle, on average, exceeded the normal values in all the examined groups of patients with COVID-19, however, the values of the thickness of the left ventricular wall and IVS were somewhat greater in patients of the 2nd study group.

It can be assumed that the smaller dimensions of the LV cavity in combination with the greater thickness of its walls in CAD with diabetes mellitus who underwent COVID-19 of the 1st group indicate a high probability of having concentric LV remodeling. The average level of LVML was significantly increased in all control groups and exceeded the standard values by 1.6 times. Both groups practically did not differ from each other in this respect. In turn, the LVMI index, which more reliably reflects the level of LV myocardial hypertrophy, had slightly higher values in CAD with diabetes mellitus who underwent COVID-19 of the 1nd group. At the same time, the OTS index, by which one can judge the type of LV remodeling, in CAD with diabetes mellitus who underwent COVID-19 of group 1 did not exceed 0.55 on average, and in women of group 2 it was less than 0.45.

We obtained data on the high prevalence of concentric hypertrophy in group 1 — in 19 (38%) patients, while in the second group — in 14 (24%) patients. Eccentric hypertrophy of the left ventricle occurred in group 1 in 27 cases (65%), and in group 2 - in 30 (41%). The data obtained allow us to suggest that there is a trend towards a concentric type of LV remodeling in CAD with diabetes mellitus who underwent COVID-19of the 1st group, and an eccentric type in CAD with diabetes mellitus of the 2nd group.

Another interesting fact is the discovery of higher IVS thickness in CAD with diabetes mellitus of the 2nd group (1.32±0.4 cm versus 1.23±0.12 cm). The participation of the LV walls in the implementation of the contractile function of the heart was reduced in all examined CAD with diabetes mellitus who underwent COVID-19, so the average EF in group 1 was less tha second one, in relation to the control group. At the same time, lower myocardial contractility was also registered in CAD with diabetes mellitus who underwent COVID-19 of the 1st group. Among endothelial functions flow mediated vasoconstriction was better in second group than group 1 ($P<0.05$). Besides, endothelin-1 also were greater in group 1 than group 2 patients ($P<0.05$).

4. Conclusion

The study showed a high prevalence of left ventricular hypertrophy in both study groups, which is an indicator of a high risk of cardiovascular complications, in this case, myocardial infarction. There was also a tendency to a greater degree of LV eccentric hypertrophy in CAD with diabetes mellitus who underwent COVID-19, compared with patients without COVID-19, which is due to a deeper restructuring of hemodynamics (systolic dysfunction and expansion of the heart cavities) in this category of patients due to extensive myocardial infarction with severe clinical course. Furthermore, endothelial dysfunction were pronounced more in CAD with diabetes mellitus who underwent COVID-19 than those without COVID-19.

Compliance with ethical standards

Acknowledgments

Authors thank to professor Bakhromkhon Alyavi for technical support.

Disclosure of conflict of interest

No conflict of interest.

Statement of ethical approval

Ethical approvement from Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation dated 04.01.2022

Statement of informed consent

Informed consent was obtained from all individual participants included in the study

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