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Heart damage in patients with cirrhosis of the liver

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Abstract

The review outlines the current understanding of the clinical syndrome of heart disease in patients with liver cirrhosis and the development of cirrhotic cardiomyopathy. Patients with cirrhosis of the liver often notice chest pain, palpitations, complaints of arterial hypotension and rapid fatigue. Echocardiography shows that the left ventricular ejection fraction in cirrhosis is preserved at rest and decreases under stress. In some patients with viral liver cirrhosis, there is a decrease in global myocardial deformation (the presence of latent systolic dysfunction). More pronounced impairment of left ventricular diastolic function is recorded in patients with ascites and patients with Child–Pugh class B and C. In patients with ascites, unfavorable left ventricular remodeling, left heart cavities enlargement, dilatation of the pulmonary artery and its branches are more common. There is an increase in pulmonary artery pressure, the development of portopulmonary hypertension and hepatopulmonary syndrome in patients with liver cirrhosis. The development of these syndromes leads to a sharp decrease in the quality of life of patients with relatively preserved liver function and a worsening of the prognosis for orthotopic liver transplantation. Approximately half of patients with liver cirrhosis have electrophysiological disorders: prolongation of the *QT* interval, tachycardia, supraventricular and ventricular extrasystoles. To date, there are no clinical guidelines for the management of cirrhotic cardiomyopathy. If a patient with liver cirrhosis develops clinically significant heart failure, then general principles of management of such patients are necessary. It is necessary to limit the use of angiotensin-converting enzyme inhibitors and cardiac glycosides. The combined use of nonselective beta-blockers and nitrates reduce cardiac output and *QT* interval. The use of potassium canrenoate, lisinopril helps reverse the development of structural and functional changes in left ventricle. The positive effect of antiviral therapy on cardiac hemodynamics in patients with viral cirrhosis was noted. Liver transplantation is known to be an effective treatment for cirrhotic cardiomyopathy, but this treatment may worsen latent heart failure. Thus, in patients with liver cirrhosis, heart damage occurs with the development of cirrhotic cardiomyopathy, while the mechanisms of the development of myocardial dysfunction are not fully understood. Further studies of the development of the syndrome are required for timely diagnosis and clinical intervention to improve the survival of patients.

Keywords: cirrhosis, pulmonary hypertension, systolic, diastolic dysfunction.

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Hepatic cirrhosis (HC) is one of the major healthcare problems. An increase in the incidence of viral hepatitis and toxic substances such as alcohol are the main factors that impair liver function [1]. As a result, patients with HC die due to gastrointestinal bleeding, pneumonia, and also as a result of cardiovascular failure.

Heart damage in patients with HC was detected for the first time back in the 1950s [2]. It was assumed for a long time that these disorders were caused by the toxic effect of alcohol on the heart, and the first reports on cardiac dysfunctions in non-alcoholic HC appeared only in the 1980s [3, 4]. It was revealed that HC was accompanied by impaired cardiac function, and this disorder was called cirrhotic cardiomyopathy (CCM) [5–10].

The primary diagnostic criteria of CCM include signs of systolic dysfunction (decreased ejection fraction less than 55%), a reduction in the cardiac output increase in response to exercise, and pharmacological stimulation [11]. Signs of diastolic dysfunction include decreased E/A ratio (<1; depending on age), an increase in the deceleration of the blood flow velocity in the early diastole phase for more than 200 ms prolongation of isovolumetric relaxation for more than 80 ms. Additional CCM criteria are prolongation of the *QT* interval, inadequate increase in heart rate in response to exercise,

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electromechanical desynchrony, myocardial hypertrophy, increased concentrations of troponin 1, and brain natriuretic peptide in the blood, and an increase in the size of the left atrium [5, 7].

CCM is registered more often in patients aged 45 to 60 years. Significant risk factors influencing CCM formation are the etiology of HC and age [5, 7, 11, 12].

HC patients often note pain in the region of the heart, palpitations, and complain about arterial hypotension and rapid fatigability [13].

According to echocardiography, the ejection fraction of the left ventricle during HC at rest is preserved. Its reduction manifests only under stress (physiological, pharmacological, physical) [11]. In some patients with viral HC, a decrease in global and segmental cardiac strain (the presence of latent systolic dysfunction) is registered [12].

According to numerous studies, diastolic dysfunction of the left and right ventricles develops in patients with HC due to fibrosis, hypertrophy, subendocardial edema, and changes in the structure of myocardial collagen [13]. More pronounced diastole disorders are recorded in patients with ascites and patients with Child-Pugh classes B and C [14–16].

Morphofunctional changes in the heart in patients with viral HC depend on the presence of ascites. In patients with ascites, adverse variants of left ventricular remodeling and increased left atrium and ventricle dimensions are more common [7, 12, 17]. In addition, structural and functional changes occur in the right sections (dilatation of the right ventricle and atrium, thickening of the right ventricle wall), and the pulmonary artery and its branches are dilated [12]. In patients with HC, the pressure in the pulmonary artery system increases with the development of portopulmonary hypertension due to gross changes in the vascular bed of the lungs against the presence of portal hypertension. Hepatopulmonary syndrome is developed because of arterial hypoxemia and intrapulmonary vascular dilatation [17]. The development of these syndromes leads to a sharp decrease in patients' quality of life with relatively safe functioning of the liver and deterioration of prognosis for orthotopic liver transplantation [18].

Approximately half of the patients with HC develop electrophysiological disorders, prolonging the *QT* interval (more than 400 ms), tachycardia, supraventricular, and ventricular extrasystoles. These disorders are hazardous in terms of the development of ventricular arrhythmias and sudden death [10, 12]. However, it is known that after treatment with β-blockers or liver transplantation, normalization of the prolonged *QT* interval is possible [19]. In addition, the literature has shown that in patients with HC with a prolonged *QT* interval, a significant increase in the time interval between electrical and mechanical ventricular systole has been established, and such electrical desynchrony contributes to a further deterioration of myocardial contractility [10].

In patients with HC, the chronotropic response is impaired, so the absence of a proper increase in the heart rate in response to the activation of the sympathetic nervous system and the need for increased cardiac output is detected. Valsalva test, mental stress, physical, or pharmacological stress do not result in a sufficient increase in heart rate. Low heart rate variability is accompanied by the risk of postoperative complications after liver transplantation [9, 19, 20].

It has been revealed that in patients with HC, the parameters characterizing the formation of heart failures such as the blood concentrations of troponin 1 and cerebral natriuretic peptide are increased [7].

Several studies showed that cardiac dysfunction in HC occur due to defects in the functioning and density of β-adrenergic receptors. A decrease in the concentration of Gs-protein occurs because of an increase in the cell membrane permeability and the current density of potassium channels. In addition, an increase in the activity of nitric oxide, carbon monoxide, nuclear factor κB, and imbalance of cannabinoid receptors also contribute to this phenomenon [7, 15, 16].

To date, there are no clinical guidelines for the treatment of CCM. Meanwhile, surgical methods for the treatment and control of portal hypertension are known to lead to a significant deterioration in hemodynamics with the appearance of fatal rhythm disturbances, myocardial ischemia, and pulmonary edema [8, 10].

If clinically significant heart failure develops in a patient, general guidelines for managing such patients are required. The use of angiotensin-converting enzyme inhibitors (resulting from peripheral vasodilation) and cardiac glycosides should be limited. To prevent bleeding from varicose veins of the esophagus, non-selective β-blockers with nitrates are used. Studies have shown that the combination of these drugs reduces cardiac output and the *QT* interval [8, 10, 19, 20]. The use of K-cancrenoatom in patients with HC has been found to have a positive effect on myocardial remodeling and improvement of left ventricular diastolic function [21].

It is noteworthy that in one-third of patients with viral HC, antiviral therapy with interferon drugs in combination with ribavirin for a year had a positive effect on some morphofunctional parameters of the heart (a decrease in the mass of the left ventricular myocardium, a reduction in the left atrium size and systolic pressure in the pulmonary artery were noted) [12, 17, 22].

Liver transplantation is an effective treatment for CCM. After surgery, cardiac functions recover in patients [23]. Meanwhile, orthotopic liver transplantation can deteriorate latent heart failure [24]. For this reason, before such treatment, a thorough examination of each patient is necessary, and electrocardiography, echocardiography, Holter monitoring, stress tests, and coronary angiography are recommended if indicated.

Thus, in patients with HC, the heart is damaged with CCM formation, while the mechanisms of the development of myocardial dysfunction are not fully understood. Therefore, further study of this syndrome development is required for its timely diagnosis and clinical intervention to improve the survival of patients.

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