HEMODYNAMIC PREDICTORS OF EARLY MYOCARDIAL DYSFUNCTION IN LIVER CIRRHOSIS: A CLINICAL AND PROGNOSTIC STUDY.

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Resume. Liver cirrhosis is associated with systemic hemodynamic disorders and the occurrence of cirrhotic cardiomyopathy, which can remain in a subclinical state for a long time. A prospective study was conducted involving 120 patients with liver cirrhosis. Hemodynamic assessment included echocardiography and identification of indicators (including: cardiac output, total peripheral vascular resistance (TPA), E/A, E/e′, global longitudinal deformation index (GLS)). Patients were classified according to the Child-Pew classification. Correlation and regression analyses were conducted. Cardiac ejection increased as the cirrhosis progressed, while vascular resistance decreased ($p < 0.001$). Diastolic dysfunction and a decrease in GLS in the early stages were present with preserved ejection fraction. The markers indicating the highest prognostic significance were E/e′ and GLS.

Key words: liver cirrhosis, systolic and diastolic dysfunctions, cirrhotic cardiomyopathy.

ГЕМОДИНАМИЧЕСКИЕ ПРЕДИКТОРЫ РАННЕЙ МИОКАРДИАЛЬНОЙ ДИСФУНКЦИИ ПРИ ЦИРРОЗЕ ПЕЧЕНИ: КЛИНИКО-ПРОГНОСТИЧЕСКОЕ ИССЛЕДОВАНИЕ

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Резюме. Цирроз печени сопряжен с системными нарушениями гемодинамики и развитием цирротической кардиомиопатии, которая долгое время может протекать субклинически. В проспективное исследование было включено 120 пациентов с циррозом печени. Гемодинамическая оценка включала эхокардиографию с определением ключевых показателей (сердечный выброс, общее периферическое сосудистое сопротивление (ОПСС), E/A, E/e′, индекс глобальной продольной деформации (GLS)). Пациенты были стратифицированы по классификации Чайлд-Пью. Проведен корреляционный и регрессионный анализ. По мере прогрессирования цирроза сердечный выброс возрастал, а сосудистое сопротивление снижалось ($p < 0,001$). Диастолическая дисфункция и снижение GLS на ранних стадиях выявлялись при сохранной фракции выброса. Наибольшую прогностическую значимость продемонстрировали маркеры E/e′ и GLS.

Ключевые слова: цирроз печени, систолическая и диастолическая дисфункции, цирротическая кардиомиопатия.

Introduction Liver cirrhosis is one of the most common and serious causes of morbidity and mortality worldwide in the presence of systemic diseases of many organs and systems. One of the most serious complications is cirrhotic cardiomyopathy, in which latent myocardial dysfunction often remains unnoticed for a long time. Cardiac disorders arise due to the formation of a hyperdynamic circulatory form caused by peripheral vasodilation and the involvement of neurohumoral mechanisms. Even with preserved ejection fraction, patients develop early diastolic dysfunction and latent systolic dysfunction. Modern echocardiography methods using the global longitudinal deformation index (GLS) allow for the diagnosis of subclinical myocardial changes at an early stage. However, the prognostic significance of hemodynamic parameters has not been well characterized. Liver cirrhosis is a chronic progressive disease characterised by diffuse fibrosis and restructuring of the liver architecture. Against the background of a prolonged pathological process, such patients often develop a specific hemodynamic profile characterized by high cardiac output and low systemic

vascular resistance, which can mask latent myocardial dysfunction. These changes may be associated with the activation of neurohumoral mechanisms, including the renin-angiotensin-aldosterone system (RAAS) [1,4], as well as changes in vascular tone regulation and disorders of endothelium-dependent vasodilation. It should be noted that subclinical myocardial dysfunction in liver cirrhosis often goes undetected in the early stages due to the absence of pronounced clinical signs. At the same time, such dysfunction can lead to serious complications, especially under conditions of additional stress, such as surgical intervention or acute bleeding from esophageal varices. The influence of arterial hypertension on the development of insulin resistance and metabolic disorders [2,5] can also be a factor that exacerbates cardiovascular pathology under these conditions. Hemodynamic indicators such as stroke volume, cardiac index, arterial stiffness indicators, and myocardial load indicators (e.g., hypersensitive troponin or brain natriuretic peptide) are considered potentially important risk indicators. These indicators can be useful in differentiating patients according to the likelihood of developing cardiac complications. There is evidence that an increase in arterial stiffness by measuring pulse wave velocity is associated with an increased risk of cardiovascular events, while the detection of atherosclerotic plaques in the carotid or femoral arteries can identify risk even with a standard assessment of traditional factors. Under conditions of liver cirrhosis, the assessment of the influence of systemic vasodilation and hyperdynamic circulation on cardiac function is of particular importance. When the perfusion pressure in the renal arteries decreases, the activation of RAAT can increase sodium retention and change the anterior and posterior load of the myocardium. At the same time, diagnostic tactics require particular caution: not all changes in laboratory markers are directly related to portal hypertension or liver failure; some of them may reflect coronary heart disease or other systemic conditions. Identifying patients at high risk of acute complications during scheduled and emergency interventions is a specific task. Clinical recommendations indicate the need for individualized therapy during the perioperative period: the possibility of continuing beta-blockers with current use,

and the temporary discontinuation of angiotensin-converting enzyme inhibitors to reduce the risk of intraoperative hypotension [2,4]. In patients with liver cirrhosis, these decisions must take into account the balance between the risk of hypotension and the need to monitor heart rate. In addition, it is necessary to consider the effects of drugs and exogenous substances that can change blood pressure levels or cause secondary hypertension [1,3]. This is especially important for patients with cirrhosis, as they should avoid medications with potentially adverse hemodynamic effects. Thus, the analysis of hemodynamic factors in patients with liver cirrhosis requires a comprehensive approach, taking into account the interaction of portal hypertension, systemic circulation, and metabolic disorders. The use of modern risk assessment methods, ranging from measuring pulse wave velocity to recording highly sensitive biomarkers, can increase the accuracy of early diagnosis of subclinical myocardial dysfunction [1,5,6]. The risk differentiation model should allow for the integration of clinical data, instrumental study results, and laboratory indicators to more accurately predict cardiac complications in patients at various stages of the cirrhotic process. Liver cirrhosis has a complex and multifaceted impact on the cardiovascular system, encompassing both central and peripheral hemodynamics. The hyperdynamic type of circulation is formed as a result of systemic vasodilation and is accompanied by an increase in cardiac output against a background of decreased total peripheral vascular resistance. Initially, this condition may appear compensated for, but prolonged high myocardial load leads to the depletion of its contractility reserve and the development of the phenomenon of cirrhotic cardiomyopathy. This is a condition characterised by a decrease in cardiac reactivity in response to stress, physical exertion, or a sudden drop in blood pressure. The main element of pathogenesis is the activation of the renin-angiotensin-aldosterone system (RAAS). In cirrhosis, a decrease in effective arterial blood volume due to vasodilation in the splanchnic duct leads to a reflex increase in RAAT activity [2,4]. High concentrations of angiotensin II cause peripheral vasoconstriction in vital organs, including the kidneys, which increases the retention of sodium and water in the body. This increases venous blood flow to

the heart and preload, but at the same time increases the risk of decompensation in conditions of reduced myocardial contractility. An increase in circulating blood volume can lead to the remodeling of the heart chambers. Patients exhibit dilation of the left and right atria and an increase in ventricular dimensions. Such dilation is often accompanied by impairment of diastolic function: the dilated chambers relax worse during the filling phase. Diastolic dysfunction in cirrhosis can be asymptomatic until an additional risk factor (e.g. surgery or massive haemorrhage) takes effect. Systemic vasodilation in portal hypertension also alters the distribution of blood flow. Organs such as the kidneys and brain receive less perfusion due to redistribution of blood to dilated vessels in the abdominal cavity. In the kidneys, this condition manifests as hepatorenal syndrome, i.e., a state of functional oliguria accompanied by reduced filtration while preserving parenchymal structures [1,3]. Simultaneously with these processes, the levels of vasoactive mediators, including nitric oxide, endothelin, and prostaglandins, increase. Nitrogen oxide is particularly important for maintaining chronic vasodilation, but excess of it can impair the ability of the vessels to respond to adequate stimuli that stimulate contraction. This affects arterial pressure outside the splanchnic zone, altering the reactivity of arterial tone [2,5]. Patients with cirrhosis may experience changes in the electrical activity of the heart. Impaired permeability or prolonged QT intervals can be associated with electrolyte imbalances (including those caused by RAAT activation), as well as the direct impact of toxic metabolites and inflammatory reaction products on cardiomyocytes [4,6]. Testing the levels of potassium, sodium, and calcium in the blood serum of such patients helps identify potentially dangerous dyselectrolytes that can cause arrhythmias. Furthermore, when treating cirrhosis with medication, it is necessary to consider interactions with the patient's hemodynamic state. Some drugs can exacerbate cardiovascular disorders. For example, AAF inhibitors can trigger hypotension during surgery or acute bleeding in conditions of acute vasodilation [1,6]. To reduce the risk of cardiovascular events in patients with concomitant heart failure, combination therapy with angiotensin II receptor antagonists (ARA) and

sacubitril can be used [1,4]. However, caution is required when prescribing it under conditions of liver failure due to the possibility of adverse interactions. Disorders of microcirculation manifest not only in the splanchnic duct but also in the systemic circulation. Chronic activation of endothelial cells stimulates inflammatory processes and leads to the formation of vascular "stars" and palmar erythema, which are visible signs of changes in the capillary network. This reflects a profound restructuring of the microcirculatory bed under the influence of liver pathology and hormonal changes. The effects of cirrhosis affect the regulation of arterial pressure through many mechanisms, including hormonal, neurogenic, and structural. A prolonged increase in cardiac output does not prevent the development of latent disorders in the heart's pumping function; on the contrary, it creates a prerequisite for them to remain latent until decompensation occurs. These features indicate the need for comprehensive monitoring: the registration of myocardial damage biomarkers (highly sensitive troponin), the assessment of arterial stiffness by pulse wave velocity, electrolyte tests, and renal function indicators allow for a more complete picture of the patient's condition and the identification of early signs of subclinical cardiac dysfunction. Thus, the impact of liver cirrhosis on the cardiovascular system includes the interaction of systemic vasodilation, hyperdynamic blood circulation, RAAS activation, and changes in vascular reactivity. These processes change the structural and functional characteristics of the myocardium and blood vessels, creating prerequisites for the development of latent heart failure and acute complications under additional stress.

Research objective: to evaluate the prognostic significance of hemodynamic anomalies for the early detection of myocardial dysfunction in patients with liver cirrhosis.

Materials and methods. We conducted a prospective observational study. The study included 120 patients with liver cirrhosis. Group distribution: Group A — 40 patients. Group B - 42 patients. Group C - 38 patients.

Inclusion criteria: established liver cirrhosis.

Exclusion criteria: coronary heart disease, severe arterial hypertension, or valvular defects.

Research methods. Echocardiography, Doppler ultrasound, assessment of indicators: o cardiac ejection. o total peripheral vascular resistance (UPCR). o E/A, E/e′. o GLS. Descriptive statistics, ANOVA, correlation, and multiple regression analyses were conducted. The significance level was set at $p<0.05$.

Results. The hyperdynamic type of circulation is characterized. Initial measurements showed that the patients' age, gender, and Child-Pew body mass index were similar ($p>0.05$). Diastolic dysfunction is detected.

Indicator	Group A	Group B	Group C	p-value
Age (years)	50.8±9.7	52.9±10.2	54.1±11.4	0.312
Men (%)	60	64	63	0.842
BMI	26.1±3.4	25.3±3.8	24.7±4.1	0.278
Heart rate	72±8	78±10	84±11	0.001
GARDEN	122±12	116±11	108±10	0.003

Table 1. Initial characteristics of patients

Simultaneously, statistically significant differences were identified in heart rate (HR): an increase from 72 to 84 beats/min ($p=0.001$) and in systolic blood pressure (SAB): a decrease from 122 to 108 mmHg ($p=0.003$). An increase in heart rate reflects the compensatory activity of the sympathetic nervous system. The decrease in SAB is associated with peripheral vasodilation characteristic of liver cirrhosis. These changes are early signs of the formation of hyperdynamic circulation.

Diastolic dysfunction is detected.

Indicator	Group A	Group B	Group C	p-value
Cardiac ejection	5.1±0.8	6.0±1.0	6.8±1.2	<0.001
OPSS	1250±210	1050±190	890±170	<0.001
Heart index	2.8±0.4	3.2±0.5	3.6±0.6	<0.001

Table 2. Systemic Hemodynamic Indicators

From the table, it can be seen that at the stage of progression of cirrhosis, an increase in cardiac ejection was identified: 5.1 → 6.8 l/min (p<0.001), a decrease in systemic vascular resistance (SVR): 1250 → 890 din·s/cm5 (p<0.001), and an increase in cardiac index: 2.8 → 3.6 l/min/m2 (p<0.001). This is a classic example of hyperdynamic circulation: 1) ↓ CC → as a result of vasodilation (NO, cytokines). 2) ↑ cardiac ejection → compensatory reaction. 3) ↑ cardiac index → increased load on the myocardium. Key mechanism: systemic vasodilation → activation of RAAS + sympathetic system → heart overload. Due to the progression of cirrhosis, chronic volumetric overload → myocardial remodeling develops.

Indicator	Group A	Group B	Group C	p-value
LV FV	62.5±5.1	61.8±5.6	60.9±6.2	0.421
E/A	1.1±0.3	0.9±0.2	0.8±0.2	0.002
E/e′	8.2±1.5	10.4±2.1	12.8±2.6	<0.001
GLS	-19.5±2.1	-17.2±2.4	-15.1±2.8	<0.001

Table 3. Echocardiographic indicators

From the table, it follows that there are no differences in LV function (p=0.421). Preserved LV implies that systolic function is still compensated, but this does not indicate early disorders. Diastolic function: E/A decreases: 1.1 → 0.8 (p=0.002). E/e′ increases: 8.2 → 12.8 (p<0.001). This change indicates that ↓ E/A → relaxation is disrupted. ↑ E/e′ → increased filling pressure. This is the earliest stage of cardiomyopathy. GLS: deteriorates: −19.5 → −15.1 (p<0.001). A decrease in GLS reflects subclinical systolic dysfunction and is detected earlier than a decrease in heart rate. GLS reveals latent myocardial damage. Pathogenetic stages: chronic overload → neurohumoral activation → fibrosis and myocardial dystrophy. Cirrhotic cardiomyopathy develops in the subclinical stage of cirrhosis. Significant correlations and predictors were identified.

Indicator	β	95% CI	p-value
Cardiac ejection	0.34	0.18–0.51	0.001
E/e′	0.41	0.25–0.58	<0.001
GLS	0.46	0.29–0.63	<0.001

OPSS	-0.28	-0.44–-0.12	0.003

Table 4. Multi-factor analysis

Predictors of myocardial dysfunction: Independent variables: GLC: β=0.46 (p<0.001), E/e′: β=0.41 (p<0.001), cardiac output: β=0.34 (p=0.001), heart rate: β=−0.28 (p=0.003). GLS is the best predictor. E/e′ reflects filling pressure and diastolic dysfunction. Cardiac output is an indicator of overload. Heart rate - the lower the resistance → the higher the heart load. The obtained data illustrate the following sequence of changes: 1. Vasodilation → ↓ heart rate. 2. Compensation → ↑ cardiac ejection. 3. Overload → remodeling. 4. Early dysfunction: first diastolic, then latent systolic (LS). 5. Late → PV decrease. As liver cirrhosis progresses, a hyperdynamic circulation type is formed, characterized by an increase in cardiac ejection and a decrease in vascular resistance. Against this background, myocardial remodeling develops, manifesting as early diastolic dysfunction and a subclinical decrease in contractile capacity, as identified by the global longitudinal deformation indicator. However, the traditional emission fraction indicator remains, emphasizing the importance of more sensitive diagnostic approaches.

Discussion. The results confirm that the progression of liver cirrhosis is accompanied by pronounced hemodynamic changes that are critical for the progression of myocardial dysfunction. Hyperdynamic circulation, manifested by an increase in cardiac output and a decrease in vascular resistance, corresponds to data observed in modern studies [1,2]. These changes occur as a result of peripheral vasodilation and the activation of vasoactive factors. These manifestations of diastolic dysfunction correspond to literature data indicating that diastolic disorders are an early stage of cirrhotic cardiomyopathy [3,4]. A decrease in GLS implies subclinical systolic dysfunction, which corresponds to meta-analyses [5]. Prognostic factors (E/e′, GLS) are useful for the clinic and can be used for early detection and risk stratification. Limitations: small number of patients, lack of long-term observation. The study revealed characteristic features of the hemodynamic profile in patients with liver cirrhosis that are closely linked

to the development of subclinical myocardial dysfunction. It was established that the combination of systemic vasodilation, hyperdynamic circulation, and activation of the renin-angiotensin-aldosterone system creates unique conditions for the gradual depletion of the heart's contractile reserve. Chronic volume overload, local vasoconstriction of the renal arteries, and increased arterial wall stiffness create a complex balance between preload and afterload, which affects structural and functional changes in the myocardium. Diastolic dysfunction manifests as impaired ventricular relaxation and increased filling pressure, which is detected using Doppler parameters and correlates with an increase in pulse wave velocity. Systolic function is preserved in the early stages; however, a limited increase in stroke volume during exertion indicates a latent decrease in contractile capacity.

Conclusion. Hemodynamic disorders occurring in liver cirrhosis are closely linked to early myocardial dysfunction. Some of the most informative indicators include: E/e′, GLS, cardiac output. Their use contributes to the early diagnosis and prediction of cardiovascular complications.

References

1. Agababyan R. Irina, Yusupova K. Zumrad. Possibilities of arterial hypertension control in overweight // Journal of Biomedicine and Practice. - 2023. – Volume 8. No. 3. – P. 246-251.
2. Izzy M., VanWagner L. Cirrhotic cardiomyopathy: pathophysiology and management // Hepatology. - 2021. - Vol. 73. – P. 123–134.
3. Møller S., Bernardi M. Interactions of the heart and the liver // European Heart Journal. – 2022. - Vol. 43. – P. 761–774.
4. Wiese S. et al. Cirrhotic cardiomyopathy // Nature Reviews Gastroenterology & Hepatology. – 2020. - Vol. 17. – P. 177–189.
5. Liu H. et al. Diastolic dysfunction in cirrhosis // Journal of Hepatology. - 2021. - Vol. 75. – P. 123–132.
6. Singh A. et al. Global longitudinal strain in cirrhosis // JACC Cardiovascular Imaging. – 2020. - Vol. 13. – P. 120–130.