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Method for Determining Liver Biomarkers as Predicts of Chronic Heart Failure

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Abstract The conducted study showed that chronic heart failure is accompanied by systemic organ disorders, the severity of which directly depends on the ejection fraction of the left ventricle. In patients with reduced blood pressure, higher levels of NT-proBNP, signs of cardiorenal dysfunction, and a significant increase in serum markers of liver fibrosis - collagen III and IV types - were detected. The obtained data indicate a significant role of chronic venous congestion and hypoxic damage in the formation of hepatic fibrosis in CHF. The use of extracellular matrix biomarkers in combination with clinical and instrumental indicators expands the possibilities of early diagnosis and prognostic assessment of organ complications, which can contribute to optimizing the management tactics of patients with various heart failure phenotypes.

Keywords Chronic heart failure, Ejection fraction, Type III collagen, Type IV collagen, Liver fibrosis, Venous congestion, Biomarkers

1. Introduction

Chronic heart failure (CHF) with reduced left ventricular ejection fraction (LV EF <40%) is a severe clinical and pathophysiological form of cardiovascular pathology characterized by progressive heart pump failure, myocardial remodeling, and pronounced systemic effects on target organs [1,2]. According to the World Health Organization, the prevalence of CHF in developed countries is 2-4% of the adult population, while in the age group over 70 years - more than 10% [3]. In Uzbekistan, according to the statistics of the Ministry of Health (2023), the level of hospitalization due to decompensation of CHF is increasing annually, reflecting the growth in the number of patients with severe forms of the disease.

One of the most vulnerable organs in CHF is the liver, whose function is impaired as a result of chronic congestion in the inferior vena cava system, decreased perfusion, and tissue hypoxia. This leads to the development of what is called "cardiogenic hepatopathy," or "heart liver," manifesting as cytolytic, cholestatic, and hypocoagulation syndromes [4,5].

Laboratory indicators - biochemical markers of liver function (ALT, AST, IF, GGTP, bilirubin, albumin, INR) - are of particular importance, which, in combination with clinical symptoms, allow not only to assess the degree of liver damage but also to predict the severity and outcome of CHF [6,7]. Their change is associated with an increased risk of hospitalization, a deterioration in the quality of life, and an increase in mortality [8].

Despite a large number of studies in the field of CHF, in the practice of primary care physicians, therapists, and cardiologists in Uzbekistan, the importance of laboratory assessment of liver function in cardiological practice is still underestimated. The lack of clear diagnostic and prognostic stratification algorithms using liver biomarkers leads to underestimation of the severity of the condition and insufficient optimization of therapy [9].

The aim of the study is to determine the clinical and prognostic significance of biochemical markers of liver damage in patients with chronic heart failure with reduced left ventricular ejection fraction, with the aim of improving risk stratification, optimizing treatment tactics, and disease prognosis.

2. Materials and Methods of Research

Clinical and laboratory studies were conducted at the Bukhara Multidisciplinary Medical Center between 2023 and 2024. The study included 98 patients who were hospitalized with a diagnosis of chronic heart failure (CHF), as well as 30 practically healthy individuals who constituted the control group.

All patients were divided into two groups depending on the left ventricular ejection fraction (LVEF) determined by echocardiography data (using Simpson's method): • Group I (n = 55): patients with CHF and reduced LV ejection fraction (LV < 40%); • Group II (n = 43): patients with CHF and preserved LV ejection fraction (LV ≥ 50%).

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Clinical, laboratory, and instrumental examination of patients with CHF was conducted, assessing NYHA, EchoCG, ECG, and ultrasound, determining biochemical parameters, NT-proBNP, and serum markers of liver fibrosis (PIIINP, collagen IV, ELISA). Statistical analysis was performed in IBM SPSS 25.0 using correlation and ROC analysis at $p<0.05$.

3. Research Results

Table 1 presents comparative laboratory and biochemical indicators in patients with chronic heart failure, depending on the left ventricular ejection fraction, as well as in the control group. The analysis was conducted to assess the severity of cardiorenal and metabolic imbalances with reduced and preserved myocardial systolic function (table 1).

Analysis of laboratory and instrumental indicators revealed significant differences between patients with reduced ejection fraction (EF <40%) and preserved ejection fraction (EF ≥50%), as well as in comparison with the control group. In patients of group I, a significant increase in the level of NT-proBNP (5647±932 pg/ml) was noted, which significantly exceeded the values of group II (2380±721 pg/ml) and control group (118±45 pg/ml; $p<0.001$), reflecting a more pronounced degree of hemodynamic overload and severity of SLE.

Kidney function indicators also had adverse changes in patients with reduced blood pressure: creatinine levels were significantly higher in group I compared to group II and control (115.6±18.4 versus 99.3±14.7 and 84.7±12.1 μmol/l; $p<0.01$), while glomerular filtration rate significantly decreased (61.2±9.8 ml/min/1.73 m2), indicating the formation of cardiorenal syndrome. In group II, CHF indicators were intermediate and significantly differed from the control values ($p<0.001$).

From the protein metabolism side, in patients with BP <40%, a significant decrease in total blood protein (66.5±4.9 g/l) was revealed compared to the II group (69.4±5.1 g/l) and the control group (73.2±4.7 g/l; $p<0.05$), which may reflect the influence of chronic venous congestion, impaired synthetic liver function, and systemic inflammation.

Carbohydrate and lipid metabolism indicators (glucose and total cholesterol levels) did not differ statistically significantly between the groups ($p>0.05$), although a tendency towards higher glucose values was noted in group I, which may indicate metabolic tension against a background of severe CHF.

To assess the severity of liver fibrotic changes in patients with chronic heart failure depending on the left ventricular ejection fraction, serum levels of type III and IV collagen, reflecting the activity of fibrogenesis and remodeling of the extracellular matrix, were analyzed (table 2).

According to the presented data, in patients of group I with BP <40%, a significant increase in the concentrations of type III collagen (38.5±6.8 ng/ml) and type IV collagen (121.3±18.7 ng/ml) was revealed compared to group II (26.2±5.4 and 89.6±14.9 ng/ml, respectively; $p<0.001$) and the control group (18.1±4.1 and 62.4±10.5 ng/ml). The obtained results indicate more pronounced fibrous changes in the liver with reduced ejection fraction, which is likely due to chronic venous congestion and hypoxic damage to hepatocytes. In patients with preserved atrial fibrillation, collagen indicators had intermediate values, but also significantly exceeded the control, indicating the presence of subclinical fibrosis even with a less severe course of CHF.

4. Conclusions

In patients with chronic heart failure, a decrease in left ventricular ejection fraction is associated with a significant increase in serum collagen levels of types III and IV, reflecting the progression of liver fibrous changes against a background of chronic venous congestion and hypoxia. Determining these markers allows for an objective assessment of the degree of liver damage and can be used for early stratification of the risk of hepatic complications in CHF.

Table 1. Cardiospecific and general laboratory indicators in patients with CHF and in the control group, (M ± SD)

Indicator	Indicator Group I (EF < 40%)	Group II (EF ≥ 50%)	Control group	p (I vs II)
NT-proBNP, pg/ml	5647 ±932	2380 ±721	118 ±45	< 0,001
Creatinine, μmol/l	115,6 ±18,4	99,3 ±14,7	84,7 ±12,1	< 0,01
glomerular filtration rate, ml/min/1.73m2	61,2 ±9,8	75,3 ±11,5	93,1 ±13,4	< 0,001
Total protein, g/l	66,5 ±4,9	69,4 ±5,1	73,2 ±4,7	< 0,05
Glucose, mmol/l	5,9 ±0,8	5,6 ±0,6	5,3 ±0,5	> 0,05
Total cholesterol, mmol/l	4,5 ±0,7	4,7 ±0,8	5,0 ±0,9	> 0,05

Table 2. Examination of type III and IV collagen levels, (M ± SD)

Indicator	Indicator Group I (EF < 40%)	Group II (EF ≥ 50%)	Control group	p (I vs II)
Type III collagen, ng/ml	38,5 ±6,8	26,2 ±5,4	18,1 ±4,1	< 0,001
Type IV collagen, ng/ml	121,3 ±18,7	89,6 ±14,9	62,4 ±10,5	< 0,001

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