NEW ASPECTS OF LABORATORY DIAGNOSTICS OF LIVER FIBROSIS

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Abstract. *Currently, the mortality rate from terminal stage liver fibrosis - cirrhosis - ranks 9th in the world among all causes of death and 6th among people of working age, amounting to 14 to 30 cases per 100 thousand people. The article presents current data on the methods used for the diagnosis of liver fibrosis. To date, liver biopsy, the study of direct and indirect serological markers, as well as instrumental methods are used. Laboratory diagnosis of fibrosis at this stage of development of medicine is aimed at the development, improvement and application of non-invasive diagnostic methods. This is due to the ability to track the dynamics of the disease, the lack of contraindications and other advantages.*

Keywords: *liver fibrosis, liver biopsy, non-invasive diagnosis of liver fibrosis, FibroTest, elastometry.*

The diagnostic assessment of liver fibrosis, a major determinant of disease severity, is an important step in the management of patients with chronic liver diseases. Currently, the mortality rate from terminal stage liver fibrosis- cirrhosis- ranks 9th in the world among all causes of death and 6th among people of working age, amounting to 14 to 30 cases per 100 thousand people. The presence of liver fibrosis is a risk factor for the development of hepatocellular carcinoma. Laboratory diagnostics of liver fibrosis is one of the most pressing problems of modern hepatology. Early and correct determination of the stage of liver fibrosis is necessary to predict the natural course of the disease and prescribe therapy aimed at reducing the progression of the process [4,6].

The "gold" standard for diagnosing liver fibrosis remains a puncture biopsy with histological examination of the material. This type of study is the most accurate. When

assessing the results of a biopsy, a scale for assessing the severity of liver fibrosis is used - the METAVIR system or the Klodell index. The degree of fibrosis is assessed in points- from 0 to 4. There are a number of disadvantages when performing a biopsy. Firstly, complications may develop (up to 3% of cases), since the procedure is invasive. Among the complications, it is necessary to highlight bleeding, including massive, subcapsular hematomas of the liver, including those with a fatal outcome. According to 9 studies, the fatality rate ranges from 0 to 3.3 per 1000 liver biopsies. Additional passes due to unsuitable material result in an increase in complication rates of up to 68%. Secondly, in 15- 35% of cases, when performing a liver puncture biopsy, unchanged tissue is obtained due to the small volume of liver tissue being examined. Erroneous data on the stage of liver fibrosis in biopsy are 10-30%. Thirdly, this method is difficult to apply to study the dynamics of the process. The presence of significant shortcomings has led to the development of numerous non-invasive serological markers of liver fibrosis. The use of two or more noninvasive methods improves diagnostic accuracy compared to using each method alone [3,6].

Serological markers of liver fibrosis are divided into direct and indirect. Direct markers characterize the metabolism of the extracellular matrix- fibrogenesis and fibrinolysis, and have high specificity and sensitivity. The classification of direct serological markers is based on molecular structure. Markers of fibrogenesis include procollagen peptides (carboxyterminal peptide of procollagen type I, aminoterminal peptide of procollagen type III (PIIINP)), hyaluronic acid (hyaluronate), laminin, tissue inhibitor of metalloproteinase-1 (TIMP-1), transforming growth factor-β (TGF-β), collagen IV. During fibrogenesis, the content of type I collagen increases 8-fold. In addition, the ratio of types I/III also changes from 1:1 in a healthy liver to 1:2 in cirrhosis [1].

The most studied class I biomarker is hyaluronic acid. Increased levels of this glycosaminoglycan are observed in liver diseases accompanied by fibrosis. A hyaluronic acid level of 85 mg/l corresponds to severe fibrosis, and 110 mg/l with a sensitivity of 79.2% and a specificity of 89.4% corresponds to liver cirrhosis. A serum level of less than 60 mg/l excludes severe fibrosis or liver cirrhosis with a probability of 93% and 95% [2,5].

Indirect serological tests can detect liver dysfunction. These markers are released in the presence of an inflammatory process in the liver, and the inflammatory process is always accompanied by fibrogenesis. The most specific and sensitive indicators of damage (inflammation and necrosis) are AST (aspartate aminotransferase), ALT (alanine aminotransferase) and their ratio- the de Ritis coefficient (in case of liver fibrosis it exceeds 1). The platelet count reflects the severity of hypersplenism. Indirect markers also include indicators of the acute phase inflammatory reaction- haptoglobin, α2-macroglobulin, apolipoprotein-A1, γ-glutamyl transpeptidase (GGTP). The

quantitative values of these indicators correlate with the clinical stage of liver fibrosis. A relationship is noted between the stage of liver fibrosis in patients with chronic viral hepatitis B and C and indirect serum markers. With an increase in the stage of liver fibrosis, the content of platelets, albumin and cholesterol in the serum decreases and the level of AST, ALT, GGT, alkaline phosphatase, and the average platelet volume increases [1,3].

To increase the diagnostic accuracy of the degree of liver fibrosis, laboratory tests and indices have been developed. The most relevant are indirect markers, combined into complex tests using discriminant analysis. Currently, there are about 40 different indices for determining the stage of liver fibrosis. Patented and commercially available are FibroTest (Paris, France), Fibrometers (Angers, France), FibroSpect II (California, USA), ELF and Hepascore (Australia) [6].

Serological methods of liver fibrosis have many advantages. These include: high sensitivity and specificity at various stages of fibrosis, the possibility of using it to monitor the course of the disease and evaluate the effectiveness of treatment; no complications or contraindications; availability, safety, and economic feasibility.

Instrumental methods for assessing the degree of liver fibrosis include liver imaging methods- ultrasound, MRI, CT, Doppler examination of liver vessels, and liver elastography. Currently, these methods are relevant due to their availability and non-invasiveness. Liver visualization methods allow you to assess the size, density, elasticity, shape, structure of the liver, the presence or absence of formations. In liver fibrosis, there is an increase in density and resistance to portal blood flow. Ultrasound angiography is widely used to assess portal hemodynamics. More informative at the moment is Doppler ultrasonography, which allows measuring the blood flow velocity in the arteries and veins of the liver and spleen and the perfusion index. The pulsation index of the splenic artery in moderate and severe liver fibrosis is 64- 88%, and in liver cirrhosis 74- 86% [7,8].

There are two main types of elastography: compression elastography and shear wave elastography. For evaluation in compression elastography of the liver, the liver fibrosis index LFI (Liver Fibrosis Index) is used, which is calculated automatically based on a formula that takes into account a large number of parameters [4].

Conclusion. Today, the number of people with liver disease exceeds 2 billion people. The high percentage of patients stimulates the development of safer, more accessible, informative and accurate diagnostic methods. The use of FibroTest has reduced the number of necessary biopsies by 46%, and therefore reduce the risk of possible complications. The high sensitivity and specificity of serological markers at the screening stage makes it more likely to deliver the correct degree of fibrosis in time and prescribe the necessary course of treatment, which is important in clinical practice.

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