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# MODERN NON-INVASIVE METHODS OF DIAGNOSTICS OF LIVER FIBROSIS IN CHILDREN

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**Abstract.** The review presents modern non-invasive methods for diagnosing liver fibrosis in children. Biochemical diagnostic tests for fibrosis are described, the structure of the liver parenchyma and the severity of fibrosis are assessed using traditional ultrasound techniques and non-invasive quantitative assessment of the liver structure: Acoustic Structure Quantification (ASQ) with determination of the density index. It is shown that ASQ allows obtaining valuable information about the acoustic structure of liver tissue in visual, parametric and numerical formats, which improves the quality, level and clinical significance of diagnostics.

**Keywords:** children, ultrasound examinations, diagnostics of liver fibrosis, fibroelastometry, quantitative assessment of liver parenchyma structure.

## INTRODUCTION

The development of liver fibrosis is a pressing problem in both adults and children. Liver fibrosis and cirrhosis have a significant impact on the outcome of these forms of pathology and the health status of patients. Over the past 30 years, mortality from liver cirrhosis among the adult population has increased to 1 million per year, and age-standardized mortality has increased by 22% [1]. Mortality in patients with cirrhosis is 66% higher than in the healthy population (HR, 1.66, 95% CI: 0.98-2.82).

## MATERIALS AND METHODS

Fibrosis develops as a result of chronic liver diseases and is characterized by the proliferation of connective tissue of the organ, replacing the damaged liver parenchyma, which occurs with excessive accumulation of extracellular matrix proteins. The rate of this degeneration depends on the cause of the disease, the general condition of the patient and environmental factors [2]. Chronic liver diseases in children are a heterogeneous group, which includes both infectious diseases affecting the liver and metabolic diseases, autoimmune hepatitis, as well as congenital anomalies of the biliary tract, bile acid synthesis, etc. [3]. The most common cause of cirrhosis in newborns is biliary atresia, while in older children, the first place is occupied by infectious etiology of liver damage [4].

## RESULTS AND DISCUSSION

Determining the degree of liver fibrosis, as well as the rate of its progression, is a key step in assessing the quality of life and the likelihood of an unfavorable outcome in patients with chronic liver diseases. With an increase in the stage of fibrosis, the risk of liver transplantation or death increases from 2 to 10.9 times for patients with fibrosis degrees I and IV, respectively (HR, 10.9; 95% CI, 6.06-19.62) [1]. Obviously, modern requirements for effective diagnostics of liver fibrosis with an assessment of the dynamics of structural and functional changes in its parenchyma are a relevant topic for the development of new technologies. Liver biopsy is considered the gold standard for assessing the morphological status of organ tissue [2]. However, liver puncture biopsy is a rather dangerous invasive method, the implementation of which in children is associated with a high risk of postoperative complications [3]. This is an important test in the diagnosis and evaluation of the effectiveness of treatment of chronic liver diseases in children. However, a biopsy should be performed only if the attending physician and parents are confident that it will help the treatment [4]. Undoubtedly, these factors contributed to the intensive development of non-invasive methods for assessing the structure and architecture of the liver. The range

of such methods is quite wide, but the main one is elastography, which is also used in pediatric practice [1]. The limitation of this technique is the ability to determine only the density of the organ, without anatomical orientation [2]. One of the important non-invasive methods for assessing the condition of the liver is a biochemical study of the activity of liver enzymes in the blood. However, when diagnosing liver fibrosis, these data correlate poorly with the degree of its severity. It has been shown that up to 40% of patients with severe cirrhosis had normal ALT values [3]. In clinical practice, the sensitivity and specificity of a number of ratios in assessing the degree of fibrosis in patients with chronic liver disease of various etiologies has been noted [3]. Among them are the AST/ALT ratio, AST to platelet count, Forn index, FIB-4 test, as well as the pediatric NAFLD fibrosis index (PNFI), fibrotest, etc. [4]. These indices are calculated based on the biochemical determination of the activity of ALT, AST, GGT and the content of albumin, cholesterol, haptoglobin, a complete blood count (platelet count), coagulogram (apoprotein A1, prothrombin), as well as the patient's age [1].

The sensitivity of these methods in diagnosing severe fibrosis and cirrhosis ranges from 65 to 98%. High sensitivity is shown for the Forna index in diagnosing liver cirrhosis, while the specificity was 27–76% and was higher for the fibrotest and APRI. However, according to S. Sökücü et al., the fibrotest is not significant in assessing the degree of fibrosis in children with viral hepatitis B [2]. In children with non-alcoholic liver disease, only the AST/erythrocyte index ratio and FIB-4 have diagnostic value in diagnosing the degree of fibrosis [3]. Another diagnostic criterion for liver fibrosis in patients with non-alcoholic liver disease may be the content of hyaluronic acid in the blood. At a concentration of hyaluronic acid (above 2100 ng/ml) with a probability of 89% associated with the presence of fibrosis F2-F4 [4]. It has also been shown that tissue inhibitor of metalloproteinase-1 (TIMP-1) serves as a good marker of the development of fibrosis in children [2]. It is noted that serological markers of fibrosis have significant sensitivity, but

low specificity, which does not interfere with their use in clinical practice. Of certain diagnostic value is also a radionuclide study of the structural and functional state of the liver - hepatoscintigraphy with labeled radiocolloid (99mTc-bromezide, 37-150 MBq), which is based on its removal from the blood due to the phagocytic function of the cells of the reticuloendothelial system (RES), the accumulation of the radiopharmaceutical drug (RPD) in the Kupffer cells of the liver and distribution in the tissue of the organ in accordance with the local values of hepatic blood flow. In this case, cirrhosis of the liver is recognized on the basis of not only the detected changes in its structure, but also hyperfixation of the labeled 99mTc colloid (up to 70%) in the spleen and bone marrow due to reduced uptake of the liver RES. Severe liver cirrhosis with portal hypertension is characterized by scintigraphic signs such as an increase in the left lobe with an uneven distribution of radiopharmaceuticals in it, splenomegaly with high accumulation of activity, and visualization of the spine and pelvic bones [3].

At the same time, more convenient modern ultrasound systems occupy a leading place in non-invasive determination of the liver parenchyma condition and diagnostics of its fibrosis. Ultrasound examination (US) is a very inexpensive visualization study that does not have an ionizing effect. In the diagnosis of fibrotic changes in the liver, ultrasound is effective in tracking the progression of the disease, as well as in detecting fibrotic septa and regeneration nodes. With the progression of cirrhosis, hypertrophy of the caudal and lateral segments of the liver and a decrease in the volume of the right lobe are observed, and in its final stage, general atrophy of the organ is noted. At the same time, at the initial stage of liver fibrosis, there may be a normal ultrasound picture [4]. To identify cirrhotic changes in the liver, at different times it was proposed to use various ultrasound parameters of the organ (blood flow velocity in the portal vein, liver size, presence of nodes, hypertrophy of the caudate lobe, echogenicity, etc.) [1]. In modern ultrasound systems, 3 parameters are used to assess the degree of fibrosis: determination of parenchymal nodularity (both

superficial and internal), assessment of the edge of the liver and its echo structure. Of these, the more sensitive and specific parameter is liver surface nodularity. Moreover, the sensitivity of cirrhosis diagnostics when assessing the degree of parenchymal nodularity is 86% compared to assessing only the unevenness of the organ surface (53%) [2]. Recently, it has been shown that traditional ultrasound is not always an effective method for diagnosing both early fibrosis and severe cirrhosis. The sensitivity of the method in determining severe fibrosis based on the degree of nodularity of the surface, the edge of the liver and the echo structure of the parenchyma was 57, 15 and 41%, respectively.

**CONCLUSION.** In modern conditions, magnetic resonance imaging (MRI) occupies a special place in the diagnosis of liver fibrosis in children, which is capable of providing conditions for visualizing organ tissue in various planes, determining changes in the density of the liver and its parenchyma associated with developing fibrosis or cirrhosis.

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