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MODERN METHODS OF DIAGNOSING NON-ALCOHOLIC FAT DISEASE OF THE LIVER (SCIENTIFIC REVIEW)

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Abstract. The review presents a scientific approach to the modern diagnostic methods used in the timely detection of hepatosis, which is one of the current problems, and their possibilities are highlighted. Along with clinical laboratory examinations, the possibilities of modern radiological examinations - computer tomography, magnetic resonance tomography, and ultrasound examinations in the detection of liver fatty hepatosis are shown. In particular, the capabilities of ultrasound elastography methods, which are rapidly developing today, are widely covered.
Key words: hepatosis, clinical and laboratory research, CT, MRI, ultrasound elastography

ЖИГАРНИНГ НОАЛКОГОЛЛИ ЁГЛИ КАСАЛЛИГИНИ ЗАМОНАВИЙ ТАШХИСЛАШ УСУЛЛАРИ (ИЛМИЙ ШАРХ)

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Аннотация. Шарҳда ҳозирги кунда долзарб муаммолардан бири бўлган гепатозларни ўз вақтида аниқлашда қўлланиладиган замонавий ташхис усулларига илмий ёндашилган ва уларнинг имкониятлари ёритиб берилган. Клиник - лаборатор текширувлар билан бир қаторда замонавий радиологик текширувлар – компьютер томография, магнит резонанс томография, ультратовуш текширувларининг жигар ёғли гепатозларини аниқлашдаги имконлари кўрсатиб ўтилган. Айниқса, ҳозирги кунда тез ривожланиб бораётган ультратовуш эластографияси усулларининг имкониятлари кенг ёритиб берилган.
Калит сўзлар: гепатозлар, клиник – лаборатор текширувлар, КТ, МРТ, ультратовушли эластография.

СОВРЕМЕННЫЕ МЕТОДЫ ДИАГНОСТИКИ НЕАЛКОГОЛЬНОЙ ЖИРОВОЙ БОЛЕЗНИ ПЕЧЕНИ (НАУЧНЫЙ ОБЗОР)

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Аннотация. В обзоре представлен научный подход к современным методам диагностики, применяемым при своевременном выявлении гепатоза, что является одной из актуальных проблем, и освещены их возможности. Наряду с клинико-лабораторными исследованиями, показаны возможности современных рентгенологических исследований - компьютерной томографии, магнитной резонансной томографии, ультразвуковое исследования при выявлении жирового гепатоза печени. В частности, широко освещаются возможности методов ультразвуковой эластографии, которая сегодня бурно развивается.

Ключевые слова: гепатозы, клинико-лабораторные исследование, КТ, МРТ, ультразвуковая эластография

Introduction. According to statistics, non-alcoholic fatty liver disease occurs in the world from 6.3 to 33%, on average every fifth person. In economically developed countries, this figure is 20-35%, in the USA 34%, and in Japan 29% among the adult population [30,33]. In Uzbekistan, NAFLD accounts for 25% and ranks first among liver diseases. It has been noted that NAFLD is more common in women aged 40-50 [30]. The ratio between men and women is 1:3. In recent years, it has also been observed in adolescents and young people aged 10-20 years [15]. It is recognized that its increase is mainly associated with the consumption of semi-finished meals (fast food) and carbonated drinks. Nonalcoholic fatty liver disease (NAFLD) is characterized by excessive accumulation of triglycerides (TG) in the cytoplasm of hepatocytes, increased activity of liver enzymes in the blood, and morphological changes in biopsy samples [21,34]. In such cases, hepatocytes lose their function and gradually transform into adipose tissue. NAFLD is characterized by obesity, an increase in the fatty layer in the abdominal region, and the symptom of metabolic syndrome (MS), which is currently relevant. The disease can progress from simple fat accumulation in the liver to necrotic inflammation, fibrosis, cirrhosis, and hepatocellular carcinoma. There are several causes of this disease, including metabolic, toxic, infectious, alimentary, and cryptogenic factors [8,18]. The disease occurs not only in obese people, but also in thin people. The reason for this is associated with impaired glucose tolerance [2,4]. NSAIDs are at the center of attention not only of therapists and gastroenterologists, but also of cardiologists, endocrinologists, and nephrologists due to the risk of causing cardiovascular diseases, type 2 diabetes mellitus, and kidney diseases[20]. Due to the fact that the disease has been asymptomatic for many years and causes complications in the liver, it requires early detection and treatment measures. Therefore, it is one of the urgent problems in the field of hepatology.

NAFLD includes two types of pathological conditions: steatosis and non-alcoholic steatohepatitis (with the development of fibrosis). Steatosis is the initial stage of steatohepatitis development, and most patients do not show clinical signs [38]. One of the main mechanisms of NAFLD development is insulin resistance (IR), which leads to disruption of lipid, carbohydrate, and fat metabolism, which leads to excessive production of free fatty acids. Recent studies in patients with excess weight or insulin resistance indicate an increasing role of epigenetic factors in the development of "hereditary" NAFLD [13].

The main clinical signs in patients with NAFLD are:

• asthenic syndrome: weakness, fatigue, sleep disturbances;
• dyspeptic syndrome: meteorism, nausea, constipation or diarrhea;
• pain syndrome: in the right hypochondrium and/or feeling of heaviness;
• Hepatosplenomegaly [36].

In the early stages, changes in laboratory parameters can be detected accidentally during continuous monitoring, clinical examination, or examination and treatment of other diseases. Biochemical blood tests usually do not reveal significant changes. For the diagnosis of NAFLD, attention is mainly paid to laboratory indicators of lipid and carbohydrate metabolism, insulin resistance [15]. Among lipid metabolism indicators, changes in triglycerides (TG), total cholesterol (TC), and high-density and low-density lipoproteins are noteworthy. In most patients, there is an increase in TG (≥1.7 mmol/l), a decrease in total cholesterol and low-density lipoproteins, as well as high-density lipoproteins (<0.9 mmol/l in men, <1.0 mmol/l in women) [9]. From biochemical analyses, it is possible to assess NAFLD based on the indicators of alanine transaminase (ALT),

aspargin transaminase (AST), gamaglutamyltransferase (GGT), bilirubin, and proteins. However, the results of biochemical analysis usually do not increase in the early stages of the disease. With the transition to the steatohepatitis stage, ALT and AST levels may increase. 20% of patients have impaired glucose tolerance [34]. **Computed tomography (CT)** is of great importance in the diagnosis of diffuse and focal liver diseases [14]. In particular, the following main features of NAFLD are characterized: a decrease in liver density by 3-5 HU and more units compared to the spleen, and an increase in the density of intrahepatic blood vessels, portal and inferior vena cava compared to liver tissue. In non-alcoholic fatty liver disease, a uniform decrease in liver structure density is observed, which allows for the timely detection of steatosis. However, it does not reliably diagnose steatohepatitis or fibrous changes. A significant disadvantage is that the patient receives a certain amount of radiation, which is limited due to its high cost in primary healthcare joints [14].

The advantages of modern CT, multispiral CT, and magnetic resonance imaging methods are: a high-contrast image of the tissue, the ability to obtain a complete image of the organ in any desired projection, as well as a large amount of information for differential diagnosis. **Magnetic resonance imaging (MRI)** helps to qualitatively assess the degree of hepatosis. However, there are a number of contraindications to perform an MRI. These include the presence of iron prostheses, pregnancy, claustrophobia (fear of enclosed spaces), body weight exceeding 100 kg, and limited examination options for individuals with seizures. The duration of the examination is 30 minutes or more, which is also a relative contraindication to MRI. [1]. Based on histological characteristics, steatosis, steatohepatitis, and cirrhosis of the liver are distinguished in NAFLD. [11].

The main morphological criteria of NAFLD are:

• large-drop steatosis, mainly in the 3rd region of the acini, characterized by the presence of large lipid droplets in the cytoplasm, with the nucleus displaced to the edge of the lobule;

• balloon dystrophy of hepatocytes;

• predominance of lobular inflammation, expressed by polymorphonuclear leukocytes and mononuclear cells;

• perisinusoidal fibrosis in the 3rd region of the acinus - the site of the worst blood supply [17, 25, 36].

Ultrasound diagnostics plays an important role in the early detection of fatty hepatosis among chronic liver diseases and in assessing the effectiveness of treatment methods.This method plays an important role in determining the course of this disease due to the widespread implementation of modern innovative methods from gray scale technology in the early detection of NAFLD, such as Doppler ultrasonography, compression, point and shear wave methods.

The main advantages of ultrasound compared to other imaging methods are: non-invasiveness, ease of implementation, harmlessness to the patient, good tolerance, the ability to study the structure of the liver without the introduction of contrast agents, and the ability to see blood vessels [30]. Allows repeatedly harmless viewing for dynamic observations. The gray scale method (B-mode) is the primary stage of ultrasound examination, distinguished by its simplicity and informativeness [19]. Ultrasound examination on a gray scale provides the necessary information for studying the size, topography, macrostructure of the liver, and the functional state of the bile ducts. However, during gray-scale examinations, only general criteria for NAFLD are assessed (increased echogenicity, decreased conductivity of ultrasound waves in liver tissues, limited visibility of blood vessels) [3]. Pathological fat accumulation in hepatocytes with increased echogenicity of the liver parenchyma makes the periportal area invisible, and ultrasound waves fade and completely disappear as they deepen into the organ [14]. At the same time, the intrahepatic

blood vessels located in the deep and posterior parts of the liver and the area of the diaphragm in the fundus of the liver are poorly visible or not visible at all. The image of the walls of the portal and hepatic veins is blurry, i.e., gives rise to the sign of a flickering image of venous vessels [12]. In this case, the method of color Dopplerography is useful. Color Dopplerography helps to see invisible blood vessels in the gray scale mode. [29]. For greater accuracy in ultrasound examination on a gray scale, it is considered a highly informative method for determining the state of blood vessels in the liver and outside it, blood flow velocity, vascular resistance (RI) and pulsation (PI) indices [32]. In cases where morphological changes in the liver parenchyma are not yet manifested on the gray scale, signs of decreased blood flow velocity in the portal vein are detected early during Doppler ultrasonography. Detection of early changes in the portal vein of the liver is recommended as a screening method for the early detection of diffuse changes in this organ [40].

Since the beginning of the 21st century, a new direction in the science and practice of hepatology, various methods of ultrasound elastography, have been introduced into practice and are being further improved. Several methods of ultrasonic elastography are being widely implemented in practice. Among them, compression elastography (Strain elastography, SE) assesses the elastic properties of tissues by applying pressure to them by pressing the sensor with the hand [4]. Compression elastography shows comparative images of tissues before and after pressure application. [14].

There are three types of displacement-wave elastography.

1. Transient elastography (Transient Elastography, TE).
2. One-dimensional - point (Acoustic Radiation Force Impulse, ARFI)
3. Two-dimensional shear wave elastography (2D Shear Wave Elastography, 2DSWE). **The method of transient elastography (Transient elastography, TE)** was performed using a Fibroscan (France) device, which is used only for liver examination [22]. The elasticity/hardness of the fabric is assessed by measuring the propagation of displacement waves in TE and their velocity (without an echogram). This device operates with two types of sensors: the M sensor has a frequency of 3.5 MHz, measuring to a depth of 2.5-6.5 cm from the skin, the XL sensor has a frequency of 2.5 MHz, measuring to a depth of 3.5-7.5 cm from the skin [24]. For the examination, it is not necessary for the patient to go on an empty stomach and not take medications. With this method, it is possible to determine the stiffness of the tissue. However, due to the inability to obtain a complete picture of the liver, it is also called the "blind" method. It is the primary method for quantitative determination of indicators from early stages of liver fibrosis to cirrhosis at a pressure of kPa. Contraindications for examination may be ascites and obesity [25,29].

In the method of one-dimensional point elastography (Acoustic Radiation Force Impulse, ARFI), the ultrasound sensor creates acoustic waves directed and amplified to a certain point and depth in the tissues of the examined organ. Maximum pressure appears at the focus point. This leads to displacement (deformation) of the surrounding tissues. As a result of the examination, the stiffness of the tissue is assessed by calculating the velocity of the displacement wave at a certain depth [26].

Two-dimensional shear wave elastography (2D Shear Wave Elastography, SWE) is a method for determining stiffness through the propagation of shear waves at different depths through a color image in B-mode. It allows obtaining information about qualitative (color) and quantitative changes in the organ parenchyma in kPa, m/sec. The higher the kPa value, the harder the fabric is [27].

Ҳозирги кунда истиқболли усуллардан бири икки ўлчамли силжиш тўлқинли эластография (2D-Shear Wave Elastography, SWE) ҳисобланади. Жумладан, Currently, one of

the promising methods is two-dimensional shear wave elastography (2D-Shear Wave Elastography, SWE). In particular, A. N. Katrich et al. (2017) compared morphological and 2D shift wave elastography studies of NAFLD in the F2 stage > 6.8 kPa (sensitivity 85.7%, specificity 52.9%); At stage F3 > 8.5 kPa (sensitivity 91%, specificity 57.1%); F4 - > 14 kPa (sensitivity 95.7%, specificity 52.2%). V.N. Diomidova et al. showed that elastography indicators in NAFLD were 94% sensitivity, 97.8% specificity, and 94.9% accuracy. This method is widely used not only for determining rigidity/elasticity, but also for dynamic observations in NAFLD, cirrhosis, and chronic hepatitis. In particular, one of the researchers from Uzbekistan, Saipova G.G., in her scientific research, widely used the method of two-dimensional shift wave elastography in patients with chronic viral hepatitis "C," determined sensitivity indicators of 93%, specificity of 72%, accuracy of 90%.

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