

**Ключевые слова:** первичная открытоугольная глаукома, хирургическое лечение, глаукомная оптическая нейропатия, прогрессирование.

### PROGRESSION OF GLAUCOMA OPTICAL NEUROPATHY AFTER DIFFERENT ANTI-GLAUCOMA OPERATIONS

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**Abstract.** Primary glaucoma, despite certain success of modern methods of conservative, laser and surgical treatment, remains one of the most urgent problems of ophthalmology. Primary glaucoma is a multifactorial disease; there are many known risk factors that lead to its development and progression and, ultimately, to glaucoma optical neuropathy (GON).

**Aim.** Compare the impact of different types of anti-glaucoma operations on the progression of glaucoma optical neuropathy.

**Object and methods.** There were 150 patients (150 eyes) with primary open-angle glaucoma (POAG) of stage I-III under observation. Longevity of the disease is 3-10 years. There were 72 men and 78 women. Age 39-69 years. The level of intraocular pressure (IOP) was  $28.5 \pm 3.0$  mm Hg. All patients received local hypotensive therapy. They made up two groups of observation. All patients before the operation, after 1, 3, 6 months and 1 year were performed visometry, static perimetry on the device Humphrey Field Analyzer model 540 i by Carl Zeiss Meditec in the program 30-2 Threshold for the study of local defects in the field of vision, MD (integral index of deviation of the level of light sensitivity in the field of vision, depending on the age norm and no more than 5,8 dB) and indicators of PSD (degree of local defects, not more than 1.78 dB), tonometry, refractometry, keratopachymetry, biomicroscopy, ophthalmoscopy using Volk Double aspheric or Ocular Small Pupil lenses, optical coherence tomography (OCT) on the device Optovue RTVue 100-2 (version of the program A6.11.0.12). In order to objectivize the progression of the GON, the parameters of the RNFL-layer of the nerve fibers of the retina and the GSS-complex of the ganglion cells were studied, and, if necessary, the anterior segment of the eye (A-OCT) was studied. The stage of the disease was determined by classification of perimetric changes of glaucoma. In the first stage the trabeculectomy (TE) with Ex-Press shunt implantation (69 eyes) was performed; in the second – two-stage treatment: 1 stage – non-penetrating deep sclerectomy (NPDS), 2 stage – laser descemetogoniopuncture in 2 weeks after the 1st stage. We studied the influence of TE with Ex-Press shunt implantation and NPDS followed by laser descemetogoniopuncture on GON progression. The observation period was 1 year.

**Results.** It was established that in 3, 6 months and 1 year after the operation the progression of GON in the first group was 4,35%, 8,69%, 12,3%; in the second group – 1,25%, 9,88%, 13,6% respectively. The frequency of GON at the terms of observation of 3, 6 months and 1 year did not differ in the first and second groups of observation and it was in spite of the fact that the performance of TE with Ex-Press shunt implantation had a lower safety profile and was accompanied by a higher frequency and spectrum of postoperative complications. At the same time, the first group of patients had a more pronounced hypotensive effect. It can be assumed that the character of the postoperative complications and their duration, as well as the IOP level, both low and high, are not the key risk factors for the progression of GON after various types of surgery.

**Conclusion.** 1. The frequency of GON progression in POAG patients in 3, 6 months and 1 year after the performance of TE with the implantation of Ex-Press shunt was 4.35%, 8.69% and 12%, respectively; after NPDS with the following laser descemetogoniopuncture – 1.25%, 9.88%, 13.6%, respectively. 2. Performance of various surgical interventions, both fistulizing (TE with Ex-Press shunt implantation) and non-penetrating (NPDS with subsequent laser descemetogoniopuncture) did not give any advantages in terms of prevention of GON progression in POAG patients in the long term. 3. Prospects of GON prognostication and prophylaxis after surgical treatment of POAG are presented to us in studying of new factors of its prognostication with the subsequent development of new directions of treatment.

**Key words:** primary open-angle glaucoma, surgical treatment, glaucoma optical neuropathy, progression.

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### NON-INVASIVE DIAGNOSTIC CRITERIA FOR STRUCTURAL LIVER CHANGES IN PATIENTS WITH CHRONIC HEPATITIS ASSOCIATED WITH VIRUS C

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**Introduction.** Chronic liver diseases rate among the first in the gastrointestinal tract pathology, which is associated with their prevalence, severity and often adverse outcome of treatment [1]. According to various studies, the chronic hepatitis with subsequent progression to cirrhosis rates number 2-4 among the causes of hospitalization and disability [2]. Therewith, the most serious danger presents hepatitis C, whose virus has af-

ected from 1 to 5% of the population in different countries [3,4].

It is known that in patients with chronic viral hepatitis the stage of fibrosis is one of the decisive factors in the choice of treatment regimen [5]. In addition, the rate of fibrosis progression in case of reinfection with the hepatitis C virus can vary significantly, therefore a timely assessment of the fibrotic transformation progression in the liver remains a topical issue in modern gastroenterology [6].

Today the liver morphology analysis is considered to be the gold standard for detecting fibrosis. However, biopsy may be associated with adverse iatrogenic effects, as well as with a sampling error and a subjective variability of assessment [7,8]. A biopsy sampling error also depends on the amount of tissue taken and the number of biopsies performed. Taking into account the above-mentioned limitations, clinical practice requires non-invasive markers of structural liver changes that are highly accurate and informative.

In recent years the evolution of ultrasound techniques has led to potentially new diagnostic approaches with the ability to quantify liver fibrosis [9,10]. Presently, shear wave elastography (SWE) is considered as one of the most promising imaging techniques. It has a number of advantages, in particular, the efficiency and ability to evaluate the stiffness of large areas of the liver parenchyma [11,12]. However, a lot of primary and even secondary healthcare institutions in Ukraine lack the necessary equipment to conduct SWE, and doctors have only B-mode ultrasound results at their disposal. Meanwhile, an early detection and evaluation of liver fibrosis primarily allows treatment at the stage where most changes are reversed, and plays a crucial role in monitoring the outcome of treatment in patients with chronic hepatitis associated with C virus (CHC).

Therefore, the purpose of the study was to determine non-invasive diagnostic criteria for structural changes in the liver in patients with CHC.

**Object and methods.** 94 patients with CHC were examined, among them 50 were men (53.2%), 44 were women (46.8%). The average age was (46.91±1.16) years old. All patients agreed to participate in the study. The control group consisted of 20 practically healthy individuals, representative by the age and gender.

All the patients underwent a sonological examination of liver and spleen on the ultrasound scanner SONIUS P7, Ultrason (Ukraine-Switzerland) in B-mode. The presence and stage of liver fibrosis were diagnosed by Young's modulus by shear wave elastography (SWE) using a convex scanner with a frequency of 3,5 MHz.

The statistical data processing was performed using MS Excel 2007 and SPSS 16.0 programs. As for the quantitative indicators – the median (Me), the lower (LQ) and upper (UQ) quartiles were calculated, as for the qualitative indicators – the absolute number (n) and the percentage of cases (%). The comparisons of indicators were performed using the chi-square test ( $\chi^2$ ) and the Student's t-test. Differences were considered statisti-

cally significant if the  $\alpha$ -error was less than 5% ( $p < 0.05$ ). The Spearman correlation analysis was performed by calculating the correlation coefficient (r) and its significance (p). Assessment of the diagnostic performance of the indicators was performed using the ROC-analysis to determine the area under the ROC-curve (AUC) and to calculate the optimal thresholds for the maximum sum of sensitivity and specificity. The prognostic parameter estimation was performed by calculating the odds ratio (OR).

**The results of the study and their discussion.** According to the data obtained from the SWE of the liver, 15 (16.0%) patients with CHC had no fibrotic changes, 42 (44.7%) were diagnosed with moderate fibrosis and 37 (39.3%) had marked fibrosis.

When performing ultrasound in B-mode, an increase in liver size was registered in 69 (73.4%) patients with CHC, as compared to the control group, with no significant difference depending on the stage of fibrosis.

The analysis of the frequency of detection of structural changes in the liver parenchyma showed that structural liver changes in the form of heterogeneity were observed in 76 of 94 (80.9%) patients with CHC. In this case, the frequency of this symptom in severe fibrosis group was 1.5 times higher than in the group without fibrosis ( $\chi^2 = 13.65$ ;  $p < 0.001$ ) and than in patients with moderate fibrosis ( $\chi^2 = 13.71$ ;  $p < 0.001$ ) (table 1).

**Table 1 – The frequency of detection of structural changes in the liver parenchyma according to ultrasound data at different stages of fibrosis (n, %)**

Indicator	Patients with CHC (n=94)					
	Without fibrosis (n=15)		Moderate fibrosis (n=42)		Severe fibrosis (n=37)	
	n	%	n	%	n	%
heterogeneous structure	10	66,7	29	69,0	37	100,0* #
granularity of liver parenchyma:						
Medium	15	100,0	33	78,6	5	13,5* #
Coarse	0	0	9	21,4	32	86,5* #
increased echogenicity	4	26,7	34	81,0*	37	100,0* #
weakly positive distal ultrasound attenuation	0	0	10	23,8* #	0	0
thickened walls of portal triads	3	20,0	40	95,2*	37	100,0* #

Notes: 1. \* –  $p < 0.001$  – a significant difference in indicators as compared to the non-fibrosis group; 2. # –  $p < 0.001$  – a significant difference in patients with moderate and severe fibrosis.

Sonographically, the structure of the liver parenchyma is divided into fine-, medium- and coarse-grained. In patients with CHC, regardless of the presence or absence of fibrotic transformation, the fine-grained structure was not observed in any of the cases. The medium-grained structure occurred in all patients without fibrosis and in 78.6% of patients with moderate fibrosis. The frequency of detection of coarse-grained liver parenchyma in patients with CHC with severe fibrosis was 86.5%, which is 4.0 times higher than in the stage of moderate fibrosis ( $\chi^2 = 33.35$ ;  $p < 0.001$ ).

An increase in liver echogenicity was observed in 79.8% of patients with CHC, the frequency of this indicator being higher in patients with the presence of fibrosis (89.9% of cases without any significant difference depending on the stage) and was observed only in 26.7% of patients without fibrosis ( $\chi^2 = 31.23$ ;  $p < 0.001$ ).

Such sonographic indicator of fatty liver dystrophy as a weakly positive distal ultrasound attenuation was observed in almost every fourth (23.8%) patient with CHC, with a moderate liver fibrosis only. Thickening of portal triad walls was 4 times more often diagnosed in patients with liver fibrosis (97.5%) than in patients without fibrotic changes ( $\chi^2 = 59.69$ ;  $p < 0.0001$ ). However, analysis of the frequency of this sign detection showed no significant difference, depending on the stage of fibrotic transformation.

In the course of correlation analysis, the stiffness of the liver parenchyma was directly related to its coarse-grained structure ( $r = 0.65$ ;  $p < 0.05$ ) and the thickened walls of portal triads ( $r = 0.62$ ;  $p < 0.05$ ).

Analysis of the prognostic probability of the use of sonological indicators as non-invasive diagnostic criteria showed that the presence of coarse-grained liver structure 34 times increased the chances of detecting patients with severe fibrosis among the patients with CHC ( $OR = 34,13$ ,  $p < 0,001$ ). Imaging the thickened walls of portal triads and detecting the increased echogenicity significantly increase the probability of diagnosing liver fibrosis in patients with CHC ( $OR = 154$ ,  $p < 0.001$  and  $OR = 24.41$ ,  $p < 0.001$ , respectively).

In patients with CHC, the values of length were in the range of 80.4-199.0 mm, width – 32.0-77.0 mm, vein diameter 6-8 mm. In all the patients, the structure of the spleen parenchyma was unchanged – homogeneous, but the increase in size, both length and width, was determined. Splenomegaly was observed in 33 (35.1%) patients with CHC, of whom only 3 (9.1%) patients had dilatation of the splenic vein. Lymphadenopathy was detected in 26 (27.7%) patients, ascites – in 2 (2.1%) patients.

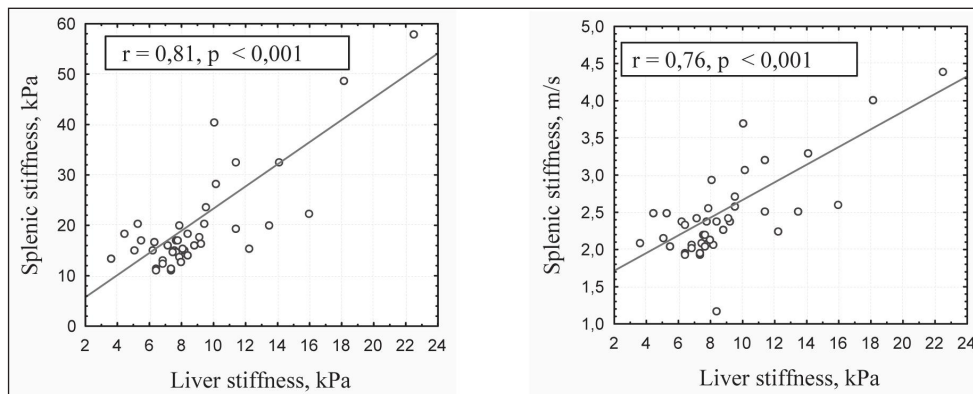
According to SWE results, the median values of spleen stiffness in patients with CHC were significantly higher than in the control group – 16.29 (14.30-22.49) kPa and 2.39 (2.12-2.62) m/s against 14.12 (12.75-16.64) kPa and 2.17 (2.03-2.28) m/s ( $p < 0.05$ ).

According to the SWE assessment of physical parameters characterizing spleen stiffness in patients with CHC depending on the severity of fibrotic changes of

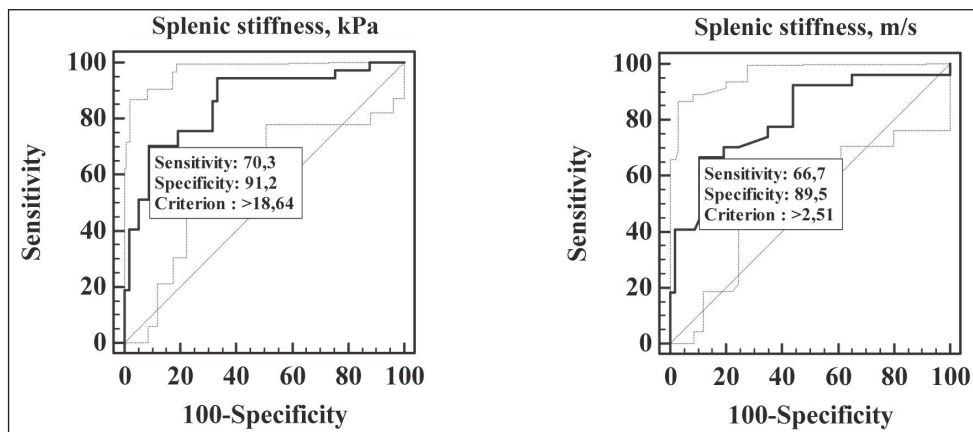
**Table 2 – SWE spleen indicators in patients with CHC depending on the stage of liver fibrosis, Me (Q1, Q2)**

Indicator	Patients with CHC (n=94)					
	Without fibrosis (n=15)		Moderate fibrosis (n=42)		Severe fibrosis (n=37)	
	Me	LQ-UQ	Me	LQ-UQ	Me	LQ-UQ
Young's modulus ( $E_{av}$ ), kPa	15,30	15,12-15,32	15,18	13,40-18,62	20,49* #	17,09-32,59
shear wave propagation velocity ( $V_{sw}$ ), m/s	2,20	2,17-2,39	2,41	2,26-2,49	3,13* #	2,33-3,21

Notes: 1. \* –  $p < 0.001$  – a significant difference in indicators as compared to the non-fibrosis group; 2. # –  $p < 0.001$  – a significant difference in patients with moderate and severe fibrosis.



**Figure 1 – Results of the correlation analysis of indicators of liver and spleen stiffness according to SWE data in patients with CHC.**



**Figure 2 – ROC-analysis results of the use of spleen stiffness indicator as a non-invasive assessment of severe liver fibrosis in patients with CHC.**

the liver, a severe fibrosis was observed to increase 1.3 times the values of the Young's modulus as compared to both – patients without fibrosis and those with a moderate liver fibrosis ( $p < 0.05$ ) (table 2).

As a result of the correlation analysis, the liver stiffness according to SWE in patients with CHC was observed to directly correlate with the splenic stiffness, in kPa ( $r = 0.81$ ;  $p < 0.001$ ) and in m/s ( $r = 0.76$ ;  $p < 0.001$ ) (fig. 1).

When performing ROC analysis, it was determined that at the value of Young's modulus above 18.64 kPa, a severe liver fibrosis at CHC is diagnosed (sensitivity 70.3% and specificity 91.2%) (fig. 2). As for the velocity of shear wave propagation in the spleen, the threshold value for non-invasive evaluation of severe liver fibrosis was more than 2.51 m/s with the sensitivity of 66.7% and the specificity of 89.5%. The obtained values of the

area under the ROC curve for both Young's modulus (AUS = 0.858,  $p < 0.001$ ) and the shear wave propagation rate (AUS = 0.812,  $p < 0.001$ ) testify to the high quality of the proposed diagnostic model.

Thus, the study allowed to determine the criteria for the formation of a risk group for the development and progression of fibrotic changes in the liver in patients with CHC. The established parallels between sonological indices in B-mode and the results of SWE indicate the viability of a comprehensive approach to the early staging of the fibrotic transformation in the liver, which is essential for monitoring and evaluating the prognosis of CHC development.

### Conclusions

1. The diagnostic criteria for the formation of the risk group as for the development of fibrotic changes in pa-

tients with CHC, according to the ultrasound in B-mode, are imaging of the thickened walls of portal triads (OR = 154,  $p < 0,001$ ) and an increased liver echogenicity (OR = 24,41,  $p < 0,001$ ).

2. The coarse-grained liver structure on the gray ultrasound scale (OR = 34.13,  $p < 0.001$ ) and the spleen stiffness according to SWE (OR = 24.58,  $p < 0.001$ ) are the non-invasive diagnostic indicators of severe liver fibrosis in patients with CHC.

**Prospects for further research.** The development of the screening algorithm for the marked liver fibrosis in patients with CHC is considered to be a promising and important scientific direction, with consideration of the taking into account the indicators of structural changes in the liver according to sonoelastography.

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## НЕІНВАЗИВНІ ДІАГНОСТИЧНІ КРИТЕРІЇ СТРУКТУРНИХ ЗМІН ПЕЧІНКИ У ХВОРИХ НА ХРОНІЧНИЙ ГЕПАТИТ, АСОЦІЙОВАНИЙ З ВІРУСОМ С

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**Резюме.** Неінвазивна діагностика фіброзу печінки у хворих на хронічний гепатит асоційований з вірусом С (ХГС) на різних етапах прогресування залишається актуальною в усьому світі. *Мета:* визначити неінвазивні діагностичні критерії структурних змін печінки у хворих на ХГС. *Об'єкт і методи:* обстежено 94 пацієнта з ХГС. Ультразвукове дослідження (УЗД) печінки та селезінки, зсувнохвильову еластографію виконано на сканері Ultrason (Україна-Швейцарія). *Результати:* частота виявлення крупнозернистої паренхіми печінки у пацієнтів з ХГС при вираженому фіброзі 86,5%, що у 4,0 рази вище, ніж при помірному ( $\chi^2=33,35$ ;  $p < 0,001$ ). При проведенні кореляційного аналізу встановлено вірогідний взаємозв'язок між жорсткістю паренхіми печінки та її крупнозернистою структурою ( $r=0,65$ ;  $p < 0,05$ ), ущільненням стінок портальних триад ( $r=0,62$ ;  $p < 0,05$ ), з жорсткістю селезінки в кПа ( $r=0,81$ ;  $p < 0,001$ ) і в м/с ( $r=0,76$ ;  $p < 0,001$ ). Візуалізація ущільнених стінок портальних триад та встановлення підвищеної ехогенності суттєво збільшують ймовірність діагностики структурних змін печінки у хворих на ХГС (OR=154,  $p < 0,001$  та OR=24,41,  $p < 0,001$ , відповідно). Отримані значення площі під ROC-кривою як для модуля Юнга (AUC=0,858,  $p < 0,001$ ), так і для швидкості розповсюдження зсувної хвилі (AUC=0,812,  $p < 0,001$ ) свідчать про високу якість запропонованої діагностичної моделі. *Висновки.* Діагностичними критеріями формування групи ризику розвитку фіброзних змін у хворих на ХГС за даними УЗД є візуалізація ущільнених стінок портальних триад (OR=154,  $p < 0,001$ ) та підвищена ехогенність печінки (OR=24,41,  $p < 0,001$ ). Крупнозерниста структура паренхіми (OR=34,13,  $p < 0,001$ ) та жорсткість селезінки (OR=24,58,  $p < 0,001$ ) є неінвазивними діагностичними ознаками вираженого фіброзу печінки у пацієнтів з ХГС.

**Ключові слова:** хронічний гепатит С, фіброз печінки, зсувнохвильова еластографія, структурні зміни печінки, селезінка.



### НЕИНВАЗИВНЫЕ ДИАГНОСТИЧЕСКИЕ КРИТЕРИИ СТРУКТУРНЫХ ИЗМЕНЕНИЙ ПЕЧЕНИ У БОЛЬНЫХ С ХРОНИЧЕСКИМ ГЕПАТИТОМ, АССОЦИИРОВАННЫМ С ВИРУСОМ С

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**Резюме.** Неинвазивная диагностика фиброза печени у больных хроническим гепатитом ассоциированным с вирусом С (ХГС) на разных этапах прогрессирования остается актуальной во всем мире. *Цель:* определить неинвазивные диагностические критерии структурных изменений печени у больных ХГС. *Объект и методы:* обследовано 94 пациента с ХГС. Ультразвуковое исследование (УЗИ) печени и селезенки в В-режиме, сдвигово-волновая эластография выполнены на сканере Ultrasign (Украина-Швейцария). *Результаты:* частота выявления крупнозернистой паренхимы печени у пациентов с ХГС при выраженном фиброзе составила 86,5%, что в 4,0 раза выше, чем при умеренном фиброзе ( $\chi^2 = 33,35$ ;  $p < 0,001$ ). При проведении корреляционного анализа установлена прямая взаимосвязь между жесткостью паренхимы печени и ее крупнозернистой структурой ( $r = 0,65$ ;  $p < 0,05$ ), уплотнением стенки портальных триад ( $r = 0,62$ ;  $p < 0,05$ ), жесткостью селезенки в кПа ( $r = 0,81$ ;  $p < 0,001$ ) и в м/с ( $r = 0,76$ ;  $p < 0,001$ ). Визуализация уплотненных стенок портальных триад и повышенная эхогенность существенно увеличивают вероятность фиброза печени у больных ХГС (OR = 154,  $p < 0,001$  и OR = 24,41,  $p < 0,001$ , соответственно). Полученные значения площади под ROC-кривой как для модуля Юнга (AUC = 0,858,  $p < 0,001$ ), так и для скорости распространения сдвиговой волны (AUC = 0,812,  $p < 0,001$ ) свидетельствуют о высоком качестве предлагаемой диагностической модели. *Выводы.* Диагностическими критериями формирования группы риска развития фиброзных изменений у больных с ХГС по данным УЗИ является визуализация уплотненных стенок портальных триад (OR = 154  $p < 0,001$ ) и повышенная эхогенность печени (OR = 24,41,  $p < 0,001$ ). Крупнозернистая структура печени (OR = 34,13,  $p < 0,001$ ) и жесткость селезенки (OR = 24,58,  $p < 0,001$ ) значатся неинвазивными диагностическими признаками выраженного фиброза печени у пациентов с ХГС.

**Ключевые слова:** хронический гепатит С, фиброз печени, сдвигово-волновая эластография, структурные изменения печени, селезенка.

### NON-INVASIVE DIAGNOSTIC CRITERIA FOR STRUCTURAL LIVER CHANGES IN PATIENTS WITH CHRONIC HEPATITIS ASSOCIATED WITH VIRUS C

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**Abstract.** Chronic liver diseases rate among the first in the gastrointestinal tract pathology, which is associated with their prevalence, severity and often adverse outcome of treatment. According to various studies, the chronic hepatitis (CHC) with subsequent progression to cirrhosis rates number 2-4 among the causes of hospitalization and disability. *Purpose of the study* to determine non-invasive diagnostic criteria for structural changes in the liver in patients with CHC. *Object and methods.* 94 patients with CHC were examined. All the patients underwent a sonological examination of liver and spleen on the scanner Ultrasign (Ukraine-Switzerland). The presence and stage of liver fibrosis were diagnosed by Young's modulus by shear wave elastography (SWE). *Research results.* According to the data obtained from the SWE of the liver, 15 (16.0%) patients with CHC had no fibrotic changes, 42 (44.7%) were diagnosed with moderate fibrosis and 37 (39.3%) had marked fibrosis. The analysis of the frequency of detection of structural changes in the liver parenchyma showed that structural liver changes in the form of heterogeneity were observed in 76 of 94 (80.9%) patients with CHC. In this case, the frequency of this symptom in severe fibrosis group was 1.5 times higher than in the group without fibrosis ( $\chi^2 = 13.65$ ;  $p < 0.001$ ) and than in patients with moderate fibrosis ( $\chi^2 = 13.71$ ;  $p < 0.001$ ). The frequency of detection of coarse-grained liver parenchyma in patients with CHC with severe fibrosis was 86.5%, which is 4.0 times higher than in the stage of moderate fibrosis ( $\chi^2 = 33.35$ ;  $p < 0.001$ ). In the course of correlation analysis, the stiffness of the liver was directly related to its coarse-grained structure ( $r = 0.65$ ;  $p < 0.05$ ) and the thickened walls of portal triads ( $r = 0.62$ ;  $p < 0.05$ ). Imaging the thickened walls of portal triads and detecting the increased echogenicity significantly increase the probability of diagnosing liver fibrosis in patients with CHC (OR = 154,  $p < 0.001$  and OR = 24.41,  $p < 0.001$ , respectively). As a result of the correlation analysis, the liver stiffness according to SWE in patients with CHC was observed to directly correlate with the splenic stiffness, in kPa ( $r = 0.81$ ;  $p < 0.001$ ) and in m/s ( $r = 0.76$ ;  $p < 0.001$ ). The obtained values of the area under the ROC curve for both Young's modulus (AUS = 0.858,  $p < 0.001$ ) and the shear wave propagation rate (AUS = 0.812,  $p < 0.001$ ) testify to the high quality of the proposed diagnostic model. *Conclusions:* the diagnostic criteria for the formation of the risk group as for the development of fibrotic changes in patients with CHC, according to the ultrasound in B-mode, are imaging of the thickened walls of portal triads (OR = 154,  $p < 0,001$ ) and an increased liver echogenicity (OR = 24,41,  $p < 0,001$ ). The coarse-grained liver structure on the gray ultrasound scale (OR = 34.13,  $p < 0.001$ ) and the spleen stiffness according to SWE (OR = 24.58,  $p < 0.001$ ) are the non-invasive diagnostic indicators of severe liver fibrosis in patients with CHC.

**Key words:** chronic hepatitis C, liver fibrosis, shear wave elastography, structural liver changes, spleen.

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