

# NON-INVASIVE ESTIMATION OF ACTIVITY OF NEKROINFLAMMATORY PROCESS IN THE PATIENTS' LIVER WITH CHRONIC HEPATITIS C

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**Abstract:** 79 patients with chronic hepatitis C were examined. Using the Geno Fibro Test system (an alternative to liver biopsy), the necroinflammatory process of the liver was evaluated in patients. Studies were conducted on the existence of a link between the main biochemical indices and the degree of necroinflammatory activity of the liver in patients. With the use of modern statistical methods of research, the level of ALT is established for minimal, moderate and high activity of the necroinflammatory process in the liver in patients with chronic hepatitis C.

**Keywords:** chronic hepatitis, non-inflammatory process in the liver, modern statistical methods.

## НЕИНВАЗИВНАЯ ОЦЕНКА АКТИВНОСТИ НЕКРОВОСПАЛИТЕЛЬНОГО ПРОЦЕССА В ПЕЧЕНИ У БОЛЬНЫХ ХРОНИЧЕСКИМ ГЕПАТИТОМ С

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**Аннотация:** было обследовано 79 больных хроническим гепатитом С. С помощью системы Geno Fibro Test (альтернатива биопсии печени) проводилась оценка некровоспалительного процесса печени у пациентов. Проведены исследования на наличие связи между основными биохимическими показателями и степенью некровоспалительной активности печени у больных. При использовании современных статистических методов исследования установлен уровень АлАТ для минимальной, умеренной и высокой активности некровоспалительного процесса в печени у больных хроническим гепатитом С.

**Ключевые слова:** хронический гепатит С, некровоспалительный процесс в печени, современные статистические методики.

According to the World Health Organization (WHO) over the past 20 years around the world, there has been a clear trend towards an increase in the number of liver disease causing high mortality. The number of people in the world today with any liver disease exceeds 2 billion people [1].

In chronic hepatitis C (CHC), the definition of the stage of hepatic fibrosis is of particular relevance. Determining the stage of fibrosis is important for predicting the natural course of the disease, assessing the possibilities of therapy and its selection. Evaluation of the index of histological activity is also an important thing. It allows you to judge the possibility of a progressive course of the disease [2]. Liver biopsy is the gold standard for determining the stage of liver fibrosis. However, it has a number of significant disadvantages: invasiveness of the procedure, physical and psychological discomfort, the risk of complications, including lethal ones - the hospitalization frequency after biopsy is 1-5%, serious complications - up to 1%, mortality - 0.12% [3]. For these reasons, interest in non-invasive markers for assessing liver status in CHC has increased significantly in recent years [4].

In connection with this, the purpose of our study was the establishment in patients with CHC of the possibility of using biochemical indicators as criteria for the activity of the necroinflammatory process in the liver.

**Materials and methods.** 79 CHC patients were under observation. 44 of them were women (55.7%), 35 - men (44.3%). The average age of the patients was  $41.16 \pm 2.45$  years. The etiology of the disease was confirmed by the detection of antibodies to HCV in the serum of blood by the method of enzyme immunoassay, RNA-HCV by polymerase chain reaction. All the patients underwent Geno Fibro Test, which is an expert system of biochemical blood counts (the content of alpha2-macroglobulin, haptoglobin, apolipoprotein A1, total bilirubin, GGT (gamma-glutamyltranspeptidase) and ALT) when examining a patient with HCV and includes 4 modules (Fibro Test, detection of viral load, polymorphism of the interleukin-28b receptor gene, genotyping). Evaluation of the liver fibrosis stage was determined by the Fibro Test system, which is a modern alternative to liver biopsy. The MEAVIR scale used in the Fibro Test system is used and involves four stages of liver fibrosis. To assess the viral necrotic inflammatory activity, the Acti Test was used. Four stages of activity were isolated according to the MEAVIR scale: no activity (A0), minimal activity (A1), moderate activity (A2), high activity (A3). The control group consisted of 30 healthy donors. Statistical processing of the data was carried out using Student's t test, including for small samples, correlation coefficient  $r$ , least squares method, Receiver Operating Characteristic (ROC) analysis, and calculation of the AUC (Area Under Curve coefficient).

**Results and its discussion.** The stage of fibrosis F0 was diagnosed in 37 (46.8%), F1 in 9 (11.4%), F2 in 13 (16.5%), F3 in 7 (8.8%), F4 in 13 (16.5%) patients. Genotypes of HCV 1b occurred in 67 (84.8%), 3a - in 11 (13.9%), 2 - in 1 (1.3%) of the examined patients. The homozygous genotype of the IL-28 b C / C receptor was detected in 21 (26.5%), T / T in 16 (20.3%), and heterozygous C / T in 42 (53.2%) patients. Data on the content of alpha2-macroglobulin, haptoglobin, apolipoprotein A1, total bilirubin, and the activity of GGT and ALT in the blood serum of patients with CHC, taking into account the stage of the necroinflammatory process in the liver, are presented in Table. 1.

Table 1. Biochemical parameters of blood serum in patients with CHC, taking into account the stage of necroinflammatory process in the liver

Indicators	F0 (n=37)	F1 (n=9)	F2 (n=13)	F3 (n=7)	F4 (n=13)
<i>The degree of inflammatory necrotic activity (A)</i>	0- 32.4% 1- 37.8% 2-16.2% 3- 13.6%	0 – 22.3% 1 – 33.3% 2 – 11.1% 3 – 33.3%	0- 7.6% 1-23.1% 2- 23.1% 3- 46.2%	3-100%	3-100%
<i>Alpha2-macroglobulin, g / l</i>	1.88±0.18	2.36±0.53	2.67±0.45	2.91±0.60	3.81±0.35 $p_1 < 0,05$ ; $p_2 < 0,05$
<i>Haptoglobin, g / L</i>	1.13±0.13	0.88±0.40	1.2±0.42	0.68±0.40	0.42±0.13 $p_1 < 0,05$
<i>Apolipoprotein A1, g / l</i>	1.65±0.08	1.52±0.18	1.34±0.18	1.37±0.22	1.34±0.10 $p_1 < 0,05$
<i>Bilirubin total, <math>\mu\text{mol/l}</math></i>	9.22±1.35	11.22±2.61	15.08±3.57	12.71±4.80	13.23±3.04
<i>GGT, ED / L</i>	42.38±15.83	53.89±15.49	71.69±23.46	128.43±30.59 $p_1 < 0,05$ ; $p_2 < 0,05$ ;	134.85±45.04
<i>ALT, ED / l</i>	64.65±14.44	122.89±10.52 $p_1 < 0,05$ ;	113.54±52.3	158.2±16.70 $p_1 < 0,05$ ;	219.77±55.55 $p_1 < 0,05$ ;

Note:  $p_1$  - compared to F0,  $p_2$  - compared to F1.

Further, based on the correlation analysis method, studies were conducted on the presence of links between the main biochemical indices and the degree of necroinflammatory activity. A statistically strong relationship was found between the level of ALT and the degree of A ( $R = 0.68$ ).

Considering the most significant connection, it is possible to represent it graphically, using approximating functions constructed on the basis of the method of least squares (Figure 1).

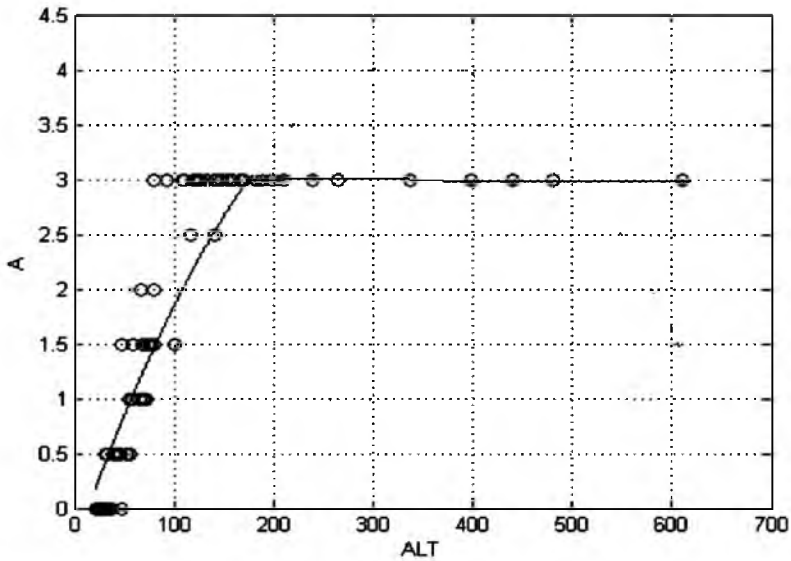


Fig. 1. Dependence of A on the level of ALT, where "o" - measured values; "-" - approximating curve

According to Fig. 1, it is determined that the ALT value in the range from 0 to 40 units/liter corresponds to the activity stage  $A \leq 1$ . At an ALT level of 40 to 59 U/l, the activity stage is determined by  $A \leq 2$  with a probability of 100%, from 60 to 100 U/l - A2 with a probability of 59%. With an ALT content of 100 to 650 U/L, the probability of A3 is 91%.

In order to verify the quality of the study, an ROC analysis of the used value was performed, which makes it possible to obtain an estimate of the accuracy of the proposed method (Fig. 2).

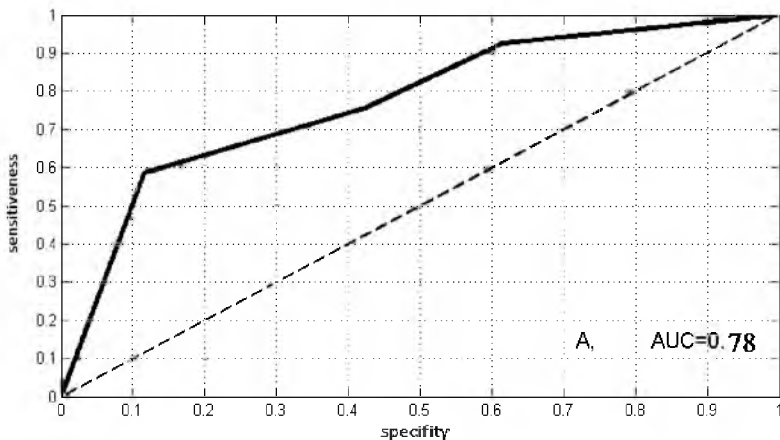


Fig. 2. ROC-curve for the evaluation of stage A on the ALT

Figure 2 shows that the quantitative value of the reliability of the difference in the informativeness of these methods indicates a high quality of the study, since the AUC area under the curve for A and ALT was 0.78.

**Conclusions.** The serum ALT level can be used to evaluate the stage of the necroinflammatory process in the liver. The range of values of this indicator from 0 to 40 U / L indicates the absence or minimal activity of the process (A0-A1), from 40 to 100 U / L - about moderate activity (A3), more than 100 U / L - high activity (A3).

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## NEW METHOD OF MODELING CHRONIC RENAL INSUFFICIENCY ON THE BACKGROUND OF DIABETIC NEPHROPATHY

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**Abstract:** in the experiment, 40 mongrel rabbits of both sexes weighing 1500-2500 g were used on a conventional laboratory ration of the vivarium. Morphological changes in kidney tissue and kidney vessels were studied, at 1, 3, 4, 10 and 20 days after the simulation. Conducted lifetime microcirculation studies in the kidneys of this series of experiments revealed the presence of intravascular disorders in the form of thromboses, an increase in arteriolo-venular relations to 1: 4-1: 6, with marked infiltration of tissues of extra vascular zones. Reproduction of the model of diabetes mellitus, taking into account the pathogenetic significance of the role of sorbitol in the development of angiopathy, makes it possible to obtain, at a reliable level, the possibilities of studying nephropathy.

**Keywords:** chronic renal failure, model of diabetes mellitus, sorbitol, diabetic nephropathy.

## НОВЫЙ СПОСОБ МОДЕЛИРОВАНИЯ ХРОНИЧЕСКОЙ ПОЧЕЧНОЙ НЕДОСТАТОЧНОСТИ НА ФОНЕ ДИАБЕТИЧЕСКОЙ НЕФРОПАТИИ

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**Аннотация:** в эксперименте были использованы 40 беспородных кроликов обоего пола массой 1500-2500 г, находившихся на обычном лабораторном рационе вивария. Изучены морфологические изменения почечной ткани и сосудов почек на 1, 3, 4, 10 и 20 суток после моделирования. Проведенные прижизненные исследования микроциркуляции в почках данной серии опытов выявили наличие внутрисосудистых нарушений в виде тромбозов, увеличение артериоло-венулярных отношений до 1:4-