https://doi.org/10.22416/1382-4376-2023-33-4-7-13
UDC 616.36-002-004.4+616.36-003.826

Practical Aspects of Clinical Manifestations, Pathogenesis and Therapy of Alcoholic Liver Disease and Non-alcoholic Fatty Liver Disease: Expert Opinion

Vladislav V. Tsukanov[1,*], Marina F. Osipenko[2], Ekaterina V. Beloborodova[3], Maria A. Livzan[4], Igor B. Khlynov[5], Sergei A. Alekseenko[6], Yury P. Sivolap[7], Julia L. Tonkikh[1], Alexander V. Vasyutin[1]

[1] *Federal Research Centre "Krasnoyarsk Science Centre" of the Siberian Branch of Russian Academy of Science", Scientific Research Institute of Medical Problems of the North, Krasnoyarsk, Russian Federation*
[2] *Novosibirsk State Medical University, Novosibirsk, Russian Federation*
[3] *Siberian State Medical University, Tomsk, Russian Federation*
[4] *Omsk State Medical University, Omsk, Russian Federation*
[5] *Ural State Medical University, Yekaterinburg, Russian Federation*
[6] *Far-Eastern State Medical University, Khabarovsk, Russian Federation*
[7] *RUDN University, Moscow, Russian Federation*

Aim: to present the results of an expert discussion of modern aspects of the clinical manifestations, pathogenesis and treatment of alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD).
Key points. ALD and NAFLD are characterized by high prevalence and have a significant impact on public health. For the diagnosis of liver pathology, it is important to determine the stage of fibrosis and the severity of the exacerbation of the disease. In the treatment of ALD, it is recommended to achieve abstinence, proper nutrition, the appointment of B vitamins, drugs with cytoprotective activity. In severe hepatitis, corticosteroids may be prescribed. In the treatment of NAFLD, diet and lifestyle modification, weight loss, the use of insulin sensitizers, vitamin E, statins (in the presence of hyperlipidemia) and drugs with metabolic activity are effective.
Currently, a point of view is being actively expressed about the synergism of the action of alcohol and the metabolic syndrome on the development of fibrosis, cirrhosis, and hepatocellular carcinoma. The current international consensus recommends a change in the nomenclature of NAFLD and ALD and proposes the terms "metabolically associated steatotic liver disease" and "metabolically associated alcoholic liver disease".
Conclusion. The closeness of the clinical manifestations and pathogenesis of NAFLD and ALD justifies attention to drugs with metabolic activity, which are recommended by the Russian Gastroenterological Association and Russian Scientific Liver Society for the treatment of these diseases. The experts support the suggestion to quantify alcohol consumption in patients with NAFLD in order to change the management of patients, if necessary.
Keywords: alcoholic liver disease (ALD), non-alcoholic fatty liver disease (NAFLD), alcohol, clinical picture, pathogenesis, treatment
Conflict of interest: the authors declare that there is no conflict of interest.

For citation: Tsukanov V.V., Osipenko M.F., Beloborodova E.V., Livzan M.A., Khlynov I.B., Alekseenko S.A., Sivolap Yu.P., Tonkikh J.L., Vasyutin A.V. Practical Aspects of Clinical Manifestations, Pathogenesis and Therapy of Alcoholic Liver Disease and Non-alcoholic Fatty Liver Disease: Expert Opinion. Russian Journal of Gastroenterology, Hepatology, Coloproctology. 2023;33(4):7–13. https://doi.org/10.22416/1382-4376-2023-33-4-7-13

Практические аспекты клинических проявлений, патогенеза и терапии алкогольной болезни печени и неалкогольной жировой болезни печени: мнение экспертов

В.В. Цуканов[1,*], М.Ф. Осипенко[2], Е.В. Белобородова[3], М.А. Ливзан[4], И.Б. Хлынов[5], С.А. Алексеенко[6], Ю.П. Сиволап[7], Ю.Л. Тонких[1], А.В. Васютин[1]

[1] *ФГБНУ «Федеральный исследовательский центр "Красноярский научный центр" Сибирского отделения Российской академии наук», обособленное подразделение «Научно-исследовательский институт медицинских проблем Севера», Красноярск, Российская Федерация*

[2] *ФГБОУ ВО «Новосибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Новосибирск, Российская Федерация*

[3] ФГБОУ ВО «Сибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Томск, Российская Федерация

[4] ФГБОУ ВО «Омский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Омск, Российская Федерация

[5] ФГБОУ ВО «Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Екатеринбург, Российская Федерация

[6] ФГБОУ ВО «Дальневосточный государственный медицинский университет» Министерства здравоохранения Российской Федерации, Хабаровск, Российская Федерация

[7] ФГАОУ ВО «Российский университет дружбы народов имени Патриса Лумумбы», Москва, Российская Федерация

Цель: изложить результаты экспертного обсуждения современных аспектов клинических проявлений, патогенеза и лечения алкогольной болезни печени (АБП) и неалкогольной жировой болезни печени (НАЖБП).

Основные положения. АБП и НАЖБП характеризуются высокой распространенностью и оказывают значительное влияние на здоровье населения. Для диагностики патологии печени большое значение имеют определение стадии фиброза и тяжести обострения заболевания. В лечении АБП рекомендуется достижение абстиненции, правильное питание, назначение витаминов группы В, препаратов с цитопротективной активностью. При тяжелом гепатите возможно назначение кортикостероидов. В терапии НАЖБП эффективны модификация диеты и образа жизни, снижение веса, применение препаратов, повышающих чувствительность клеток к инсулину, витамина Е, статинов (при наличии гиперлипидемии) и препаратов с метаболической активностью.

В настоящее время активно высказывается точка зрения о синергизме действия алкоголя и метаболического синдрома на развитие фиброза, цирроза и гепатоцеллюлярной карциномы. Современный международный консенсус рекомендует изменить номенклатуру НАЖБП и АБП и предлагает термины «метаболически ассоциированная стеатотическая болезнь печени» и «метаболически ассоциированная алкогольная болезнь печени».

Заключение. Близость клинических проявлений и патогенеза АБП и НАЖБП обосновывает внимание к препаратам с метаболической активностью, которые рекомендуются Российской гастроэнтерологической ассоциацией и Российским обществом по изучению печени для терапии этих заболеваний. Эксперты поддерживают предложение количественно оценивать потребление алкоголя у пациентов с НАЖБП для изменения при необходимости тактики ведения пациентов.

Ключевые слова: алкогольная болезнь печени (АБП), неалкогольная жировая болезнь печени (НАЖБП), алкоголь, клиника, патогенез, лечение

Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Цуканов В.В., Осипенко М.Ф., Белобородова Е.В., Ливзан М.А., Хлынов И.Б., Алексеенко С.А., Сиволап Ю.П., Тонких Ю.Л., Васютин А.В. Практические аспекты клинических проявлений, патогенеза и терапии алкогольной болезни печени и неалкогольной жировой болезни печени: мнение экспертов. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2023;33(4):7–13. https://doi.org/10.22416/1382-4376-2023-33-4-7-13

As part of the forum “ALD and NAFLD: Two sides of the same coin”, which took place on May 20, 2023, leading experts from the Urals, Siberia, the Far East and Moscow discussed various aspects of alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD) with the aim of optimizing diagnostic and treatment tactics for this category of patients. This publication outlines the panel discussion.

In the Introduction, the Forum moderator, Doctor of Medical Science Vladislav V. Tsukanov, cited the definition of non-alcoholic fatty liver disease (NAFLD) given in 1980 by J. Ludwig: “non-alcoholic steatohepatitis is a poorly studied and non-specified disease which histologically simulates alcoholic liver disease (ALD) and can further progress to fibrosis” [1]. A series of works by C. Lieber in the 1980s emphasized the metabolic aspects of the ALD pathogenesis [2]. In 2020, an international expert team proposed the term “metabolically associated fatty liver disease” (MAFLD) as more comprehensively reflecting the essence of fatty liver disease [3]. In the recent 2–3 years, the metabolic aspects of ALD and NAFLD are being heavily discussed on the international level stipulating the topic of the event presented in this article.

Experts delivered monothematic reports at the Forum. Professor E.V. Beloborodova drew attention to the importance of proper patient communication for diagnosing ALD, and the feasibility of using special questionnaires to identify alcohol consumption. For the purpose of diagnosis, it is sensible to determine the stage of liver fibrosis and severity of hepatitis exacerbation using special scales. In ALD therapy, proper nutrition and prescription of B vitamins are of great importance; for severe hepatitis, prednisolone and

antioxidants (ademetionine) can be prescribed. The paper by P.E. Tkachenko et al. demonstrates the efficacy of co-administered prednisolone and ademetionine at 1200 mg/day for 2 weeks in patients with ALD. It improved treatment response by 30 % (p = 0.01), decreased the incidence of hepatorenal syndrome by 20 % (p = 0.03) and reduced total mortality by 10 % [4]. A study by J. Mato et al. in patients with alcoholic liver cirrhosis is well known. During ademetionine therapy (continuously up to 2 years, 1200 mg/day), 2.5-fold ($p < 0.05$) decreased mortality in the group of patients with alcoholic cirrhosis vs. placebo group was reported [5].

Professor Yu.P. Sivolap emphasized the recent European epidemiological studies which demonstrate adverse health effect even of low doses of alcohol. For treatment of ALD, of utmost importance is achieving alcohol abstinence. Up to 75 % of patients are unable to abstain from alcohol consumption. To achieve abstinence, it is crucial to reduce manifestations of comorbid depression, the symptoms of which, along with conventional antidepressants, can be reduced by prescribing ademetionine.

Corresponding member of Russian Academy of Sciences, Professor M.A. Livzan highlighted NAFLD epidemy in the world today. At present, the term "metabolically associated fatty liver disease" (MAFLD) is widely discussed. Diagnosing liver fibrosis in patients with NAFLD is pivotal for prognosis and deciding on treatment tactics. NAFLD and ALD pathogenesis shares common features. No sufficient data on the safety of low alcohol doses in NAFLD are available. The treatment of NAFLD envisages diet and lifestyle modification, weight loss, the use of insulin sensitizers, vitamin E, statins (in hyperlipidemia) and drug products with cytoprotective activity.

Professor S.A. Alekseenko provided case studies of two patients. With outwardly similar clinical symptoms, one of the patients had elevated transaminases and signs of severe liver fibrosis. The second case study results were normal. It became the basis for diagnosing steatohepatitis and prescribing pharmacological treatment in the first case and recording hepatic steatosis with recommendations on the diet lifestyle modification and weight loss in the second case.

Professor M.F. Osipenko drew attention to the lack of objective methods for quantifying patient alcohol consumption which often results in erroneous diagnosis. New studies [6] demonstrate that of all patients with NAFLD, more than a quarter drinks moderate to excessive amounts of alcohol. Key elements of ALD and NAFLD pathogenesis have common features. This complicates the diagnosis. In this regard, a diagnostic approach for MAFLD may be useful.

ALD and NAFLD treatment approaches are based on stratification of pathology progression risk which determines the intensity of conducted therapy. It is reasonable to pay attention to drugs that can optimize metabolic processes that change in liver diseases. Modern scientific papers emphasize ademetionine ability to influence cell division processes, vascularization, proliferation, apoptosis, RNA stabilization, neutralization of lipid peroxidation products, and genomic stability issues [7]. A conclusion was deduced that when steatosis or steatohepatitis is detected, the possible causes of the pathology should be carefully analyzed and patients should be evaluated from the comorbidity point of view, suggesting the possibility of alcohol as a major or additional factor combined with metabolic disorders.

Doctor of Medical Science I.B. Khlynov gave a brief review of Clinical Guidelines on managing patients with NAFLD or ALD and noted that general approaches include correction of metabolic disorders for which ademetionine, ursodeoxycholic acid and essential phospholipids are used. The role of ademetionine in membrane, lipid, neurotransmitters metabolism, in regulation of transsulfuration and formation of glutathione which is a free radicals oxidation regulator [8] has been proven. As is known, the more severe the liver fibrosis the lesser the ademetionine levels in the body. Herewith, any liver pathology accompanied by fibrosis requires replacement therapy [9]. Clinical studies showed efficacy of ademetionine 800 and 1200 mg/day for 4 months in patients with NAFLD [10].

During the panel discussion, which continued not only on May 20 but also online, after the end of the Forum, experts highlighted and discussed the following publications. In 2019 Z. Younossi et al. published a paper with follow-up of 4264 patients with hepatic steatosis for 20 years. In 46 % of patients metabolic dysfunction was found. Alcohol abuse was defined as more than 3 drinks per day (1 drink equals 10 g of alcohol). Mortality was established to be higher among patients with alcohol abuse (32.2 %) vs. patients who consume much alcohol (22.2 %; p = 0.003). Alcohol abuse and metabolic syndrome were independent lethal factors [11].

The January 2023 issue of *Journal of Hepatology*, F. Aberg et al. [12] analyzed contemporary data on the importance of alcohol

consumption and metabolic syndrome in liver diseases development. The authors noted that hepatic steatosis develops in most patients consuming more than 60 g of ethanol per day for a period of more than two weeks [13]. However, the risk of liver cirrhosis increases with systematic consumption of relatively low doses of alcohol. A meta-analysis of 2,629,272 people and 5505 patients with cirrhosis showed that the risk of cirrhosis turns significant with chronic intake of one ethanol serving per day compared with abstainers. Simultaneously, liver cirrhosis and alcoholic hepatitis occur only in 10 to 20 % of patients with chronic alcoholism, which highlights the key role of alcohol effect modifiers including female gender, genetic factors, smoking, gut microbiome condition, comorbidity and metabolic disorders [14].

The results of studying the effect of metabolic syndrome on liver pathology are more unambiguous. The metabolic syndrome has been established to belong to the risk factors of liver fibrosis [15], hepatocellular carcinoma [16] and adverse outcomes of liver disorders [17].

The relationship between alcohol consumption and metabolic syndrome is a complex and controversial issue [18]. Modern papers actively express the point of view about the synergistic effect of alcohol and metabolic syndrome on the development and progression of liver diseases [19]. Possible alcohol consumption and metabolic disorders interaction mechanisms arise from similar histological manifestations of ALD and NAFLD [20], common genetic background (*PNPLA3, TM6SF2, MBOAT7*) [21], combined effect on mitochondrial dysfunction, oxidative stress [22], hepatic stellate cells activation [23], impact on gut microbiota and intestine permeability [24], effect on bile acids metabolism [25]. The authors concluded that studying the interaction between alcohol consumption and metabolic disorders is certainly promising and crucial for optimizing managing patients with liver pathology [12].

In the May 2023 issue of the *Hepatology* journal, the American Association for the Study of Liver Diseases (AASLD) published the latest Clinical Guidelines for the NAFLD patients management noting that alcohol consumption may be crucial in disease progression and should be quantitatively assessed in all patients with NAFLD. The Guidelines state that moderate alcohol consumption increases the probability of liver fibrosis, especially in people with obesity or diabetes mellitus, indicating the synergistic effects of alcohol and metabolic disorders. Therefore, the AASLD recommends people with F2 or higher stage liver fibrosis to abstain from alcohol [26].

The consensus of AASLD, EASL (European Association for the Study of the Liver), APASL (Asia Pacific Association for the Study of the Liver), ALEH (Latin American Association for the Study of the Liver) and other scientific institutions on changing the nomenclature of fatty liver disease being prepared for publication is essential and is freely available from June 2023 in *Journal of Hepatology* [27]. The consensus will be simultaneously published in *Hepatology* and *Annals of Hepatology* journals. In total, 236 people from 56 countries participated in composing of the consensus.

As a result, the term "metabolically associated fatty liver disease" (MAFLD) was chosen as a replacement for the term "non-alcoholic fatty liver disease" (NAFLD). It is recommended to consider the presence of hepatic steatosis and at least one of five cardio-metabolic factors as diagnostic criteria for MAFLD: 1) BMI > 25; waist circumference > 94 cm for men and > 80 cm for women; 2) fasting glucose > 5.6 mmol/L; 3) blood pressure ≥ 130/85 mmHg; 4) blood triglycerides ≥ 1.7 mmol/L; 5) blood high-density lipoprotein cholesterol ≤ 1 mmol/L. In hepatic steatosis without cardio-metabolic manifestations, it is recommended to evaluate the detection of changes as cryptogenic. The decision was made to retain the term steatohepatitis, modifying it to "metabolically associated steatohepatitis" (MASH).

The vast majority of experts voted that alcohol consumption > 30–60 g/day in NAFLD affects the natural course of the disease (95 %) and alters the response to therapeutic interventions (90 %). In this regard, it was decided to maintain restriction of alcohol consumption for the diagnosis of MASLD (MAFLD), and to formulate the diagnosis as "metabolically associated alcoholic liver disease" (MetALD) in patients with alcohol abuse [27].

At the "NAFLD and ALD: Two sides of the same coin" Forum, Russian experts discussed new information in detail and came to conclusion that interaction of alcohol and metabolic factors is a complex process which requires further study. Alcohol consumption can definitely influence the course of NAFLD and potentiate adverse course of liver disease. Drug products affecting metabolic processes, in particular ademetionine, are a matter of priority in patients with ALD (MAALD) and NAFLD (MAFLD).

Summary of the forum moderator Professor V.V. Tsukanov

The issue of correlation between alcohol consumption and metabolic changes indeed seems to be quite complex and of a fundamental nature. Therefore, it is reasonable to continue discussions and Expert Board meetings. Establishing a compact working group will be useful for systematic study of this issue. Works demonstrating the synergistic effect of alcohol and metabolic syndrome on the development of liver pathology are especially noteworthy. The idea to quantitatively assess alcohol consumption in NAFLD patients to alter patients' management tactics appears to be reasonable. The proposal to stratify the indicators of patients with hepatic steatosis to justify the use of metabolic therapy provokes interest. The similarity of the clinical manifestations and pathogenesis of NAFLD and ALD justifies attention to drug products with metabolic activity such as ademetionine recommended by the Russian Gastroenterological Association and Russian Scientific Liver Society for the treatment of these diseases [28, 29]. Undoubtedly, possible changes in the nomenclature of NAFLD and ALD require careful consideration at meetings of the Russian Gastroenterological Association and Russian Scientific Liver Society.

References / Литература

1. *Ludwig J., Viggiano T.R., McGill D.B., Oh B.J.* Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. *Mayo Clin Proc*. 1980;55(7):434–8.
2. *Lieber C.S.* Alcohol and the liver: 1984 update. *Hepatology*. 1984;4(6):1243–60. DOI: 10.1002/hep.1840040625
3. *Eslam M., Newsome P.N., Sarin S.K., Anstee Q.M., Targher G., Romero-Gomez M., et al.* A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. *J Hepatol*. 2020;73(1):202–9. DOI: 10.1016/j.jhep.2020.03.039
4. *Tkachenko P., Maevskaya M., Pavlov A., Komkova I., Pavlov C., Ivashkin V.* Prednisolone plus S-adenosil-L-methionine in severe alcoholic hepatitis. *Hepatol Int*. 2016;10(6):983–7. DOI: 10.1007/s12072-016-9751-4
5. *Mato J.M., Cámara J., Fernández de Paz J., Caballería L., Coll S., Caballero A., et al.* S-adenosylmethionine in alcoholic liver cirrhosis: A randomized, placebo-controlled, double-blind, multicenter clinical trial. *J Hepatol*. 1999;30(6):1081–9. DOI: 10.1016/s0168-8278(99)80263-3
6. *Staufer K., Mangal B., Trauner M.* Detection of unreported alcohol consumption in fatty liver disease. *J Hepatol*. 2023;78(2):e67–9. DOI: 10.1016/j.jhep.2022.10.016
7. *Pascale R.M., Simile M.M., Calvisi D.F., Feo C.F., Feo F.* S-adenosylmethionine: From the discovery of its inhibition of tumorigenesis to its use as a therapeutic agent. *Cells*. 2022;11(3):409. DOI: 10.3390/cells11030409
8. *Noureddin M., Sander-Struckmeier S., Mato J.M.* Early treatment efficacy of S-adenosylmethionine in patients with intrahepatic cholestasis: A systematic review. World *J Hepatol*. 2020;12(2):46–63. DOI: 10.4254/wjh.v12.i2.46
9. *Murphy S.K., Yang H., Moylan C.A., Pang H., Dellinger A., Abdelmalek M.F., et al.* Relationship between methylome and transcriptome in patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2013;145(5):1076–87. DOI: 10.1053/j.gastro.2013.07.047
10. *Барановский А.Ю., Райхельсон К.Л., Марченко Н.В.* Применение S-аденозилметионина (Гептрала®) в терапии больных неалкогольным стеатогепатитом. *Клинические перспективы гастроэнтерологии, гепатологии*. 2010;9(1):3–10. [*Baranovsky A.Yu., Raykhelson K.L., Marchenko N.V. Application* of S-adenosylmethionine (Heptral®) in treatment of patients with non-alcoholic steatohepatitis. *Klinicheskie perspektivy gastroenterologii, gepatologii*. 2010;9(1):3–10. (In Russ.)].
11. *Younossi Z.M., Stepanova M., Ong J., Yilmaz Y., Duseja A., Eguchi Y., et al.* Effects of alcohol consumption and metabolic syndrome on mortality in patients with nonalcoholic and alcohol-related fatty liver disease. *Clin Gastroenterol Hepatol*. 2019;17(8):1625–33. DOI: 10.1016/j.cgh.2018.11.033
12. *Åberg F., Byrne C.D., Pirola C.J., Männistö V., Sookoian S.* Alcohol consumption and metabolic syndrome: Clinical and epidemiological impact on liver disease. *J Hepatol*. 2023;78(1):191–206. DOI: 10.1016/j.jhep.2022.08.030
13. *Crabb D.W., Im G.Y., Szabo G., Mellinger J.L., Lucey M.R.* Diagnosis and treatment of alcohol-associated liver diseases: 2019 practice guidance from the American association for the study of liver diseases. *Hepatology*. 2020;71(1):306–33. DOI: 10.1002/hep.30866
14. *Roerecke M., Vafaei A., Hasan O.S.M., Chrystoja B.R., Cruz M., Lee R., et al.* Alcohol consumption and risk of liver cirrhosis: A systematic review and meta-analysis. *Am J Gastroenterol*. 2019;114(10):1574–86. DOI: 10.14309/ajg.0000000000000340
15. *Long M.T., Zhang X., Xu H., Liu C-T., Corey K.E., Chung R.T., et al.* Hepatic fibrosis associates with multiple cardiometabolic disease risk factors: The Framingham Heart Study. *Hepatology*. 2021;73(2):548–59. DOI: 10.1002/hep.31608
16. *Welzel T.M., Graubard B.I., Zeuzem S., El-Serag H.B., Davila J.A., McGlynn K.A.* Metabolic syndrome increases the risk of primary liver cancer in the United States: A study in the SEER-Medicare database. *Hepatology*. 2011;54(2):463–71. DOI: 10.1002/hep.24397
17. *Ren H., Wang J., Gao Y., Yang F., Huang W.* Metabolic syndrome and liver-related events: A systematic review and meta-analysis. *BMC Endocr Disord*. 2019;19(1):40. DOI: 10.1186/s12902-019-0366-3
18. *Knott C., Bell S., Britton A.* Alcohol consumption and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis of more than 1.9 million individuals from 38 observational studies. *Diabetes Care*. 2015;38(9):1804–12. DOI: 10.2337/dc15-0710
19. *Åberg F., Färkkilä M., Männistö V.* Interaction between alcohol use and metabolic risk factors for liver disease: A critical review of epidemiological studies. *Alcohol Clin Exp Res*. 2020;44(2):384–403. DOI: 10.1111/acer.14271
20. *Boyle M., Masson S., Anstee Q.M.* The bidirectional impacts of alcohol consumption and the metabolic syndrome: Cofactors for progressive fatty liver disease. *J Hepatol*. 2018;68(2):251–67. DOI: 10.1016/j.jhep.2017.11.006
21. *Jamialahmadi O., Mancina R.M., Ciociola E., Tavaglione F., Luukkonen P.K., Baselli G., et al.* Exome-wide association study on alanine aminotransferase identifies sequence variants in the GPAM and APOE associated with fatty liver disease. *Gastroenterology*. 2021;160(5):1634–46.e7. DOI: 10.1053/j.gastro.2020.12.023
22. *Li S., Tan H-Y., Wang N., Feng Y., Wang X., Feng Y.* Recent insights into the role of immune cells in alcoholic liver disease. *Front Immunol*. 2019;10:1328. DOI: 10.3389/fimmu.2019.01328
23. *Ramos-Tovar E., Muriel P.* Molecular mechanisms that link oxidative stress, inflammation, and fibrosis in the liv-

er. *Antioxidants (Basel)*. 2020;9(12):1279. DOI: 10.3390/antiox9121279
24. *Lemmer P., Manka P., Best J., Kahraman A., Kälsch J., Vilchez-Vargas R., et al.* Effects of moderate alcohol consumption in non-alcoholic fatty liver disease. *J Clin Med*. 2022;11(3):890. DOI: 10.3390/jcm11030890
25. *Idalsoaga F., Kulkarni A.V., Mousa O.Y., Arrese M., Arab J.P.* Non-alcoholic fatty liver disease and alcohol-related liver disease: Two intertwined entities. *Front Med (Lausanne)*. 2020;7:448. DOI: 10.3389/fmed.2020.00448
26. *Rinella M.E., Neuschwander-Tetri B.A., Siddiqui M.S., Abdelmalek M.F., Caldwell S., Barb D., et al.* AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*. 2023;77(5):1797–835. DOI: 10.1097/HEP.0000000000000323
27. *Rinella M.E., Lazarus J.V., Ratziu V., Francque S.M., Sanyal A.J., Kanwal F., et al.* A multi-society Delphi consensus statement on new fatty liver disease nomenclature. *J Hepatol*. 2023:S0168-8278(23)00418-X. (Online ahead of print). DOI: 10.1016/j.jhep.2023.06.003
28. *Ивашкин В.Т., Маевская М.В., Жаркова М.С., Котовская Ю.В., Ткачева О.Н., Трошина Е.А. и др.* Клинические рекомендации Российского общества по изучению печени, Российской гастроэнтерологической ассоциации, Российской ассоциации эндокринологов, Российской ассоциации геронтологов и гериатров и Национального общества профилактической кардиологии по диагностике и лечению неалкогольной жировой болезни печени. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии*. 2022;32(4):104–40. [*Ivashkin V.T., Maevskaya M.V., Zharkova M.S., Kotovskaya Yu.V., Tkacheva O.N., Troshina E.A., et al.* Clinical practice guidelines of the Russian Scientific Liver Society, Russian Gastroenterological Association, Russian Association of Endocrinologists, Russian Association of Gerontologists and Geriatricians and National Society for Preventive Cardiology on diagnosis and treatment of non-alcoholic liver disease. *Russian Journal of Gastroenterology, Hepatology, Coloproctology*. 2022;32(4):104–40. (In Russ.)]. DOI: 10.22416/1382-4376-2022-32-4-104-140
29. *Ивашкин В.Т., Маевская М.В., Павлов Ч.С., Сиволап Ю.П., Луньков В.Д., Жаркова М.С. и др.* Клинические рекомендации Российского общества по изучению печени по ведению взрослых пациентов с алкогольной болезнью печени. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2017;27(6):20–40. [*Ivashkin V.T., Mayevskaya M.V., Pavlov Ch.S., Sivolap Yu.P., Lunkov V.D., Zharkova M.S., et al.* Management of adult patients with alcoholic liver disease: Clinical guidelines of the Russian Scientific Liver Society. *Russian Journal of Gastroenterology, Hepatology, Coloproctology*. 2017;27(6):20–40. (In Russ.)]. DOI: 10.22416/1382-4376-2017-27-6-20-40

Information about the authors

Vladislav V. Tsukanov* — Dr. Sci. (Med.), Professor, Head of the Clinical Department for Gastrointestinal Pathology in Adults and Children, Federal Research Centre "Krasnoyarsk Science Centre" of the Siberian Branch of Russian Academy of Science", Scientific Research Institute of Medical Problems of the North.
Contact information: gastro@impn.ru;
660022, Krasnoyarsk, Partizana Zheleznyaka str., 3G.
ORCID: https://orcid.org/0000-0002-9980-2294

Marina F. Osipenko — Dr. Sci. (Med.), Professor, Head of the Department of Propaedeutics of Internal Diseases at the Department of General Medicine, Novosibirsk State Medical University.
Contact information: ngma@bk.ru;
630091, Novosibirsk, Krasny Avenue, 52.
ORCID: https://orcid.org/0000-0002-5156-2842

Ekaterina V. Beloborodova — Dr. Sci. (Med.), Professor, Professor of the Department of Hospital Therapy at the Department of General Medicine, Siberian State Medical University.
Contact information: belobekaterina@yandex.ru;
634050, Tomsk, Moskovsky Highway, 2.
ORCID: https://orcid.org/0000-0002-8776-5924

Maria A. Livzan — Dr. Sci. (Med.), Professor, Correspondent Member of RAS, Head of Faculty Therapy and Gastroenterology Department, Rector, Omsk State Medical University.
Contact information: mlivzan@yandex.ru;
644099, Omsk, Lenina str., 12.
ORCID: https://orcid.org/0000-0002-6581-7017

Сведения об авторах

Цуканов Владислав Владимирович* — доктор медицинских наук, профессор, заведующий клиническим отделением патологии пищеварительной системы взрослых и детей ФГБНУ «Федеральный исследовательский центр «Красноярский научный центр» Сибирского отделения Российской академии наук», обособленное подразделение «Научно-исследовательский институт медицинских проблем Севера».
Контактная информация: gastro@impn.ru;
660022, г. Красноярск, ул. Партизана Железняка, 3г.
ORCID: https://orcid.org/0000-0002-9980-2294

Осипенко Марина Федоровна — доктор медицинских наук, профессор, заведующая кафедрой пропедевтики внутренних болезней лечебного факультета ФГБОУ ВО «Новосибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: ngma@bk.ru;
630091, г. Новосибирск, Красный просп., 52.
ORCID: https://orcid.org/0000-0002-5156-2842

Белобородова Екатерина Витальевна — доктор медицинских наук, профессор, профессор кафедры госпитальной терапии лечебного факультета ФГБОУ ВО «Сибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: belobekaterina@yandex.ru;
634050, г. Томск, Московский тракт, 2.
ORCID: https://orcid.org/0000-0002-8776-5924

Ливзан Мария Анатольевна — доктор медицинских наук, профессор, член-корреспондент РАН, заведующая кафедрой факультетской терапии и гастроэнтерологии, ректор ФГБОУ ВО «Омский государственный медицинский университет Министерства здравоохранения Российской Федерации.
Контактная информация: mlivzan@yandex.ru;
644099, г. Омск, ул. Ленина, 12.
ORCID: https://orcid.org/0000-0002-6581-7017

* Corresponding author / Автор, ответственный за переписку

Igor B. Khlynov — Dr. Sci. (Med.), Associate Professor at the Department of Faculty Therapy and Geriatrics, Ural State Medical University.
Contact information: hlinov.doc@yandex.ru;
620029, Ekaterinburg, Repina str., 3.
ORCID: https://orcid.org/0000-0002-0944-9811

Sergei A. Alekseenko — Dr. Sci. (Med.), Professor, Head of the Department of Hospital Therapy at the Department of General Medicine, Far-Eastern State Medical University.
Contact information: k_gter@mail.fesmu.ru;
680000, Khabarovsk, Muravyov-Amursky str., 35.
ORCID: https://orcid.org/0000-0003-1724-9980

Yury P. Sivolap — Dr. Sci. (Med.), Professor of the Department of Psychiatry, Psychotherapy and Psychosomatic Pathology, RUDN University.
Contact information: yura-sivolap@yandex.ru;
117198, Moscow, Mikloukho-Maklaya str., 6.
ORCID: https://orcid.org/0000-0002-4494-149X

Julia L. Tonkikh — Cand. Sci. (Med.), Leading Researcher of the Clinical Department for Gastrointestinal Pathology in Adults and Children, Federal Research Center "Krasnoyarsk Science Center" of the Siberian Branch of Russian Academy of Science", Separate Division "Scientific Research Institute of Medical Problems of the North".
Contact information: tjulia@bk.ru;
660022, Krasnoyarsk, Partizana Zheleznyaka str., 3G.
ORCID: https://orcid.org/0000-0001-7518-1895

Alexander V. Vasyutin — Cand. Sci. (Med.), Senior Researcher of the Clinical Department for Gastrointestinal Pathology in Adults and Children, Federal Research Center "Krasnoyarsk Science Center" of the Siberian Branch of Russian Academy of Science", Separate Division of "Scientific Research Institute of Medical Problems of the North".
Contact information: alexander_vasyutin@mail.ru;
660022, Krasnoyarsk, Partizana Zheleznyaka str., 3G.
ORCID: https://orcid.org/0000-0002-6481-3196

Хлынов Игорь Борисович — доктор медицинских наук, доцент кафедры факультетской терапии и гериатрии ФГБОУ ВО «Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: hlinov.doc@yandex.ru;
620029, г. Екатеринбург, ул. Репина, 3.
ORCID: https://orcid.org/0000-0002-0944-9811

Алексеенко Сергей Алексеевич — доктор медицинских наук, профессор, заведующий кафедрой госпитальной терапии лечебного факультета ФГБОУ ВО «Дальневосточный государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: k_gter@mail.fesmu.ru;
680000, г. Хабаровск, ул. Муравьева-Амурского, 35.
ORCID: https://orcid.org/0000-0003-1724-9980

Сиволап Юрий Павлович — доктор медицинских наук, профессор, профессор кафедры психиатрии, психотерапии и психосоматической патологии ФГАОУ ВО «Российский университет дружбы народов имени Патриса Лумумбы».
Контактная информация: yura-sivolap@yandex.ru;
117198, г. Москва, ул. Миклухо-Маклая, 6.
ORCID: https://orcid.org/0000-0002-4494-149X

Тонких Юлия Леонгардовна — кандидат медицинских наук, ведущий научный сотрудник клинического отделения патологии пищеварительной системы взрослых и детей ФГБНУ «Федеральный исследовательский центр «Красноярский научный центр» Сибирского отделения Российской академии наук», обособленное подразделение «Научно-исследовательский институт медицинских проблем Севера».
Контактная информация: tjulia@bk.ru;
660022, г. Красноярск, ул. Партизана Железняка, 3г.
ORCID: https://orcid.org/0000-0001-7518-1895

Васютин Александр Викторович — кандидат медицинских наук, старший научный сотрудник клинического отделения патологии пищеварительной системы взрослых и детей ФГБНУ «Федеральный исследовательский центр «Красноярский научный центр» Сибирского отделения Российской академии наук», обособленное подразделение «Научно-исследовательский институт медицинских проблем Севера».
Контактная информация: alexander_vasyutin@mail.ru;
660022, г. Красноярск, ул. Партизана Железняка, 3-г.
ORCID: https://orcid.org/0000-0002-6481-3196

Submitted: 30.06.2023 Accepted: 01.08.2023 Published: 30.08.2023
Поступила: 30.06.2023 Принята: 01.08.2023 Опубликована: 30.08.2023