

O.O. Abrahamovych, M.O. Abrahamovych, M.L. Farmaha, Y.L. Leshchuk, L.V. Tsyhanyk,  
T.I. Farmaha, Y.S. Leshchuk  
Danylo Halytsky Lviv National Medical University, Lviv

## SYNTROPIC AND ASSOCIATED COMORBID LESIONS OF THE CARDIOVASCULAR SYSTEM IN PATIENTS WITH LIVER CIRRHOSIS

e-mail: leshchuk\_yaryna@meduniv.lviv.ua

Liver cirrhosis is a common disease occurring mainly among people of working age and frequently resulting in lethal outcomes. The causes of such epidemiology of liver cirrhosis are syntropic comorbid lesions, in particular lesions of the circulatory system organs. The study was carried out in three consecutive steps, namely: in the first phase the proportion of patients with liver cirrhosis with extrahepatic cardiovascular lesions was revealed, in the second, the frequency of each individual cardiovascular disease in patients was evaluated, and in the third phase the frequency of cardiovascular system lesions in every severity class of liver cirrhosis in accordance with C.G. Child-R.N. Pugh criteria and correlation between their incidence and class of cirrhosis were revealed. 81.3 % of patients with liver cirrhosis have lesions of the circulatory system, among which cirrhotic cardiomyopathy and disorders in the system of blood pressure regulation with the emergence of persistent arterial hypotension have common pathogenetic mechanisms with liver cirrhosis, namely, they are syntropic, whilst postinfarction cardiosclerosis, angina pectoris, acquired heart defects, and painless form of coronary heart disease are concomitant.

**Key words:** liver cirrhosis, cardiomyopathy, arterial hypertension, syntropic lesions.

O.O. Абрагамович, М.О. Абрагамович, М.Л. Фармага, Я.Л. Лещук, Л.В. Циганик,  
Т.І. Фармага, Є.С. Лещук

## СИНТРОПІЧНІ І СУПУТНІ КОМОРБІДНІ УРАЖЕННЯ СИСТЕМИ КРОВООБІГУ У ХВОРИХ НА ЦИРОЗ ПЕЧІНКИ

Цироз печінки є поширеною хворобою переважно людей працездатного віку та нерідко призводить до летальних наслідків. Причинами такої епідеміології цирозу є синтропічні коморбідні ураження, зокрема ураження органів системи кровообігу. Дослідження проводили у три послідовні кроки, а саме: на першому було виявлено частку хворих на цироз печінки з позапечінковими кардіоваскулярними ураженнями, на другому – вивчено частоту кожної окремої кардіоваскулярної недуги у хворих, а на третьому – визначено частоту уражень органів системи кровообігу у кожному класі тяжкості цирозу печінки згідно критеріїв С.Г. Child-R.N. Pugh та виявлено зв'язок між їх частотою і класом цирозу. У 81,3 % хворих на цироз печінки зустрічаються ураження системи кровообігу, серед яких цирозна кардіоміопатія і порушення у системі регулювання артеріального тиску із виникненням стійкої артеріальної гіпотензії, які мають спільні патогенетичні механізми з цирозом, тобто є синтропічними, а постінфарктний кардіосклероз, стенокардія, набуті вади серця та безбольова форма ішемічної хвороби серця – супутніми.

**Ключові слова:** цироз печінки, кардіоміопатія, артеріальна гіпертонія, синтропічні ураження.

*The study is a fragment of the research project “Mono- and comorbid lesions of internal organs: risk factors; etiology; pathogenesis; diagnostics; clinical features of the course; treatment; prevention”, state registration No. 0122U000169.*

Liver cirrhosis (LC) is one of the crucial and extremely complex issues of clinical hepatology as it is a common disease mainly occurring among people of working age and frequently resulting in lethal outcomes [2], which is predetermined by syntropic comorbid lesions of other organs and systems [1].

Since the circulatory system dominates the vital function of the human body, determination of cardiovascular system lesions pathogenetically caused by LC is particularly relevant [3, 4, 7, 10].

Cardiovascular complications in liver cirrhosis combine cardiac dysfunction and changes in the type of systemic hemodynamics. These complications are studied both in Ukraine and abroad, primarily due to their high prevalence (occur in 90.0 % of patients with sub- and decompensated LC) [2, 9]. The special interest of scientists in this topic is explained by the proven leading pathogenetic role of cardiovascular lesions in the occurrence of multiple organ failure, increased mortality, especially in the decompensation of the pathological process and complicated treatment of such patients [5, 6, 8].

However, impairment of the circulatory system in patients with LC requires further elucidation of the pathogenetic mechanisms of their occurrence, which will justify new principles of effective treatment of this category of critically severe patients.

**The purpose** of the study was to detect comorbid lesions of the circulatory system in patients with liver cirrhosis with the elimination of syntropic and concomitant lesions.

**Materials and methods.** After obtaining written informed consent in accordance with the Helsinki Declaration of Human Rights principles, 603 patients were randomly included in the study with pre-stratification in the presence of an LC, which were examined and treated during the period of 2010–2015 in the Lviv Regional Hepatology Center, established on the basis of Department of Internal Medicine No. 1 of Danylo Halytsky Lviv National Medical University and Gastroenterology Department of the Municipal Non-Profit Institution of the Lviv Regional Council “Lviv regional hospital”. Among them, 445 men (73.8 %) and 158 women (26.2 %), aged 19 to 80 years (mean age  $49.2 \pm 10.6$  years) were included. According to the C.G. Child-R.N. Pugh classification criteria, patients were divided into three classes – A, B, and C by severity. Accordingly, LC class A was detected in 210 patients (34.8 %), class B – in 203 patients (33.7 %), and class C – in 190 patients (31.5 %).

All patients underwent a comprehensive clinical laboratory and instrumental examination of the circulatory system organs in accordance with the requirements of the state of the art medicine (Order of the Ministry of Health of Ukraine No. 436 of 03.07.2006: On approval of protocols of providing medical care in the speciality “Cardiology”). Cardiovascular diseases were diagnosed on the basis of the approved criteria: cirrhotic cardiomyopathy (CCMP) – signs of electrical (electrocardiographic interval  $Q-Tc < 0.44$  s), diastolic and/or systolic myocardial dysfunctions and/or alteration of the structure of the heart chambers, registered by echocardiography [3]; persistent arterial hypertension – increase in systolic blood pressure  $\geq 140$  mm Hg and/or diastolic blood pressure  $\geq 90$  mm Hg, recorded by at least two-time tonometry during two or more consecutive visits; persistent arterial hypotension – a simultaneous decrease in systolic blood pressure  $< 105$  mm Hg and diastolic blood pressure  $< 65$  mm Hg, recorded by at least two tonometry sessions during two or more consecutive visits; postinfarction cardiosclerosis based on the medical history and electrocardiography; angina pectoris based on the medical history and bicycle ergometry exercise testing results; acquired heart defects based on medical history data and results of echocardiography; painless myocardial ischemia based on medical history data and bicycle ergometry exercise testing results.

The study was carried out in three consecutive steps, namely: in the first phase the proportion of patients with LC with extrahepatic cardiovascular lesions was revealed, in the second, the frequency of each individual cardiovascular disease in patients with LC was evaluated, and in the third phase the frequency of cardiovascular system lesions for every severity class of LC in accordance with C.G. Child-R.N. Pugh criteria and correlation between their incidence and class of cirrhosis were revealed.

The statistical processing of the obtained results was performed using Excel (2010 Microsoft) software using descriptive statistics and z-criterion for comparison of two samples. The difference was considered statistically significant when  $p < 0.05$ .

**Results of the study and their discussion.** At the first stage of the study, complaints of patients with LC, their history, the results of clinical examination, laboratory and instrumental examinations were studied in detail. Based on the information obtained, it was found that 490 (81.26 %) of patients with LC have extrahepatic lesions of the circulatory system.

The incidence of extrahepatic cardiovascular diseases in patients with LC, which was the second stage of the study, is given in fig. 1.

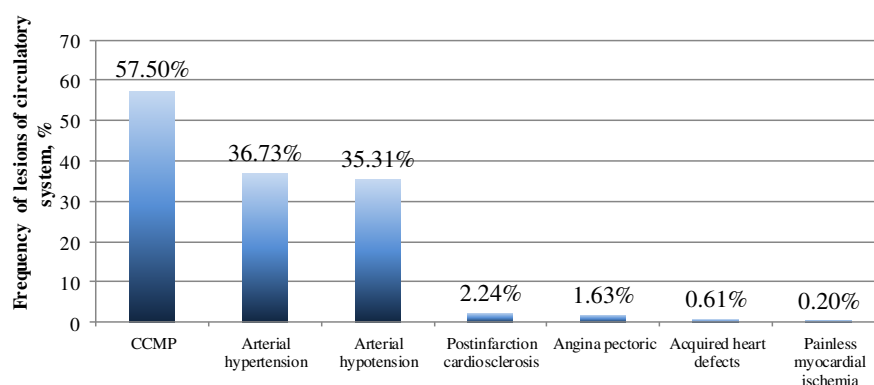


Fig. 1 – Frequency of circulatory system lesions in patients with liver cirrhosis

CCMP, namely signs of electrical (electrocardiographic  $Q-Tc$  interval  $< 0.44$  s), diastolic and/or systolic myocardial dysfunction and/or changes in the structure of the heart chambers recorded by echocardiographic examination, occurs in 280 patients (57.5 %). Arterial hypertension –

increase in systolic blood pressure  $\geq 140$  mm Hg and/or diastolic blood pressure  $\geq 90$  mm Hg, recorded during at least two tonometry on two or more consecutive visits – in 180 patients (36.7 %), and arterial hypotension – a simultaneous decrease in systolic blood pressure  $< 105$  mm Hg and diastolic blood pressure  $< 65$  mm Hg during at least two tonometry on two or more consecutive visits – in 173 (35.3 %). Postinfarction cardiosclerosis – was diagnosed in 11 patients (2.2 %), angina pectoris – 8 (1.6 %), acquired heart defects – in 3 (0.6 %), and painless form of coronary heart disease – in 1 patient with LC (0.2 %) (table 1).

Table 1

**Incidence of cardiovascular system lesions in patients with liver cirrhosis**

No	Diseases	Patients with LC (n=603)	
		N	%
1	Cirrhotic cardiomyopathy	n=487	
		280	57.5
2	Arterial hypertension	180	36.7
3	Arterial hypotension	173	35.3
4	Postinfarction cardiosclerosis	11	2.2
5	Angina pectoris	8	1.6
6	Acquired heart defects	3	0.6
7	Painless myocardial ischemia	1	0.2

The incidence evaluation of extrahepatic cardiovascular diseases in patients of each severity class of LC according to the C.G. Child-R.N. Pugh criteria is the third phase of the study, which is demonstrated in table 2.

Table 2

**Incidence of cardiovascular system lesions in patients with liver cirrhosis concerning the main disease severity by C.G. Child-R.N. Pugh classes**

No	Diseases	Patients with liver cirrhosis					
		Class A, n=210		Class B, n=203		Class C, n=190	
		N	%	N	%	N	%
1	Cirrhotic cardiomyopathy	n=116		n=181		125*#	65.8
		53	45.7	102*	56.4		
2	Arterial hypertension	105	50.0	49*	24.1	26*#	13.9
3	Arterial hypotension	35	16.7	53*	26.1	85*#	44.7
4	Postinfarction cardiosclerosis	3	1.4	5	2.5	3	1.6
5	Angina pectoris	2	1.0	4	2.0	2	1.1
6	Acquired heart defects	1	0.5	2	1.0	0	0.0
7	Painless myocardial ischemia	0	0.0	1	0.5	0	0.0

Notes: 1. \* – statistically significant difference compared to the value in class A,  $p < 0.05$ ; 2. # – statistically significant difference compared to the value in class B,  $p < 0.05$ .

The incidence of CCMP was significantly increased with increasing LC severity: in almost a half of the class A patients (53 patients, 45.7 %) were diagnosed with CCMP, which is significantly lower than their number in class B (102 patients, 56.4 %;  $p < 0.05$ ) and class C (125 patients, 65.8 %;  $p < 0.05$ ), with a statistically significant difference between the latter ( $p < 0.05$ ). The number of arterial hypertension cases was significantly decreased with increasing severity of the LC, namely in 105 patients (50.0 %) of class A high blood pressure was recorded, which is significantly higher than among patients of class B (49 patients, 24.1 %;  $p < 0.05$ ) and class C (26 patients, 13.7 %;  $p < 0.05$ ), the incidence of which also demonstrated significant difference ( $p < 0.05$ ). In its turn, the incidence of arterial hypotension increased with increasing severity of LC according to C.G. Child-R.N. Pugh: 35 people (16.7 %) of class A were diagnosed with arterial hypotension, significantly lower than in class B (53 patients, 26.1 %;  $p < 0.05$ ) and class C (85 patients, 44.7 %;  $p < 0.05$ ), which as well, demonstrated a statistically significant difference ( $p < 0.05$ ). The incidence of postinfarction cardiosclerosis was almost identical in each class of LC severity: three cases (1.4 %) were detected in the group of patients with class A LC, five (2.5 %) in the group of patients with class B LC, there were also three cases (1.6 %) among patients with class C LC. There was no statistically significant difference between the groups ( $p > 0.05$ ). Angina pectoris was diagnosed in two patients with class A (1.0 %), in four patients with class B (2.0 %) and two with class C (1.1 %). There was no significant difference between each group ( $p > 0.05$ ). In addition, we have registered few cases of acquired heart defects among patients with LC: one patient with class A (0.5 %) and two patients with class B (1.0 %). There was no significant correlation between lesions and severity of LC ( $p > 0.05$ ). We have diagnosed one case of a painless coronary heart disease in a patient with class B LC (0.5 %), there were no cases of the latter (0.0 %) among patients with class A and C, and, therefore, there was no reliable association between the severity and the presence of the lesion ( $p > 0.05$ ) (fig. 2).

Based on the obtained results, it can be asserted that CCMP and arterial hypotension have common etiologic and/or pathogenetic mechanisms with LC, and therefore can be interpreted as syntropic comorbid LC lesions. A reliable decrease in the arterial hypertension incidence and an increase in the arterial hypotension incidence were regarded as confirmation of the syntropic disorders in the system of blood pressure regulation in such patients. Such nosologies as postinfarction cardiosclerosis, angina pectoris,

acquired heart defects, and a painless form of coronary heart disease belong to the concomitant diseases of the circulatory system, since there was no correlation observed with the increase in the severity of the underlying disease.

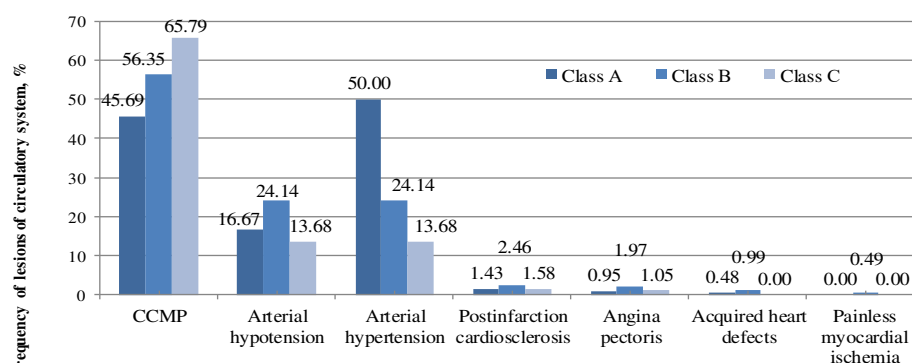


Fig. 2 – Frequency of circulatory system lesions in patients with LC and its dependence on the severity of the underlying disease depending on C.G. Child-R.N. Pugh class.

failure [1, 2]. LC is one of the six leading causes of death in patients aged 35 to 60 years, which is 16.0–44.1 cases per 100.000 population [6]. Usually the causes of death, as well as factors that determine the tactics of treatment and prognosis of such patients, are syntropic polymorbid lesions of other organs and systems, among which lesions of the circulatory system are among the most common [5, 7, 8].

The difficulty of diagnosing syntropic comorbid lesions of the circulatory system is also that, according to information in the literary sources [2, 8], the clinical manifestations of such lesions are poor and non-specific, which can often be confused with manifestations of primary underlying liver disease. Namely, such patients complain of low-intensity pain in the upper part of the heart area, feeling of shortness of breath, dyspnea, palpitations, constant rapid fatigue, reduced efficiency, edema, cardiac arrhythmias and conduction disorders.

Among 603 patients with LC, we identified 490 (81.26 %) patients with cirrhosis with extrahepatic lesions of the circulatory system. The information is confirmed by the results of other scientific studies, where the frequency of lesions of the circulatory system in the case of LC varies on average from 80.0 % to 90.0 % [3, 4].

After analyzing the frequency of circulatory system lesions in these patients, depending on the severity of LC, we identified diseases whose frequency changed significantly ( $p < 0.05$ ), and identified them as syntropic, that is, those that have pathogenetic mechanisms common to LC – secondary CCMP and persistent hypotension. Our results are consistent with studies of other authors, who describe these lesions as due to LC complications [3, 10].

## Conclusion

Lesions of the circulatory system are found in 81.3 % of patients with liver cirrhosis, among which cirrhotic cardiomyopathy and disorders in the blood pressure regulation system with the emergence of persistent arterial hypotension have common pathogenetic mechanisms with cirrhosis, namely they are syntropic, whilst postinfarction cardiosclerosis and painless form of coronary heart disease are concomitant.

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**D.S. Avetikov, M.M. Ananieva, G.A. Loban, M.O. Faustova, M.G. Skikevych,  
Yu.V. Chumak, O.S. Ivanytska**  
**Poltava State Medical University, Poltava**

## THE PROFILE OF SPECIFIC ANTIBODIES TO SARS-COV-2 IN RESIDENTS OF THE CENTRAL AND EASTERN REGIONS OF UKRAINE

e-mail: m.faustova@pdmu.edu.ua

Determination of the level of antibodies in individuals living in certain regions provides insight into the epidemiology of the infection and is crucial for the development of strategies to reduce the spread of COVID-19. The study analyzed the results of IgM and IgG tests for the SARS-CoV-2 virus in 7142 residents of eastern and central regions of Ukraine from July 2020 to January 2021. Patients' visits to COVID-19 for IgM and IgG mainly occurred in the autumn-winter period of 2020–2021, confirming the seasonality of the disease. The most popular test among residents of Poltava and Donetsk regions was the test for IgM immunoglobulins, and the vast majority of results were negative. As of January 2021, the number of people who had IgG antibodies to the pathogen COVID-19, among those surveyed approached 50 % in both Poltava and Donetsk regions.

**Key words:** COVID-19, SARS-CoV-2, antibodies, IgM, IgG.

**Д.С. Аветіков, М.М. Ананьєва, Г.А. Лобань, М.О. Фаустова, М.Г. Скікевич,  
Ю.В. Чумак, О.С. Іваницька**

## ПРОФІЛЬ СПЕЦИФІЧНИХ АНТИТІЛ ДО SARS-COV-2 У ЖИТЕЛІВ ЦЕНТРАЛЬНОГО ТА СХІДНОГО РЕГІОНІВ УКРАЇНИ

Визначення рівня антитіл у осіб, які проживають у певних регіонах, дає уявлення про епідеміологію інфекції та має вирішальне значення для розробки стратегій зниження поширення COVID-19. У дослідженні проаналізовано результати досліджень IgM та IgG до вірусу SARS-CoV-2 у 7142 жителів східного та центрального регіонів України з липня 2020 року по січень 2021 року. Звернення пацієнтів щодо визначення IgM та IgG до збудника COVID-19 переважно відбувалися в осінньо-зимовий період 2020–2021 років, що підтверджує сезонність захворювання. Найпопулярнішим тестом серед мешканців Полтавської та Донецької областей був тест на імуноглобуліни IgM, і переважна більшість результатів була негативною. Станом на січень 2021 року кількість людей, які мали антитіла IgG до збудника COVID-19, серед досліджених, наблизилася до 50 % як у Полтавській, так і в Донецькій областях.

**Ключові слова:** COVID-19, SARS-CoV-2, антитіла, IgM, IgG.

*The study is a fragment of the research project “Study of the role of opportunistic and pathogenic infectious agents with different sensitivity to antimicrobial and antiviral drugs in human pathology”, No 0118U004456.*

At the end of 2019, an emerging coronavirus infection caused by the SARS-CoV-2 virus emerged and began to spread around the world in China. Already in early 2020, COVID-19 was recognized as a global priority problem of the global health care system. On 19 January in 2022, 335 521 830 cases of COVID-19 coronavirus disease have been confirmed worldwide; 5 574 726 people have died [7].

In Ukraine, coronavirus infection COVID-19 was firstly diagnosed on March 3, 2020, in Chernivtsi. As of January 19, 2022, in Ukraine COVID -19 was diagnosed in 3 780 903 people (9.2 % of the population). However, the spread of new coronavirus infection, morbidity and mortality, the level of specific immune protection in different regions of Ukraine differed throughout the pandemic period. In particular, the analysis of epidemiological indicators in the Poltava region, which represents the central (mostly agrarian) region of Ukraine, showed that on January 19, 2022, 145 073 people fell ill on its territory (10.69 % of the region's population). The Donetsk region, which is an example of the eastern region (mostly industrialized), was identified in 171 582 cases (4.22 % of the region population) [3].

Given the rapid spread of this infection, the danger to human health and significant socio-economic consequences, diagnosis, the pathogenesis of the disease, the nature and duration of the body's immune response to the pathogen, the development of specific prevention methods have gained international