

O.Yu. Filippova, V.V. Kryvoshey  
Dnipro State Medical University, Dnipro

## QUALITY OF LIFE IN CHRONIC PANCREATITIS WITH ACCOMPANYING ARTERIAL HYPERTENSION IN AGE ASPECT AND ITS RELATIONSHIP WITH MALNUTRITION MARKERS

e-mail: filippova404dsma@gmail.com

The problem of quality of life in chronic pancreatitis remains to be actual. The presence of comorbid pathology in chronic pancreatitis can be an aggravating factor for the quality of life and malnutrition manifestations. 110 patients were included. Standardized questionnaires were used (SF-36, GSRs). The levels of total protein, serum albumin, serum iron and vitamin D, serum zinc and magnesium levels were determined. A significant decrease in quality of life was proven in the group of patients with chronic pancreatitis and hypertension. Significantly lower indicators of psychological health and role functioning were noted among the 45–55-year-old group, and among patients 56–65 years had significantly lower indicators of physical functioning, role-based physical functioning, vitality and social functioning, which correlated with markers of malnutrition. The level of total protein, albumin, vitamin D, and iron in blood serum can be markers of malnutrition in patients with chronic pancreatitis combined with hypertension.

**Key words:** quality of life, chronic pancreatitis, arterial hypertension, malnutrition, biomarkers

О.Ю. Філіппова, В.В. Кривошей

## ЯКІСТЬ ЖИТТЯ ПРИ ХРОНІЧНОМУ ПАНКРЕАТИТІ З СУПУТНЬОЮ АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ У ВІКОВОМУ АСПЕКТІ ТА ЇЇ ЗВ'ЯЗОК З МАРКЕРАМИ МАЛЬНУТРИЦІЇ

Проблема якості життя при хронічному панкреатиті залишається актуальною. Наявність коморбідної патології при хронічному панкреатиті може бути обтяжливим фактором для якості життя та проявів мальнутриції. У дослідження включено 110 пацієнтів. Використовувалися стандартизовані опитувальники (SF-36, GSRs). Визначали рівні загального білка, сироваткового альбуміну, сироваткового заліза та вітаміну D, рівні цинку та магнію. Достовірно зниження якості життя встановлено у групі хворих на хронічний панкреатит в поєднанні з артеріальною гіпертензією. Достовірно нижчі показники психологічного здоров'я та рольової діяльності відзначені у групі 45–55 років, а у пацієнтів 56–65 років – достовірно нижчі показники фізичної активності, рольової фізичної діяльності, життєздатності та соціального функціонування, що корелювали з маркерами мальнутриції. Рівень загального білка, альбуміну, вітаміну D, заліза в сироватці крові може бути маркером мальнутриції у хворих на хронічний панкреатит у поєднанні з артеріальною гіпертензією.

**Ключові слова:** якість життя, хронічний панкреатит, артеріальна гіпертензія, мальнутриція, біомаркери

*The study is a fragment of the research project "Cardiovascular risk, vascular pattern, markers of fibrosis and adipose tissue metabolism in patients with cardiovascular disease in conditions of comorbidity: optimization of treatment, prognosis and prevention of complications", state registration No. 0118U006632.*

Despite the development of the latest diagnostic and treatment technologies, chronic pancreatitis (CP) remains an urgent problem of internal medicine. Taking into account the problem of population ageing, in recent years there has been a tendency to increase the incidence of CP [9].

According to modern literature data, patients with CP have a higher share of comorbid arterial hypertension (AH) [10]. In the combined course of CP with AH clinical symptoms becomes changed: signs of cardiac pathology come to the fore, while the manifestations of CP are smoothed out or atypical [3].

A high prevalence of overweight and obesity can be observed among patients with acute and chronic pancreatitis. It should be noted that pancreatitis is characterized by the paradox of obesity [12]. Studies show that pancreatitis is more severe in people with excess body weight and obesity. Hyperlipidemia, which occurs with obesity, also contributes to fatty infiltration of the pancreas, liver and the development of CP [6, 11]. With the increasing prevalence of obesity worldwide, the incidence of pancreatitis, especially of biliary etiology, is increasing.

In recent decades, interest in research on quality of life (QL) has increased, so the role of these studies in medicine is growing. The high social significance of CP is determined by the prevalence among patients of socially active age, high costs for diagnosis and treatment, and a decrease in QL and work capacity [1]. However, there is a limited amount of data on the impact of the combined course of CP with AH on the QL of these patients.

Studies evaluating the QL in CP and AH have been conducted for more than 20 years, using various scales and questionnaires – both general and special. Studying the QL in comorbid conditions is currently of great scientific and practical interest.

In the literature, there are practically no works devoted to the study of QL in patients with CP in combination with AH. At present, there are works that study the QL in the isolated course of CP or AH. In these works was demonstrated that QL deterioration is connected precisely with the complications of CP or AH.

According to current concepts, malnutrition is a common complication of CP associated with increased morbidity and mortality among these patients. Assessment of malnutrition based on BMI alone has limitations and is currently considered inadequate for determining nutritional status of patients with CP [13].

In 2018, the Global Leadership Initiative on Malnutrition (GLIM) first published global consensus criteria for the diagnosis of malnutrition in clinical settings [4]. However, clear recommendations regarding appropriate methods and markers for determining the nutritional status of patients with CP are still lacking. Obviously, the assessment of malnutrition should be comprehensive and include not only BMI but also indicators of laboratory diagnostic methods.

**The purpose** of the study was to assess the quality of life indicators in patients with chronic pancreatitis combined with arterial hypertension in terms of age and relationship with malnutrition markers.

**Materials and methods.** The study was conducted with the approval of the Local Ethics Committee in accordance with the principles outlined in the Declaration of Helsinki. All participants of the presented study received written consent. 110 patients (46 men, 64 women) aged 45–65 years (median age – 53.7 [45.4; 64.2] years) with CP combined with AH were examined.

The diagnosis of CP was made on the basis of the anamnesis, clinical manifestations, and the results of laboratory and instrumental studies, taking into account the recent recommendations [7]. The diagnosis of AH was established according to the ESC Guidedlines [14]. The inclusion criteria were the presence of a verified diagnosis of stage II, 1st and 2nd stage hypertension; presence of a diagnosis of CP, stable CP therapy (at least 6 months) and unchanged antihypertensive therapy for 3 months, age 45-65 years, voluntary informed consent to participate in the study. Exclusion criteria from the study: an established and verified diagnosis of coronary heart disease, acute pancreatitis, III-stage and III-degree hypertension, previous therapy with hypolipidemic drugs, chronic heart failure III-IV functional class (FC), diabetes, hypothyroidism, glomerular filtration rate <60 ml/min./1.73m<sup>2</sup>, obesity 3–4 degrees.

Patients were divided into 2 groups: 1st (n=70) – patients with a combined course of CP and hypertension; 2nd (n=40) – patients with CP without concomitant hypertension. At baseline, the patients of the 1st and 2nd groups were comparable in terms of age, gender structure, BMI, and duration of CP and its course, received therapy (Table 1). Also, patients of each group were divided depending on age into subgroups in the range of 45–55 years and 56–65 years.

Table 1

**Initial characteristics of the examined patients**

Index	1st group (n=70)	2nd group (n=40)	p
Median age, years	54,3 [47.5; 64.4]	52,1 [45.4; 62.8]	0.35
gender structure (female:male)	25:45	21:19	-
BMI, kg/m <sup>2</sup>	26 [24.4; 35.2]	30 [25.3; 36.8]	0.39
duration of CP, years	3[2.4; 5.0]	3.3[2.6; 5.5]	0.44
Systolic blood pressure, mm Hg	138.5 [125.8; 144.6]	128.4 [114.2; 138.5]	0.03
Diastolic blood pressure, mm Hg	75.6 [71.4; 78.3]	71.1 [68.2; 73.7]	0.15

Note: p – between the studied and control groups (Mann-Whitney U-test)

Standardized international general and specific questionnaires were used to assess quality of life. Processing of the questionnaire results was carried out according to a special algorithm developed to assess the quality of life according to the SF-36 [5].

The Ukrainian version of the Gastro intestinal Symptom Rating Scale (GSRS). The indices of the scales range from 1 to 7, higher values correspond to more pronounced symptoms and lower quality of life.

To assess the nutritional status, the levels of total protein, serum albumin, serum iron and vitamin D, serum zinc and magnesium levels were determined [2].

Processing and analysis of data was carried out with the help of STATISTICS software packages (license No. AGAR909E415822FA). The critical level of p when testing statistical hypotheses is taken to be <0.05.

**Results of the study and their discussion.** The majority of examined patients with CP noted a loss of body weight during the last 6-12 months – 42 (60 %) among the 1st group and 21 (52.5 %) among the 2nd group. Median levels of zinc and magnesium among patients with CP and hypertension were 17.6

[12.6; 23.5] and 0.81 [0.52; 0.99], respectively, among the group of patients with isolated CP – 20.2 [14.8; 25.1] and 0.85 [0.58; 1.05] respectively.

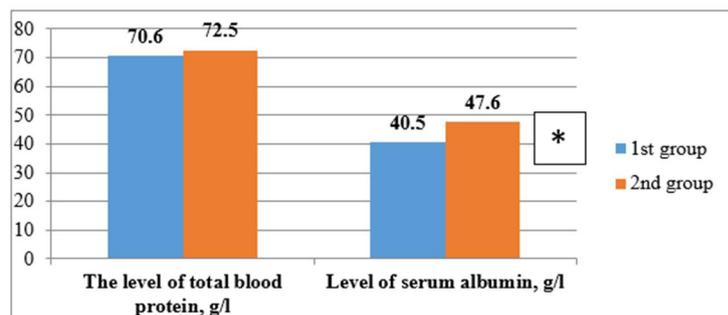


Fig. 1. Levels of total blood protein, serum albumin among patients with CP depending on the presence of AH. \* – the validity of the differences between groups ( $p < 0.05$ ).

Reliable correlations were established between the level of total blood protein, serum albumin and the duration of AH –  $r = -0.45$  ( $p < 0.05$ ), age –  $r = -0.52$  ( $p < 0.05$ ) among patients with a combined course of CP with AH.

Among the patients of the 1st group, 38 (54.2 %) had a decrease in the level of serum iron, while among the patients of the 2nd group – 14 (35 %), which is significantly lower ( $p < 0.05$ ). The median serum iron was also significantly lower by 30.6 % ( $p < 0.05$ ) among patients with a combined course of CP and hypertension (Fig. 2).

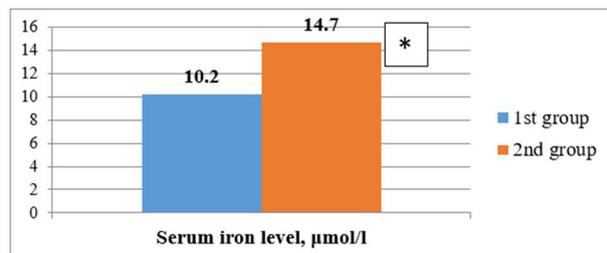


Fig. 2. The level of serum iron among patients with CP depending on the presence of hypertension. \* – the validity of the differences between groups ( $p < 0.05$ ).

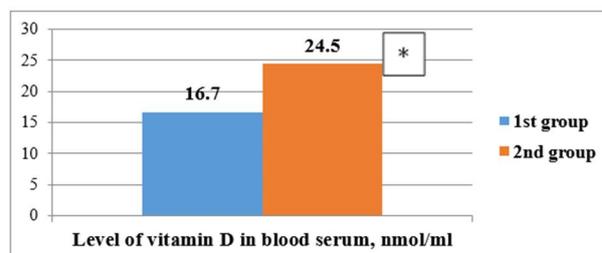


Fig. 3. The level of vitamin D in blood serum in patients with CP depending on the presence of AH. \* – the validity of the differences between groups ( $p < 0.05$ ).

Vitamin D deficiency was found in the vast majority of examined patients with CP: 61 (87.1 %) patients of the 1st group and 32 (80 %) patients of the 2nd group. At the same time, the median level of vitamin D in blood serum was 31.8 % higher in patients with CP in combination with hypertension (Fig. 3). Reliable correlations were established between the level of vitamin D and the duration of the CP disease –  $r = -0.41$  ( $p < 0.05$ ), age –  $r = -0.56$  ( $p < 0.05$ ) among patients with a combined course CP with AH.

Thus, among the examined patients with a combined course of CP and AH, 38 (54.3 %) had signs of malnutrition, among patients with isolated CP – in 18 (45 %) ( $p < 0.05$ ).

Analyzing QL indices according to the SF-36 questionnaire revealed that in patients with a combined course of CP and AH, significantly lower indices were found that characterize vitality, social functioning, psychological health, role functioning caused by emotional health – by 46.2 %, 38.2 %, 37.4 % and 47.7 % ( $p < 0.05$ ), respectively. At the same time, the index of pain intensity in patients of the first group was significantly higher compared to the second group ( $p < 0.05$ ) (Table 2).

Table 2

#### Indices of QL according to the scales of the SF-36 questionnaire in patients with CP

Questionnaire scale SF-36	1st group (CP+AH), n=70	2nd group (CP), n=40
Physical functioning	55.8 [46.5; 61.3]	61.6 [55.3; 68.6]
Role physical functioning	36.6 [30.1; 42.5]	44.0 [40.3; 48.6]
Intensity of pain	65.7 [58.9; 74.6]*	60.5 [54.3; 67.4]
General Health	34.4 [28.6; 39.5]	46.4 [40.6; 49.8]
Viability	25.5 [20.4; 31.4]*	47.4 [42.3; 52.3]
Social functioning	45.2 [39.2; 53.5]*	73.1 [61.6; 79.5]
Role functioning conditioned by emotional health	33.2 [28.5; 36.8]*	63.5 [54.6; 67.5]
Psychological health	34.0 [25.6; 42.8]*	54.3 [48.6; 59.8]

\* – the validity of the differences between groups ( $p < 0.05$ )

Analyzing the QL of patients with the combined course of CP with AH according to the SF-36 questionnaire in terms of age, it was found that among the group of 45–55 years, significantly lower indices of psychological health and role functioning caused by emotional health are noted.

At the same time, significantly lower indices of physical functioning, role-based physical functioning, vitality and social functioning were established among patients aged 56–65. Reliable correlations were established between the level of the psychological health indicator and serum albumin, iron –  $r=0.39$  ( $p<0.05$ ),  $r=0.50$  ( $p<0.05$ ), respectively. Also, among patients with a combined course of CP with AH, there was a significant positive correlation between the indicator of social functioning and the total level of protein, serum albumin, vitamin D –  $r=0.41$  ( $p<0.05$ ),  $r=0.45$  ( $p<0.05$ ),  $r=0.47$  ( $p<0.05$ ), respectively.

During the survey of patients with a combined course of CP with AH with the GSRs scale, significantly higher points characterizing reflux – by 38.9 %, diarrhea – by 30.8 %, and dyspepsia syndrome – by 27.5 % were established. The total score of the GSRs questionnaire in patients of the 1st group was also significantly higher (by 33.33 %) compared to the 2nd group ( $p<0.05$ ).

Among patients with the combined course of CP with AH in the age group of 45–55 years, there were significantly higher indicators of the GSRs scale, which characterize pain syndrome, diarrhea, and dyspeptic syndrome (Figs. 4 a, b). At the same time, the index of the total score according to the questionnaire was positively correlated with the level of serum albumin, iron, vitamin D –  $r=0.43$  ( $p<0.05$ ),  $r=0.48$  ( $p<0.05$ ),  $r=0.45$  ( $p<0.05$ ) respectively.

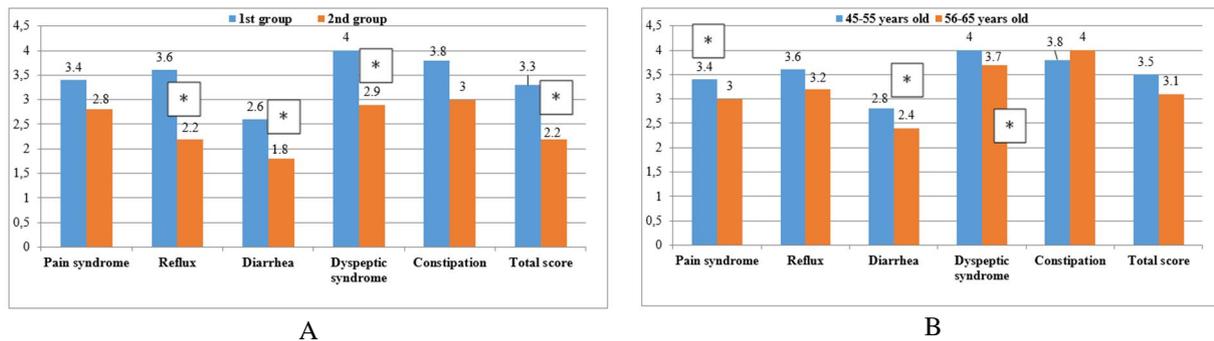


Fig. 4. Indicators of main symptoms according to the GSRs questionnaire among the examined patients (a) and AH depending on age (b). \* – the validity of the differences between groups ( $p<0.05$ ).

It should be noted that many chronic diseases can lead to a violation of the nutritional status and the development of trophic insufficiency. CP proceeds with a violation of digestion and/or absorption processes (maldigestion and malabsorption syndromes) with subsequent formation of malnutrition. Malnutrition in CP and comorbid AH in our study was associated with impaired nutrient assimilation, trophic changes that develop as a result of protein and vitamin deficiency, as well as changes in fat, carbohydrate, and mineral metabolism, which is confirmed by the results of other studies in the presence of CP-associated pathology [8].

Analyzing the obtained results, it was found that despite the presence of excess body weight and obesity of the 1st and 2nd degrees, laboratory signs of malnutrition and weight loss were observed in the majority of patients with CP and AH, which may indicate a loss of muscle mass [13]. The use of only BMI to assess nutritional status and the development of malnutrition is controversial due to the lack of a standard for the diagnosis of nutritional insufficiency. BMI does not take into account the previous condition of the patient and the decrease in the volume of muscle tissue, the main indicators of metabolism [15]. Thus, the patient may have malnutrition and nutritional deficiency both with a normal and even with an increased BMI [8], as well as with the presence of obesity, which also confirms the results of our study.

The evaluation of the results of the study using the SF-36 questionnaire showed that the QL of patients with a combined course of CP and AH compared to CP was lower on scales that assessed the psychological and physical components of health ( $p<0.05$ ). The presence of concomitant AH worsened the quality of life of CP patients on all scales that reflect the patient's physical condition, namely, physical activity, the role of physical problems in limiting life activities, pain intensity, general health, and life activity. Among patients with CP in combination with AH, low indices were also noted on psychological health scales, which indicates that the patient's daily activities are not limited to clinical manifestations of AH, but are also accompanied by negative emotional coloring, a sharp decline in strength and energy, lack of motivation and sufficient physical potential for adequate performance of everyday work, which is associated with the presence of two simultaneously existing diseases. The QL in the comorbid course of CP with AH is reduced both because of the frequency and severity of symptoms, and because of the negative emotional color they cause. The most pronounced decrease in quality of life indices, especially physical and social functioning, was noted in the group of patients aged 56–65.

Analyzing the testing data of patients with a combined course of CP with AH using a specialized gastroenterology questionnaire GSRs, it was established that the leading place in the clinic of the disease is occupied by pain, reflux and dyspeptic syndromes, which was maximally expressed among the age group

of 45–55 years. These syndromes should be considered as the main ones that reduce the quality of life in patients with CP in combination with AH. At the same time, it was the decrease in the levels of total protein, albumin, serum iron, and vitamin D that were associated with a decrease in QL in the combined course of CP and AH.

### Conclusions

1. The use of SF-36 and GSRs questionnaires allows to establish indicators of quality of life and adequately assess the main clinical syndromes characteristic of the comorbid course of chronic pancreatitis and arterial hypertension.

2. A significant decrease in quality of life according to the SF-36 questionnaire was proven in the group of patients with CP in combination with hypertension: significantly lower indices of the scales of life activity, social functioning, role functioning caused by emotional state, and mental health were found in the group of patients with concomitant hypertension ( $p < 0.05$ ). The index of pain intensity in patients of the first group was significantly higher compared to the second group ( $p < 0.05$ ). Analysis of the GSRs questionnaire revealed a significant ( $p < 0.05$ ) increase in three of the five presented scales in patients with CP and hypertension (reflux – by 38.9 %, diarrhea – by 30.8 %, and dyspeptic syndrome – by 27.5 %), which indicates deterioration of quality of life in the combined course.

3. Established changes in quality of life in age-related aspects in patients with a combined course of CP with hypertension according to the SF-36 questionnaire: significantly lower indices of psychological health and role functioning due to emotional health are noted among the 45-55 year-old group, and among patients 56-65 years of age had significantly lower indices of physical functioning, role-based physical functioning, vitality and social functioning, which correlated with markers of malnutrition ( $p < 0.05$ ).

4. Malnutrition is a common symptom complex among patients with CP in combination with hypertension (detected in 54.3 % of patients). Using BMI to assess malnutrition is uninformative. The level of total protein, albumin, vitamin D, and iron in blood serum can be markers of malnutrition in patients with CP combined with hypertension.

### References

1. Amann ST, Yadav D, Barmada MM, O'Connell M, Kennard ED, Anderson M, et al. Physical and mental quality of life in chronic pancreatitis: a case-control study from the North American Pancreatitis Study 2 cohort. *Pancreas*. 2013; 42(2) :293–300. doi: 10.1097/MPA.0b013e31826532e7.
2. Arvanitakis M, Ockenga J, Bezmarevic M, Gianotti L, Krznarić Ž, Lobo DN, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. *Clin Nutr*. 2020; 39 :612–31. doi: 10.1016/j.clnu.2020.01.004
3. Bang UC, Benfield T, Hyldstrup L, Bendtsen F, Beck Jensen JE. Mortality, cancer, and comorbidities associated with chronic pancreatitis: a Danish nationwide matched-cohort study. *Gastroenterology*. 2014; 146(4) :989–94. doi: 10.1053/j.gastro.2013.12.033.
4. de van der Schueren MAE, Keller H, Cederholm T, Barazzoni R, Compher C, Correia MITD, et al. Global Leadership Initiative on Malnutrition (GLIM): Guidance on validation of the operational criteria for the diagnosis of protein-energy malnutrition in adults. *Clin Nutr*. 2020; 39(9) :2872–2880. doi: 10.1016/j.clnu.2019.12.022.
5. Feshchenko Yu, Mostovoy Yu, Babychuk Yu. The procedure for adapting the international questionnaire for assessing the quality of life of the Ministry of Education and Culture SF-36 in Ukraine. Experience of use in patients with bronchial asthma. *Ukrainian pulmonology journal*. 2002; 3: 9–11.
6. Filippova A, Löhr M, Kryvoshei V. Blood lipid spectrum and elastic properties of arteries in patients with chronic pancreatitis in combination with arterial hypertension. *Medychni perspektyvy*. 2022; 27 (1) :42–49.
7. Löhr JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch MM, et al. United European gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United European Gastroenterol J*. 2017; 5 :153–99. doi: 10.1177/2050640616684695
8. Min M, Patel B, Han S, Bocelli L, Kheder J, Vaze A, et al. Exocrine pancreatic insufficiency and malnutrition in chronic pancreatitis: identification, treatment, and consequences. *Pancreas*. 2018; 47:1015–8. doi: 10.1097/MPA.0000000000001137
9. Ouyang G, Pan G, Liu Q, Wu Y, Liu Z, Lu W, Li S, Zhou Z, Wen Y. The global, regional, and national burden of pancreatitis in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *BMC Med*. 2020; 18(1):388. doi: 10.1186/s12916-020-01859-5.
10. Spagnolo DM, Greer PJ, Ohlsen CS, Mance S, Ellison M, Breze C, et al. Acute and Chronic Pancreatitis Disease Prevalence, Classification, and Comorbidities: A Cohort Study of the UK BioBank. *Clin Transl Gastroenterol*. 2022; 13(1): e00455. doi: 10.14309/ctg.0000000000000455.
11. Stepanov Yu, Filippova A. Dyslipidemia in patients with non-alcoholic hepatic steatohepatitis and biliary pathology and ways of its correction. *Modern gastroenterology*. 2010; 4(54):46–51.
12. Wiese ML, Aghdassi AA, Lerch MM, Steveling A. Excess Body Weight and Pancreatic Disease. *Visc Med*. 2021; 37(4):281–286. doi: 10.1159/000517147.
13. Wiese ML, Gärtner S, von Essen N, Doller J, Frost F, Tran QT, et al. Malnutrition Is Highly Prevalent in Patients with Chronic Pancreatitis and Characterized by Loss of Skeletal Muscle Mass but Absence of Impaired Physical Function. *Front Nutr*. 2022; 9:889489. doi: 10.3389/fnut.2022.889489.
14. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J*. 2018; 39(33):3021–3104. doi: 10.1093/eurheartj/ehy339.
15. Zhdan VN, Tkachenko MV, Kitura YeM, Babanina MYu, Kyrian OA. Osteoarthritis and metabolic syndrome: unity of pathogenetic mechanisms. *World of medicine and biology*. 2021; 4 (78): 56–60.