UDC 616.37-002.2:616.12-008.331.1]-07 https://doi.org/10.26641/2307-0404.2022.1.254320

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BLOOD LIPID SPECTRUM AND ELASTIC PROPERTIES OF ARTERIES IN PATIENTS WITH CHRONIC PANCREATITIS IN COMBINATION WITH ARTERIAL HYPERTENSION

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Цитування: Медичні перспективи. 2022. Т. 27, № 1. С. 42-49
Cited: Medicni perspektivi. 2022;27(1):42-49

Key words: *blood lipid spectrum, elastic properties of arteries, chronic pancreatitis, arterial hypertension*
Ключові слова: *ліпідний спектр крові, пружноеластичні властивості артерій, хронічний панкреатит, артеріальна гіпертензія*
Ключевые слова: *липидный спектр крови, упругоэластические свойства артерий, хронический панкреатит, артериальная гипертензия*

Abstract. Blood lipid spectrum and elastic properties of arteries in patients with chronic pancreatitis in combination with arterial hypertension. Filippova A.Yu., Löhr M., Kryvoshei V.V. *110 patients aged 45-65 years with chronic pancreatitis were examined. The first group consisted of patients with a combined course of chronic pancreatitis with arterial hypertension; the second group - patients with chronic pancreatitis without concomitant hypertension. All patients were examined for total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol. Arterial stiffness was determined by the pulse wave velocity. It was found that patients of the 1st group had significantly higher levels of triglycerides (37.2%), low-density lipoprotein cholesterol (13%), total cholesterol (25%), atherogenic ratio (19.6%) and significantly lower levels of high-density lipoprotein cholesterol (15.4%). Correlations between age and the level of atherogenic ratio, low-density lipoprotein cholesterol were established – r=0.35; p<0.01; r=0.37; p<0.01, respectively. The duration of chronic pancreatitis positively correlated with the level of triglycerides, low-density lipoprotein cholesterol – r=0.43; p<0.01; r=0.34; p<0.01, respectively. The level of brachial artery augmentation index was significantly lower by 43% in patients with chronic pancreatitis in combination with arterial hypertension, while the aortic augmentation index was significantly higher by 37.6% (p<0.01). It was found that patients of the 1st group had a significantly higher pulse wave velocity in the carotid-femoral segment compared to the 2nd group – by 7.5% (p<0.01). Significant correlations have been established between the brachial artery augmentation index and age, total cholesterol, atherogenic ratio, high and low density lipoprotein cholesterol, triglycerides, cardiovascular risk level by the SCORE scale in patients with a combined course of chronic pancreatitis with arterial hypertension. Conclusions. Patients with the combination of chronic pancreatitis and hypertension had significantly higher levels of triglycerides, low-density lipoprotein cholesterol and total cholesterol. Changes in the elastic properties of arteries in patients with chronic pancreatitis with comorbid hypertension were characterized by an increase in the augmentation index and the pulse wave velocity in the carotid-femoral segment.*

Реферат. Ліпідний спектр крові та пружноеластичні властивості артерій у пацієнтів з хронічним панкреатитом у поєднанні з артеріальною гіпертензією. Філіппова О.Ю., Льор М., Кривошей В.В. *Обстежено 110 хворих віком 45-65 років з хронічним панкреатитом. Першу групу склали пацієнти з поєднаним перебігом хронічного панкреатиту з артеріальною гіпертензією; другу групу – пацієнти з хронічним панкреатитом без супутньої артеріальної гіпертензії. Усім пацієнтам визначали вміст загального холестерину, тригліцеридів, холестерину ліпопротеїдів високої щільності, холестерину ліпопротеїдів низької*

щільності та холестерину ліпопротеїдів дуже низької щільності. Жорсткість артерій визначали за показником швидкості поширення пульсової хвилі. Установлено, що хворі 1-ї групи мали достовірно вищі рівні тригліцеридів (на 37,2%), холестерину ліпопротеїдів низької щільності (на 13%), загального холестерину (на 25%), коефіцієнту атерогенності (на 19,6%) та достовірно нижчий рівень холестерину ліпопротеїдів високої щільності (на 15,4%). Установлені кореляційні зв'язки між віком та рівнем коефіцієнту атерогенності, холестерину ліпопротеїдів низької щільності – r=0,35; p<0,01; r=0,37; p<0,01 відповідно. Тривалість захворювання на хронічний панкреатит позитивно корелювала з рівнем тригліцеридів, холестерину ліпопротеїдів низької щільності – r=0,43; p<0,01; r=0,34; p<0,01 відповідно. Установлено достовірно нижчий на 43% рівень індексу аугментації плечової артерії у хворих з хронічним панкреатитом у поєднанні з артеріальною гіпертензією, водночас індекс аугментації аорти був достовірно вищим на 37,6% (p<0.01). Установлено, що хворі 1-ї групи мали достовірно вищий показник швидкості поширення пульсової хвилі в каротидно-феморальному сегменті порівняно з 2-ю групою – на 7,5% (p<0.01). Установлені достовірні кореляційні зв'язки між індексом аугментації плечової артерії та віком, рівнем загального холестерину, коефіцієнтом атерогенності, холестерину ліпопротеїдів високої та низької щільності, тригліцеридів, рівнем кардіоваскулярного ризику за шкалою SCORE у хворих на поєднаний перебіг хронічного панкреатиту з артеріальною гіпертензією. Висновки. Хворі з поєднаним перебігом хронічного панкреатиту та артеріальної гіпертензії мали достовірно вищі показники тригліцеридів, холестерину ліпопротеїдів низької щільності та загального холестерину. Зміни показників пружноеластичних властивостей артерій у хворих на хронічний панкреатит із коморбідною артеріальною гіпертензією характеризувались підвищенням індексу аугментації та швидкістю поширення пульсової хвилі в каротидно-феморальному сегменті.

Chronic pancreatitis (CP) is an important public health problem with a high prevalence worldwide. CP is characterized by the development of persistent destructive inflammatory process, which can eventually lead to irreversible damage of endocrine and exocrine function of the pancreas with the subsequent development of diabetes [5, 10].

The problem of managing patients with CP is often determined by its combination with other diseases in terms of polymorbidity. Current literature suggests that exocrine pancreatic insufficiency is more likely to develop in patients with cardiovascular pathology [6]. Thus, according to the results of a recently published meta-analysis, the incidence of acute coronary syndrome is 2.5 times higher among patients with CP [6]. The authors note that CP and exocrine pancreatic insufficiency should be considered as independent risk factors for cardiovascular events.

The high prevalence of hypertension and diseases of the gastrointestinal tract in general population determine the relevance of studying the peculiarities of these comorbid pathology [1]. It is known that the main risk factors for CP include alcohol abuse, smoking, regular consumption of fatty foods, obesity and also common in the formation of hypertension [7]. It should be noted that the local angiotensin-generating system has been found in the exocrine part of the pancreas, which plays an important role in the regulation of insulin secretion and imbalance in the ratio of angiotensin-converting enzyme (ACE)/ACE2 even in man [8].

The above data determined our interest in studying the features of the combined course of CP and arterial hypertension (AH) and the search for therapeutic opportunities to improve the prognosis in this category of patients.

It is known that dyslipidemia, in particular hypertriglyceridemia, plays an important role in the pathogenesis of hyperlipidemic pancreatitis and in the formation of cardiovascular risk in patients with AH [9]. However, there are limited data on the effect of comorbid CP on lipid metabolism in patients with AH.

The aim of this study was to determine the blood lipid spectrum and elastic properties of arteries in patients with chronic pancreatitis in relation to arterial hypertension.

MATERIALS AND METHODS OF RESEARCH

The study was conducted with approval from the Local ethics committee according to principles outlined in the Helsinki declaration. All participants of presented study have been informed,, written consent. 110 patients (46 men, 64 women) aged 45-65 years (median age – 50.7 [45.4; 58.0] years) with CP in combination with AH were examined who attended the outpatient clinic between 01/2020 and 03/2021.

Diagnosis of CP was based on history, clinical manifestations and results of laboratory and instrumental studies, taking into account the recommendations of the United European Gastroenterology for the diagnosis and treatment of chronic pancreatitis, based on evidence [11]. The diagnosis of AH was established according to the recommendations of the Ukrainian Association of Cardiologists (2012), clinical recommendations of the European Society of Hypertension and the European Society of Cardiology [12]. Inclusion criteria were the presence of a verified diagnosis of stage II, grade 1 and 2 hypertension; presence of a diagnosis of CP, consistently selected therapy for CP (at least 6 months) and constant antihypertensive therapy for 1 month, age 45-65 years, voluntary informed

consent to participate in the study. Exclusion criteria: established and verified diagnosis of coronary heart disease, acute pancreatitis, stage III and III hypertension, prior therapy with hypolipidemic drugs, chronic heart failure III-IV functional class (FC), diabetes mellitus, hypothyroidism, glomerular filtration rate <60 min. / 1.73 m2, obesity 3-4 degrees.

All patients with CP received standard therapy with the inclusion of pancreatin drugs in the form of minimicrospheres and mini-tablets. At the same time, all included patients with hypertension received stably selected, unchanged (for the last three months) antihypertensive therapy (combination of perindopril with amlodipine).

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, patients in groups 1 and 2 were comparable in age, gender structure, BMI, and duration of CP and its course, received therapy (Table 1). Normal body weight was determined in 32 (29.1%) examined patients, overweight – in 35 (31.8%) patients, first-degree obesity – in 26 (23.6%) patients, second-degree – in 17 (15,5%) patients.

Table 1

Baseline characteristics of the study population

Characteristic	1st group (n=70)	2nd group (n=40)	p
Median of age, years	**66 [57.5; 74.4]**	**64 [54.4; 72.8]**	**0.35**
gender structure (female:male)	**25:45**	**21:19**	**-**
BMI, kg/m2	**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 study and control groups (the Mann-Whitney U-test).

All patients were measured for height and weight, waist circumference, and BMI according to a standard formula. The content of total cholesterol (TC), triglycerides (TG), high-density cholesterol (HDL cholesterol) in serum was determined by standard enzyme-linked immunosorbent assay. The level of low-density cholesterol (LDL cholesterol) and very low-density cholesterol (VLDL cholesterol) was calculated according to the formulas proposed by A.N. Klimov [4].

Arterial stiffness was defined as pulse wave velocity, which was calculated according to the formula proposed by the Society of Arterial Stiffness (calculated) and measured using the device BAT41-2 (carotid-femoral) [13].

Data processing and analysis were performed using Libre Office and licensed program STATISTICS (license No. AGAR909E415822FA). More than 50% of the data had a different than normal type of distribution according to the Shapiro-Wilk test, so the analysis used non-parametric statistics, the data were described as the median and 25 and 75 quartiles. Comparing quantitative indicators, the Mann – Whitney test was used; Pearson's Chi-square test ($\chi 2$) was used to compare qualitative indicators. Correlation analysis was performed using the non-parametric Spearman correlation coefficient (ρ). The trend lines on the charts correspond to the linear regression lines. The significant level of p for statistical hypotheses is taken <0.05 [14].

RESULTS AND DISCUSSION

In lipid profiles of patients with CP, elevated levels of TG, LDL cholesterol and TC were observed in 95 (86.4%), 104 (94.5%) and 101 (91.8%) patients, respectively. Decreased levels of HDL cholesterol were found in 38 (34.5%) patients. It was established that patients of the 1st group had significantly higher levels of TG (37.2%), LDL cholesterol (13%), TC (25%), atherogenic ratio (19.6%) and significantly lower HDL (by 15.4%), the medians of the indicators are given in Table 2. The correlations between age and the level of atherogenic ratio, LDL were estimated – r=0.35; p<0.01; r=0.37; p<0.01, respectively. The duration of CP was positively correlated with the level of TG, LDL – r=0.43; p<0.01; r=0.34; p<0.01, respectively.

Table 2

The indicators of lipid spectrum in examined patients

Indicator	All patients (n=110)	CP+AH (n=70)	CP (n=40)	p
TC, mmol/l	6.9 [6.0;7.8]	7.6 [7.0;8.2]	5.7 [5.3;6.1]	<0.01
HDL, mmol/l	1.1 [1.0;1.3]	1.1 [0.9;1.1]	1.3 [1.2;1.4]	<0.01
LDL, mmol/l	3.6 [3.3;4.3]	3.9 [3.4;4.5]	3.4 [2.8;3.6]	<0.01
VLDL, mmol/l	0.9 [0.8;1.0]	0.9 [0.8;1.0]	0.8 [0.8;0.9]	>0.01
TG, mmol/l	3.9 [3.1;4.4]	4.3 [3.9;4.6]	2.7 [1.8;3.3]	<0.01
Atherogenic ratio	4.2 [3.7;4.8]	4.6 [4.1;4.9]	3.7 [3.2;4.1]	<0.01

Notes: TC – total cholesterol, TG – triglycerides, HDL – high-density cholesterol, LDL – low-density cholestero, VLDL – very low-density cholesterol.

In the analysis of lipid spectrum in patients with combined CP and hypertension depending on gender structure, it was found that men had a significantly higher level of cholesterol, LDL, TG, atherogenic ratio compared to women – by 16.4%, 14.4%, 31.5% and 25.3%, respectively (Table 3).

Table 3

Indicators of the lipid spectrum in patients with a combined course of CP and hypertension depending on gender structure

Indicator	Men CP+AH (n=25)	Women CP+AH (n=45)	p
TC, mmol/l	7.85 [6.6;8.5]	6.56 [5.9;7.2]	<0.01
HDL, mmol/l	1.18 [1.0;1.18]	1.12 [0.9;1.2]	>0.01
LDL, mmol/l	4.11 [3.6;4.8]	3.52 [3.12;3.96]	<0.01
VLDL, mmol/l	0.93 [0.82;1.2]	0.71 [0.65;1.0]	>0.01
TG, mmol/l	4.63 [3.96;4.89]	3.17 [2.78;3.87]	<0.01
Atherogenic ratio	4.75 [4.23;5.1]	3.55 [3.41;4.0]	<0.01

Notes: TC – total cholesterol, TG – triglycerides, HDL – high-density cholesterol, LDL – low-density cholestero, VLDL – very low-density cholesterol.

Determining the elastic properties of arteries in patients with combined CP and AH, a significantly lower level of augmentation index (Aix) of the brachial artery was found (by 43%), while the aortic augmentation index was significantly higher by 37.6% ($p<0.05$). It was found that patients of the 1st group had a significantly higher pulse wave velocity in the carotid-femoral segment compared to the 2nd group – by 7.5% ($p<0.05$) (Table 4).

It should be noted that men with a combined course of CP and AH were characterized by significantly higher indicators of brachial artery stiffness in comparision to women (Table 5).

Table 4

The indicators of elastic properties of arteries in the examined patients.

indicators	All patients (n=110)	CP+AH (n=70)	CP (n=40)	p
RR brachial artery, mm	40.0 [35.0;48.0]	43.0 [37.0;53.5]	39.0 [34.5;43.5]	>0.01
PP aorta, mm	32.0 [26.0;38.0]	36.0 [29.2;43.8]	27.0 [23.5;32.0]	<0.01
Aix brachial artery, %	-39.7 [-63.1;-24.2]	-32.1 [-47.3;-11.7]	-56.3 [-71.6;-40.5]	<0.01
Aix aorta, %	20.2 [11.9;25.8]	22.9 [17.5;30.2]	14.3 [8.8;19.9]	<0.01
Aix.75. brachial artery, %	-40.5 [-55.2;-21.5]	-34.0 [-46.3;-16.6]	-52.6 [-64.5;-40.8]	<0.01
Aix.75. aorta, %	17.1 [9.7;26.8]	20.4 [14.2;29.2]	11.0 [5.0;17.0]	<0.01
PWVcf, m/s	8.9 [8.4;9.5]	9.3 [8.5;9.7]	8.6 [8.1;8.9]	<0.01
SAI, %	48.8 [45.4;54.4]	48.8 [45.4;54.6]	49.5 [45.4;54.0]	>0.01
DAI, %	51.3 [46.1;55.3]	52.1 [46.3;55.3]	50.5 [46.0;54.6]	>0.01
SEVR, %	176.1 [153.6;194.9]	177.6 [153.8;194.1]	171.9 [153.6;196.2]	>0.01

Notes: Aix – augmentation index, DAI – diastolic index of the area of the cardiac cycle, PP – pressure increasing rate, PWVcf – pulse wave velocity in the carotid-femoral segment, SAI – systolic index of cardiac area cycle, SEVR – index of subendocardial blood flow efficiency, RR – diameter increasing rate.

Table 5

Indicators of elastic properties of arteries in patients with CP in combination AH depending on gender structure

indicators	Men CP+AH (n=25)	Women CP+AH (n=45)	p
RR brachial artery, mm	45.2 [37.4;54.4]	40.2 [34.8;53.7]	>0.01
PP aorta, mm	39.2 [32.5;44.9]	35.5 [28.0;39.7]	>0.01
Aix brachial artery, %	-29.8 [-55.8;-9.9]	-35.7 [-46.7;-14.3]	<0.01
Aix aorta, %	25.7 [19.1;32.1]	20.2 [14.6;29.9]	>0.01
Aix.75. brachial artery, %	-39.0 [-48.9;-22.4]	-30.4 [-39.5;-14.9]	<0.01
Aix.75. aorta, %	23.8 [12.8;30.4]	17.4 [9.4;24.7]	>0.01
PWVcf, m/s	9.9 [8.1;10.5]	9.0 [7.9;9.4]	>0.01
SAI, %	49.9 [45.2;55.0]	46.1 [44.9;55.7]	>0.01
DAI, %	52.8 [46.8;57.4]	50.2 [45.3;58.5]	>0.01
SEVR, %	178.9 [159.7;196.3]	180.4 [152.4;198.7]	>0.01

Notes: Aix – augmentation index, DAI – diastolic index of the area of the cardiac cycle, PP – pressure increasing rate, PWVcf – pulse wave velocity in the carotid-femoral segment, SAI – systolic index of cardiac area cycle, SEVR – index of subendocardial blood flow efficiency, RR – diameter increasing rate.

Significant correlations have been established between the brachial artery augmentation index and age, cholesterol level, atherogenic ratio, HDL, LDL, TG, cardiovascular risk level on the Systematic COronary Risk Evaluation (SCORE) scale in patients with combined CP with AH (Fig. 1). At the same time, the aortic augmentation index in these patients correlated only with age and TC, TG (Fig. 2). The level of pulse wave velocity in the carotid-femoral segment was most associated with LDL (Fig. 3).

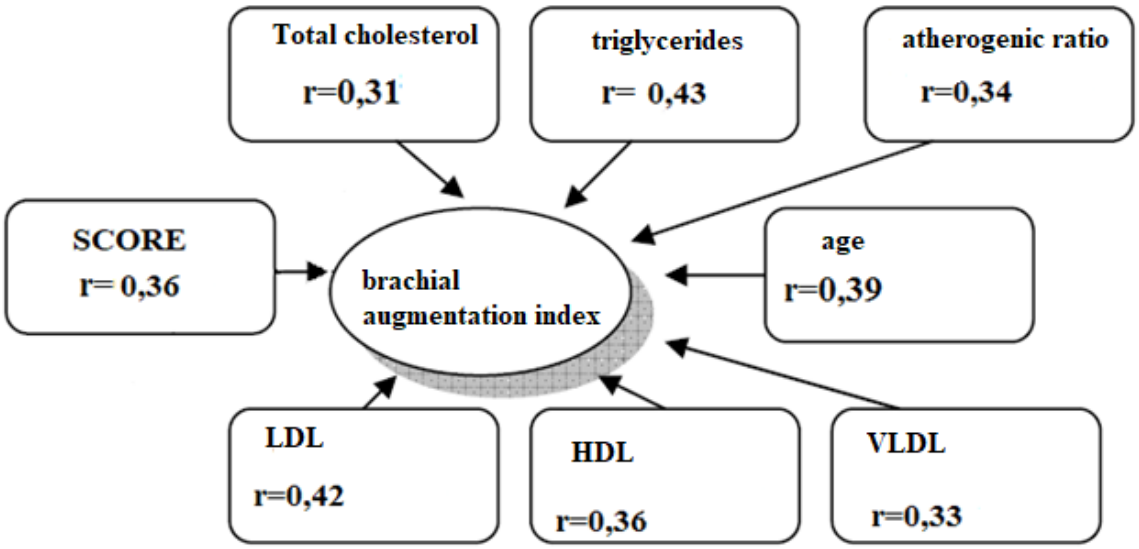

Fig. 1. Correlation between lipid complex parameters and brachial artery augmentation index in patients with CP in combination with AH

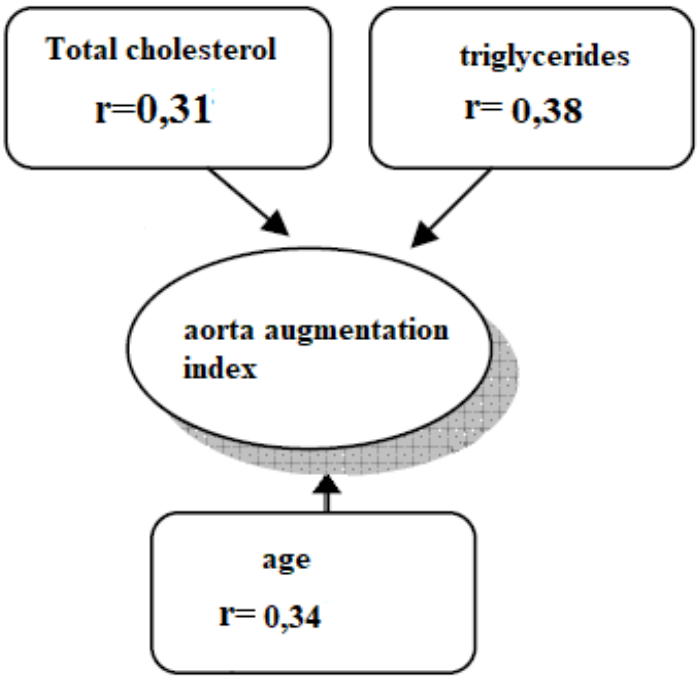

Fig. 2. Correlation between lipid complex parameters and aortic augmentation index in patients with CP in combination with AH

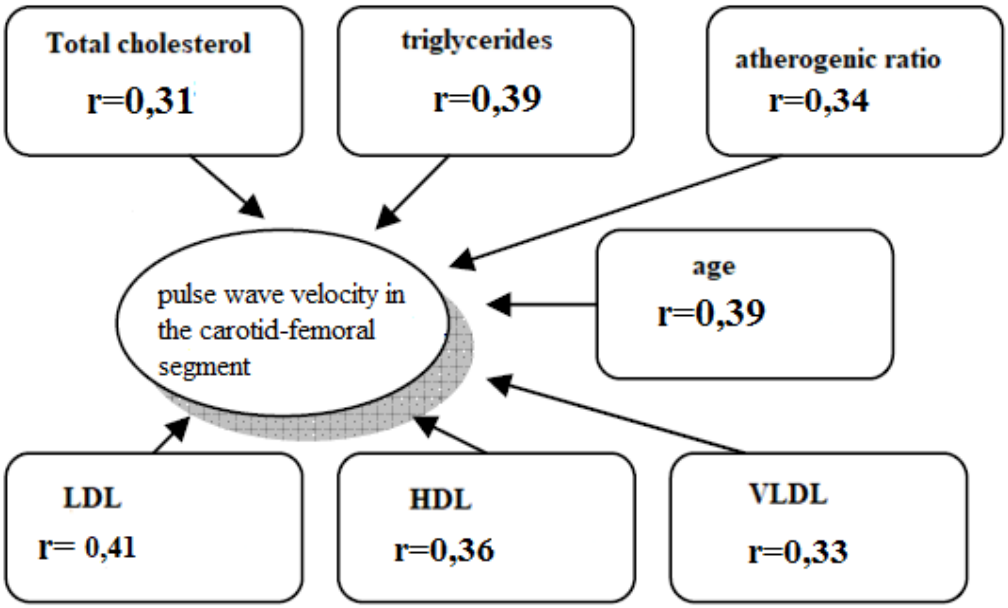

Fig. 3. Correlation between lipid complex parameters and pulse wave velocity in carotid-femoral segment in patients with CP in combination with AH

The obtained results indicate that patients with a combined course of CP with AH in comparison with isolated CP had statistically more significant changes that characterize the proatherogenic blood lipid spectrum. The influence of AH on lipid metabolism may be related to genetic factors, as the predisposition to the development of AH and dyslipidemia may be the result of inheritance of common genetic alleles [15]. On the other hand, hypertension can directly effect on the development of dyslipidemia in comorbid conditions [2, 3]. Therefore, the possible influence of antihypertensive therapy on lipid spectrum parameters, in particular thiazide diuretics and beta-blockers, should be noted [15].

It should be emphasized that the majority of enrolled patients with CP and AH were overweight, so there is an accumulation of a number of phenotypic prerequisites for the formation of high cardiovascular risk: lifestyle, unbalanced diet, low physical activity. Significantly higher levels of proatherogenic lipid fractions in men might associate with low treatment compliance, non-compliance with dietary guidelines, bad habits, and so on.

According to the results of the analysis of elastic properties of arteries in patients with CP, it was found that the presence of concomitant AH was associated with significantly higher arterial stiffness, which correlated with proatherogenic lipid fractions, especially TG. It should be noted that according to the obtained data, men with a combined course of CP and AH had the most significant increasing in the stiffness of the brachial artery. It is worth noting the data of a recent large-scale study showed an increase in the number of patients aged 30-79 with AH from 1990 to 2019 from 331 million women and 317 million men in 1990 to 626 (584-668) million women and 652 (604-698) millions of men in 2019 [15]. As a result, men show a greater increase in the prevalence of AH, which may be related to vascular remodeling in these patients.

Thus, the presence of concomitant AH had a negative impact on lipid metabolism and elastic properties of arteries in patients with CP, which requires early detection and active drug exposure.

CONCLUSIONS

1. Men with a combined course of chronic pancreatitis and arterial hypertension had significantly higher levels of TG, LDL cholesterol and total cholesterol.
2. Changes in the elastic properties of arteries in patients with chronic pancreatitis with comorbid arterial hypertension were characterized by significant increasing of augmentation index and pulse wave velocity in the carotid-femoral segment.

Contributors:

Filippova A.Yu. – methodology, formal analysis, resources, writing – original draft, writing – review & editing, visualization, supervision, project administration;

Löhr M. – conceptualization, writing – riginal draft, writing – review & editing, visualization, funding acquisition;

Kryvoshei V.V. – software, validation, formal analysis, resources, data curation, writing – original draft, writing – review & editing, visualization.

Funding. This research received no external funding.

Conflict of interests. The authors declare no conflict of interest.

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Стаття надійшла до редакції
28.12.2021