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LIPID METABOLISM INDICATORS IN PATIENTS WITH STAGE II ESSENTIAL HYPERTENSION DEPENDING ON THE PRESENCE OF CONCOMITANT METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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170 patients with stage II hypertension were examined. Based on the presence of metabolic dysfunction-associated steatotic liver disease (confirmed by ultrasound and FibroTest), all examined patients were divided into two clinical groups. The first clinical group included 109 patients with stage II hypertension and steatotic liver disease, and the second group included 61 patients with stage II hypertension without liver damage. The control group included 30 practically healthy individuals. In addition to general clinical and laboratory examinations, all patients underwent determination of serum lipid profile indicators and lipoprotein (a). Comorbidity of stage II hypertension and metabolic dysfunction-associated steatotic liver disease was accompanied by a significant ($p<0.05$) increase in the concentration of total cholesterol, LDL-cholesterol, VLDL cholesterol, triglycerides, atherogenicity index, and lipoprotein (a) both in comparison with healthy individuals and patients with stage II hypertension without concomitant liver damage, which may indicate a significantly increased risk of developing atherosclerosis and other cardiovascular diseases in these patients.

Key words: arterial hypertension, hypertensive disease, metabolic dysfunction-associated steatotic liver disease, lipoprotein (a), lipid spectrum.

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ПОКАЗНИКИ ЛІПІДНОГО ОБМІНУ У ХВОРИХ НА ГІПЕРТОНІЧНУ ХВОРОБУ II СТАДІЇ В ЗАЛЕЖНОСТІ ВІД НАЯВНОСТІ СУПУТНЬОЇ МЕТАБОЛІЧНО-АСОЦІЙОВАНОЇ СТЕАТОТИЧНОЇ ХВОРОБИ ПЕЧІНКИ

Обстежено 170 хворих з гіпертонічною хворобою II стадії. Залежно від наявності метаболічно-асоційованої стеатотичної хвороби печінки (підтвердженої за допомогою ультразвукового методу обстеження та фібротесту) всі обстежені пацієнти були поділені на дві клінічні групи. До першої клінічної групи увійшло 109 пацієнтів з гіпертонічною хворобою II стадії та стеатотичною хворобою печінки, до другої – 61 пацієнт з гіпертонічною хворобою II стадії без ураження печінки. До групи контролю увійшло 30 практично здорових осіб. Усім пацієнтам, окрім загальноклінічних і лабораторних методів обстеження, було проведено визначення показників ліпідного спектру сироватки крові та ліпопротеїну (а). Коморбідність гіпертонічної хвороби II стадії та метаболічно-асоційованої стеатотичної хвороби печінки супроводжувалась суттєвим ($p<0,05$) зростанням концентрації загального холестерину, холестерину в ЛПНЩ та ЛПДНЩ, тригліцеридів, індексу атерогенності та ліпопротеїну (а) як порівняно із здоровими особами, так і хворими на гіпертонічну хворобу II ст. без супутнього враження печінки, що може свідчити про суттєво підвищений ризик розвитку атеросклерозу та інших серцево-судинних захворювань у даних пацієнтів.

Ключові слова: артеріальна гіпертензія, гіпертонічна хвороба, метаболічно-асоційована стеатотична хвороба печінки, неалкогольна жирова хвороба печінки, ліпопротеїн (а), ліпідний спектр.

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Today, arterial hypertension (AH) is considered not only an independent disease, essential hypertension (EH), but also a leading risk factor for the development of other cardiovascular diseases [4, 5, 9]. Accumulated clinical experience provides grounds for considering AH as one of the etiological factors of metabolic disorders, including liver disease [1, 3]. According to recent studies, among patients with metabolic dysfunction-associated steatotic liver disease (MASLD), cardiovascular mortality is ahead of the incidence of hepatocellular carcinoma and other specific liver diseases [6, 10]. Life expectancy assessment among patients with MASLD has established that mortality in this group is the highest, namely due to cardiovascular disease. It accounted for 48 % of total mortality, while the indicator associated with liver damage was only 7 % [8].

In clinical practice, it is quite common (almost 70 % of cases) to encounter comorbidity of EH and MASLD [5, 6], which are united not only by significant prevalence and, therefore, by a high probability of combination, but also by common risk factors [9]. Given the lack of a clear clinical picture, MASLD is often detected during a "targeted" examination of patients with increased body weight and is very rarely diagnosed among patients without excess body weight and obesity [1, 6]. Today, the hypothesis of the common pathogenetic mechanisms of their development is confirmed, and the presence of MASLD is considered a factor that

can change the prognosis in patients with hypertension [8]. On the other hand, according to many researchers, MASLD acts as an independent risk factor for the progression of cardiovascular pathology, as it is considered an "additional" component of the metabolic syndrome [3, 6].

Therefore, in the case of comorbidity of EH and MASLD, a detailed assessment of lipid metabolism indicators can provide additional information to clarify the role of concomitant MASLD in assessing the overall cardiovascular risk of patients with EH stage II.

The purpose of the study was to evaluate lipid metabolism indicators in patients with stage II hypertension depending on the presence of concomitant metabolic-associated steatotic liver disease.

Materials and methods. In accordance with the study objectives, 170 patients with stage II EH who were undergoing inpatient treatment in the cardiology department of the Vinnytsia Regional Pirogov Clinical Hospital from August 2018 to September 2024 were randomly selected and examined. The study began with screening, careful collection of complaints and anamnesis, and obtaining written informed consent from the patient to participate in the study, in accordance with the ethical norms of the Declaration of Helsinki and the local bioethics committee.

Inclusion criteria: patients with a verified diagnosis of stage II EH: men and women aged 30 to 69 years with and without concomitant MASLD. The diagnosis of EH was established after a detailed clinical and instrumental examination in accordance with the clinical recommendations of the ESH, ESC (2024) [4, 5]. The diagnosis of MASLD was established based on anamnesis data, clinical examination with mandatory consideration of generally accepted laboratory indicators, and results of instrumental methods. Viral hepatitis B and C were excluded by detecting specific antibodies to virus antigens by ELISA (Roche Diagnostics e601, Switzerland) using reagent sets "Alere Medical Determine HBsAg" and "Mikrogen, Immunoblot HCV IgG, 20", respectively. The size, contour, acoustic structure, and echogenicity of liver tissue were assessed using ultrasound (TOSHIBA XARIO 100, Japan). To confirm the diagnosis of MASLD, patients with stage II EH underwent the biochemical test "FibroMax" (BioPredictive, France), which included five diagnostic algorithms: "FibroTest", "ActiTest", "SteatoTest", "NashTest", and "AshTest". Only 109 patients with concomitant MASLD participated in the study – the "SteatoTest" index was 0.41 units and was estimated within S1-S2 (from 6 to 32 % of "fatty" liver infiltration) without signs of cytolysis syndrome, fibrosis, or alcoholic liver damage.

Exclusion criteria: The study did not include patients with stage I and III hypertension, symptomatic hypertension, concomitant coronary artery disease, the presence of chronic heart failure stage II–III (according to M. D. Strazhesko – V. Kh. Vasylenko), FC III–IV (according to NYHA), cardiac arrhythmias (ventricular extrasystole of high gradations, atrial fibrillation), congenital and acquired heart defects, concomitant liver diseases of viral, alcoholic, autoimmune, and other etiologies, kidney diseases with impaired function, diabetes mellitus, stage III obesity, chronic obstructive pulmonary disease, respiratory failure and systemic connective tissue diseases.

170 patients with stage II EH were examined (98 (57.6 %) women and 72 (42.4 %) men) aged 35 to 69 years (mean age 49.3±0.5 years). The ratio of women to men was 1.3:1; in the main clinical array, female patients significantly predominated ($p<0.02$). The control group included 30 people without any clinically significant verified chronic diseases of internal organs, without signs of cardiovascular and hepatobiliary pathology, aged 34 to 66 years (mean age 48.1±2.1 years). The main clinical array and the control group were matched by age and sex.

All subjects were divided into 2 groups depending on the presence of concomitant MASLD. The 1st group consisted of 109 (64 %) patients with concomitant MASLD, among whom there were 39 (35.8 %) men and 70 (64.2 %) women with a significant ($p<0.05$) predominance of female patients; the 2nd group included 61 (36 %) patients (28 (45.9 %) women and 33 (54.1 %) men) without signs of concomitant liver damage.

The initial examination of the subjects included the collection of complaints and anamnesis data, which included family, professional, and social anamnesis, the presence of psycho-emotional stress, bad habits, past and concomitant diseases, nutritional characteristics (abuse of table salt, strong tea or coffee, excessive consumption of animal fats), and physical activity.

Blood pressure (BP) was measured according to recommendations using a sphygmomanometer (Microlife). BP measurements were performed in the morning between eight and ten o'clock after 15 minutes of rest. Systolic BP and diastolic BP in a sitting position were recorded on the same arm twice, with an interval of 2 minutes if the BP values did not differ by more than 5 mm Hg. If a greater difference between the obtained values was detected, a third measurement was performed, and the average value of two or three consecutive measurements was calculated.

All subjects underwent general laboratory tests, which included a complete blood count, a complete urine test, blood sugar, creatinine, electrolytes, and additional biochemical tests that allowed for a more complete assessment of the state of lipid metabolism (determination of lipid spectrum indicators and serum lipoprotein (a) (Lp(a)) levels).

The level of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) was determined by the spectrophotometric method using standard reagent sets "Cholesterol-F", "Triglycerides-F", and "HDL-cholesterol" manufactured by "Filisit-Diagnostics" (Ukraine). The level of very low-density lipoprotein cholesterol (VLDL-C) was determined by the formula: TG x 0.45. The level of low-density lipoprotein cholesterol (LDL-C) was calculated by the formula of W. Friedwald: LDL-C = LDL-C – HDL-C – (0.45 x TG). The atherogenic index (IA) was calculated as the ratio of the amount of cholesterol in proatherogenic lipoproteins to HDL-C: IA = LDL-C – HDL-C / HDL-C.

The level of Lp(a) was determined by the "sandwich" variant of solid-phase ELISA using the "Human Lp(a) ELISA Kit" reagent sets (Assaypro, USA) on the STAT FAX 303/PLUS analyzer.

The obtained values of all indicators of instrumental and laboratory diagnostic methods were compared with the corresponding results of the control group.

Statistical analysis of the study results was performed using variational statistics methods in the StatSoft "Statistica" v. 10.0.228.8 program, according to the recommendations. The results of the study are presented as quantitative values (median and interquartile range [25th and 75th percentiles]) and as relative values (%). The reliability of the difference % was calculated using the $\chi 2$ criterion. To determine the relationship between individual parameters, a single-factor nonparametric correlation analysis and the Spearman Rank Order Correlation method were used.

Results of the study and their discussion. When examining all patients with stage II EH, proatherogenic changes in the lipid profile were observed compared with healthy individuals. The presence of concomitant MASLD in patients with stage II EH, in turn, was associated with greater changes in blood lipid levels (Table 1).

Table 1

Analysis of biochemical parameters in groups of patients with stage II EH, depending on concomitant MASLD

Indicators	Control (n=20)	EH II (n=61)	EH II and MASLD (n=109)	P1-2	P1-3	P2-3
	1	2	3			
Lp (a), mcg/ml	89.8 (71.6; 125.4)	105.2 (87.7; 133.4)	166.2 (121.2; 218.5)	0.03	<0.0001	0.0007
TC, mmol/L	4.6 (4.3; 5.0)	5.2 (4.6; 5.6)	5.6 (5.1; 6.7)	0.02	<0.0001	0.0009
HDL-C, mmol/L	1.19 (1.06; 1.22)	0.98 (0.89; 1.04)	0.99 (0.91; 1.06)	<0.0001	<0.0001	ns
TG, mmol/L	1.44 (1.34; 1.56)	1.67 (1.39; 2.02)	2.00 (1.55; 2.50)	0.03	<0.0001	0.02
VLDL-C, mmol/L	0.65 (0.60; 0.70)	0.76 (0.63; 0.91)	0.90 (0.70; 1.12)	0.03	<0.0001	0.01
LDL-C, mmol/L	2.8 (2.5; 3.1)	3.4 (2.8; 3.8)	3.8 (3.3; 4.5)	0.05	0.0001	0.01
IA	2.97 (2.69; 3.47)	4.41 (3.61; 5.10)	4.82 (4.20; 5.79)	<0.0001	<0.0001	0.04
FibroTest	0 (0; 0)	0.07 (0.02; 0.12)	0.24 (0.14; 0.28)	<0.0001	<0.0001	0.003
ActiTest	0 (0; 0)	0.07 (0.02; 0.12)	0.24 (0.16; 0.32)	<0.0001	<0.0001	0.003
SteatoTest	0.015 (0.005; 0.04)	0.17 (0.12; 0.22)	0.41 (0.37; 0.56)	<0.0001	<0.0001	0.002
NashTest	0 (0; 0)	0.12 (0.12; 0.13)	0.21 (0.17; 0.23)	<0.0001	<0.0001	0.002
AshTest	0 (0; 0)	0.03 (0.00; 0.07)	0.02 (0.01; 0.04)	0.003	0.004	ns

Thus, the level of TC among the examined patients without additional liver damage was significantly ($p<0.05$) higher than in the control group by 13 %. The course of stage II EH combined with MASLD was accompanied by a significant increase in TC levels, by 22 % compared to the control ($p<0.05$) and by 7.6 % compared to patients with stage II EH without signs of MAFLD ($p<0.05$) (Fig. 1).

A significant ($p<0.05$) increase in the average serum TG concentration was found among all subjects compared with healthy individuals. The presence of MASLD in patients with stage II EH was associated with a significant ($p<0.05$) 39 % increase in TG compared with the control value and a 20 % increase ($p<0.05$) compared with the similar indicator in patients with stage II EH without MASLD.

In patients with stage II EH, LDL and VLDL cholesterol levels were significantly higher ($p<0.05$) than in controls. Comorbidity of stage II EH and MASLD was accompanied by a significant ($p<0.05$) increase in LDL and VLDL cholesterol concentrations both in comparison with healthy individuals and patients with stage II EH without concomitant liver damage (LDL – by 35.7 % and 11.8 %, respectively ($p<0.05$), VLDL – by 38.5 % and 18.4 %, respectively ($p<0.05$)).

The level of HDL cholesterol among all patients included in the study was significantly ($p<0.05$) lower than in the control group: in the group of patients with stage II EH without concomitant liver damage – 18 %, and in the combination of stage II EH with MASLD – by 17 % (without a significant difference depending on the presence of MASLD, $p>0.05$).

Among patients with comorbidity of stage II EH and MASLD, the highest value of IA was recorded – 4.82 (4.20; 5.79), which significantly ($p<0.05$) differed from the similar indicator among healthy

individuals (2.97 (2.69; 3.47) and from patients with isolated stage II (4.41 (3.61; 5.10)).

It is especially necessary to highlight the existing reliable direct correlation between IA and the "SteatoTest" indicator (rs=0.33, p<0.05), which indicates the associative relationships between the development of MASLD and proatherogenic changes in blood lipids.

Among the examined patients with stage II EH, the level of Lp(a) (Fig. 2) significantly (p<0.05) increased compared to the control: by 13.8 % in the group without concomitant MASLD and by 85.7 % in the comorbid course of stage II EH and MASLD. A significant (p<0.05) difference in the level of Lp(a) was recorded in the groups of patients with stage II EH depending on the presence of concomitant MASLD: in the presence of "fatty infiltration" of the liver, the level of Lp(a) was 58 % higher compared to that among patients without signs of liver damage (p=0.0001).

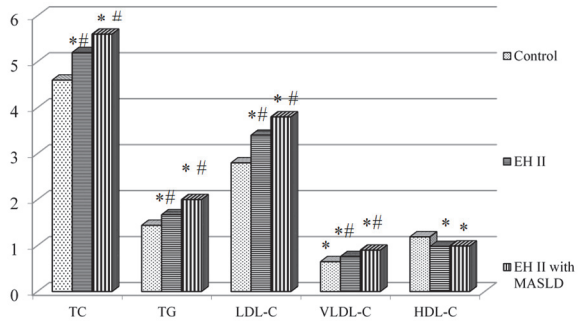

Fig. 1. Indicators of the lipid spectrum of blood serum in patients with stage II EH, depending on the presence of MASLD. Notes (here and hereafter): * – significance of the difference compared to the control (p<0.05); # – significance of the difference between groups without/with MASLD (p<0.05).

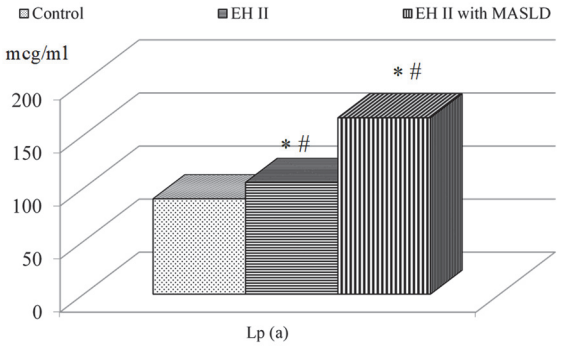

Fig. 2. Serum Lp(a) concentration indicators in patients with stage II EH depending on the presence of MASLD.

The increase in IA was also associated with pathological changes in the lipid transport system ((significant (p<0.05) direct correlations were noted between the IA index and the level of Lp(a), (rs=0.23)). The obtained data confirm the hypothesis of the commonality of certain pathogenetic mechanisms underlying the development of AH and MASLD, which lead to pronounced metabolic shifts and increase overall cardiovascular risk [2, 7, 8].

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Comorbid course of stage II EH and MASLD is characterized by profound destabilization of lipid metabolism, which has a multifactorial nature. Our results confirm the complex and ambiguous role of Lp(a) in the pathogenesis of cardiometabolic disorders. Although today the role of Lp(a) in the development of atherosclerosis, hypertension and MASLD remains a subject of discussion in the scientific community [10, 11, 12], our study recorded direct reliable correlations between the level of Lp(a) and key indicators of the lipid spectrum. In particular, positive correlations were found with the level of total cholesterol, triglycerides, as well as cholesterol in VLDL and LDL (r_s from 0.21 to 0.32, p<0.05). The most significant was the relationship with the atherogenic index (AI) (r_s=0.23), which emphasizes the potential role of Lp(a) as a marker of high atherogenic risk. Analysis of the literature data demonstrates contradictory conclusions regarding the relationship between Lp(a) and MASLD. Some authors point to a paradoxical inverse correlation, where lower levels of Lp(a) are associated with more severe liver fibrosis. However, our data on the direct relationship of Lp(a) with atherogenic lipids in patients with fatty hepatosis indicate that in a certain cohort of patients Lp(a) may act as an additional independent cardiovascular risk factor, independent of the degree of steatosis, which coincides with the opinion of some researchers [12, 13]. Changes in the lipid profile in the combination of EH and MASLD indicate that the liver loses the ability to adequately regulate lipoprotein metabolism, which, against the background of arterial hypertension, creates the prerequisites for accelerated damage to target organs. An increase in the level of Lp(a) by 58 % (p=0.0001) in patients with a combination of EH and MASLD compared with patients without liver damage also indicates a pronounced increase in vascular risk in this category of patients, since this indicator itself is an independent factor in the development of atherosclerosis and systemic inflammation.

An important aspect is that Lp(a) is a genetically determined factor, the level of which practically does not change under the influence of standard diet therapy, taking statins or other currently known drugs [7]. This makes its assessment critically important for a personalized approach to determining cardiovascular risk. Inclusion of Lp(a) determination in the comprehensive diagnosis of patients with MASLD allows identifying individuals who require

more active attention and actions to prevent vascular catastrophes.

Thus, a significantly higher level of Lp(a) in the comorbidity of EH and MASLD reflects the aggressiveness of the atherogenic process, increased cardiovascular risk and requires the implementation of more intensive strategies for correcting the condition. This emphasizes the need for comprehensive monitoring of lipid metabolism for timely prevention of cardiovascular complications in this category of patients.

Limitations. The limitations of the study include the lack of the possibility of verifying MASLD using a liver biopsy, given the invasiveness of this method and the lack of absolute indications in patients with the initial stage of MASLD (steatosis). Another limitation was the lack of long-term dynamic observation of patients, which reduces the ability to assess the impact of genetically determined elevated Lp(a) levels on the incidence of cardiovascular events in the long term in patients with comorbidity of hypertension and MASLD.

Conclusions

1. It was established that the comorbidity of EH and MASLD is accompanied not only by an increase in proatherogenic shifts in the lipid spectrum, but also by a specific restructuring of the blood lipid transport system. The key feature of this course is a statistically significant increase in the concentration of lipoprotein (a) by 58 % compared with patients with isolated stage II EH (p=0.0001).

2. A significant increase in Lp(a) levels in patients with a combination of EH and MASLD indicates a pronounced increase in cardiovascular risk in this category of patients.

3. Determination of Lp(a) levels in EH comorbid with MASLD has significant prognostic value for assessing cumulative metabolic risk.

Prospects for further research. Further studies of changes in the metabolic profile in patients with comorbid conditions with hypertension will allow stratifying cardiovascular risk and improving the prognosis of the disease.

References

1. Badmus OO, Hinds TD Jr, Stec DE. Mechanisms Linking Metabolic-Associated Fatty Liver Disease (MAFLD) to Cardiovascular Disease. Curr Hypertens Rep. 2023 Aug;25(8):151-162. doi: 10.1007/s11906-023-01242-8.
2. Cui D, Yu X, Guan Q, Shen Y, Liao J, Liu Y, et al. Cholesterol metabolism: molecular mechanisms, biological functions, diseases, and therapeutic targets. Mol Biomed. 2025 Oct 9;6(1):72. doi: 10.1186/s43556-025-00321-3.
3. Dongier A, Delwaide J, Louis É, Loly JP. Nouvelles recommandations concernant les maladies stéatosiques du foie : ce qu'il faut en retenir [Updated recommendations on metabolic dysfunction-associated steatotic liver disease]. Rev Med Liege. 2025 May;80(5-6):401-409. PMID: 40518897. [in French].
4. ESC/ESH 2018 Guidelines for the management of arterial hypertension. Eur Heart J. 2018; 39 (33): 3021-3104. DOI:10.1093/eurheart/ehy339.
5. ESC 2024 Guidelines for the management of elevated blood pressure and hypertension. Eur Heart J. 2024. DOI:10.1093/eurheartj/ehae178.
6. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. 2024 Sep;81(3):492-542. doi: 10.1016/j.jhep.2024.04.031.
7. Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias. ESC/EAS Scientific Document Group et al. Atherosclerosis. 2025; Volume 409, 120479.
8. Gofton C, George J. Updates in fatty liver disease: Pathophysiology, diagnosis and management. Aust J Gen Pract. 2021 Oct;50(10):702-707. doi: 10.31128/AJGP-05-21-5974.
9. Gribenyuk OV, Kuzminova NV, Osovska NY, Knyazkova II. Arterial hypertension, obesity and non-alcoholic fatty liver disease: is there any connection. Arterial Hypertens, 2016; 20 (4), 216-227. doi:10.5603/AH.2016.0025.
10. Muñoz Rossi FA, Salazar Agudelo J, Quinapanta Castro NI, Mosquera SZ, Mejia Fajardo MC, Mosquera López ED, et al. Relationship Between Metabolic Dysfunction-Associated Steatotic Liver Disease and Lipoprotein (a) and Other Biomarkers. Cureus. 2024 Jun 24;16(6):e63019. doi: 10.7759/cureus.63019.
11. Nam JS, Park K, Baik SJ, Park JS. Lipoprotein(a) level predicts the development of nonalcoholic fatty liver disease in Korean adults: A retrospective longitudinal study. Medicine (Baltimore). 2024 May 31;103(22):e38411. doi: 10.1097/MD.0000000000038411.
12. Nikoli A, Orfanidou M, Goulas A, Goulis DG, Polyzos SA. Circulating lipoprotein(a) in patients with nonalcoholic fatty liver disease: a systematic review and meta-analysis. J Gastroenterol Hepatol. 2024 Dec;39(12):2572-2581. doi: 10.1111/jgh.16768.
13. Wu T, Ye J, Shao C, Lin Y, Wang W, Feng S, et al. The Ability of Lipoprotein (a) Level to Predict Early Carotid Atherosclerosis Is Impaired in Patients With Advanced Liver Fibrosis Related to Metabolic-Associated Fatty Liver Disease. Front Med (Lausanne). 2023 Aug 24;10:1229064. doi: 10.3389/fmed.2023.1229064.

Conflict of interest. The authors have no conflicts of interest to declare.

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