Review article

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The complex role of lipoprotein(a) in the pathophysiology of non-alcoholic fatty liver disease: A systematic review

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ABSTRACT

Aim: The aim of the present systematic review was to summarize the epidemiological studies that have examined the association between lipoprotein(a) (Lp(a)) and liver steatosis or fibrosis.

Methods: A computer-assisted systematic literature search was performed by 2 independent experts for manuscripts that examined the association between Lp(a) and non-alcoholic fatty liver disease (NAFLD).

Results: Overall, n=9 studies were considered as eligible for the present systematic review. In all studies participants' origins were from Asian [n=4 from China, n=3 from Korea and n=1 from Japan] with only one study where participants were recruited from a clinic in Italy. In all studies, the association between Lp(a) and NAFLD was cross-sectional. In n=3 studies, the diagnosis of NAFLD accompanied by histological characteristics of non-alcoholic steatohepatitis (NASH) and liver fibrosis was performed with the gold standard method of liver biopsy. Four studies focused on the association between Lp(a) and liver fibrosis. Most of the selected studies revealed a significant inverse association between Lp(a) and liver fibrosis implying the use of the lipidemic molecule combined with conventional hepatic markers to detect advanced NAFLD stages. In addition to this and considering the aggravating role of Lp(a) in prediction of CVD onset, some scientific teams suggested that in case of advanced hepatic fibrosis this lipid marker should not be used as an indicator of vascular health.

Conclusion: Additional studies are required to clarify the role of Lp(a) in NAFLD and other metabolic diseases in different reference populations.

KEY WORDS: *Lipoprotein(a), steatotic liver disease, liver fibrosis*

INTRODUCTION

Compelling evidence from pathophysiological, observational, and genetic studies suggest a potentially causal association between high lipoprotein(a) (Lp(a)) levels, atherosclerotic cardiovascular disease (CVD), and calcific aortic valve stenosis. The attribute of Lp(a) that affects CVD risk is not established. Low levels of Lp(a) have been also associated with type 2 diabetes (T2DM).[1] In addition to this, evidence has demonstrated that elevated Lp(a) levels are associated with a residual CVD risk irrespective to traditional risk factor optimization, includ-

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ing the reduction in low density lipoprotein cholesterol (LDL-C).[2] This "risk-factor" hypothesis is supported by the accumulation of Lp(a) particles in human atherosclerotic lesions, the findings of Mendelian randomization studies and the amplification of plaque area in animal models expressing apolipoprotein (a).[3] These findings have led to the formulation of the Lp(a) hypothesis, namely that Lp(a) lowering leads to CVD risk reduction, intensifying the search for Lp(a)-reducing therapies.[4]

Advanced non-alcoholic fatty liver disease (NAFLD) in terms of steatohepatitis (NASH) and fibrosis result in increased CVD risk.[5] Besides, the relationship between serum Lp(a) level and NAFLD – especially NASH – is unknown. Dyslipidemia and cardiovascular complications are comorbidities of NAFLD, which range from simple steatosis to steatohepatitis, fibrosis, and cirrhosis up to hepatocellular carcinoma. Lp(a) has been associated with CVD risk and metabolic abnormalities, but its impact on the severity of liver damage in patients with NAFLD remains to be clarified. The aim of the present systematic review was to summarize the epidemiological studies that have examined the association between Lp(a) and liver steatosis or fibrosis.

METHODS

Search strategy

Following the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) 2009 guidelines, a computer-assisted systematic literature search was performed by 2 independent experts, using Medline (PubMed), Scopus and the ISI Web of Knowledge for manuscripts that examined the association between Lp(a) and NAFLD.[6] The search strategy was mainly based on Medical Subject Headings terms, as follows; ("lipoprotein(a)" OR "Lp(a)" OR "apoprotein a" OR "apolipoproteins a" OR "apo(a)") AND ("Non alcoholic Fatty Liver Disease" OR "NAFLD" OR "Nonalcoholic Fatty Liver Disease" OR "fatty liver" OR "Nonalcoholic Steatohepatitis" OR "Nonalcoholic Steatohepatitides" OR "liver fibrosis" OR "liver disease" OR "liver steatosis"). The search was limited to publications in English from April 1 2013 to April 15 2023. The reference lists of retrieved articles were also considered when these were relevant to the issue examined yet not allocated in the basic search. The relevance of studies was assessed by using a hierarchical approach based on: title, abstract and full manuscript. For papers in which additional information was required, the authors were contacted via email.

Selection criteria

Studies were eligible if they were published research epidemiological studies that evaluated the association between Lp(a) and overall NAFLD or specific elements of NAFLD such as liver steatosis, liver fibrosis or liver enzymes. Eligible studies included original research articles retrieved from prospective studies (cohort studies or case-cohort studies) or retrospective or cross-sectional studies with a sample size of at least 100 participants. The exclusion criteria were review articles, letters-to-the editors, editorials and animal studies.

Flow of included studies

The literature search flow diagram is illustrated in Figure 1. Initially, *n*=146 papers were retrieved while after duplicates removal *n*=125 were selected for evaluation. The *n*=107 manuscripts were disregarded on the basis of Title/Abstract because they were irrelevant or were Letters to the Editors or replies to Letters or reviews. Among the rest, *n*=18 manuscripts, *n*=9 manuscripts with *n*=9 studies were considered as relevant to the present work[7-15] (Figure 1).

RESULTS

Overall, n=9 studies were considered as eligible for the present systematic review. The specific characteristics and results of the selected studies are summarized in Table 1. In brief, in all studies participants' origins were from Asia [n=4 from China (12–15), n=3 from Korea (7,10,11) and n=1 from Japan[8]] with only one study where participants were recruited from a clinic in Italy.[16] In all studies, the association between Lp(a) and NAFLD was cross-sectional. In n=3 studies, the diagnosis of NAFLD accompanied by histological characteristics of NASH and liver fibrosis was performed with the gold standard method of liver biopsy.[8,9,15] Four studies focused on the association between Lp(a) and liver fibrosis[8,9,11,13] (Table 1).

The association between Lp(a) and biopsy-proven NAFL, NASH and liver fibrosis

One study in China with biopsy-proven NAFLD showed a positive association between the severity of NAFLD and the serum concentration of Lp(a). In particular, ranking from no NAFLD to NASH there was a significant increase in Lp(a) metrics with the values being about 40% higher in NASH patients compared with the NAFL subgroup.[15] This trend was retained in age- and sex- adjusted models; yet no other potential confounders such as liver enzymes, insulin resistance, lipid markers were taken into account.[15] Additional analysis to examine the differentiation potential of Lp(a) in relation to the presence vs. absence of NASH showed that a model which combines liver enzymes (i.e. aspartate aminotransferase (AST), alanine aminotransferase (ALT)) with Lp(a) had an area under the curve which reached the 0.830.[15]

Similar analyses in the context of a cross-sectional study with a bigger sample (i.e. n=600 NAFLD patients)

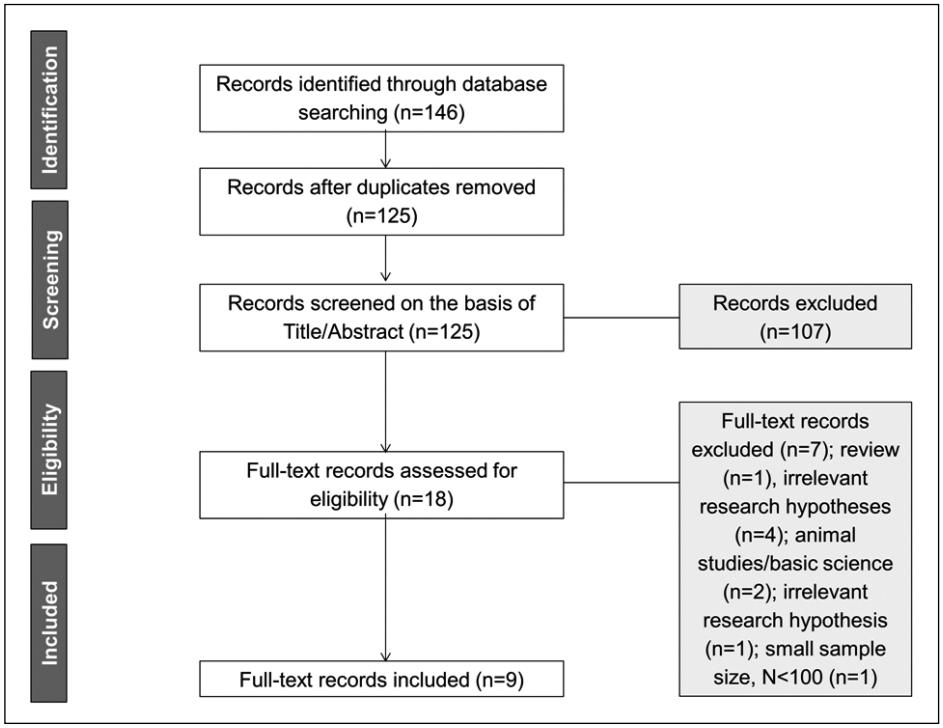

FIGURE 1. The flow diagram of the selected studies

in Italy were recently published.[9] The mean Lp(a) levels of the sample had a range of 14-37 nmol/L. Multi-adjusted analysis with liver enzymes, lipidemic and glycemic confounders taken into account, revealed that per 1 nmol/L increase in Lp(a), the odds of liver fibrosis (presence vs. absence), fibrosis grade 3-4 vs. 0-2 and cirrhosis (presence vs. absence) was reduced by 24%, 52% and 69%, respectively; implying that the more advanced fibrosis in the liver the lower the Lp(a) metrics in serum.[9] The authors concluded that this observation suggests Lp(a) as a novel biomarker to predict advanced liver damage. In addition to this, they saw that the accuracy of this biomarker to differentiate the presence vs. absence of advanced fibrosis was further increased when combined with transaminases.[9]

Another study with 181 NAFLD patients diagnosed through liver biopsy in an Hepatology Clinic in Japan evaluated among others the Lp(a) in serum (range: 5.3-16.9 mg/dL).[8] An inverse association between Lp(a) levels and the likelihood of advanced liver fibrosis (i.e. Grade 3 and 4) was observed even after adjusting for various lipidemic, glycemic markers as well as liver enzymes. Additionally, the authors underscored the limited accuracy of Lp(a) as a predictor of CVD risk in patients with advanced NAFLD.[8]

The association between Lp(a) and advanced liver fibrosis assessed through non-invasive diagnostic tools

A very recent study from Korea with 14,419 adults who underwent abdominal ultrasonography showed that metabolic associated fatty liver disease (MAFLD) patients with liver fibrosis defined using NAFLD fibrosis score (NFS) or fibrosis-4 score (FIB-4) or AST to platelet ratio index (APRI) presented significantly lower Lp(a) values compared with their MAFLD without fibrosis or no MAFLD counterparts.[11] However, this analysis was univariate.

In another work from China, interesting non-linear associations of liver fibrosis, liver stiffness and liver fat content with Lp(a) were revealed.[13] In particular, Lp(a) increased slowly between −5.0 and 0 as NFS increased and became stable when NFS reached 0. By contrast, when it comes to liver stiffness assessed through high-resolution B-mode ultrasonography, Lp(a) decreased sharply between 3.5 and 6.3 as liver stiffness increased and decreased much more slowly, and the curve became smooth when liver stiffness was higher than 6.3. In MAFLD patients with hepatic fibrosis stages F0–F1, the curve fluctuated as liver fat content accumulated. However, in patients with hepatic fibrosis stage F2, Lp(a) decreased sharply between 5% and 20% as liver fat content increased and fluctuated when liver fat content was higher than 20%. In patients with hepatic fibrosis stages F3–4, Lp(a) exhibited a sharply increasing trend between 5% and 12% and then fluctuated between 12% and 20%. After the liver fat content was higher than 20%, Lp(a) held a stable increasing trend. The authors also concluded that the predictive value of Lp(a) for carotid atherosclerosis was reduced as hepatic fibrosis aggregated.[13]

TABLE 1. Description and main results of selected studies.

First author, publication year	Country; N; Age, years (mean(SD) OR range)	Type of analysis between Lp(a) and liver health	Outcome(s) related with liver health	Type of Lp(a) variable	Adjustments	Main results
Park K. J., 2023 (11)	Korea; N=14,419; Age: 45 (45-46)	Cross-sectional	Abdominal ultrasonography diagnosed liver steatosis MAFLD – APASL criteria Liver fibrosis (defined as positive score in >2 of the following NIT methods: NFS>0.676, FIB-4>2.67, and APRI>0.562	Continuous	Crude analysis	Lp(a) level was reduced in subjects with MAFLD, especially with liver fibrosis. **Lp(a) values** • Non-MAFLD: 9.93mg/dL • MAFLD: 7.68mg/dL • MAFLD with fibrosis: around 5-6mg/dL
Wang J., 2022 (12)	China; N= 4,335; Age=46.9 (9.7) in subgroup without carotid plaque Age=57.7 (9.5) in subgroup with carotid plaque	Cross-sectional	Abdominal ultrasonography diagnosed NAFLD	Categorical (cut-off points: 30mg/dL; 10mg/dL)	Age, sex, albumin, ALT, total bile acid, creatinine, hypertension, and dyslipidemia	NAFLD patients with diabetes & Lp(a)<10 mg/dL OR 10≤Lp(a)<30 mg/dL had 56% higher likelihood to have carotid plaques compared with their counterparts with Lp(a)<10mg/dL)
Ye J., 2022 (14)	China; N=1,038; Age= 41.3 (12.4) (validation in another Chinese cohort, international cohort and a cohort in the United Kingdom)	Cross-sectional	MAFLD – APASL criteria MRI-PDFF or ultrasonography diagnosed liver steatosis	Continuous	Unsupervised cluster analysis including age, BMI, HbA1c, TC/HDL-C ratio, and triglyceride and Lp(a) levels	One cluster was characterized by an extremely high Lp(a) level, but relatively lower triglyceride level, TC/HDL-C ratio and HOMA-IR. This cluster presented the highest incidence of 16-year coronary heart disease and the 2nd highest incidence of 16-year type 2 diabetes.
Wu T., 2022 (13)	China; N=4,348; Age=46.4	Cross-sectional	MAFLD-Asia-Pacific guidelines 2020; Fatty liver disease through high-resolution B-mode ultrasonography	Continuous; quartiles	Age, sex, BMI, smoking status, alanine aminotransferase, uric acid, homeostasis model assessment-HOMA-IR, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and ApoB/ApoA ratio.	• L-shaped trend between Lp(a) levels and liver stiffness in patients with MAFLD; • Non-MAFLD patients had higher levels of Lp(a) than MAFLD patients with or without advanced fibrosis; • Advanced liver fibrosis significantly reduces the predictive value of Lp(a) levels for the risk of carotid atherosclerosis in patients with MAFLD.

TABLE 1. Description and main results of selected studies (Continued).

First author, publication year	Country; N; Age, years (mean(SD) OR range)	Type of analysis between Lp(a) and liver health	Outcome(s) related with liver health	Type of Lp(a) variable	Adjustments	Main results
Meroni M., 2022 (9)	Italy; N=600; Age= 54 (13)	Cross-sectional	Liver biopsy	Continuous	Age, sex, BMI, IFG/ type 2 diabetes, statin use, ALT, total cholesterol and triglycerides.	Circulating Lp(a) combined with transaminases may represent a novel noninvasive biomarker to predict advanced fibrosis in patients with NAFLD.
Jung I., 2020 (7)	Korea; N=22,534; Age=37.7	Retrospective longitudinal study	Abdominal ultrasonography	Quartiles	Age, sex, BMI, fasting glucose, AST, systolic blood pressure, total cholesterol, LDL-C, smoking amount, exercise, alcohol frequency, HOMA-IR.	• Serum Lp(a) levels were inversely associated with the presence of NAFLD; • Subjects with low Lp(a) and high HOMA-IR showed an increased risk of NAFLD.
Zhang Y., 2020 (15)	China; N=167; $Age_{controls}$=38.9 (5.4) Age_{NAFL}=38.9 (9.8) Age_{NASH}=40.6 (10.6)	Cross-sectional	Abdominal ultrasound; Liver biopsy	Continuous	Age, sex.	• In NAFLD patients, Lp(a) was a potential risk factor for NASH; • Combination of Lp(a), ALT, and AST had a greater predictive efficiency for NASH.
Konishi K., 2020 (8)	Japan; N=176; Age=20-79	Cross-sectional	Liver biopsy	Continuous	Age, sex, BMI, ALT, Creatinine, HbA1c, HDL-C, LDL-C, triglycerides and lipid lowering agents.	• Advanced NASH is associated with low serum Lp(a) levels. • Lp(a) levels in advanced NASH may not be useful in evaluating cardiovascular risk.
Nam JS., 2016 (10)	Korean; N=2,242; Mean age range=52.4-53.2	Cross-sectional	Ultrasonography	Tertiles	Age, sex, smoking status, BMI, systolic and diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, HDL-C, LDL-C, AST, ALT, HOMA-IR.	• Lp(a) is not an independent predictor of NAFLD; • The association was mediated by HOMA-IR.

Abbreviations: Alanine transaminase (ALT); Aspartate aminotransferase (AST); Aspartate aminotransferase to Platelet Ratio Index (APRI); Asian Pacific Association for the Study of the Liver (APASL); Body mass index (BMI); Fibrosis-4 (FIB-4); High Density Lipoprotein Cholesterol (HDL-C); Hemoglobin A1C (HbA1c); High-density lipoprotein cholesterol (HDL-C); Homeostatic Model Assessment for Insulin Resistance (HOMA-IR); Impaired Fasting Glucose (IFG); Lipoprotein a (Lp(a)); Low-density lipoprotein cholesterol (LDL-C); Metabolic-associated fatty liver disease (MAFLD); Non-alcoholic fatty liver disease (NAFLD); Non-alcoholic steatohepatitis (NASH); Non-alcoholic fatty liver disease fibrosis score (NFS); Standard Deviation (SD); Total cholesterol (TC).

The association between Lp(a) and ultrasonography-diagnosed liver steatosis

In 2016, a Korean study with 2,242 subjects free of type 2 diabetes assessed with abdominal ultrasonography the severity of NAFLD according to the level of liver steatosis.[10] Ranking from no NAFLD to severe NAFLD a trend of reduced Lp(a) metrics was observed; participants without NAFLD had around 15mg/dL Lp(a) levels with the respective metric in participants with severe NAFLD being close to 9mg/dL. Multi-adjusted analysis showed that participants assigned in 3rd Lp(a) tertile (higher Lp(a) values) had about 34% lower odds of severe NAFLD compared with their 1st Lp(a) tertile counterparts. Of interest, this association lost its significance when insulin resistance was take into account.[10] This observation comes in line with the results from another study in China launched in 2022 which suggested an interaction between glucose metabolism and Lp(a) in carotic plaques risk in NAFLD patients.[12]

In a Korean study with more than 22,000 participants the mean Lp(a) levels was lower in subjects with NAFLD than in those free of NAFLD (70.0 vs 73.8 nmol/L, respectively).[7] Multi-adjusted analysis showed that participants assigned in 4th Lp(a) quartile (highest Lp(a) level) had 19% lower odds of NAFLD. The main conclusion of this study was that this observation was reversed when combined with increase insulin resistance; in particular, the group of participants with low Lp(a) and high Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) (using the median value of these metrics to define each group) had close to two times higher likelihood to have NAFLD compared with the reference group of participants with high Lp(a) and low HOMA-IR.[7]

The Lp(a) oriented pattern of NAFLD

A very recent study with MAFLD patients from China revealed through unsupervised cluster analysis that there is a pattern of MAFLD characterized by extremely high Lp(a) levels, but relatively lower triglyceride levels, total cholesterol/HDL-C ratio and HOMA-IR. This cluster presented the highest incidence of 16-year coronary heart disease and the 2nd highest incidence of 16-year T2DM.[14]

DISCUSSION

In the present systematic review, the potential role of Lp(a) in the pathophysiological paths of NAFLD is discussed in the context of observational studies. Most of the selected studies revealed a significant inverse association between Lp(a) and liver fibrosis implying the use of this lipidemic molecule combined with conventional hepatic markers to detect advanced NAFLD stages. In addition to this and considering the aggravating role of Lp(a) in predicting CVD onset, some scientific teams suggested that in case of advanced hepatic fibrosis this lipid marker should not be used as an indicator of vascular health.

Lp(a) is an LDL-like particle of a single apolipoprotein B100 covalently linked by a disulphide bond to a single apolipoprotein (a) (Apo(a)).[17] The concentration of Lp(a) is genetically determined by the Lp(a) gene. The Apo(a) molecular mass ranges from 275 kDa to 800 kDa in association with the allelic variance of the Lp(a) gene to encode different numbers of kringle type IV type 2 (KIV 2) repeat sequences. Hence, the Apo(a) size determines the Lp(a) isoform size; >40 Apo(a) isoforms have been detected which result in 40 Lp(a) molecules of different size.[18] The biggest part of the available literature on Lp(a) is related with its independent aggravating effect on atherosclerotic CVD. In 2009, a meta-analysis of 36 cohorts from the Emeringing Risk Factors Collaboration found that per 3.5-fold higher than usual Lp(a) levels amplified risk ratio of coronary heart disease by 13%.[19] The latest meta-analysis on this topic retrieving data from 43 publications, reporting on 75 studies and 957,253 participants provided additional evidence that higher Lp(a) levels are associated with higher risk of all-cause mortality and CVD-death in the general population and in patients with CVD.[20] These findings support the Guidelines from the European Society of Cardiology and the European Atherosclerosis Society which recommend that Lp(a) should be measured at least once in each adult person's lifetime.[21]

Insulin resistance and other relevant mechanisms have been found to affect the concentration of Lp(a), although the results of this association remains controversial. In the meantime, an inverse association between markers of insulin resistance and this lipid molecule have been suggested.[22] This interaction of Lp(a) with insulin resistance has raised questions about its potential involvement in the path of metabolic syndrome, T2DM and other relevant cardiometabolic conditions. The evidence on the role of of Lp(a) on metabolic syndrome is still questioned. A very recent meta-analysis of observational studies retrieved data from 18 studies on the association between Lp(a) and the odds of metabolic syndrome.[23] Even if a significant inverse association was observed the heterogeneity of studies was high due to the different assays used to assess Lp(a) as well as the various definitions for metabolic syndrome.[23] In addition to this, when studies with high risk of bias were excluded from the analysis the pooled effect of the remaining studies did not reach the level of significance.[23] In a meta-analysis of 5 prospective studies the association between 5 prospective studies the T2DM was investigated revealing a higher risk of T2DM at low Lp(a) concentrations (approximately <7 mg/dL).[24]

Overall, the pathophysiological role of Lp(a) in the development of metabolic disease remains unclear. NAFLD – or the recently renamed metabolic dysfunction-associated steatotic liver disease (MASLD)[25,26] – ranks among the most common metabolic liver diseases with an increasing prevalence worldwide. Considering that no pharmaceutical agent has been accepted for this condition and especially its advanced stages (i.e. NASH) identifying molecules that can be treatment target remains a very active field.[27] Besides, the relationship between serum Lp(a) level and NAFLD – especially NASH – is unknown. The limited existing literature – presented herein – suggest that low Lp(a) levels could be an indicator of advanced hepatic fibrosis. Lp(a) subunits are synthesized in the liver while it has been seen that the expression of Apo(a) in the liver and serum LDL-C levels are low in advanced NASH.[8] Additionally, an interaction between Lp(a) and insulin resistance on advanced NAFLD stages was observed yet this actual mechanism is still not clear.[7,10] On the other side, genetically predicted higher circulating Lp(a) levels were recently associated with increased risk of metabolic diseases including T2DM as revealed in a phenome-wide Mendelian randomization study.[28] This raises some questions in the field about which is the cause and which is the outcome of the cross-sectional associations presented in this systematic review.

Limitations of existing studies

The selected studies that investigate the association between Lp(a) and NAFLD stages or liver fibrosis have several limitations which need to be taken into consideration for better interpretation of the outcomes. Most of the studies have a cross-sectional design with no potential to reach causal associations. Additionally, generalization of the conclusions of the present systematic review cannot be performed since most of study samples are Asian while the selected samples were not representative to the general population from which the sample was selected. On the other side, the assays used to assess Lp(a) levels varied among studies which result in high heterogeneity. Lastly, only 3 studies presented herein used the gold standard method of liver biopsy to define the presence of NAFLD and specific disease stages.

CONCLUSIONS

Although the causal relationship between Lp(a) levels and NAFLD development could not be addressed here, this systematic review summarizes for the first time the available evidence in the field. Additional studies are required to clarify the role of Lp(a) in NAFLD and other metabolic diseases in different reference populations.

Declaration of competing interest

Dr Kouvari was supported with a grant from the Hellenic Atherosclerosis Society.

CSM reports grants through his institution from Merck, Massachusetts Life Sciences Center and Boehringer Ingellheim, has been a shareholder of and has received grants through his Institution and personal consulting fees from Coherus Inc. and AltrixBio, he reports personal consulting fees from Novo Nordisk, reports personal consulting fees and support with research reagents from Ansh Inc., collaborative research support from LabCorp Inc., reports personal consulting fees from Genfit, Lumos, Amgen, Corcept, Intercept, 89 Bio, Madrigal and Regeneron, reports educational activity meals through his institution or national conferences from Esperion, Merck, Boehringer Ingelheim and travel support and fees from TMIOA, Elsevier, and the Cardio Metabolic Health Conference. None is related to the work presented herein.

ΠΕΡΙΛΗΨΗ

Ο αμφιλεγόμενος ρόλος της λιποπρωτεΐνης(α) στην παθοφυσιολογία της μη αλκοολικής λιπώδους διήθησης ήπατος: συστηματική ανασκόπηση

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Σκοπός: Σκοπός της παρούσας συστηματικής ανασκόπησης ήταν να συγκεντρώσει τις πρόσφατες επιδημιολογικές μελέτες οι οποίες εξετάζουν τη σχέση των επιπέδων λιποπρωτεΐνης(α) (συντομογραφία στα αγγλικά: Lp(a)) με την ηπατική στεάτωση και ίνωση μη αλκοολικής αιτιολογίας.

Μεθοδολογία: Δύο ανεξάρτητοι ερευνητές πραγματοποίησαν βιβλιογραφική αναζήτηση σε διάφορες βάσεις δεδομένων σχετικά με μελέτες που διερευνούν το ρόλο της Lp(a) στην παθοφυσιολογία της μη αλκοολικής λιπώδους διήθησης ήπατος (συντομογραφία στα αγγλικά: NAFLD).
Αποτελέσματα: Συνολικά, στην παρούσα ανασκόπηση συμπεριελήφθησαν ν=9 μελέτες. Σε όλες τις μελέτες η προέλευση του πληθυσμού ήταν από την Ασία (ν=4 από Κίνα, ν=3 από Κορέα και ν=1 από Ιαπωνία) με εξαίρεση μία μελέτη με πληθυσμό από την Ιταλία. Όλες οι μελέτες ήταν συγχρονικές. Μόνο σε ν=3 μελέτες η διάγνωση της νόσου έγινε με βιοψία ήπατος. Τέσσερις μελέτες διερεύνησαν τη σχέση της Lp(a) με την ίνωση ήπατος. Οι περισσότερες μελέτες ανέδειξαν αντίστροφη συσχέτιση μεταξύ της Lp(a) και της ηπατικής ίνωσης ενισχύοντας την υπόθεση περί αξιοποίησης του συγκεκριμένου βιοδείκτη ως ένδειξης προχωρημένης μορφής της νόσου. Επιπρόσθετα, προτείνεται η αποφυγή χρήσης της Lp(a) για την εκτίμηση καρδιαγγειακού κινδύνου σε περίπτωση σοβαρής ηπατικής ίνωσης.
Συμπεράσματα: Περαιτέρω έρευνα απαιτείται για την κατανόηση του ρόλου της Lp(a) στην παθοφυσιολογία της NAFLD σε διαφορετικούς πληθυσμούς.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: *Λιποπρωτεΐνη(α); ηπατική στεάτωση; ηπατική ίνωση*

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