



ORIGINAL ARTICLE

Lipoprotein (a) is a predictor of non-achievement of LDL-C goals in patients with chronic heart disease

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Abstract

Introduction and objectives: Lipoprotein (a) [Lp(a)] concentration influences serum low-density lipoprotein cholesterol (LDL-C) levels. How it influences the achievement of LDL-C targets established in the guidelines is not well studied. Our aim was to know the prevalence of elevated Lp(a) levels in patients with coronary artery disease (CAD), and to assess its influence on the achievement of LDL-C targets.

Method: We conducted a cross-sectional study in a Cardiology department in Spain. A total of 870 patients with stable CAD had their lipid profile determined, including Lp(a). Patients were stratified into two groups according to Lp(a) >50 mg/dL and Lp(a) ≤50 mg/dL. The association of Lp(a) >50 mg/dL with achievement of LDL-C targets was assessed by logistic regression analysis. **Results:** The prevalence of Lp(a) >50 mg/dL was 30.8%. Patients with Lp(a) >50 mg/dL had higher baseline (142.30 ± 47.54 mg/dL vs 130.47 ± 40.75 mg/dL; $p=0.0001$) and current (72.91 ± 26.44 mg/dL vs 64.72 ± 25.30 mg/dL; $p=0.0001$), despite the fact that they were treated with more high-potency statins (77.2% vs 70.9%; $p=0.058$) and more combination lipid-lowering therapy (LLT) (37.7% vs 25.7%; $p=0.001$). The proportion of patients achieving target LDL-C was lower in those with Lp(a) >50 mg/dL. Independent predictors of having elevated Lp(a) levels >50 mg/dL were the use of high-potency statins (OR 1.5; 95% CI 1.08–2.14), combination LLT with ezetimibe (OR 2.0; 95% CI 1.45–2.73) and failure to achieve a LDL-C ≤55 mg/dL (OR 2.3; 95% CI 1.63–3.23).

Conclusions: Elevated Lp(a) levels influence LDL-C levels and hinder the achievement of targets in patients at very high cardiovascular risk. New drugs that act directly on Lp(a) are needed in these patients.

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PALABRAS CLAVE

Colesterol-LDL;
Lipoproteína (a);
Enfermedad arterial
coronaria;
Tratamiento
hipolipemiente

Lipoproteína (a) es un factor predictor de no consecución de objetivos de C-LDL en pacientes con cardiopatía isquémica crónica

Resumen

Introducción y objetivos: La concentración de lipoproteína (a) [Lp(a)] influye en los niveles séricos de colesterol de las lipoproteínas de baja densidad (C-LDL). Cómo influye en la consecución de objetivos de C-LDL establecidos en las guías no está bien estudiado. Nuestro objetivo fue conocer la prevalencia de niveles elevados de Lp(a) en pacientes con enfermedad arterial coronaria (EAC), y evaluar su influencia en la consecución de objetivos de C-LDL.

Método: Realizamos un estudio transversal en un servicio de Cardiología en España. A un total de 870 pacientes con EAC estable les determinamos el perfil lipídico, incluida Lp(a). Los pacientes se estratificaron en dos grupos según Lp(a) >50 mg/dL y Lp(a) ≤50 mg/dL. La asociación de Lp(a) >50 mg/dL con la consecución de objetivos de C-LDL se evaluó mediante análisis de regresión logística.

Resultados: La prevalencia de Lp(a) >50 mg/dL fue de 30,8%. Los pacientes con Lp(a) >50 mg/dL tenían un C-LDL más elevado, tanto basal ($142,30 \pm 47,54$ mg/dL vs $130,47 \pm 40,75$ mg/dL; $p=0,0001$) como actual ($72,91 \pm 26,44$ mg/dL vs $64,72 \pm 25,30$ mg/dL; $p=0,0001$), a pesar de que estaban tratados con más estatinas de alta potencia (77,2% vs 70,9%; $p=0,058$) y más tratamiento hipolipemiente (THL) de combinación (37,7% vs 25,7%; $p=0,001$). La proporción de pacientes que alcanzaron el objetivo de C-LDL fue menor en aquellos con Lp(a) >50 mg/dL. Fueron predictores independientes de tener niveles elevados de Lp(a) >50 mg/dL, la utilización de estatinas de alta potencia (OR 1.5; 95% CI 1.08–2,14), el THL de combinación con ezetimiba (OR 2,0; 95% CI 1,45–2,73) y la no consecución de un C-LDL ≤55 mg/dL (OR 2,3; 95% CI 1,63–3,23).

Conclusiones: Los niveles elevados de Lp(a) influyen en los niveles de LDL-C y dificultan la consecución de objetivos en pacientes de muy alto riesgo cardiovascular. En estos pacientes son necesarios nuevos fármacos que actúen directamente sobre Lp(a).

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Introduction

Lipoprotein (a) [Lp(a)] is a molecule that resembles low density lipoprotein (LDL) covalently bound by a disulphide bond from apolipoprotein B100 to apolipoprotein (a).^{1,2}

Lp(a) has proatherogenic, proinflammatory, and prothrombotic properties, and several studies have demonstrated that it is involved in the pathophysiological process of atherosclerosis of the coronary arteries, as well as of other vascular territories.^{3,4} There is ample scientific evidence from both epidemiological and genetic studies of the association between cardiovascular risk and elevated Lp(a) levels^{5–8} that shows that it is a continuous and independent risk factor for coronary artery disease (CAD) and that elevated Lp(a) levels predict the occurrence of cardiovascular events.⁹

Genetics accounts for more than 90% of plasma Lp(a) levels, while environmental factors have little influence,^{10,11} and in the general population the distribution is skewed to the left, with 35% of all people presenting values >30 mg/dL.¹² Other genetic dyslipidaemias, such as familial hypercholesterolaemia, are associated with a higher prevalence of elevated Lp(a).¹³

Whilst CAD mortality has declined in recent years, a percentage of patients do not meet guideline-recommended low-density lipoprotein cholesterol (LDL-C) reduction targets,^{14,15} even with intensive treatment strategies,¹⁶ and

those subjects who fail to attain the recommended targets continue to be at high risk for cardiovascular morbidity and mortality.

There is little evidence as to the role of high Lp(a) levels in not reaching the strict LDL-C targets of the latest guidelines,^{17–19} and, inasmuch as Lp(a) levels are often not determined in people with CAD, the correlation between Lp(a) and successful achievement of LDL-C goals in these patients has been scarcely explored.

The objective of the present study was to investigate the prevalence of elevated Lp(a) levels in a population of patients with CAD and how they impact LDL-C concentrations and the achievement of the LDL-C goals set forth in the guidelines for very high-risk CAD patients.

Patients and method**Study population**

The study population consisted of 870 consecutive cases with CAD seen at a cardiology clinic at a Spanish tertiary hospital between September 2016 until March 2020.

Two Lp(a) categories were established based on the threshold proposed by the European Atherosclerosis Society for Lp(a),²⁰ setting a limit of 50 mg/dL, thereby dividing

cases into one group with Lp(a) concentrations of ≤ 50 and another one with values of > 50 mg/dl.

Using our centre's computerised analytical system, we collected the highest LDL-C recorded in said system (baseline LDL-C), which comprised 72.5%, prior to commencing with lipid-lowering treatment (LLT) and then distributed the patients according to whether their baseline LDL-C was $\leq$ or > 130 mg/dl.

In those subjects who had already started LLT prior to the implementation of our hospital's computerised analysis registry (240 patients), we inferred pre-LLT LDL-C concentrations using the published conversion factors.¹⁷

All the participants signed an informed consent form and that had been previously approved by the local ethics committee.

Clinical and biochemical determinations

The diagnosis of CAD was established by coronariographic proof of at least one coronary stenosis of 50% or more in an epicardiac coronary artery.

Clinical parameters were chosen that were related with the presence of hyperlipidaemia and the use of LLT.

Lp(a) concentrations (in mg/dl) were determined by means of immunoturbidimetry on the Hitachi 917 analyser (Roche Diagnostics, Indianapolis, IN, USA), using calibrators, controls, and reagents from the same brand.

Total cholesterol, high-density lipoprotein cholesterol (HDL-C) and triglyceride values were quantified in the laboratory; LDL-C values were determined by means of the Friedewald formula when triglyceride levels were less than 200 mg/dl and by direct method when they were higher.²¹ The LDL-C corrected for the cholesterol content of Lp(a) [C-Lp(a)] was obtained by using Dahlen's equation (corrected LDL-C = LDL-C – Lp(a) mass $\times 0.3$).²²

High potency statins were deemed [appropriate], such as rosuvastatin at doses of 20–40 mg/day or atorvastatin at doses of 40–80 mg/day.

Statistical analysis

All statistical analyses were performed using the SPSS 25.0 software package (IBM Corporation, Armonk, NY, USA) for Windows.

The Kolmogorov-Smirnov test was applied to determine that the Lp(a) concentrations followed no normal pattern of distribution ($p < .0001$).

The categorical variables are presented as frequencies with percentages and were compared using the Chi-squared test. The continuous variables are expressed as the mean and standard deviation, except for Lp(a) levels, which are presented as the median and interquartile range (IQR), and were compared with Student's t-test for independent samples when the distribution is normal, or with the Mann-Whitney U test when the data are not normally distributed.

The odds ratio (OR) and 95% confidence Interval were calculated using multivariate logistic regression.

Statistical significance was set at a p value $< .05$.

Results

Baseline population characteristics

A total of 870 outpatient subjects with CAD were enrolled. Just over 43% (43.2%) (376 participants) had Lp(a) levels > 30 mg/dl and 30.8% (268 subjects) displayed concentrations of > 50 mg/dl. The median Lp(a) value was 22.10 mg/dl (IQR 8.28–60.70).

We divided the study population into two groups – those with Lp(a) concentrations of ≤ 50 mg/dl and Lp(a) > 50 mg/dl. The main clinical and biochemical characteristics can be found on [Table 1](#).

There were no differences in terms of age or sex of the individuals with Lp(a) $>$ and those with Lp(a) ≤ 50 mg/dl, or with respect to family history of premature CAD.

Hyperlipemia was reported more often among the participants in the higher Lp(a) level group. LLT was similar in both groups, although the use of high-potency statins was higher in those with Lp(a) > 50 mg/dl; patients on high-potency statin treatment had significantly higher Lp(a) levels than those not receiving such treatment: 24.35 mg/dl (IQR 8.63–62.55) vs. 18.55 mg/dl (IQR 7.40–52.38) ($p = 0.019$ as per Mann-Whitney U).

Combination LLT with ezetimibe was more common in participants with Lp(a) > 50 mg/dl, and those who took ezetimibe exhibited significantly higher Lp(a) values than those who did not: 31.80 mg/dl (IQR 10.90–76.85) vs. 18.15 mg/dl (IQR 7.50–54.13) ($p = .0001$ on the basis of the Mann-Whitney U test).

Association between Lp(a) and LDL-C

We have analysed both groups of patients: those with a baseline LDL-C concentration of ≤ 130 mg/dl and those who started off with a baseline LDL-C value > 130 mg/dl ([Table 2](#) [Table 2](#)).

The subjects with baseline LDL-C levels of > 130 mg/dl and Lp(a) > 50 mg/dl exhibited significantly higher concentrations of LDL-C at baseline, as well as LDL-C values at present, in comparison with those in the Lp(a) ≤ 50 mg/dl group.

Participants with baseline LDL-C values ≤ 130 mg/dl displayed similar baseline LDL-C concentrations, regardless of whether it was $>$ or ≤ 50 mg/dl; that being said, their current LDL-C levels were significantly greater when Lp(a) was > 50 mg/dl.

The percentage of LDL-C decrease was similar in individuals with baseline LDL-C > 130 mg/dl, irrespective of Lp(a); among those with baseline LDL-C of ≤ 130 mg/dl, the ones having Lp(a) concentrations of > 50 mg/dl revealed significantly smaller decreases than those with Lp(a) values ≤ 50 mg/dl.

Lp(a) concentrations and LDL-C target values achieved

The percentage of participants who attained the target LDL-C levels established in the European dyslipidaemia guidelines²³ (both below 70 mg/dl, as well as 55 mg/dl) was

Table 1 Baseline characteristics of the study subjects.

	Patients (N = 870)	Lp(a) ≤50 mg/dl (n = 602)	Lp(a) >50 mg/dl (n = 268)	p
<i>Clinical parameters</i>				
Age (years)	64.34 ± 11.93	64.73 ± 11.80	63.47 ± 12.19	.150
Females	17.90 (156)	16.6 (100)	20.9 (56)	.151
Family history	52.00 (452)	51.5 (310)	53.0 (142)	.713
Hyperlipidaemia	67.7 (588)	65.1 (392)	73.4 (196)	.018
Statins	96.00 (835)	95.7 (576)	96.6 (259)	.579
High-potency statins	72.9 (634)	70.9 (427)	77.2 (207)	.058
Ezetimibe	30.3 (264)	26.6 (160)	38.8 (104)	.000
Combination therapy	29.4 (256)	25.7 (155)	37.7 (101)	.001
<i>Biochemical parameters</i>				
Current cholesterol	137.92 ± 32.69	135.48 ± 32.16	143.40 ± 33.28	.001
Current LDL-C	67.24 ± 25.92	64.72 ± 25.30	72.91 ± 26.44	.000
Baseline LDL-C	134.11 ± 43.27	130.47 ± 40.75	142.30 ± 47.54	.000
HDL-C	46.78 ± 13.64	46.51 ± 14.14	47.40 ± 12.45	.378
Triglycerides	120.84 ± 73.31	122.98 ± 78.93	116.02 ± 58.54	.197
Non-HDL cholesterol	91.17 ± 30.05	89.01 ± 29.33	96.01 ± 31.14	.002
LDL-C <70 mg/dl	59.1 (511)	62.9 (376)	50.6 (135)	.001
LDL-C <55 mg/dl	31.8 (275)	36.3 (217)	21.7 (58)	.000

Quantitative variables are expressed as the mean ± standard deviation. Qualitative variables are expressed as percentages (n). HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; Lp(a): lipoprotein (a).

Table 2 Baseline and currently levels of LDL-C in individuals with baseline LDL-C values of > and ≤130 mg/dl, according to Lp(a) concentrations.

	Baseline LDL-C > 130 mg/dl			Baseline LDL-C ≤ 130 mg/dl		
	Lp(a) ≤50 mg/dl	Lp(a) >50 mg/dl	p ^a	Lp(a) ≤50 mg/dl	Lp(a) >50 mg/dl	p ^a
Baseline LDL-C	164.37 ± 29.00	176.18 ± 37.27	.0001	98.71 ± 19.40	101.80 ± 18.18	.135
Current LDL-C	70.06 ± 29.04	76.85 ± 30.83	.028	60.28 ± 20.40	68.18 ± 19.38	.0001
Percentage reduction of LDL-C	56.90 ± 17.76	55.29 ± 18.29	.383	37.85 ± 20.52	31.28 ± 19.00	.003

LDL-C: low density lipoprotein cholesterol; Lp(a): lipoprotein (a).

^a Student's t.

lower among the individuals with Lp(a) >50 mg/dl, despite the greater use of high-potency statins and combination LLT in combination with ezetimibe in these cases (Table 1).

When we corrected LDL-C in accordance with Lp(a) concentration levels using Dahlen's formula, the percentage of participants achieving LDL-C targets improves with respect to the LDL-C calculated. An LDL-C value of <70 mg/dl was achieved by 76.1 vs. 59.1% (p = .0001) of the subjects and an LDL-C value of <55 mg/dl was obtained by 54.4 vs. 31.8% (p = .0001).

Target LDL-C <70 mg/dl is improved when corrected LDL-C was considered both in patients with Lp(a) ≤50 mg/dl (71.6 vs. 62.9%; p = .0001) and those with Lp(a) >50 mg/dl (86.3 vs. 50.6%; p = 0.0001), albeit the magnitude is greater in the latter group. Likewise, the target level of LDL-C of <55 mg/dl was better among individuals with Lp(a) ≤50 mg/dl (46.9 vs. 36.3%; p = .0001), but, especially, among those with Lp(a) > 50 mg/dl (71.4 vs. 21.7%; p = .0001).

Median Lp(a) values differed depending on the LDL-C level achieved: individuals who achieved LDL-C ≤55 mg/dl had significantly lower Lp(a) values than those who attained LDL-C values of between 55–70 mg/dl and >70 mg/dl. Consequently, it would appear that elevated Lp(a) values

hamper the achievement of the targets set out in the clinical practice guidelines (Table 3).

Variables independently associated with elevated Lp(a) concentrations

In the multivariate analysis, the clinical variables independently associated with elevated Lp(a) (>50 mg/dl) were LLT with high-potency statins (OR 1.5, 95% CI 1.1–2.1, p = .017), combined LLT with ezetimibe (OR 2.0, 95% CI 2.5–2.7, p = 0.0001), and failure to achieve the LDL-C target (OR 1.5–2.7, 95% CI 1.5–2.7, p = 0.0001); 95% CI 1.5–2.7; p = 0.0001), and failure to achieve the LDL-C target of <55 mg/dl set forth in the ESC/EAS 2019 dyslipidaemia guidelines²³ for patients at very high cardiovascular risk (OR 2.3; 95% CI 1.6–3.2; p = .0001) (Table 4 Table 4).

Discussion

The results of this study reveal that a high percentage of individuals with CAD and elevated Lp(a) levels are less likely to achieve guideline-recommended lipid targets despite the

Table 3 Lp(a) values according to LDL-C target achieved.

LDL-C levels achieved	<55 mg/dl	55–69.9 mg/dl	>70 mg/dl
Median Lp(a) (IQR)	15.9 (6.0–40.9) (1)	23.8 (8.1–62.9) (2)	30.1 (10.62–67.3) (3)

Mann–Whitney U test.
 LDL-C: low density lipoprotein cholesterol; Lp(a): lipoprotein (a); IQR: interquartile range.
 1 and 2 = 0.0001; 1 and 3 = 0.000; 2 and 3 = 0.160.

Table 4 Clinical predictors of Lp(a) > 50 mg/dl in the multivariate analysis.

	OR	95% CI	p
<high-potency statins	1.5	(1.08–2.14)	.017
Ezetimibe	2.0	(1.45–2.73)	.0001
LDL-C ≤55 mg/dl	2.3	(1.63–3.23)	.0001

LDL-C: low density lipoprotein cholesterol; 95% CI: 95% confidence interval; OR: odds ratio.

use of intensive LLT with high-potency statins or LLT in combination with ezetimibe.

The EAS proposed that the optimal level of Lp(a) is <50 mg/dl; this corresponds to the 80th percentile of the Caucasian population, which accounts for 20% of the population with the highest values.²⁰ In the present study, we detected a 30.8% prevalence of elevated Lp(a) levels (>50 mg/dl) among CAD patients. This prevalence is similar to that reported in other studies of individuals with CAD and higher than in the general population, which indicates that elevated Lp(a) is an important risk factor for developing CAD. We have also established that Lp(a) appears to be strongly positively associated with hyperlipidaemia. Participants in the PRAXY study of premature acute coronary syndrome had a higher prevalence of high Lp(a) relative to the general population (20 vs. 31%; $p < 0.001$), in line with the findings of our study. Compared to patients with lower Lp(a) (≤50 mg/dl), subjects with high Lp(a) levels (>50 mg/dl) had a higher prevalence of hyperlipidaemia.²⁴ In our country data from the registry of Arrobas Velilla et al.,²⁵ 29.58% of the samples analysed were found to have Lp(a) concentrations of >50 mg/dl and 1.52% of them displayed values of >180 mg/dl.

LDL-C determination includes Lp(a)-C, which can potentially contribute approximately 30–45% to the measured LDL-C.²⁶ Thus, when the total mass of Lp(a) is high, the contribution of Lp(a)-C to LDL-C is substantial.^{26,27} Thus, high levels of genetically generated Lp(a) falsely increase the amount of LDL-C calculated and, independently, the risk of CAD.²⁸ Consequently, the calculated LDL-C should be modified to factor in the cholesterol associated with Lp(a) using Dalhen's formula.²²

The LLT routinely used to treat hypercholesterolaemia (statins and ezetimibe) do not lower Lp(a) levels; as a result, lowering LDL-C to the values recommended by the current ESC/ EAS guidelines (<55 mg/dl) may be more difficult in patients with cardiovascular disease and high Lp(a) levels.

In our study, participants with Lp(a) >50 mg/dl had a more unfavourable lipid profile than those with Lp(a) ≤50 mg/dl; total cholesterol and LDL-C levels were higher in the former. This reflects the fact that the LDL-C calculated also gauges Lp(a). None of the methods used to quantify LDL-

C enable us to discern between LDL particulate cholesterol and Lp(a); consequently, both should be reported together as LDL-C, which includes «LDL-C + Lp(a)-C».²⁶ In cases in which Lp(a) is very low, this limitation is not clinically relevant, however, as Lp(a) increases so too does its contribution to LDL-C, and limits the accurate interpretation of the contribution of each. Biochemical studies have evidenced that the Lp(a)-C content as a percentage of Lp(a) mass ranges from 20 to 45% depending on the individual and their baseline Lp(a),^{26,29} such that in patients with extreme Lp(a) elevations and controlled LDL-C, the latter may consist predominantly or almost entirely of Lp(a)-C. Thus, in patients treated with high doses of statins and in whom we do not achieve an 'expected' LDL-C reduction, their true LDL-C may be very low and they are less sensitive to further LDL-C reduction given that a significant proportion of their LDL-C is in the form of Lp(a) particles. In these individuals with elevated Lp(a), a major fraction of LDL-C, both current and at baseline, may be transported by Lp(a) particles and contribute substantially to the calculated LDL-C, and in these cases statins and ezetimibe only lower LDL-C, not Lp(a)-C.

A recent study³⁰ found a strong positive correlation between serum Lp(a) concentrations and the percentage of overestimation of LDL-C, and that as Lp(a) levels went up, there was no significant variation in the percentage of corrected LDL-C decline during treatment with atorvastatin.

We observed that in the subgroup of patients with a baseline LDL-C level of >130 mg/dl and who also presented Lp(a) values of >50 mg/dl, we achieved smaller LDL-C reductions than in those in whom the concentration of Lp(a) was ≤50 mg/dl, despite more intensive use of LLT. These observations may bear implications for both treatment and LDL-C treatment targets. In our study, the use of combination LLT was significantly more frequent in people with higher Lp(a) levels. Despite this, LDL-C levels achieved in subjects with Lp(a) >50 mg/dl were significantly higher than among those with Lp(a) ≤50 mg/dl, which reflects a certain «resistance» in achieving targets in patients with elevated Lp(a) values. This «resistance» to high-intensity LLT that we have verified in our study had already been demonstrated in the FOURIER

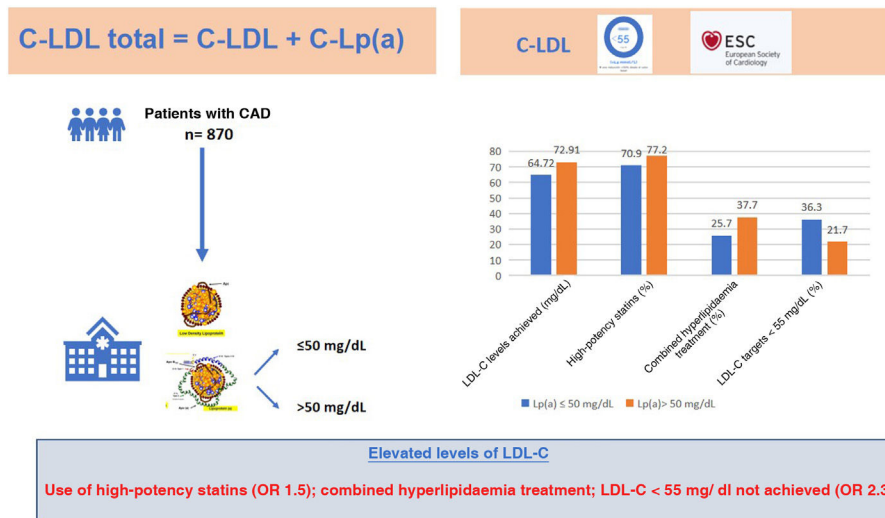


Figure 1 Summary of the study that includes the most relevant results in patients with Lp(a) levels in excess of >50 mg/dl and Lp(a) values of ≤50 mg/dl.

LDL-C: low-density lipoprotein cholesterol; Lp(a)-C: cholesterol bound to lipoprotein (a); CAD: coronary artery disease; OR: odds ratio; LLT: lipid-lowering treatment.

trial, in which the participants with the highest baseline Lp(a) levels were unable to achieve very low LDL-C levels (<20 mg/dL).³¹ In the study by Verbeek et al., the authors highlight the clinical significance of this fact,³² inasmuch as for the same given LDL-C level, the risk of CAD increased by 40–50% when Lp(a) values were ≥50 mg/dL. Moreover, they noted that high Lp(a) levels are also closely associated with adverse clinical outcomes in subjects with low LDL-C values.

This indicates that it will be extremely challenging for current LLTs to be able to achieve the targets in subjects with elevated Lp(a) and CAD, and that new drugs that also lower Lp(a) levels will be needed.

In our study, although a larger percentage of participants with elevated Lp(a) levels (>50 mg/dL) were treated with high-potency statins and LLT in combination with ezetimibe, we did not achieve a reduction to target LDL-C levels compared to those with lower Lp(a) levels (≤50 mg/dL). This leads us to promote the use of drugs that can lower Lp(a).

Fig. 1 illustrates a summary of the leading conclusions of the study.

Conclusions

The prevalence of elevated concentrations of Lp(a) (>50 mg/dL) is greater among people with CAD than among the general population.

High Lp(a) values are associated with higher levels of LDL-C and, in these patients, achieving optimal LDL-C levels as stipulated in clinical guidelines is challenging.

In the context of very high cardiovascular risk and elevated Lp(a), the use of drugs specifically targeting Lp(a) are needed, given that high-potency statin therapy and ezetimibe is not efficacious in lowering Lp(a) and, consequently, reaching the LDL-C targets as per clinical guidelines is a challenge.

Strengths and limitations of the study

One of the primary strengths of the study is how well the study population was characterised, with angiographic evidence of CAD and comprehensive lipid profiles. One limitation is the absence of baseline LDL-C values prior to initiating lipid-lowering therapy in 27.5% of individuals, which had to be calculated without prior treatment using published conversion factors.

What is known about the subject?

- LDL-C determination includes the cholesterol that is transported by LDL and Lp(a).
- The concentration of Lp(a) impacts LDL-C levels.
- Little is known about how Lp(a) concentrations affect achieving LDL-C targets in high-risk patients as established by current clinical practice guidelines.

What does it contribute?

- Patients with Lp(a) concentrations exceeding 50 mg/dl present higher LDL-C values.
- In subjects with coronary artery disease and Lp(a) values of >50 mg/dL, it is more difficult to attain target LDL-C levels of <55 mg/dL as set forth in the guidelines.
- These individuals with elevated Lp(a) have more potent LLT, with high-potency statins and combination treatment with ezetimibe.
- If a target concentration of LDL-C levels of <55 mg/dL are to be achieved in people with Lp(a) values of >50 mg/dL, new drugs are needed, such as PCSK9 inhibitors or anti-RNA.

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Conflict of interests

The authors have no conflict of interests to declare.

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