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Association of elevated lipoprotein(a) with future major adverse cardiovascular events in recurrent ASCVD patients: analysis of a large US electronic health record database

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BACKGROUND

- Elevated lipoprotein(a) [Lp(a)] is an independent, primarily genetically determined and causal atherosclerotic cardiovascular disease (ASCVD) risk factor[1,2]; 1 in 5 individuals globally are estimated to have elevated Lp(a)[3]
- In addition to increasing primary ASCVD risk, elevated Lp(a) levels may increase the risk of recurrent ASCVD events, but more evidence is needed[4]

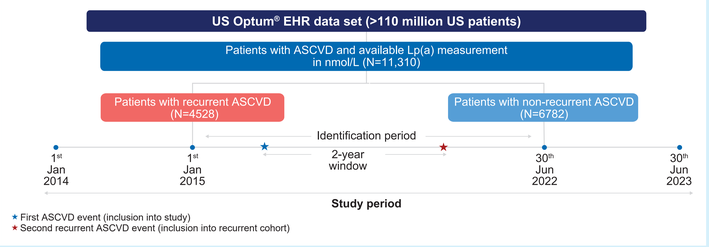
PURPOSE

- To describe the prevalence of elevated Lp(a) among patients with recurrent ASCVD and its association with future major adverse cardiovascular events (MACE)

METHODS

- This was a retrospective, non-interventional cohort study conducted in patients with recurrent ASCVD using the Optum® de-identified Electronic Health Record data set (Optum® EHR) between 01 January 2014 to 30 June 2023 (**Figure 1**)
- Eligibility criteria included adults (aged ≥18 years) with recurrent ASCVD who had an Lp(a) measurement in nmol/L
- Recurrent ASCVD was defined as having two consecutive records of a myocardial infarction (MI)–, ischemic stroke–, or peripheral artery disease (PAD)–related event or procedure, with the second record occurring within two years of the first record
- Baseline characteristics and post-index occurrence of MACE (MI, ischemic stroke, coronary revascularization, and all-cause death) are described in patients with recurrent and non-recurrent ASCVD
- Cumulative incidence rate ratios (CIRRs) and hazard ratios (HRs) of MACE, stratified by Lp(a) levels (<65 nmol/L and ≥150 nmol/L) were generated with age– and sex–adjusted Poisson and Cox proportional hazard models

Figure 1. Study design and number of patients analysed with recurrent and non-recurrent ASCVD



ASCVD, atherosclerotic cardiovascular disease; EHR, electronic health record; Lp(a), lipoprotein(a); N, number of patients in the group; US, United States.

RESULTS

Baseline characteristics

- Demographic and disease characteristics are detailed in **Table 1**
- In patients with recurrent ASCVD, the median Lp(a) was 47.0 nmol/L; 25.6% had Lp(a) ≥150 nmol/L
- In patients with non-recurrent ASCVD, the median Lp(a) was 35.0 nmol/L; 19.9% had Lp(a) ≥150 nmol/L

Table 1. Demographic and disease characteristics of patients with recurrent and non-recurrent ASCVD

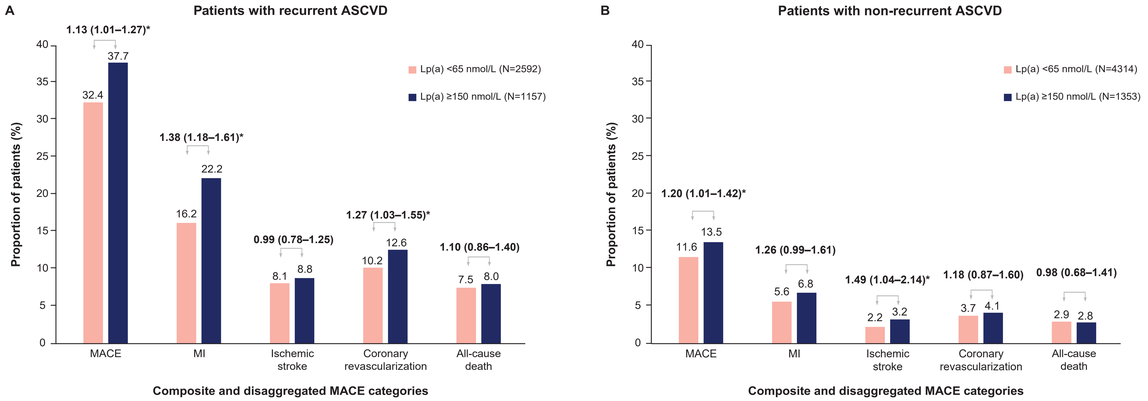
Characteristic	Patients with recurrent ASCVD (N=4528)	Patients with non-recurrent ASCVD (N=6782)
Age, mean±SD, years	62.6±12.2	59.7±12.1
Sex, n (%)		
Male	2744 (60.6)	3787 (55.8)
Female	1784 (39.4)	2995 (44.2)
Race, n (%)		
White	3453 (76.3)	5557 (81.9)
Black	414 (9.1)	416 (6.1)
Asian	261 (5.8)	280 (4.1)
BMI, mean±SD, kg/m²	29.8±6.9 (N=2207)	29.3±8.2 (N=2522)
Systolic blood pressure, mean±SD, mmHg	130.1±19.5 (N=4320)	129.7±18.1 (N=5133)
Current smoker, n (%)	681 (15.0)	464 (6.8)
Atherogenic lipids, mean±SD, mg/dL		
LDL-C	93.1±42.9 (N=3410)	111.0±40.9 (N=3341)
Total cholesterol	167.4±51.9 (N=3454)	191.9±48.2 (N=3334)
Non-HDL-C	120.9±49.2 (N=2441)	138.7±47.4 (N=1793)
Triglycerides	145.4±132.6 (N=3452)	138.7±146.8 (N=3383)
Lp(a), median (Q1, Q3), nmol/L	47.0 (15.0, 152.0)	35.0 (11.0, 119.0)
Comorbidities, n (%)		
Diabetes	942 (20.8)	557 (8.2)
Hypertension	2838 (62.7)	1892 (27.9)
Heart failure	586 (12.9)	139 (2.0)
Chronic kidney disease	564 (12.5)	195 (2.9)
Lipid-lowering therapies, n (%)		
Statins	3527 (77.9)	2834 (41.8)
PCSK9i	106 (2.3)	29 (0.4)
Ezetimibe	417 (9.2)	264 (3.9)
Fibrates	264 (5.8)	163 (2.4)
Bile acid sequestrants	67 (1.5)	56 (0.8)

ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; n, number of patients with characteristic; N, number of patients in the group; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; Q, quartile; SD, standard deviation.

MACE in patients with and without recurrent ASCVD

- Among those with recurrent ASCVD, more patients with Lp(a) ≥150 nmol/L (37.7%) had a subsequent MACE vs. patients with Lp(a) <65 nmol/L (32.5%) over a median of 3.75 years of follow-up (**Figure 2A**); similar trends were observed in patients with non-recurrent ASCVD, but were lower in magnitude (**Figure 2B**)
- Patients with recurrent ASCVD with Lp(a) ≥150 nmol/L had 38% more MIs, 27% more coronary revascularizations, and 13% more MACE compared with those with Lp(a) <65 nmol/L: (CIRR [95% CI]: 1.38 [1.18-1.61], 1.27 [1.03-1.55], and 1.13 [1.01-1.27], respectively, all p<0.05) (**Figure 2A**). Similar trend was observed in non-recurrent ASCVD patients (**Figure 2B**)

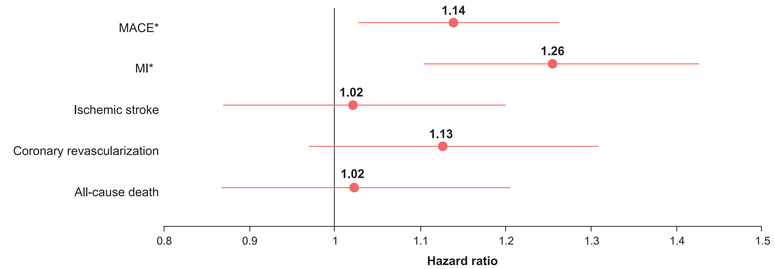
Figure 2. Proportion of patients with MACE and associated cumulative incidence rate ratios (CIRR) in patients (A) with recurrent ASCVD and (B) with non-recurrent ASCVD, stratified by Lp(a) levels



*p<0.05.
Data in bold above the bar graphs indicate CIRRs (95% CI) between Lp(a) levels (<65 nmol/L vs. ≥150 nmol/L).
ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; CIRR, cumulative incidence rate ratio; Lp(a), lipoprotein(a); MACE, major adverse cardiovascular events; MI, myocardial infarction; N, number of patients in the group.

- Patients with recurrent ASCVD with Lp(a) ≥150 nmol/L had a 14% greater risk of a subsequent MACE (HR=1.14, 95% CI: 1.03–1.26, p=0.013) and a 26% greater risk of subsequent MI (HR=1.26, 95% CI: 1.10–1.43, p<0.001) vs. patients with Lp(a) <65 nmol/L **(Figure 3)**
- In patients with non-recurrent ASCVD, there were no significant differences in terms of MACE risk between patients with Lp(a) ≥150 nmol/L vs. Lp(a) <65 nmol/L

Figure 3. Forest plot detailing the hazard ratios for MACE associated with Lp(a) ≥150 nmol/L vs. Lp(a) <65 nmol/L in patients with recurrent ASCVD



*p<0.05.
ASCVD, atherosclerotic cardiovascular disease; Lp(a), lipoprotein(a); MACE, major adverse cardiovascular events; MI, myocardial infarction.

CONCLUSIONS AND KEY TAKEAWAYS

- Elevated Lp(a) is common in patients with recurrent ASCVD with 1 in 4 having Lp(a) ≥150 nmol/L
- Elevated Lp(a) was a significant predictor of future MACE in patients with recurrent ASCVD, with 14% and 26% increased risk of MACE and MI, respectively
- Elevated Lp(a) was also associated with greater cumulative events including 13% more MACE, 38% more MIs and 27% more coronary revascularizations in patients with recurrent ASCVD
- Testing Lp(a) in patients with recurrent ASCVD is critical for risk assessment and risk management in the secondary prevention settings

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