JACC: CARDIOVASCULAR INTERVENTIONS VOL. 14, NO. 18, 2021

PUBLISHED BY ELSEVIER

Association of Lipoprotein(a) With Recurrent Ischemic Events Following Percutaneous Coronary Intervention

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ABSTRACT

OBJECTIVES This study evaluated the association between elevated levels of lipoprotein(a) [Lp(a)] and risk of recurrent ischemic events in patients who underwent percutaneous coronary intervention (PCI).

BACKGROUND Elevated levels of Lp(a) have been identified as an independent, possibly causal, risk factor for atherosclerotic cardiovascular disease in a general population study.

METHODS A prospective single-center registry was used to identify 12,064 patients with baseline Lp(a) measurements who underwent PCI between 2003 and 2013. The primary outcomes were a composite of cardiovascular death, spontaneous myocardial infarction, and ischemic stroke.

RESULTS From the registry, 3,747 (31.1%) patients had high Lp(a) (>30 mg/dL) and 8,317 (68.9%) patients had low Lp(a) (≤30 mg/dL). During a median follow-up of 7.4 years, primary outcomes occurred in 1,490 patients, and the incidence rates of primary outcomes were 2.0 per 100 person-years in the high-Lp(a) group and 1.6 per 100 person-years in the low-Lp(a) group (adjusted hazard ratio [aHR]: 1.17; 95% confidence interval [CI]: 1.05-1.30; $P = 0.004$). Increased risk of recurrent ischemic cardiovascular events in the high-Lp(a) group was consistent in various subgroups including patients receiving statin treatment at discharge (aHR: 1.18; 95% CI: 1.03-1.34; $P = 0.011$). In addition, the risk of repeated revascularization was significantly higher in the high-Lp(a) group (aHR: 1.13; 95% CI: 1.02-1.25; $P = 0.022$).

CONCLUSIONS Elevated levels of Lp(a) were significantly associated with the recurrent ischemic events in patients who underwent PCI. This study provides a rationale for outcome trials to test Lp(a)-lowering therapy for secondary prevention in patients undergoing PCI. (J Am Coll Cardiol Intv 2021;14:2059–2068) © 2021 by the American College of Cardiology Foundation.

Lipoprotein(a) [Lp(a)] is a low-density lipoprotein (LDL)-like particle composed of an apolipoprotein(a) [apo(a)] bound to an apo B-100. Elevated Lp(a) levels have proatherogenic, proinflammatory, and prothrombotic properties, and Lp(a) is now recognized as a mediator of myocardial infarction, stroke, and peripheral arterial disease. Large epidemiologic studies, meta-analyses, Mendelian randomization studies, and genome-wide association studies have identified elevated Lp(a) as an independent, possibly causal, risk factor for atherosclerotic cardiovascular disease (1-3).

However, the robust and growing evidence is mostly based on studies of the general population without known established cardiovascular disease. There is still conflicting evidence for the role of

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received October 31, 2019; revised manuscript received June 30, 2021, accepted July 13, 2021.

ISSN 1936-8798/$36.00 https://doi.org/10.1016/j.jcin.2021.07.042

ABBREVIATIONS AND ACRONYMS

aHR = adjusted hazard ratio

apo(a) = apolipoprotein(a)

CI = confidence interval

LDL = low-density lipoprotein

Lp(a) = lipoprotein(a)

PCI = percutaneous coronary intervention

elevated Lp(a) level in secondary prevention (4). Some studies have demonstrated that elevated Lp(a) was associated with subsequent coronary heart disease (5-9), but others did not find worse clinical outcomes in patients with elevated Lp(a) (10-12). Recently, the large-sized clinical trial that addressed patients presenting with acute coronary syndrome who mostly underwent percutaneous coronary intervention (PCI) showed a clinical benefit from effective Lp(a)-lowering therapies (13). In this study, we aimed to assess whether elevated Lp(a) is associated with long-term recurrent ischemic cardiovascular events in patients who underwent PCI from a large unselected real-world registry.

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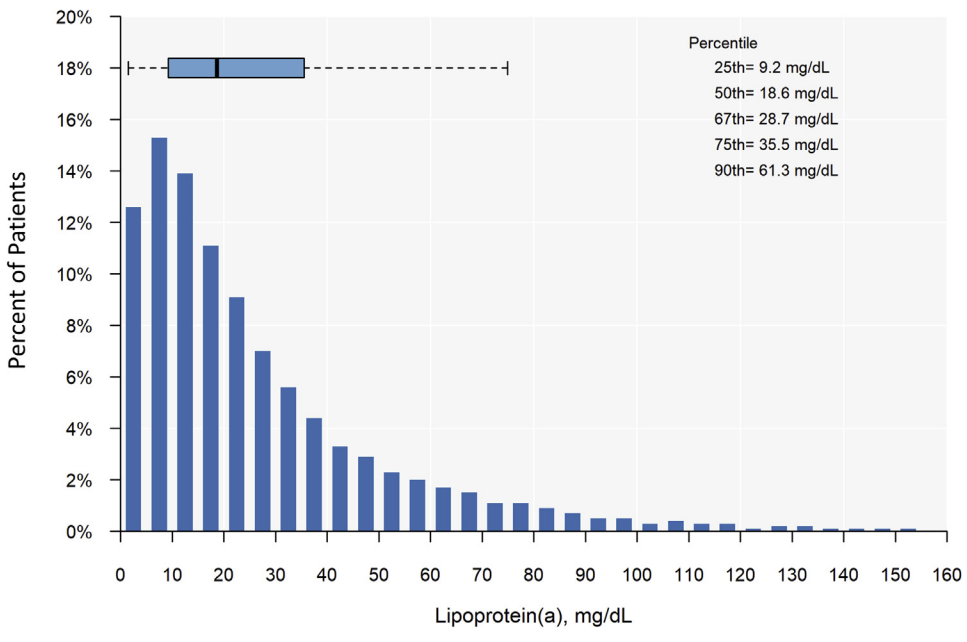
METHODS

STUDY DESIGN AND POPULATION. The ASAN PCI registry (NCT01788592) prospectively enrolled consecutive unselected real-world patients to assess the outcomes of PCI with various types of drug-eluting stents in a tertiary, high-volume center in Korea (14). This registry includes patient, procedure, and follow-up data. Selection of stent type and the use of intravascular imaging were at the discretion of the attending physician. The PCI procedure and post-PCI medical treatment were performed in accordance with accepted guidelines and established standards of practice. After PCI with a drug-eluting stent, aspirin was continued indefinitely and either clopidogrel or ticlopidine was prescribed for at least 12 months. An Institutional Review Board approved the registry.

LP(A) MEASUREMENT AND GROUP CATEGORIZATION. Blood samples for all patients were routinely obtained in the morning on the day of the index procedure and was directly sent to the laboratory. At the Asan Medical Center, Lp(a) levels have been measured in all patients who underwent diagnostic coronary angiogram or PCI for the cardiovascular risk evaluation since 2001 by using the immune nephelometric assay (BN II, Siemens Corp), which was a method to measure Lp(a) level in units of mg/dL and was known to be sensitive to the individual size heterogeneity of the apo(a) isoform. Detection limit of the Lp(a) analysis in our study was 0.2 mg/dL. The coefficient of variation was as follows: intra-assay (2.1% at 29 mg/dL, 2.4% at 61 mg/dL, 2.1% at 177 mg/dL) and interassay (3.5% at 28 mg/dL, 2.8% at 59 mg/dL, 3.5% at 175 mg/dL). The Lp(a) value was standardized to internal reference preparation from Siemens Healthcare Diagnostics.

Other lipid profiles, including total cholesterol, LDL, high-density lipoprotein, and triglyceride levels were also measured simultaneously. Because there is

FIGURE 1 The Distribution of Lipoprotein(a) Levels in the Study Population



no widely used recommended target value for Lp(a), we defined high Lp(a) as baseline Lp(a) level >30 mg/dL. This level was selected according to previous studies that found that the cardiovascular risk increased from 30 mg/dL (15,16). In addition, the gradual relationship between Lp(a) level and the risk of clinical outcomes was evaluated after patients were stratified into 4 groups (baseline Lp(a) level ≤15, 15-30, 30-50, and >50 mg/dL) according to a previous study (16).

OUTCOMES, DEFINITIONS, AND FOLLOW-UP. The primary outcome of the study was the composite of cardiovascular death, myocardial infarction, and ischemic stroke. Additional outcomes were also assessed including individual components of the primary outcome, death from any cause, any repeat revascularization, target vessel revascularization, target lesion revascularization, and new lesion revascularization.

Cardiovascular death was regarded as any death from a cardiovascular cause or if there was no identified cause of death. Spontaneous myocardial infarction was defined as an increase in cardiac enzyme above the upper reference limit with ischemic symptoms or signs that were not related to PCI. Stroke was defined as neurological deficits confirmed by neurological and imaging findings. Transient ischemic attack was not considered to be stroke. Any repeat revascularization included any percutaneous or surgical revascularization procedure, regardless of target. Target vessel revascularization was defined as any revascularization procedure in previously treated vessels. Target lesion revascularization was classified as the repeat revascularization was performed within 5 mm of previous stent border, while new lesion revascularization was performed further than 5 mm from the previous stent border. All event occurrences were adjudicated by an independent group of clinicians who were unaware of the baseline Lp(a) level.

TABLE 1 Baseline Characteristics of the Study Population

	Low Lp(a) (n = 8,317)	High Lp(a) (n = 3,747)	*P* Value
Age, y	61.6 ± 10.4	62.4 ± 10.0	<0.001
Male	6,186 (74.4)	2,581 (68.9)	<0.001
Clinical presentation			0.19
Stable angina	4,406 (53.0)	1,992 (53.2)	
Unstable angina	2,261 (27.2)	993 (26.5)	
Non-ST-segment elevated myocardial infarction	1,007 (12.1)	497 (13.3)	
ST-segment elevated myocardial infarction	643 (7.7)	265 (7.1)	
Body mass index, kg/m^2	25.1 ± 3.0	24.7 ± 2.9	<0.001
Hypertension	4,858 (58.4)	2,213 (59.1)	0.52
Diabetes	2,590 (31.1)	1,182 (31.5)	0.67
Current smoker	2,381 (28.6)	945 (25.2)	<0.001
Dyslipidemia	3,869 (46.5)	1,859 (49.6)	0.002
Total cholesterol	165.1 ± 39.2	169.5 ± 41.3	<0.001
HDL cholesterol	42.5 ± 11.2	41.7 ± 11.1	<0.001
LDL cholesterol	99.8 ± 34.0	105.3 ± 35.9	<0.001
Corrected LDL cholesterol[a]	96.4 ± 33.8	88.4 ± 36.6	<0.001
Prior myocardial infarction	642 (7.7)	314 (8.4)	0.23
Prior stroke	498 (6.0)	239 (6.4)	0.43
Prior peripheral vascular disease	171 (2.1)	117 (3.1)	<0.001
Chronic kidney disease	957 (11.5)	589 (15.7)	<0.001
History of chronic lung disease	612 (7.4)	260 (6.9)	0.43
Ejection fraction <45%	527 (6.3)	286 (7.6)	0.010
Left main disease	715 (8.6)	344 (9.2)	0.31
Multivessel disease	4,711 (56.6)	2,258 (60.3)	<0.001
Number of stents used	1.9 ± 1.1	2.0 ± 1.2	0.005
Discharge medication			
Aspirin	8,085 (97.2)	3,648 (97.4)	0.69
$P2Y_{12}$ inhibitor	7,720 (92.8)	3,491 (93.2)	0.52
Dual antiplatelet therapy	7,659 (92.1)	3,466 (92.5)	0.73
Beta-blocker	5,787 (69.6)	2,602 (69.4)	0.90
Calcium-channel blocker	6,284 (75.6)	2,849 (76.0)	0.59
ACE inhibitor or ARB	2,625 (31.6)	1,208 (32.2)	0.47
Statin	6,394 (79.0)	3,158 (79.5)	0.50

Values are mean ± SD or n (%). [a]Corrected LDL cholesterol was calculated by the equation of LDL cholesterol minus 0.3 × Lp(a).

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; HDL = high-density lipoprotein; LDL = low-density lipoprotein; Lp(a) = lipoprotein(a).

STATISTICAL ANALYSIS. Categorical variables were analyzed as frequencies with percentages and continuous variables were analyzed as mean ± SD. Comparisons between groups were performed using Student's *t*-test for continuous variables or Fisher exact test for categorical variables. Survival curves were drawn using the Kaplan-Meier method. The annualized event rate was calculated as a total number of events divided by the total follow-up period and expressed as the number of events per 100 person-years. Cox proportional hazards models were used to adjust for confounding factors including age, sex, initial presentation, body mass index, history of hypertension, history of diabetes, current smoking status, prior myocardial infarction, prior stroke, prior peripheral vascular disease, chronic kidney disease, baseline ejection fraction, presence of left main disease, presence of multivessel disease, enrollment period (year), LDL corrected for Lp(a), high-density lipoprotein cholesterol, and antithrombotics and statin prescription at discharge. The subjects were also stratified by 4 Lp(a) levels to compare risk for primary outcome. *P* values for trends were calculated by regarding groups as a continuous variable in the final multivariable models. Category-free net reclassification improvement and integrated

TABLE 2 Clinical Outcomes

	Number of Events (Incidence per 100 Person-Years)					
	Low Lp(a) (n = 8,317)	High Lp(a) (n = 3,747)	Unadjusted HR (95% CI)	*P* Value	Adjusted HR (95% CI)	*P* Value
Primary outcomes: the composite of cardiovascular death, spontaneous myocardial infarction, and ischemic stroke	954 (1.6)	536 (2.0)	1.28 (1.15-1.42)	<0.001	1.17 (1.05-1.30)	0.005
The composite of cardiovascular death excluding unknown cause of death, spontaneous myocardial infarction, and ischemic stroke	649 (1.1)	378 (1.1)	1.32 (1.17-1.50)	<0.001	1.22 (1.07-1.39)	0.002
The composite of cardiovascular death and spontaneous myocardial infarction	807 (1.3)	449 (1.7)	1.26 (1.12-1.41)	<0.001	1.14 (1.02-1.29)	0.025
Death from any cause	853 (1.4)	468 (1.7)	1.24 (1.11-1.39)	<0.001	1.13 (1.01-1.27)	0.033
Cardiovascular death	489 (0.8)	280 (1.0)	1.29 (1.11-1.49)	0.001	1.15 (0.99-1.33)	0.072
Cardiovascular death excluding unknown cause of death	157 (0.4)	103 (0.3)	1.47 (1.15-1.89)	0.002	1.24 (0.97-1.60)	0.089
Spontaneous myocardial infarction	369 (0.6)	202 (0.8)	1.24 (1.05-1.47)	0.013	1.16 (0.98-1.38)	0.088
Periprocedural peak CK-MB elevation						
>3× upper reference limit	764 (13.9)	365 (14.4)	1.04 (0.91-1.19)	0.577	1.01 (0.88-1.16)	0.864
>5× upper reference limit	657 (12.0)	323 (12.8)	1.07 (0.93-1.24)	0.334	1.05 (0.91-1.22)	0.480
>10× upper reference limit	546 (10.0)	250 (9.9)	0.99 (0.85-1.16)	0.895	0.97 (0.83-1.14)	0.731
Ischemic stroke	195 (0.3)	117 (0.4)	1.36 (1.08-1.71)	0.009	1.24 (0.99-1.57)	0.065
Any repeat revascularization	1133 (2.1)	570 (2.4)	1.15 (1.04-1.27)	0.008	1.13 (1.02-1.25)	0.022
Target vessel revascularization	790 (1.4)	414 (1.7)	1.19 (1.06-1.34)	0.004	1.15 (1.02-1.30)	0.025
Target lesion revascularization	674 (1.2)	357 (1.4)	1.21 (1.06-1.37)	0.004	1.17 (1.02-1.33)	0.020
New lesion revascularization	634 (1.1)	324 (1.3)	1.16 (1.02-1.33)	0.029	1.16 (1.01-1.33)	0.030
Cardiovascular death, spontaneous myocardial infarction, ischemic stroke, and any repeat revascularization	1,773 (3.3)	940 (4.0)	1.22 (1.12-1.32)	<0.001	1.14 (1.06-1.24)	0.001

Values are n (%) unless otherwise indicated. Adjusted covariates including age, sex, initial presentation, body mass index, history of hypertension, history of diabetes, current smoking status, prior myocardial infarction, prior stroke, prior peripheral vascular disease, chronic kidney disease, baseline ejection fraction, presence of left main disease, presence of multivessel disease, enrollment period (year), LDL corrected for Lp(a), HDL cholesterol, antiplatelet therapy, statin prescription at discharge.

CK-MB = creatinine kinase-myocardial band; other abbreviations as in Table 1.

discrimination improvement indices were calculated by competing prediction models at 10 years and were used to evaluate the prognostic performance of Lp(a). All reported *P* values are 2-sided. A *P* value <0.05 was considered statistically significant. Analyses were performed using R software version 3.4.4 (R Foundation for Statistical Computing).

RESULTS

STUDY POPULATION AND LP(A) DISTRIBUTION. Of 12,567 consecutive patients who underwent PCI with drug-eluting stents at Asan Medical Center between January 2003 and December 2013, Lp(a) levels at baseline were available in 12,064 (96.0%) patients.

The median level of Lp(a) was 18.6 mg/dL (interquartile range: 9.2 and 35.5 mg/dL) (Figure 1). A total of 3,747 (31.1%) patients had high Lp(a) levels (>30 mg/dL), and 8,317 (68.9%) patients had low Lp(a) levels (≤30 mg/dL). Baseline demographics and angiographic findings are listed in Table 1. The high-Lp(a) group was older and had more peripheral vascular disease, chronic kidney disease, and low ejection fraction. The high-LP(a) group more frequently had multivessel disease and then underwent PCI with more stents.

CLINICAL OUTCOMES. The median follow-up duration was 7.4 years (interquartile range: 4.7-10.2 years) (Supplemental Figure 1), and the primary outcomes occurred in 1,490 patients (cardiovascular death in 769 patients, spontaneous myocardial infarction in 571 patients, and ischemic stroke in 312 patients). The incidence rate of primary outcomes was 2.0 per 100 person-years in the high-Lp(a) group and 1.6 per 100 person-years in the low-Lp(a) group (adjusted hazard ratio [aHR]: 1.17; 95% confidence interval [CI]: 1.05-1.30; $P = 0.005$) (Figure 2). Individual clinical outcomes are presented in Table 2. The risk of death from any cause more frequently occurred in patients with high Lp(a) (aHR: 1.13; 95% CI: 1.01-1.27; $P = 0.033$). There was a tendency for higher risk of spontaneous myocardial infarction and ischemic stroke in the high-Lp(a) group. In addition, the adjusted risk of any repeat revascularization, target lesion revascularization, and new lesion revascularization was significantly higher in the high-Lp(a) group. Interestingly, the Kaplan-Meier curves diverged after 4 years after index PCI procedures.

Figure 3 shows the gradual relationship between primary outcomes and increasing Lp(a) levels categorized into 4 groups. As the level of Lp(a) increased, the risk for primary outcome was significantly increased (P for trend = 0.005).

INCREMENTAL PROGNOSTIC PERFORMANCE. Table 3 shows improvement in predicting the primary outcome by adding Lp(a) to a model including conventional clinical, angiographic, and procedural risk factors, and lipid profile; when Lp(a) was incorporated into the model, the net reclassification improvement significantly increased.

SUBGROUP ANALYSIS. The effect of Lp(a) group on the primary outcome was consistent across subgroups (Figure 4). Receiving statin treatment at discharge (aHR: 1.18; 95% CI: 1.03-1.34; P = 0.011) was also associated with the higher risk of recurrent ischemic cardiovascular events.

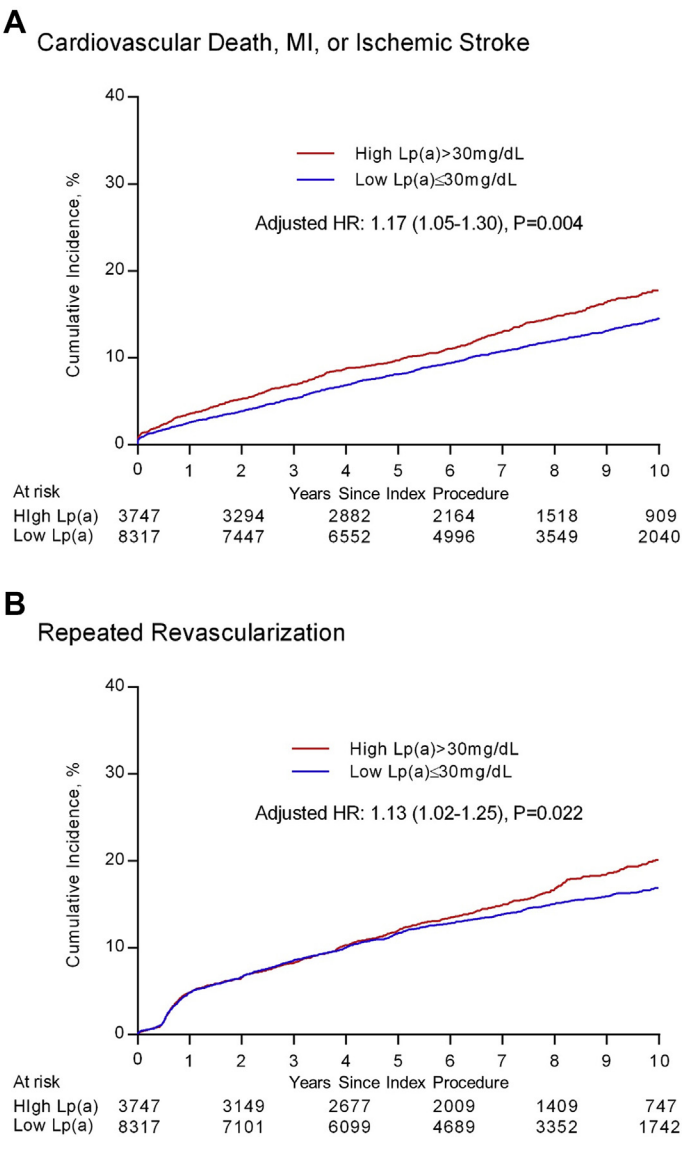
DISCUSSION

This large observational study demonstrated that elevated baseline Lp(a) levels were significantly associated with recurrent ischemic events including cardiovascular death, myocardial infarction, and ischemic stroke in patients who underwent PCI. These findings were consistent in various subgroups including patients who were receiving statin treatment at discharge and patients with low LDL cholesterol at baseline. This suggests that elevated Lp(a) could be a significant residual risk factor for the recurrent ischemic events and provides a rationale for outcome trials to test Lp(a)-lowering therapy for secondary prevention in patients undergoing PCI (Central Illustration).

Previous large epidemiologic and genetic studies based on the general population without established coronary artery disease had shown that Lp(a) levels are genetically determined and could be a causal factor for the development of atherosclerotic cardiovascular disease (15,17-19). Elevated Lp(a) levels are associated with dose-dependent increase in risk of cardiovascular events (15). In addition, the addition of Lp(a) to the conventional risk assessment model improved the cardiovascular risk prediction (20).

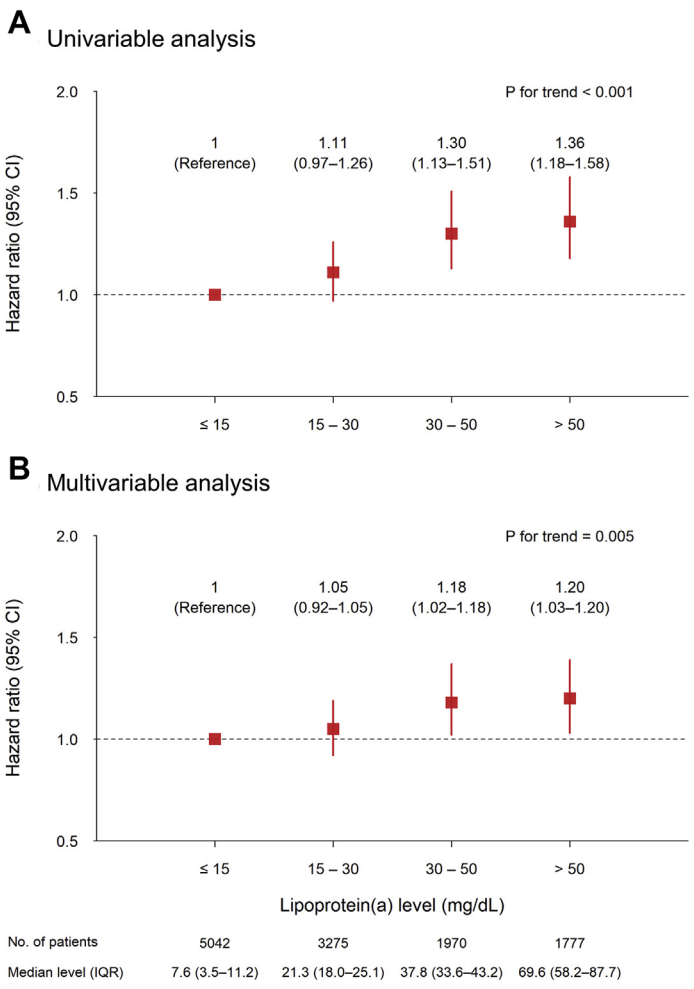
Contrary to the setting of primary prevention, the prognostic utility of Lp(a) in the setting of secondary prevention is less robust (4-12). The conflicting findings among these studies are likely to be explained by the difference in patient characteristics, distribution of Lp(a), confounding factors, and index event bias. Our study enrolled a large population of patients with high Lp(a) [3,747 patients with Lp(a) >30 mg/dL; 1,777 patients with Lp(a) >50 mg/dL] and with primary outcomes (n = 1,490) and, thereby, is powered sufficiently to identify the associations between Lp(a) and the risk of recurrent cardiovascular events even after statistical adjustment. This study added more evidence on the top of previous studies that Lp(a) would be useful as a risk marker to predict recurrent ischemic events in patients with established obstructive coronary artery disease undergoing PCI.

FIGURE 2 Kaplan-Meier Curves for Clinical Outcomes



(A) The primary outcome of cardiovascular death, myocardial infarction, and stroke. **(B)** Any repeat revascularization. Lp(a) = lipoprotein(a).

FIGURE 3 The Gradual Relationship Between Lipoprotein(a) Level and the Primary Outcome



(A) Univariate analysis; **(B)** multivariate analysis. IQR = interquartile range.

Previous studies suggested the interaction between LDL levels and clinical impact of Lp(a) levels (2,21). The association between Lp(a) and cardiovascular events was significant only in studies of patients with high LDL cholesterol, and the relationship was attenuated in those with low LDL cholesterol. Similarly, in our study, elevated Lp(a) was significantly associated with higher risk of recurrent cardiovascular events only in patients with LDL >70 mg/dL, while Lp(a) was not responsible for the primary outcome in patients with LDL ≤70 mg/dL, although we did not observe the significant interaction effect. Previous studies showed that elevated Lp(a) was associated with a risk of cardiac events in patients on statin treatment (16,22). In this study, approximately 80% of the patients received statin therapy at discharge, and consistently, elevated Lp(a) was also a significant risk factor in this subgroup.

The European Atherosclerosis Society proposed <50 mg/dL as an optimal Lp(a) level (2). However, mounting evidence suggests that the risk of adverse cardiovascular events begins to increase with Lp(a) levels as low as 24 to 30 mg/dL in general population (15,23-25). Additionally, the improvement in prediction of cardiovascular events was more pronounced when using the Lp(a) threshold of 30 mg/dL (26). A recent meta-analysis also confirmed that cardiovascular risk was significantly elevated at the levels of Lp(a) >30 mg/dL (16). Our findings also suggested that a desirable Lp(a) level in patients undergoing PCI could be <30 mg/dL. However, unexpectedly, the risk of recurrent cardiovascular events remained relatively constant above Lp(a) levels of 30 mg/dL. Whether this is an incidental finding or a result of other characteristics of the study population should be evaluated further.

The risk of target lesion revascularization was significantly higher in the high-Lp(a) group. Direct and indirect effects of Lp(a) on the progression of background atherosclerosis and smooth muscle cell proliferation within stent could be contributing factors (27). The later divergence of the event curve for repeated revascularization is not easily explained but suggests an association between high Lp(a) levels and the development of neoatherosclerosis within the coronary stent (28). Further study is necessary.

Currently available therapies can reduce Lp(a) level by as much as 20% to 30%, but the cardiovascular benefit of Lp(a) lowering has not been demonstrated (6,9,29). However, a potential pharmacologic intervention that lowers Lp(a) level by up to 90% is in development (30). A phase 2 trial in patients with established cardiovascular disease showed that antisense oligonucleotides targeting apo(a) synthesis effectively reduced Lp(a) levels with minimal side effects (31). Patients who undergo successful PCI and optimal medical treatment thereafter are still at higher risk of recurrent ischemic events, and would be a primary target for such a therapy. In addition, our findings from patients who have undergone PCI may have implications for the design and conduct of future trials that evaluate whether lowering Lp(a) levels will reduce cardiovascular events.

STUDY LIMITATIONS. First, this was post hoc observational study of prospective registry. Despite rigorous adjustment, unmeasured confounders could influence the observed findings. Second, our study population with established obstructive coronary artery disease who underwent PCI may have a higher

TABLE 3 The Incremental Prognostic Performance of Lp(a) to Predict the Primary Outcomes

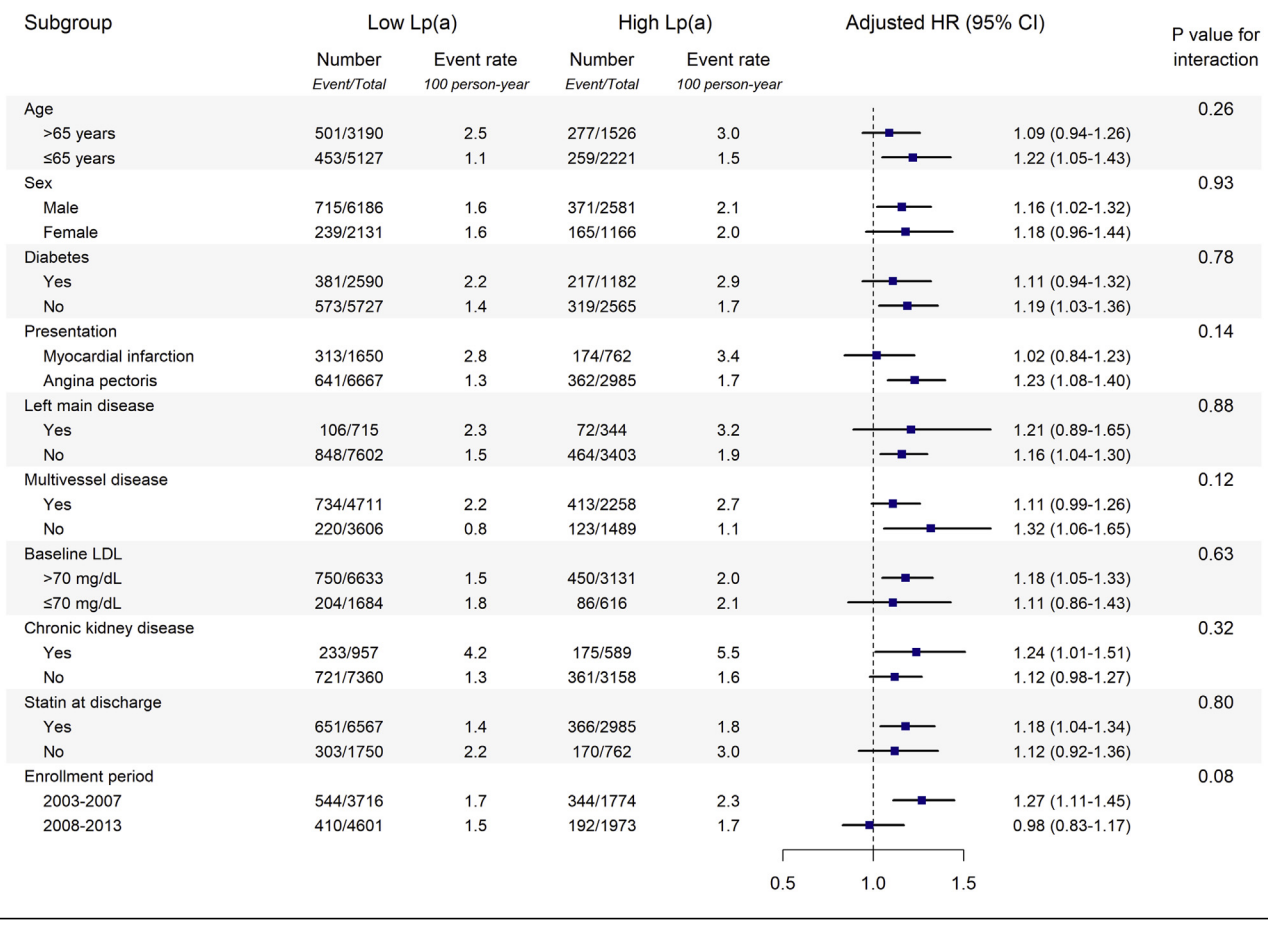
Model	C-Index (95% CI)	NRI (95% CI)	*P* Value	IDI (95% CI)	*P* Value
Model 1: clinical risk factors	0.726 (0.712 to 0.740)	-	-	-	-
Model 2: clinical risk factors plus corrected LDL and HDL cholesterol	0.727 (0.713 to 0.741)	0.020 (-0.012 to 0.062)	0.116	0.001 (0.000 to 0.003)	0.113
Model 3: model 2 plus Lp(a), >30 mg/dL	0.728 (0.714 to 0.741)	0.046 (0.012 to 0.077)	0.013	0.001 (0.000 to 0.003)	0.133

NRI and IDI were calculated by competing prediction models at 10 years. Clinical risk factors in the model 1included age, sex, initial presentation, body mass index, history of hypertension, history of diabetes, current smoking, prior myocardial infarction, prior stroke, prior peripheral vascular disease, chronic kidney disease, baseline ejection fraction, presence of left main disease, presence of multivessel disease, enrollment period (year), antiplatelet therapy, and statin prescription at discharge.

CI = confidence interval; IDI = integrated discrimination improvement; NRI = net reclassification improvement; other abbreviations as in Table 1.

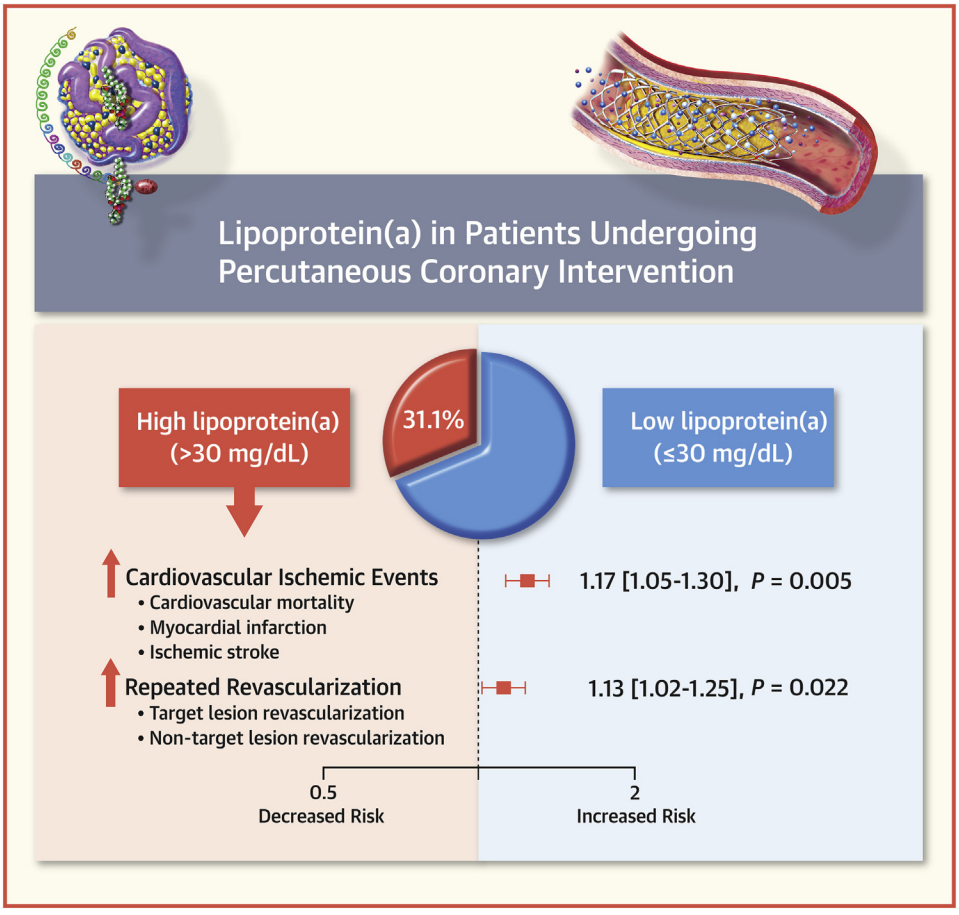
Lp(a) value compared with the general Korean population (32,33). Given the heterogeneity of Lp(a) according to the patient characteristic and ethnicities, direct inferences cannot be made to other ethnicities and clinical circumstances. Third, Lp(a) levels used in this study relied on a single measurement at baseline; however, generally, the Lp(a) level has been known to be maintained stable during life. Fourth, Lp(a) assays were in Lp(a) mass (mg/dL), rather than molar (nmol/L) concentration, because of test availability. However, the molar concentration more accurately reflects real particle number of Lp(a) than

FIGURE 4 Subgroup Analyses of the Primary Outcomes



LDL = low-density lipoprotein; Lp(a) = lipoprotein(a).

CENTRAL ILLUSTRATION **The Relationship Between Baseline Lipoprotein(a) and Future Cardiovascular Events in Patients Undergoing Percutaneous Coronary Intervention**



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the mass unit because of kringle IV type 2 variation (formerly polymorphism). The immune nephelometric assay used in our study is known to be more sensitive to the apo(a) isoform than is the immune turbidimetry assay. Fifth, several important variables and outcomes were not available for the analysis, including antiplatelet agent compliance during follow-up, familial history of premature atherosclerotic cardiovascular events, and stent thrombosis in the outcomes. Sixth, the routine use of aspirin after PCI may mitigate the risk of elevated Lp(a) on cardiovascular events in our study (34).

In conclusion, this study demonstrated that elevated Lp(a) level was significantly associated with recurrent cardiovascular events in patients undergoing PCI. This finding should be confirmed or reputed by Lp(a)-lowering therapy trials in the future.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (grant number: HC19C0022), and by the CardioVascular Research Foundation. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

WHAT IS KNOWN? Lp(a) was an independent risk factor for cardiovascular events in general population.

WHAT IS NEW? Our study showed that high Lp(a) defined as >30 mg/dL was an independent risk for future cardiovascular events in patients who underwent PCI.

WHAT IS NEXT? Further studies are warranted to confirm the results of our study, and clinical trials are needed to evaluate the treatment of reducing Lp(a) on top of current guideline-directed medical therapy in patients undergoing PCI.

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KEY WORDS coronary disease, lipoprotein (a), prognosis, stent

APPENDIX For a supplemental figure, please see the online version of this paper.