# The Association of Lipoprotein(a) with Recurrent Ischemic Events Following Percutaneous Coronary Intervention

Yong-Hoon Yoon[1], Do-Yoon Kang[2], Pil Hyung Lee[2], Jung-Min Ahn[2], Duk-Woo Park[2], Seung-Whan Lee[2], Seong-Wook Park[2], Seung-Jung Park[2]

[1]Department of Cardiology, Chungnam National University School of Medicine, Chungnam National University Hospital, Daejeon, Korea
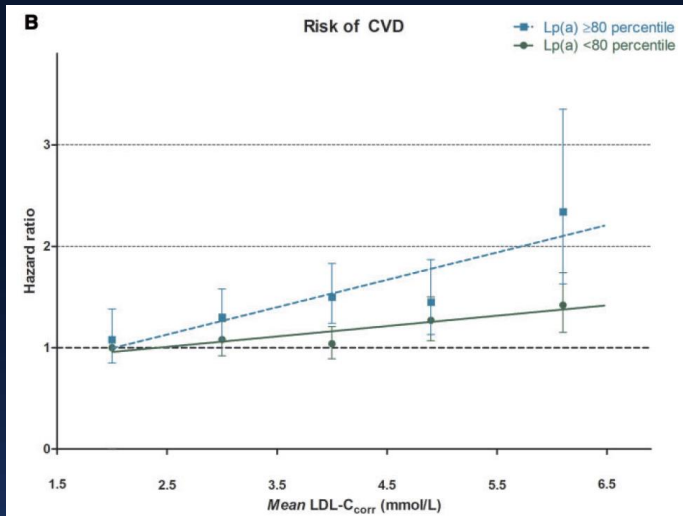
[2]Heart Institute, University of Ulsan College of Medicine
Asan Medical Center, Seoul, Korea
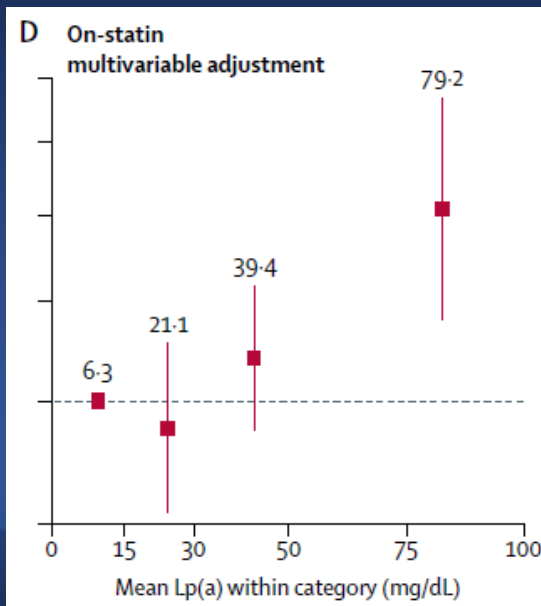
Backgrounds
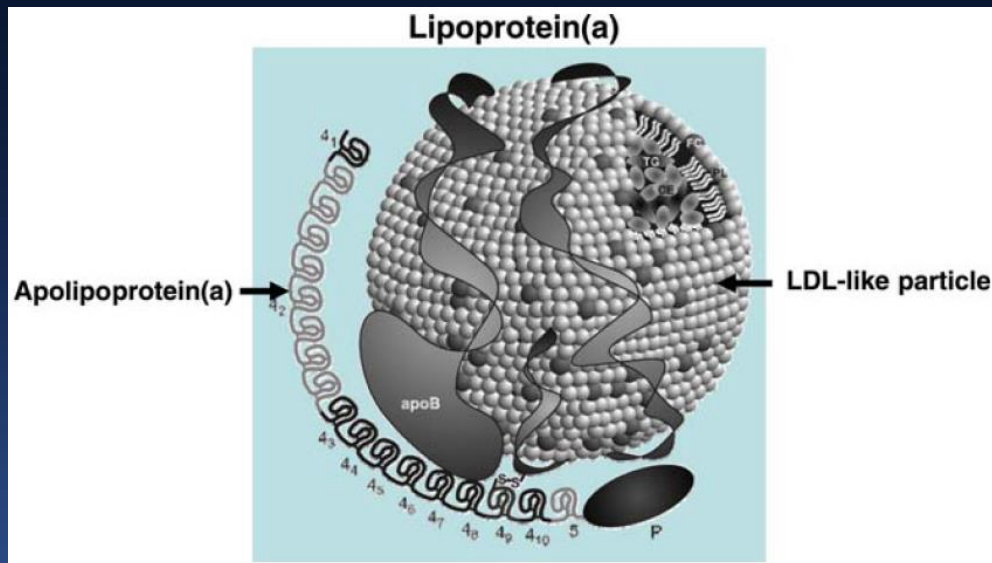
- Lipoprotein(a) [Lp(a)]
  ; LDL-like particle bound with apolipoprotein(a)

- Causal relationship with atherosclerosis or thrombosis

- Considered as CV risk factors from many studies

Backgrounds

- High Lp(a)

   ; related to cardiovascular disease

   independently with LDL level

- A recent meta-analysis

   ; High Lp(a) was associated with

   cardiovascular disease

   It was also evident in patients on

   statin treatment

Objective

- However, the robust and growing evidence is mostly based on studies with general population without known established cardiovascular disease.

- Therefore, we aimed to assess whether elevated Lp(a) is associated with long-term recurrent ischemic cardiovascular events in patients underwent PCI from a large unselected real-world registry.

Study Population

- The ASAN-PCI registry

  ; enrolled consecutive patients who underwent PCI at

    single tertiary referral center in Korea (AMC)

- Between Jan 2003 – Dec 2013

- A total of 12,567 patients

Lp(a) measurement

- Lp(a) measurement : before index angiography or PCI

- Immune-nephelometric assay (*BN II*, *Behring, Germany*)

- High Lp(a) : defined as baseline Lp(a) > 30 mg/dL

- Also categorized into 4 groups
  ; baseline Lp(a) level ≤ 15, 15-30, 30-50, and >50 mg/dL

Endpoints

- **The primary endpoint**

  ; composite of cardiovascular death, myocardial infarction,

    or ischemic stroke

- **The secondary endpoints**

  ; cardiovascular death, all-cause death,

    myocardial infarction, ischemic stroke,

    target vessel revascularization,

Statistical Analysis

Categorical variables are analyzed as frequencies with percentages and continuous variables as mean with standard deviation.

Comparisons between groups were performed using the Student t test for continuous variables or Fisher's exact test for categorical variables.

Survival curve was drawn by Kaplan-Meier method

Cox proportional hazards models were used to adjust confounding factors; 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 multi-vessel disease, enrollment period (year), and statin prescription at discharg.

Results

Study Population

- Baseline Lp(a) level : available in 12064 patients (96.0%)

  out of 12567 total population

- Median follow-up duration : 7.4 years (4.7 – 10.2)

- Median Lp(a) level = 18.6 mg/dL (9.2 – 35.5)

- High Lp(a) group – 3747 patients (31.1%)
- Low Lp(a) group – 8317 patients (68.9%)

Distribution of Lp(a) level
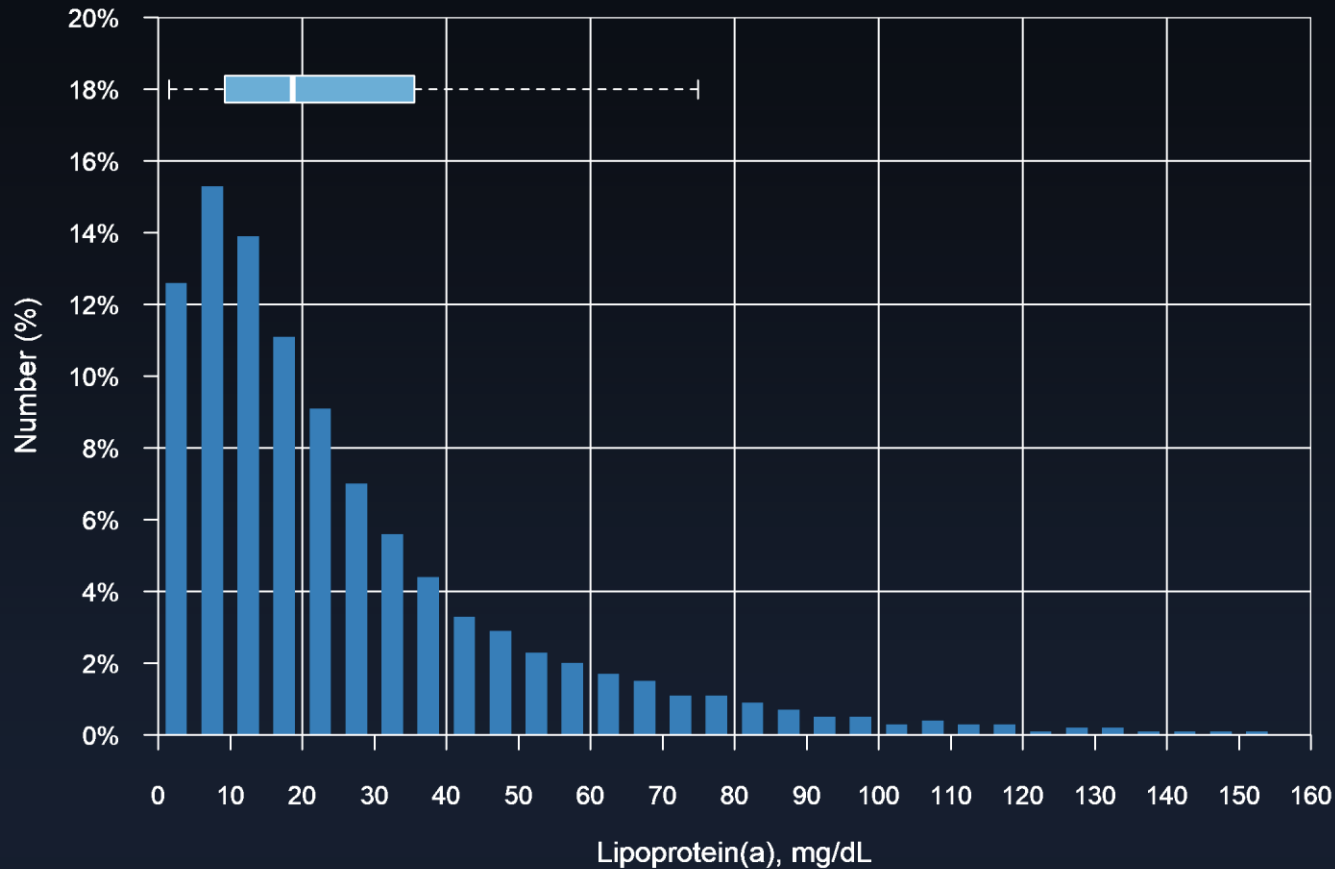
Baseline Characteristics (1)

	Low Lp(a) (N=8317)	High Lp(a) (N=3747)	P Value
			N (%) or Mean±SD
Age, y	61.6 ± 10.4	62.4 ± 10.0	<0.001
Male	6186 (74.4)	2581 (68.9)	<0.001
Clinical presentation			0.19
Stable angina	4406 (53.0)	1992 (53.2)	
Unstable angina	2261 (27.2)	993 (26.5)	
NSTEMI	1007 (12.1)	497 (13.3)	
STEMI	643 (7.7)	265 (7.1)	
Body mass index, kg/m^2	25.1 ± 3.0	24.7 ± 2.9	<0.001
Hypertension	4858 (58.4)	2213 (59.1)	0.52
Diabetes	2590 (31.1)	1182 (31.5)	0.67
Current smoker	2381 (28.6)	945 (25.2)	<0.001
Dyslipidemia	3869 (46.5)	1859 (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

Baseline Characteristics (2)

	Low Lp(a) (N=8317)	High Lp(a) (N=3747)	P Value
			N (%) or Mean±SD
Prior MI	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	4711 (56.6)	2258 (60.3)	<0.001
Number of stents used	1.9 ± 1.1	2.0 ± 1.2	0.005
Discharge medication			
Aspirin	8085 (97.2)	3648 (97.4)	0.69
$P2Y_{12}$ inhibitor	7720 (92.8)	3491 (93.2)	0.52
Beta blocker	5787 (69.6)	2602 (69.4)	0.90
Calcium channel blocker	6284 (75.6)	2849 (76.0)	0.59
ACEi or ARB	2625 (31.6)	1208 (32.2)	0.47
Statin	6394 (79.0)	3158 (79.5)	0.50

Primary endpoint
Composite of CV Death, MI, or Stroke

Secondary endpoint
All-cause death

Secondary endpoint
CV death
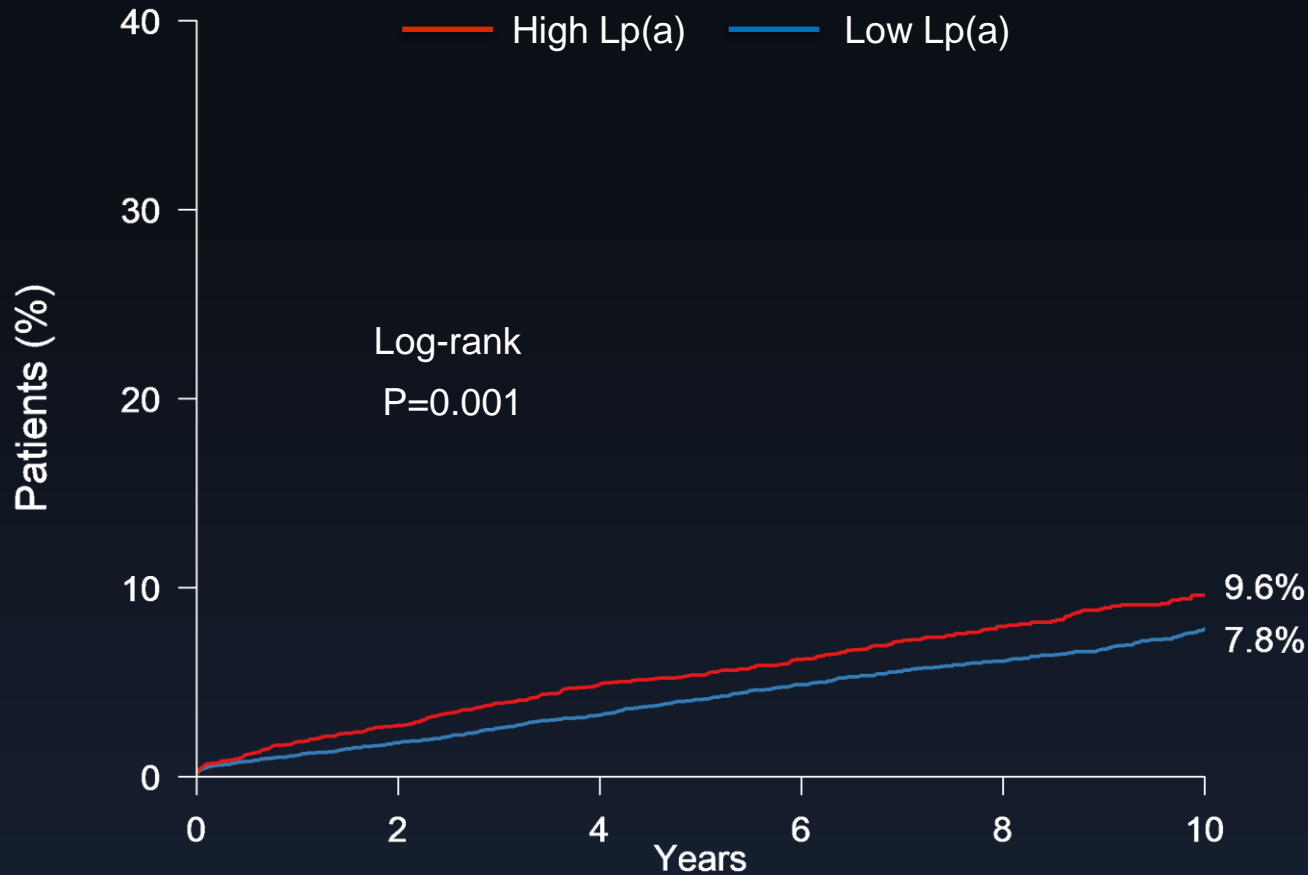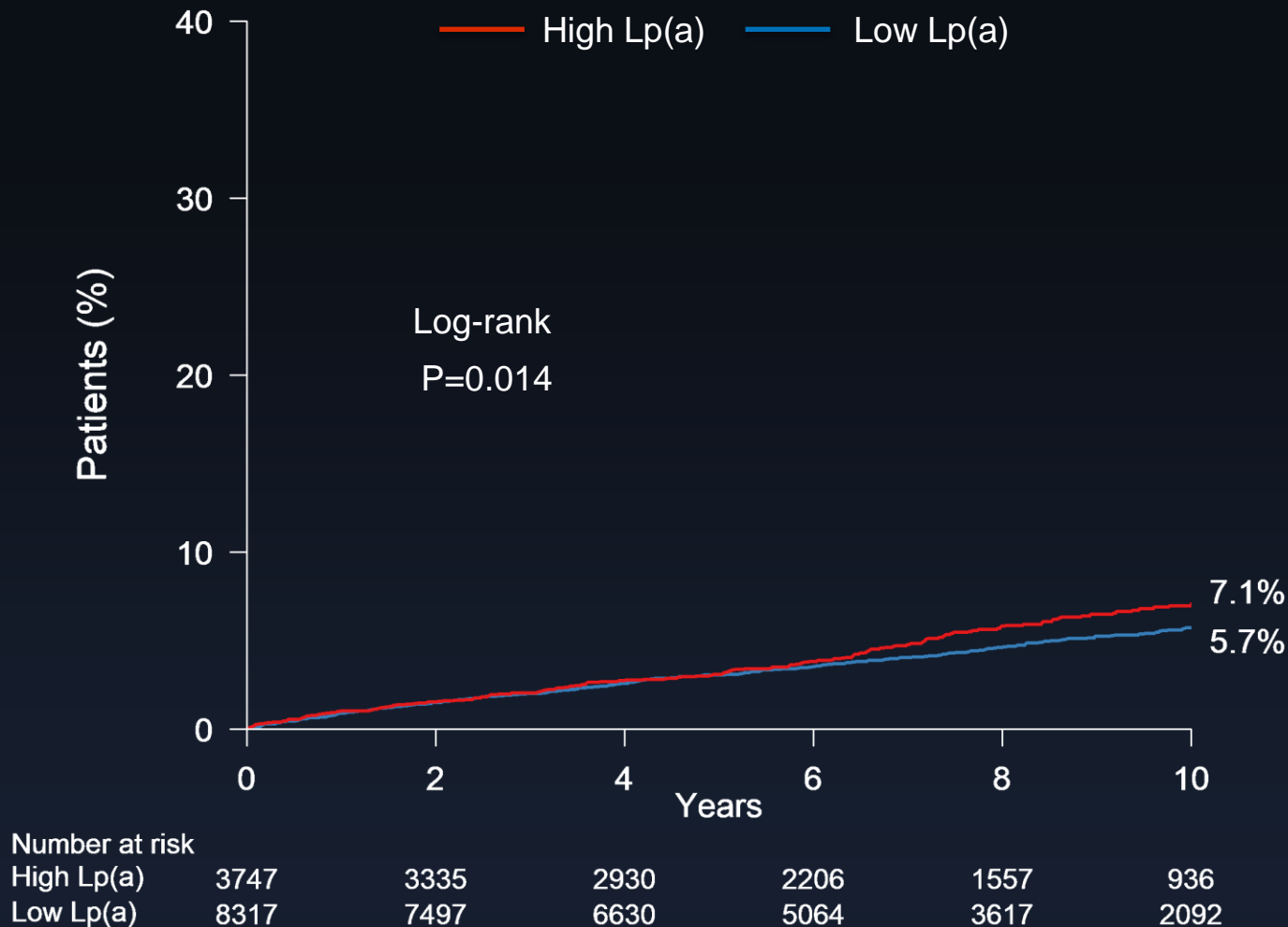
Secondary endpoint
MI

Secondary endpoint Stroke
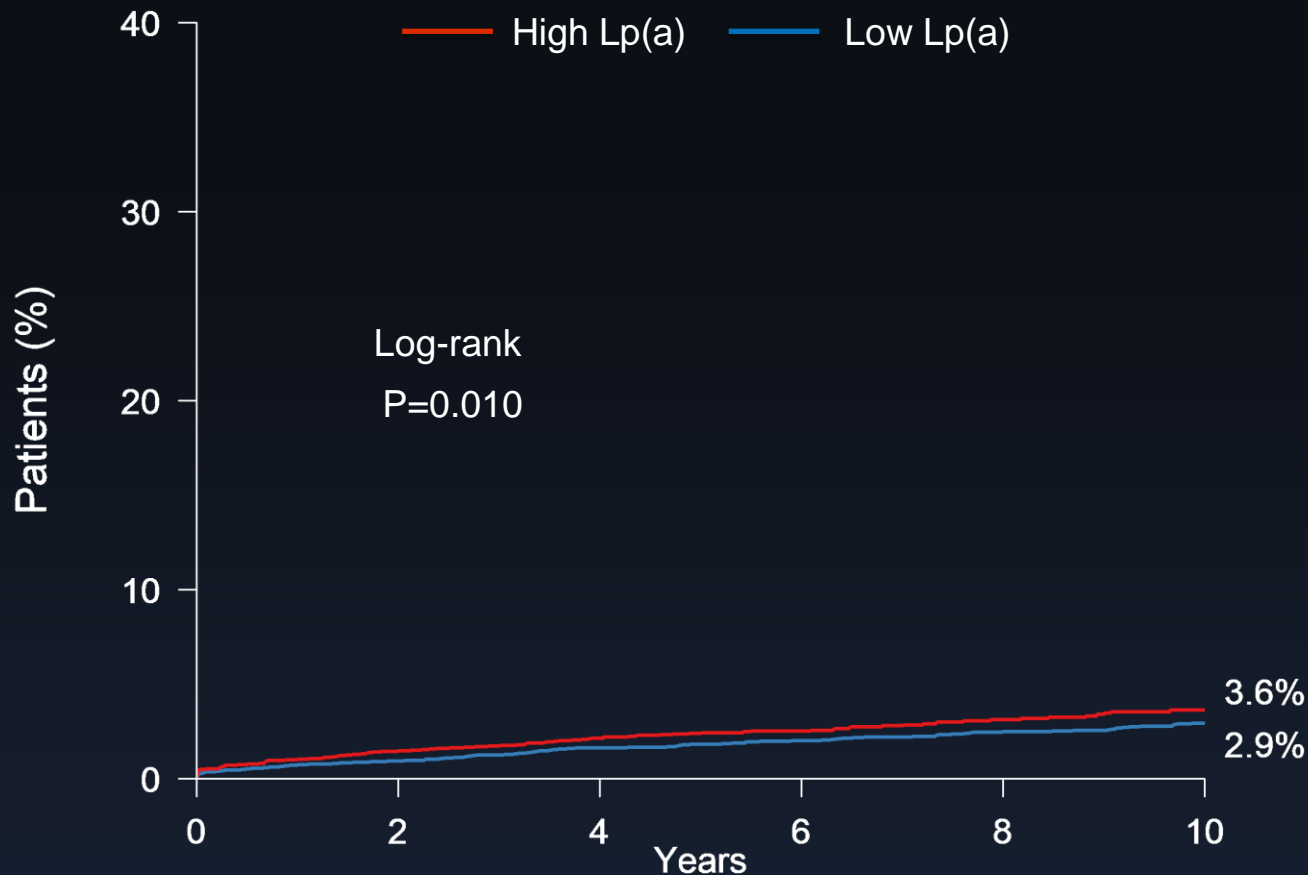
Secondary endpoint
TVR
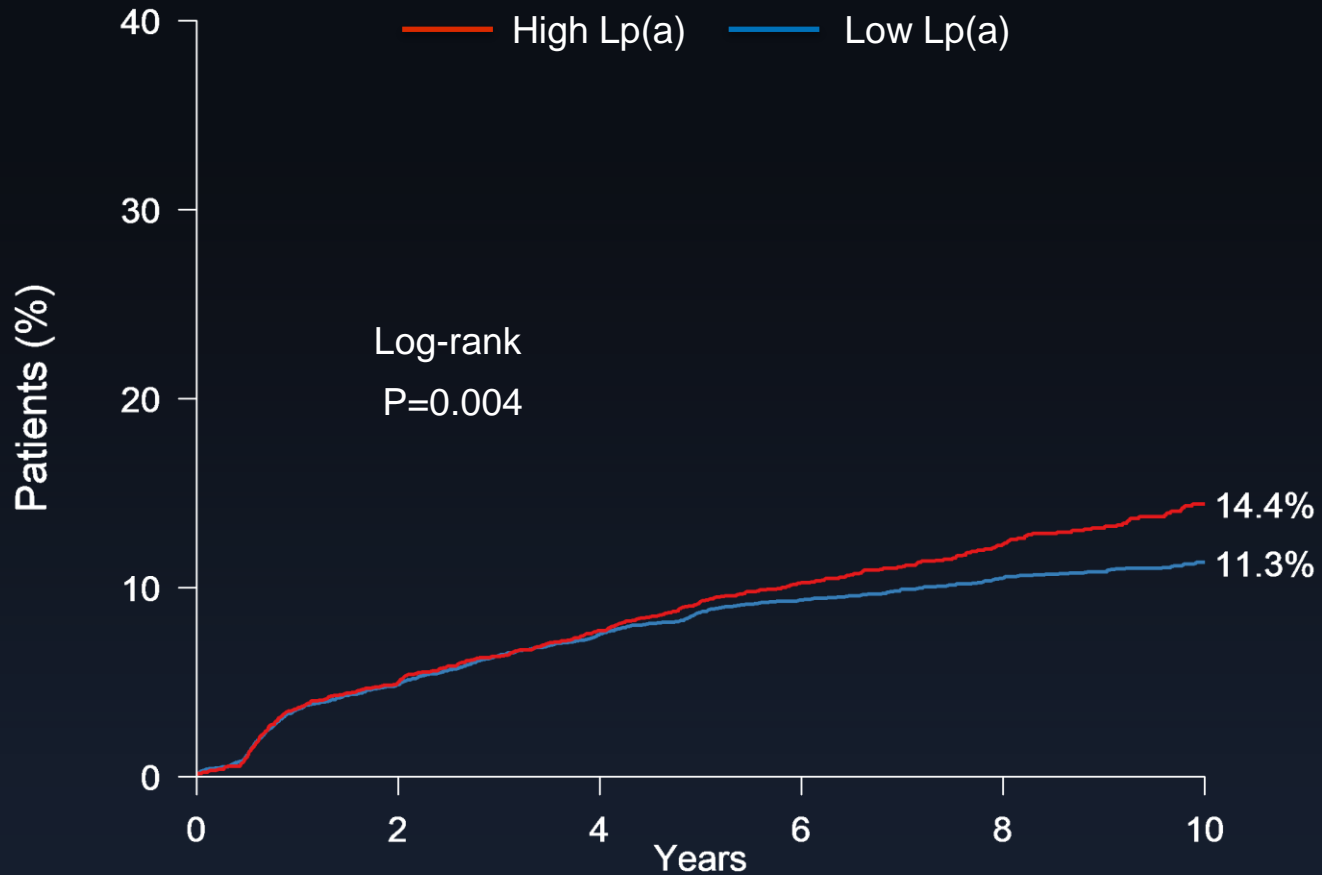
Hazards ratio of outcomes

	Unadjusted HR (95% CI)	P	Adjusted HR (95% CI)	P
Composite of cardiovascular death, myocardial infarction, or ischemic stroke	1.28 (1.15-1.42)	<0.001	1.17 (1.05-1.30)	0.004
Death from any cause	1.24 (1.11-1.39)	<0.001	1.13 (1.01-1.26)	0.038
Cardiovascular death	1.29 (1.11-1.49)	0.001	1.13 (0.97-1.31)	0.109
Myocardial infarction	1.24 (1.05-1.47)	0.013	1.19 (1.00-1.41)	0.052
Ischemic stroke	1.36 (1.08-1.71)	0.009	1.25 (1.00-1.58)	0.055
Any repeat revascularization	1.15 (1.04-1.27)	0.008	1.13 (1.03-1.26)	0.015
Target vessel revascularization	1.19 (1.06-1.34)	0.004	1.16 (1.03-1.31)	0.015
Target lesion revascularization	1.21 (1.06-1.37)	0.004	1.17 (1.03-1.33)	0.017
New lesion revascularization	1.16 (1.02-1.33)	0.029	1.17 (1.02-1.34)	0.021

Primary endpoint by 4 prespecified groups; Univariate analysis

A Univariable analysis
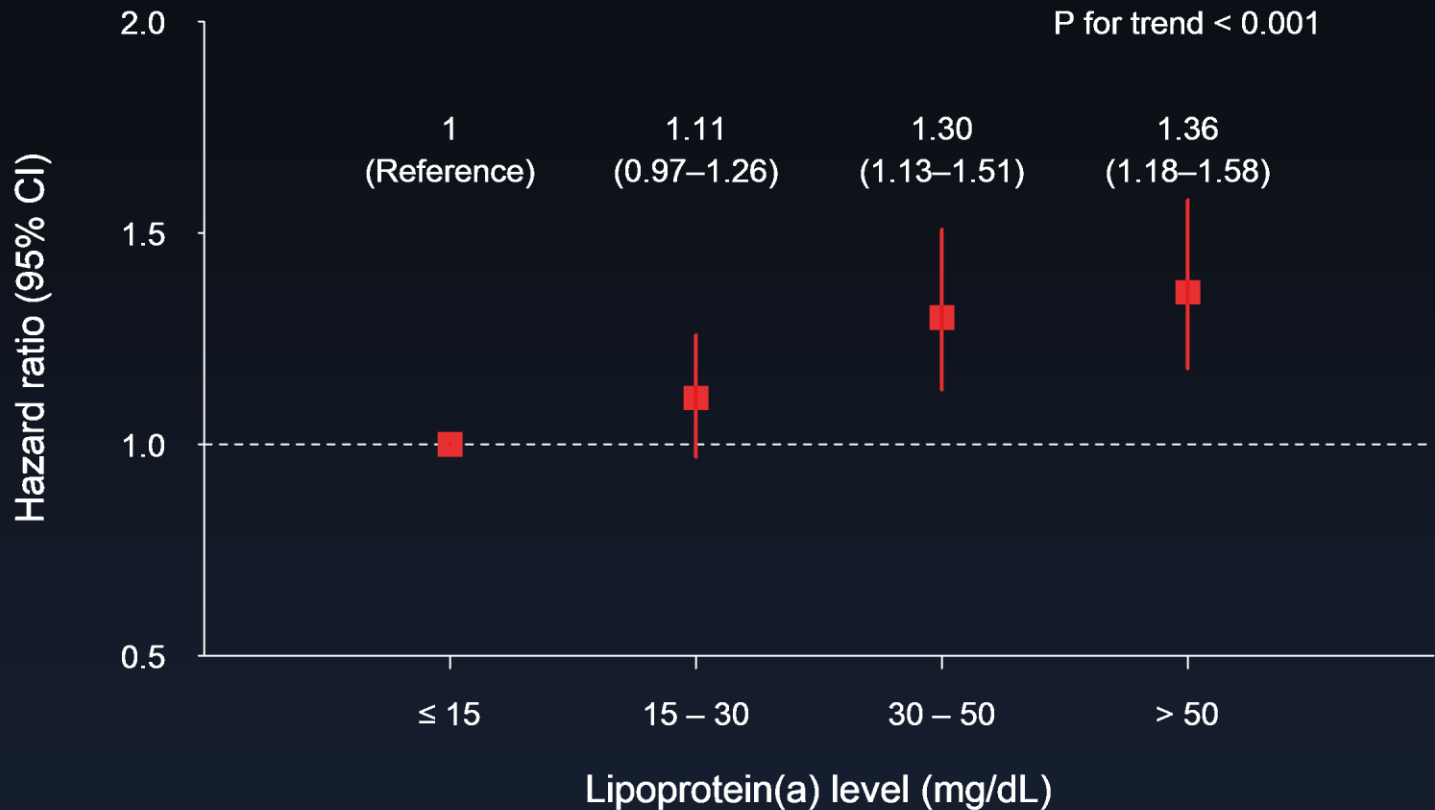
P for trend < 0.001

1 (Reference)	1.11 (0.97–1.26)	1.30 (1.13–1.51)	1.36 (1.18–1.58)

Hazard ratio (95% CI)

Lipoprotein(a) level (mg/dL)

	≤ 15	15 – 30	30 – 50	> 50
No. of patients	5042	3275	1970	1777
Median level (IQR)	7.6 (3.5–11.2)	21.3 (18.0–25.1)	37.8 (33.6–43.2)	69.6 (58.2–87.7)

Primary endpoint by 4 prespecified groups; Multivariate analysis

B Multivariable adjustment

Lipoprotein(a) level (mg/dL)	≤ 15	15 – 30	30 – 50	> 50
Hazard ratio (95% CI)	1 (Reference)	1.04 (0.91–1.04)	1.18 (1.02–1.18)	1.20 (1.03–1.20)
No. of patients	5042	3275	1970	1777
Median level (IQR)	7.6 (3.5–11.2)	21.3 (18.0–25.1)	37.8 (33.6–43.2)	69.6 (58.2–87.7)

P for trend = 0.005

Subgroup	Low Lp(a)		High Lp(a)		Adjusted HR (95% CI)		P value for interaction
	Number *Event/Total*	Event rate *100 person-year*	Number *Event/Total*	Event rate *100 person-year*			
Age							0.24
>65 years	501/3190	2.5	277/1526	3.0		1.08 (0.93-1.26)	
≤65 years	453/5127	1.1	259/2221	1.5		1.23 (1.05-1.43)	
Sex							0.94
Male	715/6186	1.6	371/2581	2.1		1.16 (1.02-1.32)	
Female	239/2131	1.6	165/1166	2.0		1.18 (0.96-1.44)	
Diabetes							0.76
Yes	381/2590	2.2	217/1182	2.9		1.11 (0.94-1.32)	
No	573/5727	1.4	319/2565	1.7		1.19 (1.03-1.36)	
Presentation							0.14
Myocardial infarction	313/1650	2.8	174/762	3.4		1.02 (0.84-1.23)	
Angina pectoris	641/6667	1.3	362/2985	1.7		1.23 (1.08-1.40)	
Left main disease							0.89
Yes	106/715	2.3	72/344	3.2		1.21 (0.89-1.65)	
No	848/7602	1.5	464/3403	1.9		1.16 (1.03-1.30)	
Multivessel disease							0.13
Yes	734/4711	2.2	413/2258	2.7		1.11 (0.99-1.26)	
No	220/3606	0.8	123/1489	1.1		1.32 (1.06-1.65)	
Baseline LDL							0.79
>130 mg/dL	171/1543	1.5	123/841	2.0		1.18 (0.93-1.49)	
≤130 mg/dL	783/6774	1.6	413/2906	2.1		1.15 (1.02-1.30)	
Chronic kidney disease							0.32
Yes	233/957	4.2	175/589	5.5		1.24 (1.01-1.51)	
No	721/7360	1.3	361/3158	1.6		1.11 (0.98-1.27)	
Statin at discharge							0.77
Yes	651/6567	1.4	366/2985	1.8		1.18 (1.04-1.34)	
No	303/1750	2.2	170/762	3.0		1.11 (0.92-1.35)	

0.5   1.0   1.5

Conclusion

- The baseline Lp(a) was significantly associated with recurrent cardiovascular events in patients undergoing PCI.

- The magnitude of future risks were similar in several ischemic endpoints.

- The results were also consistent in various subgroups including patients on statin treatment at discharge and patients with low LDL cholesterol at baseline.

Thank you !