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Impact of Baseline LDL-C and Lp(a) Elevation on Coronary Revascularization in Patients with Acute Coronary Syndrome One-Year after First Percutaneous Coronary Intervention

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Abstract

Objective: The aim of this study was to investigate the effect of Lipoprotein-a [Lp(a)] on Coronary Revascularizaton (CR) on one year follow up in patients with Acute Coronary Syndrome (ACS) after the first Percutaneous Coronary Intervention (PCI). **Method:** A retrospective study was designed. A total of 475 patients that underwent their first PCI treatment due to ACS between January 2016 and December 2017 were recruited and followed for one year at the Zhongda Hospital, China. The clinical end point after first PCI was prevalence of Major Adverse Cardiovascular Events (MACE) including nonfatal Myocardial Infarction (MI), cardiovascular death, ischemic stroke and Coronary Revascularization (CR). According to the cut point of Lp(a), participants were divided into low Lp(a) subgroup (Lp(a) < 300 mg/L) and high Lp(a) subgroup (Lp(a) ≥ 300 mg/L). Furthermore, based on baseline Low Density Lipoprotein Cholesterol (LDL-C) level, participants were divided into low LDL-C (LDL-C < 1.8 mmol/L) and high LDL-C (LDL-C ≥ 1.8 mmol/L) subgroups. **Results:** The number of prevalence of CR was higher with elevated serum Lp(a) in both low LDL-C subgroup and high LDL-C subgroup, and was significantly different in both the low LDL-C subgroup and high LDL-C subgroup (p = 0.009 and p = 0.006, respectively). Multivariate Cox-hazard regression analysis for CR showed increase in serum LDL-C and Lp(a) increased prevalence of CR by 1.514 and 1.002 folds respectively. Furthermore, Kaplan-Meier cumulative survival curves showed that increased prevalence of CR within one year after first PCI in patients with high Lp(a) [log rank p = 0.000]. **Conclusion:** Baseline increase of serum LDL-C and Lp(a) significantly increases the prevalence of CR after first PCI within one year. It indicates

that after PCI treatment, in patient with serum LDL-C and Lp(a) elevation, treatment with high-dose statin therapy or PCSK9 inhibitors may alleviate the adverse effects imposed by Lp(a) elevation.

1. Introduction

Hyperlipidemia, especially high serum level of low density lipoprotein-cholesterol (LDL-C) has been well documented as an important risk factor of atherosclerosis and its manifestation of atherosclerotic cardiovascular diseases (ASCVD) [1]. Although a significant progress have been made in recent years in the traditional risk factor control and treatment of Acute Coronary Syndrome (ACS). However, there are still a large number of patients with residual risk of cardiovascular events [2]. Hence, some epidemiological studies show that, although target LDL-C level has been achieved by statin therapy, residual cardiovascular risk such as coronary restenosis after Percutaneous Coronary Intervention (PCI) is still very high [3] [4]. It suggests that other risk factors besides LDL-C could also play a contributory role in the progression and recurrence of ACS after PCI, and identifying those potential risk factors would be beneficial for further improving cardiovascular outcome [3] [4].

Recently, some studies show that elevated plasma level of lipoprotein-a [Lp(a)] and LDL-C is associated with increased risk of Coronary Artery Disease (CAD) [5] [6]. Lp(a) is a lipoprotein particle with an LDL-like structure linked to apolipoprotein(a) [apo(a)] [6]. So, it has the effect similar to the LDL-C, and also carries atherothrombotic and proinflammatory properties [7] [8]. The combination of all these prothrombotic and atherosclerotic factors could trigger its atherosclerotic property. There is considerable heterogeneity with regards to the plasma level of Lp(a) among different ethnicities. Its cut-off value of significant risk for the Caucasians was recommended as 500 mg/L, whereas for the Chinese population, it is 300 mg/L considering far lower than the Caucasians [9] [10].

Currently, PCI is the preferred choice for ACS. The main strategy in the clinical practice after PCI is still focusing on atherogenic lipid profiles other than Lp(a), especially LDL-C, which is the main treatment target recommended by several guidelines [10] [11]. Although LDL-C has been recognized as one of the major risk factors for ACS, the residual risk for ACS despite intensive statin therapy indicates the important role for Lp(a) [12]. Therefore, preventing the incidence of coronary atherosclerosis after PCI is of paramount importance. Notably, the pathophysiological process of coronary artery atherosclerosis is featured by endothelial dysfunction, smooth muscle cells proliferation and fibrin

accumulation, and with respect to Lp(a)'s unique features such as atherosclerotic and proinflammatory properties, we speculated that Lp(a) elevation might be the potential risk factor responsible for the increased incidence of CAD due to coronary restenosis after PCI. A limited number of studies are available on the effect of LDL-C and Lp(a) on ACS patients after PCI treatment in Chinese patients. So, this study was conducted to determine the effect of Lp(a) elevation on ACS patients within one year after first therapeutic PCI, and also studied whether or not this effect of Lp(a) is dependent on LDL-C.

2. Method

2.1. Study Design

A retrospective study was conducted from January 2016 and December 2017 at the Department of Cardiology, Zhongda Hospital, China. All the patients were diagnosed with ACS through thorough angiographic assessment by 2 seasoned cardiologists.

2.2. Study Population

In our hospital from January 2016 and December 2017, total 1600 patients have undergone PCI treatments due to Coronary Artery Disease (CAD) and ACS. We have identified and enrolled 475 ACS patients who have undergone first PCI treatment. The study population consisted of patients presented with ACS consisting of Unstable Angina (UA), Non-ST segment Elevation ACS (NSTE-ACS) and ST segment Elevation ACS (STE-ACS) that necessitated therapeutic PCI after thorough angiographic assessment. Of the total enrolled patients, 51 patients were excluded due to in accordance with our exclusion criteria. A total of 424 patients were enrolled in our study (Figure 1). All the patients were prescribed with recommended dose of statin and anti-platelet therapy following PCI and have been followed for one year for any cardiovascular events *i.e.* Major Adverse Cardiovascular Events (MACE) including, Coronary Revascularization (CR) due to coronary restenosis, hemorrhagic stroke, nonfatal Myocardial Infarction (MI) and cardiovascular death. Baseline demographic and laboratory information (*see* Table 1), including age, gender, smoking status, lipid profile, hypertension, diabetes mellitus, family history and previous medications, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and coronary artery occlusion were obtained retrospectively in all the patients.

The inclusion criteria for current study were 1) patients aged 18 - 80 y/o, 2) the patients undergone first PCI due to any form of CAD *i.e.* SAP or ACS including Unstable Angina (UA) or STE-ACS or NSTE-ACS. The exclusion criteria was 1) patients with previous PCI, 2) patients with plasma creatinine level of >132 μmol/L, 3) patients with plasma alanine transaminase level of >3 times upper normal limit, 4) patients with unavailability of lipid record, 5) patients with thyrotoxicosis and malignancy or systemic inflammatory disorder.

Accordingly [6], patients after PCI are recommended to achieve target LDL-C
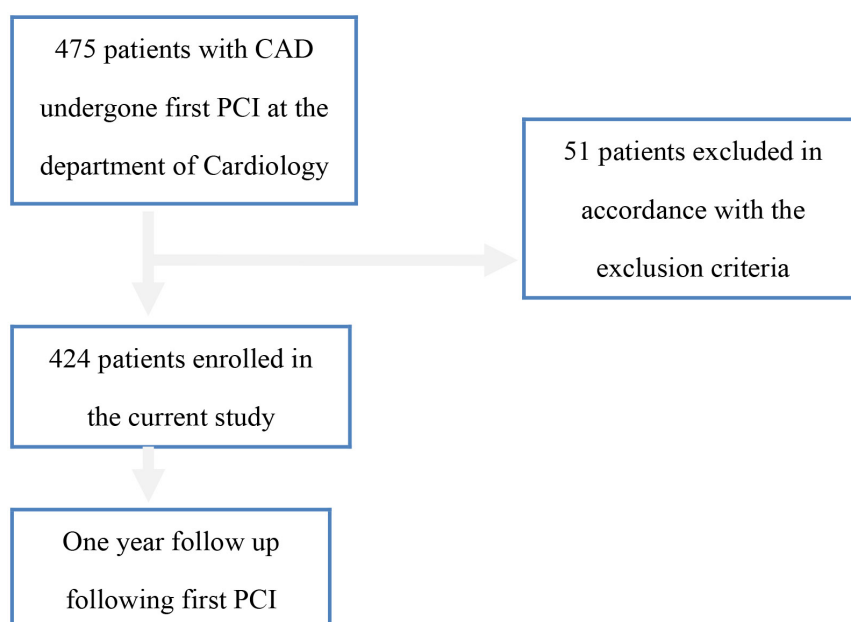
Figure 1. Flow diagram of study population.

Table 1. Comparison of baseline characteristics of low-Lp(a) and high-Lp(a) groups.

	Variables	Lp-a < 300 mg/L (n = 256)	Lp-a ≥ 300 mg/L (n = 168)	P-value
Demographic	Age (years)	67.54 ± 10.36	65.74 ± 11.22	0.519
	Sex (%)			0.188
	Male (%)	164 (64.1%)	118 (70.2%)	
	Female (%)	92 (35.9%)	50 (29.8%)	
	Blood Pressure			
	SBP (mmHg)	131.52 ± 19.96	130.92 ± 19.45	0.990
	DBP (mmHg)	85.29 ± 15.00	84.70 ± 14.17	0.614
	Smoking (%)	79 (30.9%)	47 (28.5%)	0.603
	Alcohol (%)	74 (28.9%)	45 (27.1%)	0.688
Coronary risk factors	HTN (%)	185 (72.3%)	120 (71.4%)	0.851
	DM (%)	92 (35.9%)	57 (33.9%)	0.672
	Stroke (%) [previous]	64 (25%)	43 (25.6%)	0.890
Lipid profile	HDL-C (mmol/L)	1.06 ± 0.28	1.08 ± 0.25	0.748
	LDL-C (mmol/L)	1.84 ± 0.72	2.21 ± 0.88	0.058*
	Lp (a)	140.31 ± 78.17	617.71 ± 352.86	0.000*
	Cholestrol (mmol/L)	3.52 ± 0.96	3.71 ± 1.09	0.104
	Triglyceride (mmol/L)	1.55 ± 1.27	1.49 ± 1.08	0.201
	Apo-A1 (g/L)	1.15 ± 0.26	1.00 ± 0.28	0.395
	Apo-B (g/L)	0.59 ± 0.22	0.67 ± 0.23	0.829
Laboratory	Glucose (mmol/L)	6.52 ± 2.03	6.24 ± 2.03	0.681

Continued

tests	S-Cr (umol/L)	86.30 ± 30.28	92.77 ± 50.21	0.033*
	hsCRP (mg/L)	1.54 ± 1.03	1.65 ± 1.15	0.508
Cardiac	CKMB (ng/mL)	9.61 ± 22.79	11.70 ± 20.68	0.493
biomarkers	BNP (pg/mL)	393.53 ± 1145	809.13 ± 1542	0.009*
	MYO (ng/mL)	99.20 ± 165.56	127.42 ± 156.85	0.318
	aTnI (ng/mL)	0.30 ± 1.41	0.78 ± 3.25	0.001*
Coronary	LM (%)	17 (6.6%)	9 (5.4%)	0.590
Artery	LAD (%)	190 (74.2%)	128 (76.2%)	0.647
Occlusion	LCX (%)	101 (39.5%)	75 (44.6%)	0.289
	RCA (%)	137 (53.5%)	98 (58.3%)	0.329
	Single Vessel (%)	144 (56.2%)	86 (51.2%)	0.306
	Two Vessels (%)	52 (20.3%)	29 (17.3%)	0.434
	Three Vessels (%)	60 (23.4%)	53 (31.5%)	0.065
Medications	Aspirin (%)	254 (99.2%)	166 (98.8%)	
	Clopidogrel (%)	136 (53.1%)	92 (54.8%)	
	Ticagrelor (%)	121 (47.3%)	76 (45.2%)	
	Atorvastatin (%)	91 (35.5%)	61 (36.3%)	
	Rosuvastatin (%)	165 (64.5%)	107 (63.7%)	
	Metoprolol (%)	209 (81.6%)	136 (81%)	

HTN: Hypertension, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, DM: diabetes mellitus, TC: Total Cholesterol, TG: Triglyceride, S-Cr: Serum Creatinine, hsCRP: high sensitive C-Reactive Protein, LM: left main trunk, HDL-C: High Density Lipoprotein Cholestrole, LDL-C: Low Density Lipoprotein Cholestrol, Apo-A1: Apolipoprotein A1, Apo-B: Apolipoprotein B, CKMB: Creatinine Kinase-MB, BNP: Brain Natriuretic Peptide, MYO: Myoglobin, aTnI: Troponin-I, LAD: Left Anterior Descending Artery, LCX: Left Circumflux Artery, RCA: Rgiht Coronary Artery.

level of less than 1.8 mmol/L; therefore, we used 1.8 mmol/L of LDL-C as cut-off point to categorize all patients into two subgroups. Plasma level of Lp(a) lower than 300 mg/L is considered within the normal range for the Chinese patients, therefore we considered plasma level of Lp(a) equal to or higher than 300 mg/L as abnormal [3].

2.3. Laboratory Measurement

For variable measurements in the hospital laboratory, blood samples were taken when the patients had been fasting for about 8 hours. Plasma Lp(a) level was analyzed with sandwich Enzyme Linked Immune-sorbent Assays (ELISA kit, Yaji Biosystems, Shanghai, China). All the procedures for variable measurements were performed according to the manual instruction and were evaluated by SYNCHRON LX20 UniCel DxC800 analyzer (Beckman Coulter Inc., USA).

2.4. Primary End Point

All the participants have been followed up for the cardiovascular events such as

MACE. MACE after PCI was prevalence of non-fatal MI, ischemic stroke, cardiovascular death and CR within the duration of one year. CR was defined as the angioplasty or PCI within one year after the first PCI. Stroke was defined as the loss of neurological function due to ischemic or hemorrhagic stroke. Cardiovascular death was defined as death due to cardiovascular issues. MI was defined as the prevalence of MI within one year after the first PCI.

2.5. Statistical Analysis

Continuous data was presented as mean ± SD or median (interquartile range) appropriately and compared by Student's *t*-test when data was normally distributed, otherwise compared by the Wilcoxon rank-sum test. Categorical data was presented as percentage and compared by χ^2 test. Cox-hazard regression analysis [Hazard Ratio (HR)] was performed to address predictors for CR. Kaplan-Meier survival estimation analysis was used to address one year survival effect for CR. Statistical analyses were performed by using SPSS software version 20.0 (SPSS, Inc., Chicago, Illinois). A value of $P < 0.05$ was considered significant.

3. Results

Baseline Characteristics of CAD patients with Lp-a < 300 mg/L subgroup and Lp-a ≥ 300mg/L subgroup One Year after first PCI:

All the enrolled patients were classified into High Lp(a) [Lp(a) ≥ 300 mg/L] group (n = 168) and Low Lp(a) [Lp(a) < 300 mg/L] group (n = 256). The baseline characteristics of the enrolled patients of the 2 groups are shown in Table 1. The study population consisted of 282 males (66.5%) and 142 females (33.5%), and mean age 66.83 ± 11 years. In brief, lipid profile observation has shown that LDL-C and Lp(a) are to be significantly different (p < 0.05) between the two groups. Mean value of HDL-C, Cholestrol, Triglyceride and Apo-B is elevated in patients with high Lp(a), though they weren't statistically significant between the groups. Observation of lab analysis showed that Serum Creatinine (S-Cr) was significantly different between low and high Lp(a) groups (p = 0.033). The mean value of high sensitive C-Reactive Protein (hsCRP) was higher in high Lp(a) group but was not significant. Meanwhile, the analysis of coronary vessels has shown increased prevalence of stenosis in 3 coronary vessels stenosis, though they weren't significant [53(31.5%) (p = 0.065)]. The stenosis in Right Coronary Artery (RCA), Left Cricumflex Artery (LCX) and Left Anterior Descending (LAD) artery tend to be more in high Lp(a) group though they were not significant. The values of Brain-type Natriuretic Peptide (BNP) and cardiac Troponin-I (cTnI) were significantly different in high Lp(a) group (p = 0.009 and p = 0.001 respectively). Meanwhile, the mean value of CKMB and MYO were higher in high Lp(a) group but they weren't significant. It shows that high level Lp(a) is associated with necrosis of myocardial fibers.

Cardiovascular Outcomes Comparison in the CAD Patients One Year after first PCI in the Subgroup of LDL-C < 1.8 mmol/L subgroup and LDL_C ≥ 1.8

mmol/L:

Selecting LDL-C level of 1.8mmol/L as the cut-off point, 424 patients were divided into two subgroups, low LDL-C (LDL-C < 1.8 mmol/L) and the high LDL-C (LDL-C ≥ 1.8 mmol/L) of LDL-C equal or higher than the 1.8 mmol/L. In the subgroup of low LDL-C (n = 211) subgroup, there were 147 patients with Lp(a) level lower than 300 mg/L, while another 64 were with Lp(a) level higher than 300 mg/L. As shown in Table 2, the number of prevalence of CR was higher as compared to the other adverse events of the total MACE in high Lp(a). In our study prevalence of total MACE and CR was significantly different between low and high Lp(a) groups (p = 0.002 and p = 0.009, respectively) in patients with low LDL-C. The prevalence of Stroke was higher in high Lp(a) subgroup and was significantly different (p = 0.031). It shows that elevated level of serum Lp(a) is a causative factor for adverse events *i.e.* CR and stroke even after achieving low LDL-C level.

Another 213 patients with LDL-C level equal to or higher than 1.8 mmol/L were divided into two subgroups according to the cut-off point of Lp(a). As shown in Table 2, same as in the subgroup with low LDL-C, in the subgroup of patients with high LDL-C level the number of prevalence of CR was higher as compared to the other adverse in total MACE. In this subgroup of patients with high LDL-C level the prevalence of CR and total MACE was significantly different (p = 0.006 and p = 0.001, respectively). Moreover, prevalence of other adverse events of MACE *i.e.* MI, stroke and Death were higher in high Lp(a) subgroup than the low Lp(a) subgroup though they weren't significant. So it shows that elevated level of both serum LDL-C and Lp(a) were associated with increased prevalence of MACE especially CR.

Table 2. Cardiovascular outcomes comparison in the subgroup of patients with LDL-C Lower than 1.8 mmol/L and higher than 1.8 mmol/L after PCI.

		Lp-a < 300 mg/L (n = 147)	Lp-a ≥ 300 mg/L (n = 64)	p
	MACE	15 (10.2%)	17 (26.6%)	0.002*
LDL_C	*CR*	13 (8.8%)	14 (21.9%)	0.009*
<1.8 mmol	*Stroke*	0 (0%)	2 (3.1%)	0.031*
(n = 211)	*Death*	1 (0.7%)	0 (0%)	0.508
	MI	1 (0.7%)	1 (1.6%)	0.543
		Lp-a < 300 mg/L (n = 109)	Lp-a≥300 mg/L (n = 104)	p
LDL-C	**MACE**	18 (16.5%)	37 (35.6%)	0.001*
≥1.8 mmol/L	*CR*	10 (9.2%)	24 (23.1%)	0.006*
(n = 213)	*Stroke*	3 (2.8%)	4 (3.8%)	0.654
	Death	2 (1.8%)	4 (3.8%)	0.375
	MI	3 (2.8%)	5 (4.8%)	0.430

MACE: Major Adverse Cardiovascular Events, CR: Coronary Revascularization, MI: non-fatal Myocardial Infarction, Death: Cardiovascular death, Stroke: Ischemic stroke after PCI.

Cox Regression Hazards Model for Factors Associated with Coronary Revascularizartion (CR) with CAD after first PCI within One Year:

We performed Cox regression Hazard analysis to analyze the predictors for CR. After performing univariate Cox analysis, significant predictors for CR were Lp(a), total Cholestrol, Triglyceride, Apo-A1, hsCRP, Creatinine and LDL-C, Table 3. Multivariate Cox-analysis showed increase in serum LDL-C and Lp(a) increases the prevalence of CR by 1.514 and 1.002 folds respectively. Multivariate analysis also showed that Total Cholesterol (TC) [0.651 (0.507 - 0.835), p = 0.001], Creatinine (Cr) [0.991 (0.985 - 0.997) p = 0.003] and Triglyceride (TG) [0.775 (0.635 - 0.941) p = 0.010] were significantly different when combining with all the other factors together.

Kaplan-Meier Survival Estimation Plot for Coronary Revascularization (CR) in Patients with CAD after first PCI within One Year:

We compared the prevalence of CR in CAD patients one year after first PCI between low Lp(a) group and high Lp(a) group through Kaplan-Meier cumulative survival analysis as shown in Figure 2. Kaplan-Meier cumulative survival curves for all cause CR for one year showed that the prevalence of CR after the

Table 3. Cox Regression hazards model for univariate and multivariate factors associated with coronary revascularizartion.

Variables	Univariable			Variables	Multivariate		
	HR	CI (95%)	p-value		HR	CI (95%)	p-value
Age	1.001	0.994 - 1.007	0.807	Lp (a)	1.002	1.001 - 1.002	0.000
LDL-C	1.272	1.029 - 1.571	0.026*	LDL-C	1.514	1.125 - 2.038	0.006
HDL-C	0.859	0.426 - 1.730	0.670	TC	0.651	0.507 - 0.835	0.001
TC	0.819	0.676 - 0.992	0.041	Cr	0.991	0.985 - 0.997	0.003
TG	0.826	0.692 - 0.986	0.035	TG	0.773	0.635 - 0.941	0.010
Apo-A1	0.444	0.227 - 0.871	0.018				
Apo-B	1.534	0.780 - 3.014	0.215				
Gucose	1.041	0.924 - 1.174	0.505				
hsCRP	0.611	0.442 - 0.843	0.003				
Cr	0.991	0.986 - 0.997	0.005				
SBP	1.008	0.999 - 1.017	0.076				
DBP	1.005	0.990 - 1.019	0.534				
HTN	1.304	0.836 - 2.034	0.241				
DM	1.296	0.879 - 1.930	0.203				
Smoking	0.742	0.506 - 1.090	0.128				
Alcohol	1.018	0.687 - 1.508	0.929				
Lp(a)	1.001	1.001 - 1.002	0.000*				

HTN: Hypertension, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, DM: diabetes mellitus, TC: Total Cholesterol, TG: Triglyceride, S-Cr: Serum Creatinine, hsCRP: high sensitive C-Reactive Protein, HDL-C: High Density Lipoprotein Cholestrole, LDL-C: Low Density Lipoprotein Cholestrol, Apo-A1: Apo-lipoprotein A1, Apo-B: Apolipoprotein B.
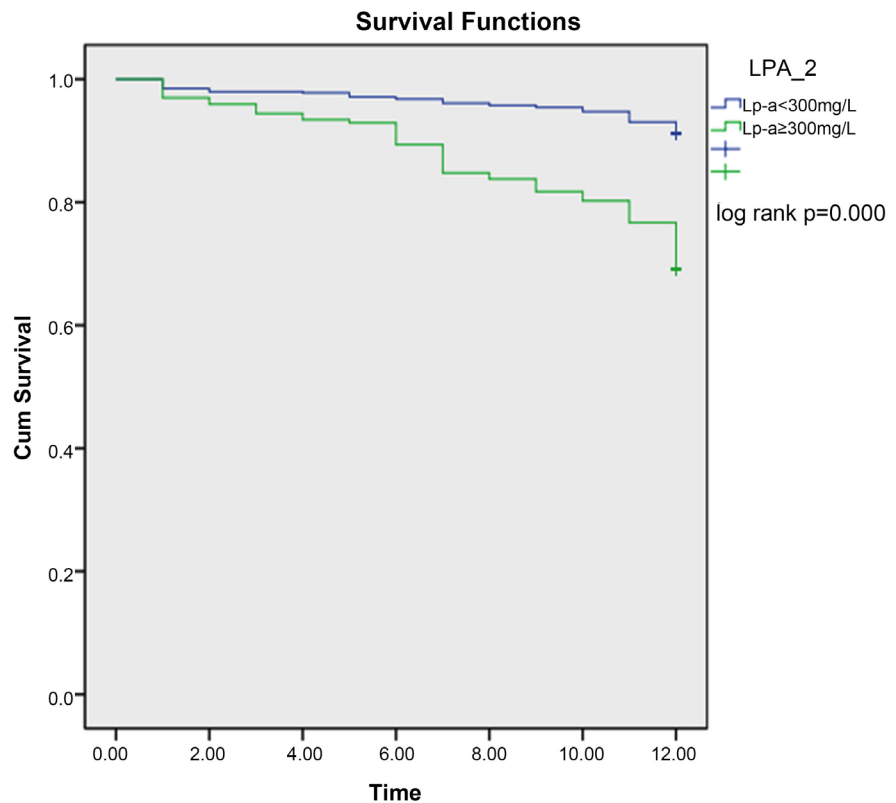
Figure 2. Kaplan-meier survival estimation plot of coronary revascularization (CR) in patients with CAD after first PCI within one year.

first PCI was significantly higher in the group with high Lp(a) than the low Lp(a) group (log rank p = 0.000).

4. Discussion

Our study showed that the number of prevalence of stent-restenosis and CR was higher as compared to the other adverse events of the total MACE in high Lp(a) in patients with low LDL-C subgroup. The increase in serum LDL-C and Lp(a) were associated with increase in prevalence of total MACE and CR. The prevalence of CR after the first PCI was significantly higher in the group with high Lp(a) subgroup than low Lp(a) subgroup. Our study also showed that LDL-C and Lp(a) increases prevalence of CR by 1.514 and 1.002 folds respectively. This association was significant even after adjustment for other independent variables. After the treatment with PCI all the patients were well followed up and were prescribed with recommended medications such as antiplatelet and statin therapies.

At present, PCI is largely applied in patients with significant coronary artery stenosis, and this reperfusion approach has overwhelmingly enhanced cardiovascular outcomes during last two decades. However, the accumulation of evidence from retrospective and perspective studies show that, despite the patients treated with PCI and strictly adhering to recommended guidelines, a significant

number of patients still have a high residue of cardiovascular risk, especially the revascularization of the target vessel requiring atherosclerosis. With regard to these findings, many strategies to reduce residual cardiovascular risk have been introduced, and a more aggressive LDL-C reduction treatment is considered as one of the most attractive and potential strategy.

Recently LIPID [13] study has shown the relationship between serum Lp(a) and further CVD events in patients with CAD on statin therapy. Formerly, observation of patients with CAD treated with intensive statin therapy in PROVE IT-TIMI [14], IDEAL [4] and TNT [15] clinical trials have shown, during their follow-ups they have found increased frequency of CR even with intensive statin treatment. In addition, the IDEAL and TNT trials have shown residual CVD risk during their 5 years follow up (12.0% and 8.7%, respectively). The results of these important clinical trials have repeatedly shown that despite aggressive reduction of LDL-C, significant cardiovascular residual risks remain in the patient and that LDL-C alone is not sufficient to reduce cardiovascular risk. Although Lp(a) was an attractive topic in clinical research, until recently it was widely accepted and considered a unique predictor of CAD risk. Evidence from genetic study show that Lp(a) is more of a causal risk factor for cardiovascular disease than just a marker [16]. There were considerable studies that have been previously reported about the possible role of Lp(a) in the development of CAD [17] [18] [19]. Lp(a) could be a risk factor for plaque destabilization and thrombosis and not the severity of coronary heart disease, and associated with myocardial lesions in patients with unstable angina [17]. High concentrations of serum Lp(a) could predict ischaemic heart disease (IHD) and myocardial infarction (MI) in the general public, and the predictive capability was not exaggerated by normal food intake, but was minimally elevated to a level high CRP [18]. A study by Juan Chen *et al.* demonstrated that Lp(a) is an independent predictor for the severity of coronary heart disease (CHD) in type 2 diabetes patients (T2DM) [19]. It has been shown that Lp(a) has shown that the severity of coronary atherosclerosis is predicted independently of conventional CV risk factors. [20]. In a study, Cho *et al.* demonstrated that high serum levels of Lp(a) were significantly related to long-term side effects in Acute Myocardial Infarction (AMI) patients, particularly in patients with a high killip class. Proatherogenic and prothrombotic effects of Lp(a) might be associated with adverse CV events throughout follow-up.

We therefore speculate that the possible pathophysiological mechanism for CAD might be due to the atherothrombotic and pro-inflammatory properties of Lp(a) [7] [8]. There are some possible mechanisms behind atherosclerosis and restenosis after PCI. 1) Lp(a) inhibits the activation of the transforming growth factor and causes growth of atherosclerotic arterial lesions via increased vascular smooth muscle cells and the migration of muscle cells smooth endothelial cells [21] [22]. 2) Lp(a) inhibits plasminogen binding site on the surface of endothelial cells and reduces the activity of the tissue-type Plasminogen Activator (t-PA).

3) Lp(a) directly increases the activity of plasminogen activator inhibitors in human endothelial cells and promotes atherorombosis [23]. Lp(a) was involved in the activation of endothelial uptake, oxidative alteration and cell formation. Additionally, Lp(a) is also associated with 1) thrombus formation due to vascular lesion, 2) elastic recoil, 3) migration of smooth muscle cells in Intima and 4) vascular remodelling. A study by Minz *et al.* [24] used intravascular ultrasound to study CAD patients for coronary restenosis through Percutaneous angiography without stent treatment and reported that 73% of the mechanism underlying a decrease in lumen diameter is because of remodelling and 27% is due to an increase in plaque and intima. On the other hand, another study by Hoffmann *et al.* [25] demonstrated that in-stent restenosis results from neo-intimal tissue proliferation, which has been accredited due to Lp(a) *in vitro* [8]. In the present study, Lp(a) was significantly associated with CR which is in parallel with the previous studies. Recently a meta-analysis on statin therapy following PCI show beneficial role of high intensity loading dose of statin therapy was more beneficial to patients with ACS in Chinese patients and was suitable for clinical application [26]. In addition, a study by Zhi Liu *et al.* [27] demonstrated that high-intensity atorvastatin therapy over the duration of 1 year after PCI was superior in ACS patients in decreasing MACE. Moreover, novel drugs, including PCSK9 inhibitors, as well as antisense oligonucleotide for Apo-A, have exhibited efficacy in decreasing Lp(a) substantially [28] [29].

Several limitations of this retrospective study should be given consideration. It's a single-center retrospective study, enrolling data of 2 years of patients and other confounding factors might have influenced the outcomes independently of adjustments in the statistical analysis. Thus an observational study with larger population is required for further proper analysis. In addition we had no proper knowledge about the patients' compliance with the prescribed medications.

5. Conclusion

In conclusion, this study revealed that in patients with first PCI, Lp(a) elevation is positively associated with coronary restenosis and CAD within one year which requires revascularization and the prevalence of CR is significantly higher in elevated level of serum LDL-C and Lp(a). It indicates that after PCI treatment, in patient with serum LDL-C and Lp(a) elevation, treatment with high-dose statin therapy or PCSK9 inhibitors may alleviate the adverse effects imposed by Lp(a) elevation.

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Author's Contribution

All the authors read and approved this study for publication.

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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