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Change in lipoprotein-associated phospholipase A2 and its association with cardiovascular outcomes in patients with acute coronary syndrome

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Abstract

Lipoprotein-associated phospholipase A2 (Lp-PLA2) probably plays an important role in the development of acute coronary syndrome (ACS). However, alterations of Lp-PLA2 levels during ACS and its association with cardiovascular outcome are unclear. Our aim was to investigate the change in Lp-PLA2 and its association with cardiovascular outcome in patients with ACS.

A total of 79 patients with ACS came from the coronary care unit (CCU) between June 1, 2015 and August 31, 2016 in this longitudinal study. Serum levels of Lp-PLA2, troponin I, and creatine kinase isoenzymes MB (CK-MB) were measured at admission, on the first morning (D1), on the second morning of hospitalization (D2), and on the last second morning before discharge (D4). The patients were followed up till November 30, 2016. The primary outcomes were cardiovascular death and cardiovascular rehospitalization. Kaplan–Meier analysis and Cox proportional hazard models were used to identify risk factors for poor outcome in patients with ACS.

All patients were followed up for 10.6 ± 4.7 months. The patients were divided into 2 groups according to the median of Lp-PLA2: lower Lp-PLA2 group and higher Lp-PLA2 group. Elevated levels of Lp-PLA2 significantly decreased during the early phases of ACS in higher Lp-PLA2 group. And Lp-PLA2 level increased at first and then decreased in lower Lp-PLA2 group. Kaplan–Meier analysis showed that patients with elevated Lp-PLA2 had a lower cardiovascular event-free survival (log-rank $\chi^2 = 4.736$, $P = .030$) than those with lower Lp-PLA2. Cox regression analysis indicated that high Lp-PLA2 level (hazard ratio [HR] = 1.005, 95% confidence interval [CI] = 1.002–1.008, $P = .003$), time delay from symptom onset to admission (HR = 1.088, 95% CI = 1.038–1.139, $P < .001$) independently predicted cardiovascular event in patients with ACS after adjusting for potential confounders.

Serum level of Lp-PLA2 altered considerably during the early phase of ACS and increased Lp-PLA2 independently predicted cardiovascular outcome in patients with ACS after adjustment for potential confounders.

Abbreviations: ACS = acute coronary syndrome, BMI = body mass index, BNP = B-type natriuretic peptide, CAD = coronary artery disease, CCU = coronary care unit, CI = confidence interval, CK-MB = creatine kinase isoenzymes MB, CRP = C-reactive protein, DBP = diastolic blood pressure, HR = hazard ratio, INR = international normalized ratio, IVUS = intravenous ultrasound, LDL = low-density lipoprotein, Lp-PLA2 = lipoprotein-associated phospholipase A2, SBP = systolic blood pressure, TnI = troponin I.

Keywords: acute coronary syndrome, lipoprotein-associated phospholipase A2, outcome

1. Introduction

Cardiovascular diseases are the leading cause of death and disability in human. Atherosclerosis and thrombosis are the major pathogenic mechanisms responsible for cardiovascular events. Recently, because conventional risk factors do not explain the changes in atherosclerosis, efforts to identify vulnerable plaques have focused on developing novel biomarkers. The studies have shown that inflammation plays an important casual role on the initiation and progression of atherosclerosis and atherosclerotic cardiovascular disease.[1,2]

Lipoprotein-associated phospholipase A2 (Lp-PLA2), known as a novel inflammatory biomarker, is involved in pathophysiology of atherosclerosis.[3] The Lp-PLA2, which can hydrolyze oxidized phospholipids and then produce lysophosphatidylcholine and nonesterified fatty acids, causes endothelial dysfunction and takes part in the formation of vulnerable plaques.[3–6]

Prior studies have indicated that Lp-PLA2 is associated with cardiovascular events in healthy populations,[7] patients with stable coronary artery disease (CAD),[8] and patients with acute coronary syndrome (ACS).[9,10] In systematic review by Madjid et al, they finally enrolled 33 studies on Lp-PLA2 and 30 studies showed that increased Lp-PLA2 levels could predict cardiovascular events.[6] However, there are some conflicting results.[6,11,12] Blake et al[11] found that Lp-PLA2 was not a strong predictor of future cardiovascular risk in the Women's Health Study. Oldgren et al[12] suggested that Lp-PLA2 did not

predict future cardiovascular events or mortality in patients with ACS. Subsequently, Lp-PLA2 inhibitor (darapladib) also failed to reduce the risk of major coronary events in both SOLID-TIMI (Stabilization of Plaque Using Darapladib-Thrombolysis in Myocardial Infarction) 52[13] and STABILITY (Stabilization of Atherosclerotic plaque By Initiation of darapLadIb TherapY) studies.[14,15]

In addition, some studies demonstrated that the Lp-PLA2 concentration was high at first and decreased gradually in patients with ACS over the first 3 days following hospital admission and then remained stable.[16,17] By contrast, Kocak et al found that Lp-PLA2 enzyme activity was significantly lower during the early stage of ACS.[18]

As a result, Lp-PLA2 is suspected not to be a useful biomarker to assess the long-term cardiovascular risk. Therefore, our aim was to investigate the change in Lp-PLA2 and its association with cardiovascular outcome in patients with ACS in the present study.

2. Materials and methods

2.1. Patients

The patients with ACS admitted to the coronary care unit (CCU) at Beijing Tiantan Hospital, Capital Medical University, People's Republic of China, between June 1, 2015 and August 31, 2016 were eligible for this study. The patient inclusion criteria were: the first ACS; age >18 years; having full data; signed informed consent form. None of patients had systemic immune disease, liver dysfunction, chronic renal impairment, or cerebrovascular disease. The patients who had any clinical manifestation of congestive heart failure (NYHA classes III–IV), or had an underlying active malignancy, acute infection, hemorrhagic diathesis, or coagulation disorders were excluded from the study. The patients with primary cardiomyopathy, endocarditis, or severe valvular heart disease were also excluded from the study. The ACS was defined as unstable angina pectoris, ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI). Finally, a total of 79 patients with ACS completing the original study were recruited in the present study and followed up till November 30, 2016. And all data in terms of height, weight, smoking, alcohol consumption, blood pressure, previous history, GRACE score, and medications were collected. Body mass index (BMI) was calculated as body weight in kilograms divided by the height in meters squared. Blood pressure was measured by mercury sphygmomanometer using Korotkoff phase V for diastolic, according to the WHO guidelines. Left ventricular ejection fraction was obtained by Simpson method on echocardiography. Coronary angiography, serum Lp-PLA2 measurement, and other biochemistry were performed in all enrolled patients. The information was obtained from hospital records and personal interviews. The ethical committee of the hospital approved the study and informed consent was obtained from each patient. The study was performed according to the recommendations of the Declaration of Helsinki.

2.2. Laboratory measurements

Blood samples for the measurement of Lp-PLA2, troponin I (TnI), and creatine kinase isoenzymes MB (CK-MB) levels were drawn at admission, on the first morning (D1), the second morning of hospitalization (D2), and the last second morning before discharge (D4). Blood samples were centrifuged at room temperature (3000 rpm) for 10 minutes and aspirated and stored at −80°C until Lp-PLA2 was measured. Serum Lp-PLA2 concentration was measured using an enzyme-linked immunosorbent assay (ELISA) kit (CSB-E08110h; Cusabio Biotech Co, Ltd, Wuhan, China) according to the manufacturer's instructions. This assay employs the quantitative sandwich enzyme immunoassay technique. The intra-assay coefficient of variation was <8%, and the inter-assay coefficient of variation was <10%. The Abbott-Architect TnI and CK-MB assay were performed with the use of the Architect system (Abbott Diagnostics, Lisnamuck, Longford Co. Longford, Ireland) immediately after taking blood.

Serum lipid profiles, serum glucose, urea, creatinine, uric acid, glycosylated hemoglobin A1C, C-reactive protein (CRP), B-type natriuretic peptide (BNP), and international normalized ratio (INR) were measured using routine methods in the morning of the first day after admission to the CCU.

2.3. Coronary angiography

Coronary angiography was performed in all patients immediately after admission in STEMI and within 24 hours after admission in NSTEMI or unstable angina pectoris. Coronary angioplasty was performed using the standard Judkins technique and a movable guide wire system through the radial or femoral artery. CAD was diagnosed if there was at least 1 lesion with ≥50% stenosis in luminal diameter on coronary angiography according to the American College of Cardiology/American Heart Association lesion classification.[19]

2.4. Clinical outcome

All patients were regularly followed up through telephone interview of doctors in our department every 3 to 6 months until November 30, 2016. The primary end point was a composite of cardiovascular death, myocardial infarction, unstable angina pectoris, revascularization, heart failure, or stroke that required hospitalization.

2.5. Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median (interquartile range), while categorical variables were expressed as ratio or percentage. The independent-sample t test or 1-way analysis of variance with repeated measures (for post hoc analysis, least significant difference was performed if equal variance was assumed and Tamhane T2 test was performed if equal variance was not assumed) was used as appropriate to compare differences for continuous variables. When the variables were not normally distributed, the nonparametric Kruskal–Wallis test was used. The comparison of categorical variables was performed using the Chi-squared test. Pearson correlation was used to analyze the associated factors for Lp-PLA2. Cardiovascular event-free survival was plotted as Kaplan–Meier curves between the 2 groups, and the differences were assessed by the log-rank test. The associations between Lp-PLA2 and cardiovascular outcomes were analyzed in multivariable Cox regression models, after adjusting for potential confounders, including BMI, blood pressure, biochemistry, and GRACE score. Adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were reported separately. A 2-tailed P-value <.05 was considered to be statistically significant.

3. Results

3.1. Baseline characteristics of the study population

The demographic data of the 79 patients were shown in Table 1. The mean age was 60.0 ± 11.5 (33, 86) years, and 72.2% of them were males. All patients were followed up until an event happened or to the end of the study. During an average follow-up of 10.6 ± 4.7 months, 10 patients experienced cardiovascular events, including 4 (5.1%) unstable angina pectoris, 2 (2.5%) recurrent myocardial infarction, 2 (2.5%) ischemic stroke, 1 (1.3%) stent thrombosis, and 1 (1.3%) heart failure.

The patients were divided into 2 groups according to the median of Lp-PLA2 (367.3 ng/mL) at admission: lower Lp-PLA2 group (39 patients) and higher Lp-PLA2 group (40 patients). Compared with those with lower Lp-PLA2, patients with higher Lp-PLA2 level had a longer time from symptom onset to admission, higher GRACE score, INR, and incidence of cardiovascular events ($P < .05$). However, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), and uric acid decreased in patients with higher Lp-PLA2 than patients with lower Lp-PLA2. There were no significant differences in age, TnI, or CK-MB between the 2 groups at baseline.

3.2. Dynamic changes in blood biomarker over time in patients with ACS

The sequential changes of Lp-PLA2, TnI, and CK-MB levels in both groups were shown in Figure 1. The mean time on the last second morning before discharge (D4) was the 4th day of hospitalization. In higher Lp-PLA2 group, serum level of Lp-PLA2 decreased significantly from 523.2 ± 150.3 ng/mL at admission, 500.6 ± 143.9 ng/mL at D1, 494.4 ± 156.4 ng/mL at D2 to 429.8 ± 124.7 ng/mL at D4 ($P < .001$, D4 vs admission, D1, D2). TnI decreased from 7.3 ± 8.4 ng/mL at admission, 11.2 ± 8.6 ng/mL at D1, 7.2 ± 6.5 ng/mL at D2 ($P = .001$, D2 vs D1) to 4.8 ± 4.1 ng/mL at D4 ($P = .040$, D4 vs admission; $P < .001$, D4 vs D1). CK-MB also showed a decrease from 29.4 ± 26.7 ng/mL at admission, 35.8 ± 35.5 ng/mL at D1, 10.9 ± 9.3 ng/mL at D2 ($P < .05$, D2 vs admission, D1) to 2.6 ± 1.5 ng/mL at D4 ($P < .01$, D4 vs admission, D1).

Table 1

Baseline characteristics of all patients grouped according to Lp-PLA2 level.

Parameters	Total	Lower Lp-PLA2	Higher Lp-PLA2	P
Number	79	39	40	−
Age, y	60.0 ± 11.5	58.9 ± 10.6	61.1 ± 12.2	.391
Gender, male/female	57/22	30/9	27/13	.350
BMI, kg/m^2	25.4 ± 3.7	26.2 ± 4.1	24.5 ± 3.2	*.046*
Time from symptom onset to admission, h	2.5 (1.0, 5.0)	2.0 (1.0, 5.0)	3.0 (2.0, 7.3)	*.041*
Previous history, n (%)				
Hypertension	47 (59.5)	24 (61.5)	23 (57.5)	.715
Diabetes	23 (29.1)	9 (23.1)	14 (35.0)	.243
Stroke	11 (13.9)	6 (15.4)	5 (12.5)	.711
Hyperlipidemia	15 (19.0)	7 (17.9)	8 (20.0)	.816
Previous statin, n (%)	28 (35.4)	16 (41.0)	12 (30.0)	.306
Smoking, n (%)	47 (59.5)	24 (61.5)	23 (57.5)	.715
Drinking, n (%)	14 (17.7)	8 (20.5)	6 (15.0)	.521
Type of ACS, n (%)				
STEMI	70 (88.6)	34 (87.2)	36 (90.0)	.693
NSTEMI	7 (8.9)	3 (7.7)	4 (10.0)	
UAP	2 (2.5)	2 (5.1)	0 (0)	
SBP, mm Hg	125.2 ± 21.6	130.8 ± 23.6	119.8 ± 18.1	*.023*
DBP, mm Hg	74.5 ± 14.7	78.4 ± 16.0	70.8 ± 12.5	*.022*
LVEF, %	60.5 ± 6.7	60.6 ± 6.6	60.3 ± 6.8	.854
GRACE score	121.0 ± 29.8	113.3 ± 28.0	128.5 ± 29.9	*.022*
Lp-PLA2, ng/mL	401.1 ± 169.3	275.9 ± 62.2	523.2 ± 150.3	*<.001*
Serum albumin, g/L	38.8 ± 2.9	38.7 ± 3.0	39.0 ± 2.8	.675
Serum glucose, mmol/L	5.56 (4.72, 7.67)	5.56 (4.82, 8.62)	5.95 (4.60, 7.46)	.984
Triglycerides, mmol/L	1.43 (0.99, 2.14)	1.45 (0.94, 2.17)	1.35 (1.03, 2.05)	.988
Total cholesterol, mmol/L	4.56 ± 0.96	4.50 ± 1.02	4.63 ± 0.90	.573
LDL cholesterol, mmol/L	2.95 ± 0.84	2.85 ± 0.83	3.06 ± 0.84	.261
HDL cholesterol, mmol/L	1.06 ± 0.20	1.07 ± 0.19	1.05 ± 0.22	.571
Uric acid, μmol/L	319.3 ± 93.7	342.1 ± 91.6	296.5 ± 91.4	*.031*
Urea, mmol/L	5.47 ± 1.76	5.75 ± 1.82	5.19 ± 1.67	.160
Creatinine, μmol/L	68.6 ± 19.7	72.6 ± 20.5	64.5 ± 18.3	.070
Glycosylated hemoglobin A1C, %	6.1 (5.5–8.0)	6.1 (5.5–7.7)	5.9 (5.4–8.1)	.834
INR	0.94 ± 0.08	0.93 ± 0.07	0.96 ± 0.08	*.046*
CRP, mg/L	3.6 (1.5, 9.3)	3.4 (0.9, 9.3)	3.7 (1.8, 9.3)	.477
BNP, pg/mL	58.2 (27.9, 162.0)	49.1 (32.4, 150.0)	64.0 (26.3, 211.5)	.717
Cardiovascular events, n (%)	10 (12.7)	1 (2.6)	9 (22.5)	*.014*

ACS = acute coronary syndrome, BMI = body mass index, BNP = B-type natriuretic peptide, CRP = C-reactive protein, DBP = diastolic blood pressure, HDL = high-density lipoprotein, INR = international normalized ratio, LDL = low-density lipoprotein, Lp-PLA2 = lipoprotein-associated phospholipase A2, LVEF = left ventricular ejection fraction, NSTEMI = non-ST-segment elevation myocardial infarction, SBP = systolic blood pressure, STEMI = ST-segment elevation myocardial infarction, UAP = unstable angina pectoris.
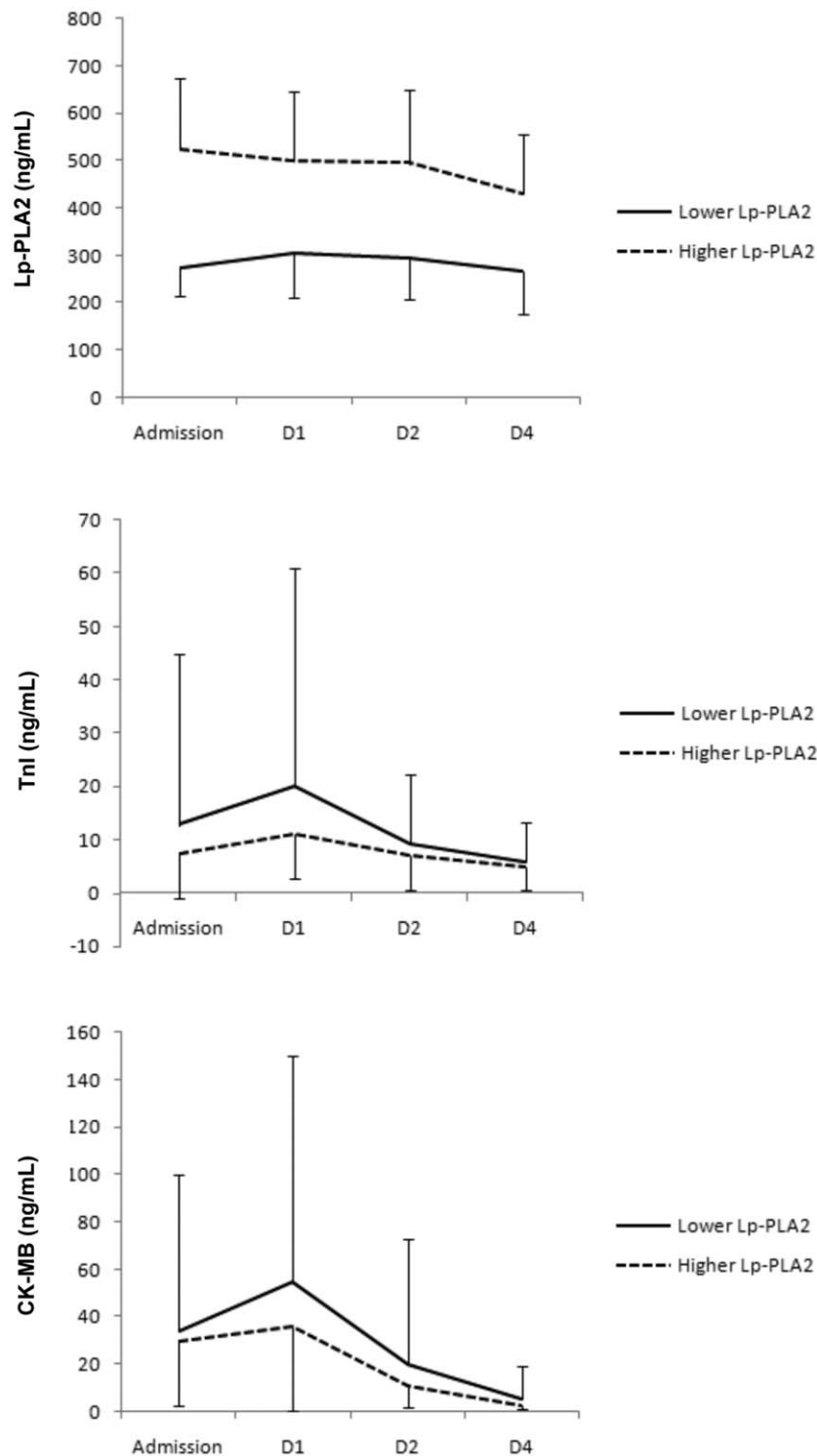Italicized P values showed statistical significance.

Figure 1. Changes in lipoprotein-associated phospholipase A2 (Lp-PLA2), troponin I (TnI), creatine kinase isoenzymes MB (CK-MB) level over time during hospitalization.

In lower Lp-PLA2 group, serum level of Lp-PLA2 increased from 275.9 ± 62.2 ng/mL at admission to 306.7 ± 95.9 ng/mL at D1 ($P = .011$), and then decreased from 297.8 ± 90.6 ng/mL at D2 ($P = .033$, D2 vs admission) to 268.0 ± 92.1 ng/mL at D4 ($P < .05$, D4 vs D1, D2). TnI did not change obviously among the 4th time point. CK-MB decreased from 34.3 ± 66.0 ng/mL at admission,

55.1 ± 95.0 ng/mL at D1, 20.3 ± 52.3 ng/mL at D2 to 5.6 ± 13.8 ng/mL at D4 ($P = .015$, D4 vs D2).

As compared with lower Lp-PLA2 group, serum levels of Lp-PLA2 were significantly higher at each time point in higher Lp-PLA2 group ($P < .001$). However, there were no differences in TnI or CK-MB at each time point between the 2 groups.

Table 2

Correlation of Lp-PLA2 with other biomarkers.

Covariate	Lp-PLA2, ng/mL			
	Admission	D1	D2	D4
LDL-C, mmol/L				
r	0.280	0.244	0.206	0.218
P	.013	.031	.080	.095
CRP, mg/L				
r	0.074	0.117	−0.005	0.130
P	.517	.305	.970	.320
TnI, ng/mL				
r	−0.012	−0.149	0.021	0.095
P	.933	.226	.865	.490

CRP = C-reactive protein, LDL = low-density lipoprotein, Lp-PLA2 = lipoprotein-associated phospholipase A2, TnI = troponin I.
Italicized P values showed statistical significance.

3.3. Correlation analysis of Lp-PLA2 with other biomarkers

Lp-PLA2 correlated with significantly positively low-density lipoprotein (LDL) cholesterol at admission and D1 ($P < .05$). However, there were no correlations between Lp-PLA2 and CRP or TnI (Table 2).

3.4. Kaplan–Meier survival analysis

Kaplan–Meier curves were reported in Figure 2. Patients with higher Lp-PLA2 showed a significantly reduced cardiovascular event-free survival (log-rank $x^2 = 4.736$, $P = .030$) than those with lower Lp-PLA2.

3.5. Risk factors for cardiovascular events

By performing Cox proportional hazard models, we found that high Lp-PLA2 level (HR = 1.005, 95% CI = 1.002–1.008, $P = .003$) and time from symptom onset to admission (HR = 1.088, 95% CI = 1.038–1.139, $P < .001$) were identified as independent predictors for cardiovascular outcome in patients with ACS after adjustment for potential confounders including

Table 3

Cox regression analysis of cardiovascular outcome in all patients.

Covariate	HR	95% CI	P
Lp-PLA2, ng/mL	1.005	1.002–1.008	.003
Time on symptom to admission, h	1.088	1.038–1.139	<.001
SBP, mm Hg	0.958	0.918–1.000	.051

Adjusted for body mass index ($P = .874$), uric acid ($P = .181$), international normalized ratio ($P = .656$), GRACE score ($P = .409$).
CI = confidence interval, HR = hazard ratio, Lp-PLA2 = lipoprotein-associated phospholipase A2, SBP = systolic blood pressure.
Italicized P values showed statistical significance.

BMI, uric acid, INR, GRACE score, and SBP level at baseline (Table 3).

4. Discussion

In the present study, we found that elevated levels of Lp-PLA2 significantly decreased during the early phases of ACS in higher Lp-PLA2 group. And Lp-PLA2 level increased at first and then decreased in lower Lp-PLA2 group. Kaplan–Meier analysis found that patients with higher Lp-PLA2 showed a significantly reduced cardiovascular event-free survival than those with lower Lp-PLA2. Furthermore, Cox regression demonstrated that high Lp-PLA2 level independently predicted cardiovascular outcome in patients with ACS after adjustment for potential confounders.

Prior studies have evaluated the prognostic value of Lp-PLA2 in primary and secondary prevention populations.[7–12] Some studies showed a positive association between Lp-PLA2 and cardiovascular outcomes.[7–10,20–22] Daniels et al[7] reported that elevated Lp-PLA2 levels predicted CAD events in apparently healthy older adults, independent of CAD risk factors. Sabatine et al[8] indicated that an elevated level of Lp-PLA2 was a significant predictor of nonfatal adverse cardiovascular outcomes in patients with stable CAD. Gerber et al[21] suggested that high Lp-PLA2 levels measured early after myocardial infarction were independently associated with mortality. Maiolino et al[22] showed that Lp-PLA2 activity, but not Lp-PLA2 mass, predicted
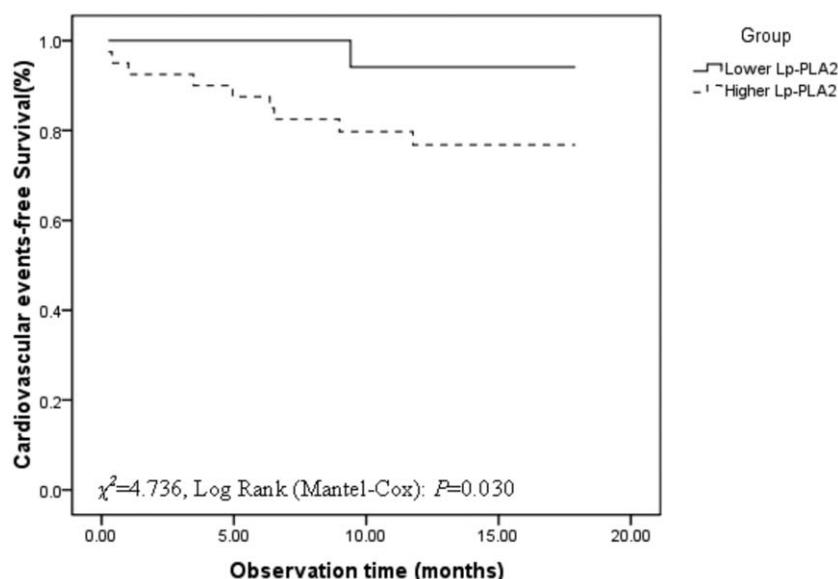

Figure 2. Kaplan–Meier survival curves for all patients for cardiovascular outcome. Lp-PLA2 = lipoprotein-associated phospholipase A2.

cardiovascular events and ACS in high-risk Caucasian patients with CAD. Similarly, among 3265 patients with ACS enrolled in the PROVE IT-TIMI 22 (PRavastatin Or atorVastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) trial, Lp-PLA2 activity measured at 30 days after an ACS event was positively associated with increased risk of cardiovascular events, even after adjustment for various risk indicators.[23] Our result was consistent with the above studies.

However, when measured early after ACS, no predictive value was found for Lp-PLA2 in the PROVE IT-TIMI 22 trial.[23] In Oldgren et al study,[12] a random subset of patients with ACS in the FRISC II (n=1362) and GUSTO IV (n=904) studies were included, and they found no association between Lp-PLA2 level and cardiovascular events, including the composite of death and myocardial infarction at 30 days (GUSTO IV) or 180 days (FRISC II), and the 1 year mortality in the FRISC II and GUSTO IV. In addition, Blake et al[11] did not find a relationship between Lp-PLA2 levels and future cardiovascular risk in healthy women. Our results were opposite to these reports.[6,11,12,23]

There are some differences between our study and the previous reports. Firstly, most of studies were based on single measurement of circulating Lp-PLA2,[7–12,21] and only a few observed the change of Lp-PLA2 over time.[16,17] Ostadal et al.[16] found that serum levels of Lp-PLA2 were significantly elevated in patients with ACS, but decreased within the first 24 hours after admission and subsequently remained stable. In our study, dynamic changes in Lp-PLA2 were observed. We noticed that serum Lp-PLA2 level decreased gradually in higher Lp-PLA2 group, while Lp-PLA2 showed an increase at first and then decrease in lower Lp-PLA2 group. Contrarily, Kocak et al[18] reported that Lp-PLA2 enzyme activity was lower in patients with ACS than in control group. Secondly, the time window for blood sample collection was different. Oldgren et al[12] reported that the time delay from symptom onset to blood sampling did not influence Lp-PLA2 levels. In PROVE IT-TIMI 22, Lp-PLA2 level measured very early after ACS was not predictive of future cardiovascular events, whereas predictive ability did emerge when Lp-PLA2 was remeasured 30 days later.[23] However, our result was not consistent with them. The time from symptom onset to admission was 2.5 hours (interquartile range 1.0–5.0) in our study. In contrast, the median time from symptom onset to randomization was 7 days in PROVE IT-TIMI 22,[23] 38 hours (interquartile range 28–53) in FRISC II[12] and 15 hours (interquartile range 9.4–20) in the GUSTO IV[12] study cohort, in which they were more prolonged than that in our study. Thirdly, patients with diabetes mellitus were excluded in some studies[9,24,25]; in contrast, patients with diabetes mellitus were included in the present study. Fourthly, different blood sample storage and Lp-PLA2 measurement method maybe had an influence on exploring the relationship between serum Lp-PLA2 and cardiovascular outcome. Serum Lp-PLA2 mass or activity was measured in different studies.[6,18,23,26] The standardization of assay calibration needs to be setup.

In this study, as compared with lower Lp-PLA2 group, serum levels of Lp-PLA2 were significantly higher at each time point in higher Lp-PLA2 group. In contrast, there were no differences in CK-MB at each time point between the 2 groups. CK-MB is a well-known ACS biomarker and a significant increase in CK-MB level indicates myocardial damage. However, CK-MB is not an earlier biomarker and do not have a better prognostic value in patients with ACS. Some studies have indicated that CK-MB can be safely removed from the routine laboratory menu without adversely affecting patient care.[27,28] TnI is used to determine acute myocardial infarction in clinical practice. However, we did not find a significant difference in TnI between the 2 groups.

In this study, we found that Lp-PLA2 was positively associated with LDL cholesterol. However, there was no correlation between TnI and Lp-PLA2, CK-MB, and Lp-PLA2. Our results were similar to previous reports.[12,16]

In Wang et al study,[29] quantitative intravenous ultrasound (IVUS) examination was performed in 194 patients with single-vessel and intermediate coronary lesions, and demonstrated that glycosylated hemoglobin A1C and Lp-PLA2 were strong independent predictors of plaque burden and area of fibro-fatty tissue and necrotic core at the minimum lumen lesion in patients with single-vessel and intermediate coronary lesions. Dohi et al[17] studied 40 patients with ACS, found that circulating Lp-PLA2 levels and plaque volume significantly decreased between baseline and 6 months of follow-up, and circulating Lp-PLA2 levels were associated with changes in coronary plaque determined by IVUS in patients with ACS. Our results were consistent with Dohi report.[17] Therefore, it still offers new insight in the pathophysiologic development of ACS. Some studies found that Lp-PLA2 expression levels were significantly upregulated during the early phases of ACS.[3,13] Lp-PLA2 was found strongly expressed in the vicinity of macrophages of vulnerable and ruptured plaques.[3] It is speculated that increased serum level of Lp-PLA2 promotes endothelial dysfunction, contributes to coronary artery stenosis progression, and accelerates atherosclerotic plaque rupture.[3] Lp-PLA2 can be believed as an early biomarker for predicting adverse cardiovascular outcome in patients with ACS.

As compared with lower Lp-PLA2 level, patients with higher Lp-PLA2 showed a prolonged time from symptom to admission. Cox regression found that time from symptom to admission correlated with patient outcome, which suggest that early revascularization is very important for improving patient prognosis.

It should be noted that there are some limitations in our study. Firstly, this study is a single-center study. Patient selection biases cannot be avoided. Secondly, the present study comprised a relatively small number of patients. In addition, it was in absence of control group.

In summary, our study showed that serum level of Lp-PLA2 altered considerably during the early phase of ACS and increased serum level of Lp-PLA2 independently predicted cardiovascular outcome in patients with ACS after adjustment for potential confounders.

Author contributions

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