Plasma Lipoprotein-associated Phospholipase A2 in Patients with Metabolic Syndrome and Carotid Atherosclerosis

Hui-ping Gong¹†, Yi-meng Du¹†, Li-na Zhong², Zhao-qiang Dong¹, Xin Wang¹, Yong-jun Mao²*, Qing-hua Lu¹*

Abstract
Background: Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) is a recently identified and potentially useful plasma biomarker for cardiovascular and atherosclerotic diseases. However, the correlation between the Lp-PLA₂ activity and carotid atherosclerosis remains poorly investigated in patients with metabolic syndrome (MetS). The present study aimed to evaluate the potential role of Lp-PLA₂ as a comprehensive marker of metabolic syndrome in individuals with and without carotid atherosclerosis.

Methods: We documented 118 consecutive patients with MetS and 70 age- and sex-matched healthy subjects served as controls. The patients were further divided into two groups: 39 with carotid plaques and 79 without carotid plaques to elucidate the influence of Lp-PLA₂ on carotid atherosclerosis. The plasma Lp-PLA₂ activity was measured by using ELISA method and carotid intimal-media thickness (IMT) was performed by ultrasound in all participants.

Results: Lp-PLA₂ activity was significantly increased in MetS subgroups when compared with controls, and was higher in patients with carotid plaques than those without plaques (P < 0.05). Furthermore, we found that significant difference in Lp-PLA₂ was obtained between patients with three and four disorders of metabolic syndrome (P < 0.01). Age (β = 0.183, P = 0.029), LDL-cholesterol (β = 0.401, P = 0.000) and waist-hip ratio (β = 0.410, P = 0.000) emerged as significant and independent determinants of Lp-PLA₂ activity. Multiple stepwise regression analysis revealed that LDL-cholesterol (β = 0.309, P = 0.000), systolic blood pressure (β = 0.322, P = 0.002) and age (β = 0.235, P = 0.007) significantly correlated with max IMT, and Lp-PLA₂ was not an independent predictor for carotid IMT.

Conclusions: Lp-PLA₂ may be a modulating factor for carotid IMT via age and LDL-cholesterol, not independent predictor in the pathophysiological process of carotid atherosclerosis in patients with MetS.

Background
The metabolic syndrome (MetS) is a constellation of atherogenic risk factors including abdominal obesity, hypertension, insulin resistance, dyslipidemia, proinflammatory, and prothrombotic state [1]. Recent publications have probed that patients with MetS are at higher risk of cardiovascular morbidity and mortality [2] and are more prone to atherosclerosis than normal subjects, even in the young adults [3,4]. Although the relationship between MetS and the risk of cardiovascular disease is still a matter of debate, MetS has been associated with carotid plaque formation and intima-media thickening [5]. Inflammatory processes have been increasingly recognized as a critical step in the pathogenesis of both metabolic syndrome and carotid atherosclerosis and may be important midways linking MetS to the increased arteriosclerotic events [6,7].

Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) was recently characterized as a novel inflammatory biomarker correlated with several components constituting the MetS and implicated in atherosclerosis, incident cardiovascular disease [8,9]. Lp-PLA₂ is preferentially secreted by monocytes and macrophages and hydrolyzes

* Correspondence: mmc168@126.com; lqhzhy@163.com
† Contributed equally
¹Department of Cardiology, the Second hospital of Shandong University, Jinan, Shandong, 250033, China
²Department of Geriatric, affiliated hospital of medical college, Qingdao University, Qingdao, Shandong, 266003, China
Full list of author information is available at the end of the article

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oxidatively modified low-density lipoprotein by cleaving oxidized phosphatidylcholines thereby generating lyso-
phosphatidylcholine and oxidized free fatty acids [10].
Such chemoattractants are thought to play pivotal role in
inflammatory reactions and particularly in vascular
inflammation and atherosclerosis [11]. However, the
potential role of Lp-PLA2 in atherogenesis and the anti-
or proatherogenic characteristic of this enzyme in
humans is less well understood [12]. Almost all pro-
spective and nested case cohort studies suggested that
Lp-PLA2 is proatherogenic [13]. One recent trial [14]
demonstrated that symptomatic carotid artery plaques
are characterized by increased levels of Lp-PLA2 and its
product lysoPC in correlation with markers of tissue oxi-
dative stress, inflammation, and instability. In contrast,
previous investigations reported no associations observed
between carotid intima-media thickness and Lp-PLA2
levels in primary hyperlipidemia patients [15,16].

To the best of our knowledge, few studies have explored
the atherosclerotic risk for carotid arteries correlated with
MetS is confounded by an association with activity of
Lp-PLA2. Additionally, carotid intima-media thickness
(IMT) of arteries is a useful measure of clinical athero-
sclerosis as assessed noninvasively by ultrasonography.
Alternations in carotid IMT has been validated as a vascular
marker of the progression of atherosclerosis [17]. Therefore,
in the present study, we measured the plasma Lp-PLA2
activity in patients with MetS (including with and without
carotid atherosclerosis) and correlated it with anthropo-
metric parameters and carotid IMT to evaluate the possible
contribution of Lp-PLA2 to carotid atherosclerosis.

Methods

Study Population
A total of 118 patients with MetS (53 men and
65 women, aged from 32 to 71 years), were recruited
from the Second Hospital of Shandong University
according to the criteria proposed by the International
Diabetes Federation [18]. Individuals were excluded if
they had a clinical history of cerebrovascular disease or
present neurological abnormalities, cerebral hemorrhage
and severe cardio-renal or nutritional disorders, lipid
and glucose metabolism. The control group consisted of
70 age- and sex-matched healthy subjects who visited
our hospital for a routine physical check-up and without
a history of cardiac disease, hypertension or diabetes
and having normal findings on physical examination,
chest roentgenography, and echocardiography. Informed
consent was obtained from all participants and the
study was approved by the local ethics committee.

Definition of metabolic syndrome
In our study, metabolic syndrome was defined by the
presence of 3 or more of the following conditions based on
the criteria of IDF [18]: (1) visceral obesity; waist circum-
ference was ≥ 90 cm in men and ≥ 80 cm in women,
(2) hypertriglyceridemia: ≥ 150 mg/dl (1.7 mmol/l) or
specific treatment for this lipid abnormality, (3) low
HDL cholesterol: <40 mg/dl (1.03 mmol/l) in men and
<50 mg/dl (1.29 mmol/l) in women or specific treatment
for this lipid abnormality, (4) hypertension: systolic blood
pressure ≥ 130 mmHg or diastolic blood pressure
≥ 85 mmHg or treatment of previously diagnosed hyper-
tension, and (5) impaired fasting glucose concentration
≥ 100 mg/dl (5.6 mmol/l) or those who had been treated
for type 2 diabetes.

Clinical measurements
The baseline and clinical characteristics of all partici-
pants were determined. The details of age, gender and
the weight and height were obtained, with the body
mass index calculated as the body weight in kilogram
divided by the height in meters squared. Waist circum-
ference was measured at the level of the umbilicus, sys-
tolic and diastolic blood pressures were obtained with a
mercury sphygmomanometer using auscultory methods.

The laboratory measurements were carried out follow-
ing overnight fasting. Blood was collected at baseline for
glucose, HbA1c, total cholesterol, triglycerides, high
density lipoprotein (HDL)-cholesterol and low-density
lipoprotein (LDL)-cholesterol. Serum insulin levels were
determined by a radio-immunoassay kit (Dongya Ltd,
Beijing, China). Insulin resistance was assessed by the
homeostasis model assessment equation [19].

Lp-PLA2 activity assay
The total plasma Lp-PLA2 activity was measured using
a PAF Acethylhydrolase enzyme immunoassay (EIA) kit
(Catalogue No. 760901, Cayman chemical Company,
USA) with a lower limit of sensitivity of 0.02-0.2 umol/
min/ml. Samples were measured in duplicate in a single
experiment. Lp-PLA2 activity was expressed as micro-
moles of platelet-activating factor hydrolyzed per minute
per milliliter of plasma samples and the inter-assay coeffi-
cient of variance was < 5%.

Carotid ultrasonography
All participants were examined in the supine position
(head turned 45°) by the same trained operator with a
high resolution B-mode ultrasonography equipped with a
5-10 MHz linear array transducer (iE33, Philips Ultra-
sound, Washington, USA). ECG leads were attached to
the ultrasound recorder for on-line continuous heart
rate monitoring. All the images were recorded and
stored on magneto optical disk for later playback and
analysis. The right and left common carotid arteries
(CCAs) and internal carotid arteries (including bifurca-
tions) were evaluated. IMT, plaque extent of the near
and far walls of the common and internal carotid arteries (ICAs) and bifurcations were measured according to the ACAPS protocol. AA thickened IMT was defined as ≥1.0 mm in either carotid artery. Presence of atherosclerotic plaques, defined as localized lesions with protrusion into the arterial lumen or regional IMT ≥1.1 mm [20], was considered when found in either or both CCAs. IMT was therefore measured at the point of maximal thickness in the walls of both CCAs. Maximal and mean IMT were defined as the greatest and mean values, respectively, of IMT measured from 3 contiguous sites at 1-cm intervals. Maximal IMT represented the highest single measurement at any site with plaque. Both thickened IMT and plaques were reconfirmed by re-examining the lesions on the printouts from the ultrasound scanner.

Statistical analysis
Data are presented as mean ± SD for continuous variables or proportions. After testing for normal distribution of variables, student’s 2-tail t-test and one-way analysis of variance (anova) followed by the post hoc least significant difference test were used where appropriate. The correlations between two variables were assessed by Pearson correlation analysis. Multiple linear regression analysis was used to evaluate the contribution of independent factors. Statistical analyses were performed using SPSS v. 15.0 (SPSS, Chicago, IL) software. A two-tailed P value <0.05 was considered statistically significant.

Results
Baseline and clinical characteristics of participants
The baseline and clinical characteristics of the metabolic syndrome patients and controls were shown in Table 1. All MetS patients were divided into subgroups according to presence or absence of plaques, carotid atherosclerotic plaques was identified in 39 patients, and no stenosis or occlusion was found. There were no statistical differences in age or gender among three groups. Patients with MetS showed increased levels of systolic blood pressure, diastolic blood pressure, BMI, waist circumference, waist-hip ratio, triglyceride, total cholesterol, fasting glucose, insulin, HbA1c, HOMA-insulin resistance and more prescription medications, and decreased levels of HDL-cholesterol when compared with controls (all P < 0.05-0.01), but there were no significant differences in any of those parameters between patients with and without carotid plaques. LDL-cholesterol was found to increase from controls to MetS patients with and without carotid plaques, moreover, with significant difference between two patient subgroups (P < 0.05). Mean IMT values were significantly higher in MetS patients with and without carotid plaques than in controls (0.74 ± 0.11 mm vs. 0.51 ± 0.15 mm, 0.86 ± 0.20 mm vs. 0.51 ± 0.15 mm, all P < 0.01, respectively), and were highest in patients with carotid plaques. Max IMT values increased significantly in MetS patients with carotid plaques, whereas no difference was found between the other two groups.

Lp-PLA2 activity
Distribution of Lp-PLA2 activity approximates a normal distribution. Lp-PLA2 activity was significantly increased in MetS subgroups when compared with controls (all P < 0.01), and was higher in patients with carotid plaques than those without plaques (34.10 ± 9.51 umol/min/mL vs. 29.62 ± 8.98 umol/min/mL, P < 0.05) (Table 1, Figure 1). There were no age (<65 vs. ≥65 years) and gender differences of Lp-PLA2 activity in patients (Data not shown). To assess the association of metabolic syndrome components with Lp-PLA2 activity, we further found that significant difference in Lp-PLA2 was obtained between patients with three (n = 89) and four (n = 28) disorders of metabolic syndrome (38.79 ± 9.22 umol/min/mL vs. 30.60 ± 9.58 umol/min/mL, P < 0.01).

Relationship of max IMT and risk factors
Pearson’s correlation coefficient and multiple regression analysis were performed to examine the relationship of max IMT to Lp-PLA2 activity and other biomarkers in overall MetS patients in order to identify a parameter that reflects carotid atherosclerosis. As shown in Table 3, Lp-PLA2 activity (r = 0.261, P = 0.006), total cholesterol (r = 0.371, P = 0.000), HDL-cholesterol (r = 0.402, P = 0.000), glucose (r = 0.188, P = 0.042) and HbA1c (r = 0.188, P = 0.042) in the patients with MetS. We also found Lp-PLA2 activity correlated with waist-hip ratio weakly but not significantly (r = 0.174, P = 0.061). However, in multivariable stepwise regression analyses, age (β = 0.183, P = 0.029), HDL-cholesterol (β = 0.401, P = 0.000) and waist-hip ratio (β = 0.410, P = 0.000) emerged as significant and independent determinants of Lp-PLA2 activity (Table 2).
variables, the associations between Lp-PLA2 activity and carotid IMT did not reach statistical significance.

**Discussion**

The present study identified elevated total plasma Lp-PLA2 activity in patients with the MetS, especially in those with carotid atherosclerosis when compared to the control subjects. We demonstrated that the Lp-PLA2 activity correlated with age, LDL-cholesterol and waist-hip ratio in patients with metabolic syndrome. Unfortunately, our data provided no evidence that Lp-PLA2

| Table 1 Baseline and clinical characteristics of the MetS subgroups and controls |
|-----------------------------|-------------------------------|-----------------|-----------------------------|
| Variables                   | Controls                      | No carotid plaque | MetS with carotid plaque   |
| Number                      | 70                            | 79               | 39                         |
| Sex (male/female)           | 30/40                         | 35/44            | 18/21                       |
| Age (years)                 | 52.4 ± 8.8                    | 53.8 ± 7.8       | 55.4 ± 6.6                 |
| BMI (kg/m²)                 | 24.49 ± 2.22                  | 28.99 ± 4.05     | 28.07 ± 3.45               |
| Waist circumference (cm)    | 84.51 ± 8.05                  | 98.08 ± 10.16    | 96.45 ± 8.58               |
| Waist-to-hip ratio          | 0.86 ± 0.05                   | 0.92 ± 0.06      | 0.93 ± 0.08                |
| Systolic BP (mmHg)          | 116 ± 10                      | 151 ± 22         | 152 ± 23                   |
| Diastolic BP (mmHg)         | 77 ± 7                        | 95 ± 14          | 94 ± 13                    |
| Total cholesterol (mmol/L)  | 4.42 ± 0.78                   | 5.36 ± 1.12      | 5.55 ± 0.99                |
| Triglyceride (mmol/L)       | 0.99 ± 0.42                   | 2.34 ± 1.19      | 2.23 ± 0.94                |
| HDL cholesterol (mmol/L)    | 1.53 ± 0.33                   | 1.22 ± 0.31      | 1.25 ± 0.26                |
| LDL cholesterol (mmol/L)    | 2.82 ± 0.72                   | 3.63 ± 0.88**    | 4.03 ± 0.99**              |
| Glucose (mmol/L)            | 4.99 ± 0.54                   | 6.37 ± 2.09**    | 6.76 ± 3.01**              |
| Insulin (uU/mL)             | 12.15 ± 5.37                  | 21.39 ± 12.09**  | 19.63 ± 10.20**            |
| HbA1c (%)                   | 4.58 ± 0.32                   | 5.38 ± 1.05      | 5.57 ± 1.52                |
| HOMA-insulin resistance     | 2.74 ± 1.38                   | 6.24 ± 4.90**    | 5.83 ± 3.45**              |
| Mean IMT (mm)               | 0.51 ± 0.15                   | 0.74 ± 0.11      | 0.86 ± 0.20**              |
| Max IMT (mm)                | 0.61 ± 0.52                   | 0.77 ± 0.09      | 1.87 ± 0.73**              |
| Lp-PLA2 activity            | 24.14 ± 6.33                  | 29.62 ± 8.98**   | 34.10 ± 9.51**             |
| Medications                 |                               |                  |                            |
| Aspirin                     | -                             | 70(88%)          | 35(91%)                    |
| Anti-hypertensive drugs     | -                             | 30(38%)          | 17(43%)                    |
| Oral hypoglycaemic drugs    | -                             | 9(12%)           | 4(11%)                     |
| Lipid regulating agents     | -                             | 9(12%)           | 5(14%)                     |

Values are mean ± SD; *P < 0.05 and **P < 0.01 compared to control; ▲P < 0.05 and ▲▲P < 0.01 compared to MetS without carotid plaque.

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![Figure 1 Lp-PLA2 activity in the MetS subgroups and controls](image)

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| Table 2 Linear regression analysis of variables correlated with Lp-PLA2 in MetS patients |
|-----------------------------------------------|-------------------------------|-----------------|-----------------------------|
|                                               | Simple Multiple r | P | β | P          |
| Age (years)                                  | 0.250                      | 0.006                      | 0.183                  | 0.029                      |
| Sex                                           | 0.164                      | 0.076                      | 0.185                  | 0.073                      |
| BMI (kg/m²)                                   | -0.092                     | 0.326                      | 0.148                  | 0.270                      |
| Waist-to-hip ratio                            | 0.174                      | 0.061                      | 0.410                  | 0.000*                     |
| Systolic BP (mmHg)                            | -0.081                     | 0.386                      | -0.068                 | 0.407                      |
| Diastolic BP (mmHg)                           | -0.150                     | 0.106                      | -0.065                 | 0.435                      |
| Total cholesterol (mmol/L)                    | 0.371                      | 0.000                      | 0.065                  | 0.618                      |
| Triglyceride (mmol/L)                         | 0.082                      | 0.380                      | 0.065                  | 0.791                      |
| HDL cholesterol (mmol/L)                      | -0.025                     | 0.786                      | -0.071                 | 0.407                      |
| LDL cholesterol (mmol/L)                      | 0.402                      | 0.000                      | 0.401                  | 0.000*                     |
| Glucose (mmol/L)                              | 0.188                      | 0.042                      | 0.084                  | 0.305                      |
| Insulin (uU/mL)                               | -0.153                     | 0.099                      | -0.122                 | 0.142                      |
| HbA1c                                        | 0.188                      | 0.042                      | 0.084                  | 0.305                      |
| HOMA-insulin resistance                       | -0.069                     | 0.458                      | -0.084                 | 0.311                      |

Gong et al. Lipids in Health and Disease 2011, 10:13
http://www.lipidworld.com/content/10/1/13
activity independently influence carotid IMT in MetS patients. The associations of Lp-PLA2 activity with carotid atherosclerosis may be mediated through age and LDL-cholesterol level.

The biological mechanisms involving plasma Lp-PLA2 in the pathogenesis of the MetS and atherosclerosis are not well-characterized. Recent evidence suggests inflammation is an important pathogenic factor in atherosclerosis and coronary heart disease, particularly in the context of insulin resistance, obesity [21], and the metabolic syndrome [6]. Furthermore, atherosclerosis is now recognized as manifestations of vascular inflammation [7]. Inflammatory factors such as adhesion molecules (ICAM-1 and VCAM-1), CD40 ligands, C-reactive protein (CRP) and myeloperoxidase (MPO) participate in induction of insulin resistance and atherosclerotic disease [21,22]. Lp-PLA2, originally named platelet-activating factor acetylhydrolase (PAF-AH), is an enzyme involved in lipoprotein metabolism and inflammatory pathways [10]. In human, 80% of Lp-PLA2 circulates bound to LDL-cholesterol, 10-15% circulates with HDL-cholesterol, and the remaining 5-10% circulates with VLDL-cholesterol [18]. Lp-PLA2 enzymatic activity results in generation of lysophosphatidylcholine (lysoPC) and oxidized non-esterified fatty acids, two pro-inflammatory mediators [10]. The lysoPC stimulates macrophage proliferation, up-regulates cytokines and CD40 ligands, and increases the expression of vascular adhesion molecules, implying a complex interaction between Lp-PLA2 and other inflammatory mediators [23,24]. Based on that, Lp-PLA2 has been implicated in inflammation and considered as an inflammatory marker in the MetS. Recently, several epidemiological studies demonstrate that an elevated activity of Lp-PLA2 is associated with MetS and number of the metabolic syndrome components as well as incident fatal and non-fatal CVD regarding MetS [25,26].

In the current study, we observed that plasma Lp-PLA2 activity was higher in patients with the MetS than in controls, suggesting that Lp-PLA2 activity may increase significantly when metabolic syndrome was present. Furthermore, our findings showed that there was a linear rise in Lp-PLA2 activity with an increment of number of metabolic syndrome components. These data were in line with previous research [19] and enlarged our scope for potential role of Lp-PLA2 in patients with MetS.

Results for studies of the associations of components of MetS with Lp-PLA2 activity have shown that abdominal obesity may have been independently responsible for the changes of Lp-PLA2 observed in this study. Additionally, we found Lp-PLA2 correlated with glucose and HbA1c weakly but significantly only in simple regression. Our findings were in accordance with the previous studies, in which Lp-PLA2 correlated with abdominal adiposity [27,28] but differed from the results of Noto et al [25] and Rana et al [29], who found that plasma Lp-PLA2 activity did not appear to be associated with waist circumference. It was possible that obesity was associated with decreases in local and peripheral insulin resistance [30]. Adipose tissue located in intra-abdominal or visceral cavities is likely to be infiltrated by macrophage, which is an important cause of the inflammatory state associated with abdominal obesity and the metabolic syndrome [29]. Lp-PLA2, as an inflammatory marker, is mainly secreted by macrophages. Thus, our results suggested that central obesity may contribute to the Lp-PLA2 activity changes in patients with MetS. Our results also indicated that there was parallel increase in Lp-PLA2 activity with an increment of components of metabolic syndrome, which was consistent with the findings of Noto at al. [25].

In the present study, our results have shown that Lp-PLA2 activity was elevated among MetS patients with carotid plaques. However, we further found independent determinants for thickened IMT as being LDL-cholesterol and age in multiple regression models. The Lp-PLA2 activity was not independently facilitates the morbidity of carotid atherosclerosis. Previous studies have revealed the plasma Lp-PLA2 activity in atherosclerotic disease, but consensus is still lacking [8,9,31]. Biologically, Lp-PLA2 is a vascular-specific proinflammatory enzyme that operates physiologically in the arterial intima [32]. Evidence has shown that Lp-PLA2 is expressed in human and rabbit atherosclerotic plaques [33]. Vickers et al [34] revealed that carotid tissue concentrations of Lp-PLA2 was notably very high in the rupture-prone shoulder region of thin fibrous cap atheromas, and Lp-PLA2 colocalized with macrophages and oxidized LDL in atherosclerotic carotid plaques.
However, several clinical studies suggested that premature coronary atherosclerosis [31] as well as carotid intima-media thickness plasma was not influenced by Lp-PLA₂ activity and gene polymorphisms in hypercholesterolemic individuals [15,16]. Thus, consistent with results of previous study [35], role of this enzyme in predicting independently the thicken IMT attenuated in our study, especially after adjustment for age and lipid variables.

Although the exact mechanisms underlying contribution of Lp-PLA₂ to carotid atherosclerosis in MetS patients remain to be elucidated, there are several possible explanations. Firstly, our study demonstrated that lipid parameters may contribute to Lp-PLA₂ activity changes. An increase in plasma Lp-PLA₂ activity, reflecting LDL-cholesterol values, has been established in several investigations [9,36]. Stafforini et al investigated that Lp-PLA₂ participated in the key oxidative steps of atherogenesis due to the association of Lp-PLA₂ and LDL-cholesterol via an interaction with apolipoprotein B (apoB) [37]. Kawamoto et al [38] reported that LDL-cholesterol was independently associated with carotid atherosclerosis in addition to clustering of cardiovascular risk factors regarding MetS. Several studies [39-41] suggested that the components of metabolic and LDL-cholesterol played a role to synergistically influence vascular thickness. Our results revealed that levels of LDL-cholesterol were significantly increased in MetS patients with carotid plaques than those without. Secondly, in present study, multivariate linear regression showed that age had a similar positive association with Lp-PLA₂ activity and contributed strongly to the variation in IMT. Thus, taken together previous important results [38-41] and our intriguing findings implied that Lp-PLA₂ activity was intimately associated with carotid thicken IMT and atherosclerosis via correlation with age and LDL-cholesterol in our study. Lp-PLA₂ may be a modulating factor in the process of carotid atherosclerosis. Lastly, owing to the prominent biological activities, the opposing proinflammatory and antiatherogenic properties of Lp-PLA₂ have been demonstrated both in human and animal models. In rabbit models, administration of Lp-PLA₂ inhibited myocardial ischemia/reperfusion injury [42], and local expression of Lp-PLA₂ reduced accumulation of oxidized LDL-cholesterol in balloon-injured arteries [43]. However, previous findings did not ascertain a causal relationship between Lp-PLA₂ and the clinical consequences of atherosclerotic disease in patients with primary hyperlipidemia [15,16] and diabetes mellitus [44]. Interestingly, elevated Lp-PLA₂ has been identified in human symptomatic carotid atherosclerotic plaque and its product lysophosphatidylcholine (lysoPC) correlated with markers of tissue oxidative stress, inflammation, and instability [14]. These paradoxical results may partly be explained by the relatively small study populations and selected inclusion criteria. Further studies are required to clarify whether Lp-PLA₂ is a risk marker that participates in the pathogenesis of carotid atherosclerosis in patients with MetS.

Despite of interesting findings, potential limitations of this study merit consideration. Our results are based on single measurements of circulating Lp-PLA₂, which may not reflect the true activity of Lp-PLA₂ over time or true expression in carotid atherosclerotic plaques. Several studies have shown that activity of Lp-PLA₂ was impacted by lipid-lowering drugs such as statins and fibric acid derivatives (fibrates) [25,45]. Thus, we could not eliminate the possible effect of medications for Lp-PLA₂ activity on the present findings. Finally, even though intriguing, results obtained in further confirmatory studies need to be considered to clarify the validity of Lp-PLA₂ in large series of patients.

Conclusions

In conclusion, our results of increased plasma Lp-PLA₂ activity in patients with the metabolic syndrome, especially in those with carotid atherosclerosis, suggest that Lp-PLA₂ may be an inflammatory marker of metabolic syndrome. However, multiple stepwise regression analysis suggested that Lp-PLA₂ may be a modulating factor, not independent risk predictor in the pathophysiological process of carotid atherosclerosis in MetS patients. Because Lp-PLA₂ activity may represent a novel pathway associated with thicken IMT, further research using large samples and general population need to be done to clarify the exact role of Lp-PLA₂ on carotid atherosclerosis in metabolic syndrome subjects.

Acknowledgements

This work was supported by the key science and technology program of Shandong Province of China (Grant No.2009GG20002034) and the Foundation of Science and Technology Commission of Shandong Province of China (Y2005C12).

Author details

1Department of Cardiology, the Second hospital of Shandong University, Jinan, Shandong, 250033, China. 2Department of Geriatric, affiliated hospital of medical college, Qingdao University, Qingdao, Shandong, 266003, China.

Authors’ contributions

HPG and YMD participated in the design of the study and drafted the manuscript; ZQD and LNZ performed research; HPG and YWW analyzed data. YJM and QHL were responsible for the study design and the funding. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Received: 25 December 2010 Accepted: 19 January 2011 Published: 19 January 2011
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doi:10.1186/1476-511X-10-13
Cite this article as: Gong et al.: Plasma Lipoprotein-associated Phospholipase A2 in Patients with Metabolic Syndrome and Carotid Atherosclerosis. Lipids in Health and Disease 2011 10:13.