Measurement of oxidized lipoprotein (a) in patients with acute coronary syndromes and stable coronary artery disease by 2 ELISAs: Using different capture antibody against oxidized lipoprotein (a) or oxidized LDL

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A R T I C L E   I N F O

Keywords:
Atherosclerosis
Coronary artery disease
Acute coronary syndromes
Lipoproteins
Lipoprotein(a)
Oxidation
Risk factor

A B S T R A C T

Objective: To evaluate clinical value of oxidized lipoprotein(a) [ox-Lp(a)] levels.

Design and methods: Ox-Lp(a) were measured by 2 ELISAs using antibodies against ox-Lp(a) [ox-Lp(a)1] or oxidized low-density lipoprotein [ox-Lp(a)2], and studied in 161 acute coronary syndromes (ACS) patients, 114 stable coronary artery disease (CAD) and 100 control subjects.

Results: Ox-Lp(a)1 was found related with ox-Lp(a)2 (r = 0.864, P = 0.000). Controlling for plasma lipids, Lp(a) and clinical characteristics, odds ratios of ox-Lp(a)1 on ACS and stable CAD were 5.06 (95% confidence interval 1.82–14.04) and 2.20 (0.78–6.22); those of ox-Lp(a)2 were 3.37 (1.67–10.63) and 1.35 (0.41–4.48), respectively. Receiver-operating characteristic curve analysis confirmed that performances of ox-Lp(a)1 were significantly superior to those for ox-Lp(a)2 in ACS (area: 0.803 vs. 0.723, P<0.001) and stable CAD (area: 0.670 vs. 0.607, P<0.01).

Conclusion: Ox-Lp(a) levels using antibodies against ox-Lp(a) may represent a better risk marker than those using antibodies against oxidized low-density lipoprotein for ACS and stable CAD.

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Introduction

Lipoprotein(a) [Lp(a)] is an atherogenic particle that structurally resembles a low density lipoprotein (LDL) particle but contains a molecule of apolipoprotein(a) [apo(a)] attached to apoB-100 by a disulfide bond [1]. Elevated plasma concentrations of Lp(a) have been shown to be of the independent risk factor for atherosclerosis [2–4]. Oxidized Lp(a) [ox-Lp(a)] has been reported to play more potent role than native Lp(a) in atherosclerosis [5–9]. Ox-Lp(a), autoantibodies, and Lp(a) immune complexes have all been detected in vivo [10–17], while the association of circulating ox-Lp(a) with cardiovascular events remains to be established.

Apo(a) and apoB proteins of Lp(a) molecule can both be oxidatively modified in vivo. The degree of oxidized apo(a) or apoB protein of Lp(a) has been detected to estimate circulating ox-Lp(a) levels [10,11]. Ox-Lp(a) levels have been reported to be present in newborns and children [12], and increased in rheumatoid arthritis patients with excessive cardiovascular events [13]. Furthermore, elevated ox-Lp(a) levels have been found to be associated with the presence of stable coronary artery disease (CAD) and acute coronary syndromes (ACS), and with severity of ACS [14].

We have developed 2 enzyme-linked immunosorbent assays (ELISA) for measuring plasma ox-Lp(a) level, one using human autoantibodies against ox-Lp(a) to capture ox-Lp(a) and a second using polyclonal antibodies against ox-LDL to capture oxidized apoB of Lp(a). As the autoantibodies isolated from human pooled plasma can recognize both oxidized apo(a) and apoB of Lp(a), the developed ELISA for ox-Lp(a) by autoantibody may accurately reflect the state of Lp(a) oxidation in vivo [18]. In all our previous clinical studies [12–14], ox-Lp(a) level has been measured by using antibodies against ox-LDL to capture oxidized apoB of Lp(a). Hence we designed this study to evaluate clinical value of ox-Lp(a) levels detected by the 2 assays in stable and unstable syndromes.

Materials and methods

Study subjects

The present study included 161 patients with ACS, 114 patients with stable CAD, and 100 control subjects (part of the data published [14]). The control subjects selected from routine health examination
were found normal in physical and electrocardiography and laboratory tests, and without diseases such as hyperlipemia, hypertension, diabetes mellitus, or any clinical evident sign of atherosclerosis. All the subjects were living in Nanjing of China, Han population, which is the major ethnic group in China.

The CAD patients in this study were selected from admitted patients under the department of cardiology of Jinling Hospital between January 2005 and March 2009, who were undergoing clinically indicated coronary angiography. Angiograms of all the CAD patients showed at least 50% stenosis of 1, 2, or 3 coronary arteries. One hundred sixty-one patients with ACS included acute myocardial infarction patients and unstable angina (UA) with Braunwald classification II or III. One hundred fourteen patients with angiographically documented CAD and no cardiac events/procedures for more than 1 year were considered to have stable CAD. The exclusion criteria of the CAD patients included mild disease of angiography (a stenosis of 10% to 50% of the luminal diameter in all the 3 coronary arteries), prior coronary revascularization, and the presence of renal disease. In patients with ACS, blood samples were taken on admission. Blood samples were collected at least 12 h after fasting from control subjects and patients with stable CAD. The blood sample was collected into EDTA (1 mg/mL) containing tube and plasma was separated immediately and stored at −70 °C until analysis. All laboratory assays were conducted within 1 year of blood sampling.

This study protocol was approved by the Ethics Committee of Jinling Hospital, and all the subjects provided written informed consent.

**Angiographic analysis**

Catheterization was performed by either the Sones or the Judkins technique. Multiple views including angulated views were obtained, and the angiograms were evaluated. The extent of angiographically documented CAD was quantified in the left anterior descending coronary artery, the left circumflex artery, or the right coronary artery as follows: normal coronary arteries (smooth, with either no stenosis or a stenosis of <10% of the luminal diameter), mild disease (a stenosis of 10% to 50% of the luminal diameter in one or more coronary arteries), or one-vessel, two-vessel, or three-vessel disease, defined as a stenosis of more than 50% of the luminal diameter in one, two, or three coronary arteries. To eliminate bias of judgment, angiographic observation and laboratory assays were conducted by different investigators in a double-blind way until all results were recorded and ready for statistical analysis.

**Assays**

**Ox-Lp(a)** was measured by 2 “sandwich” ELISAs, using autoantibodies against ox-Lp(a) [ox-Lp(a)1] or polyclonal antibody against ox-LDL [ox-Lp(a)2] as the capture antibody and quantitating with monoclonal anti-apo(a) enzyme conjugate as previously described [18]. Autoantibodies against ox-Lp(a) were isolated and identified from pooled plasma of healthy subjects by affinity chromatography. Antibodies to ox-LDL were obtained by immunization of New Zealand white female rabbits with ox-LDL. The resulting rabbit antiserum was first fractionated by affinity chromatography with immobilized protein G, and the IgG fractions were then absorbed in a column of immobilized native LDL. The washout from the column of immobilized native LDL, containing antibodies to ox-LDL and irrelevant IgG, was used to capture ox-LDL which had no reactivity with native LDL. A pooled fresh-frozen plasma sample was used as reference plasma of ox-Lp(a). The value of ox-Lp(a) was determined by 2 ELISAs, repeatedly, based on the concentration of copper ion oxidized Lp(a) as the standard. Lp(a) level was also detected by a “sandwich” ELISA as previously described [19]. With the use of monoclonal anti-apo(a) as capture antibody, bounded Lp(a) particles were quantitated with polyclonal anti- apo(a) enzyme conjugates. Polyclonal sheep anti-apo(a) was self-made. Antibodies against LDL, plasminogen and other apolipoproteins in the Lp(a) antisera were removed by absorbing on an affinity chromatographic column of Sepharose 4B (Pharmacia) coupled with plasminogen and pooled sera obtained from Lp(a)-negative subjects. Reference serum of Lp(a) was from Immuno AG Vienna. Total cholesterol, triglyceride, high density lipoprotein (HDL) cholesterol (Daichi Pure Chemicals, Japan) were measured on a Hitachi 7600 analyzer. LDL cholesterol was estimated with the use of the Friedewald formula [20].

**Statistical analysis**

Statistical analyses were performed with SPSS 11.5. The values were expressed as mean ± standard deviation. Lp(a) and ox-Lp(a) levels of non-normal distribution were logaritmically transformed. Correlations between variables were calculated by Pearson correlation coefficient. The differences of variants among groups were analyzed by ANOVA, and the differences between groups were subsequently determined by Fisher LSD test when appropriate. Differences of rates between groups were analyzed by Fisher exact test. The differences of ox-Lp(a) levels and the ratio of ox-Lp(a) to Lp(a) detected by 2 assays were analyzed by paired samples t test. Binary logistic regression was used to analyze the relationships of ACS and stable CAD with the levels of plasma ox-Lp(a), controlling for plasma lipids, Lp(a) and clinical characteristics. Receiver-operating characteristic (ROC) curve analysis was used to confirm the performance of ox-Lp(a) and Lp(a) in identifying ACS and stable CAD. Partial correlation analysis was used to study associations of ox-Lp(a) with the extent of angiographically documented disease. Values of \( P < 0.05 \) were considered statistically significant.

**Results**

**Relationship and difference between ox-Lp(a)1 and ox-Lp(a)2**

In the entire population (n = 375), a strong relationship was noted between ox-Lp(a)1 levels and ox-Lp(a)2 (\( r = 0.864, P = 0.000 \) (Fig. 1). The mean difference, ox-Lp(a)1 minus ox-Lp(a)2, was 6.11 μg/mL and the SD was 15.00. The lower 95% limit was −23.29 μg/mL and the upper was 35.51 μg/mL (mean plus or minus 1.96 SD). The difference against average ox-Lp(a)1 and ox-Lp(a)2 was shown in Fig. 2. There was an increase in bias with increasing magnitude of average ox-Lp(a), shown by the positive slope of the regression line (\( r = 0.489, P = 0.000 \)). The difference was also found positively related with ox-Lp(a)1.
Compared with control: Data are presented as the mean value±SD or number (%) of subjects. Furthermore, ox-Lp(a) levels detected by 2 assays were both found increased in both ACS and stable CAD patients. Moreover, ox-Lp(a) levels were found related with ACS and stable CAD patients. Furthermore, ox-Lp(a) levels detected by 2 assays were found higher in the ACS patients than in stable CAD patients. The baseline clinical characteristics of the patients and control subjects, indications for coronary angiography, and lipid concentrations were also listed in Table 1.

Association with the presence of ACS and stable CAD

Compared to control subjects, ox-Lp(a) detected by 2 assays and Lp(a) levels were found increased in both ACS and stable CAD patients. Furthermore, ox-Lp(a) levels detected by 2 assays were both significantly higher in the ACS patients than those in the stable CAD patients (Table 2).

To exclude the influence of Lp(a), we also examined the association of the ratio of ox-Lp(a) to Lp(a) [ox-Lp(a)/Lp(a)] with the presence of ACS and stable CAD. The ratios of ox-Lp(a)/Lp(a) detected by 2 assays were found higher in the ACS patients than in control subjects, as well as the stable CAD patients. Furthermore, the ratios of ox-Lp(a)1/Lp(a) were found higher in the stable CAD than in control, while the ratios of ox-Lp(a)2/Lp(a) remained similar between them. In addition, compared to control, ox-Lp(a)1 and 2 levels increased 203% and 109% in ACS, and 61% and 33% in stable CAD, respectively. Ox-Lp(a)1 and ox-Lp(a)1/Lp(a) were found both significantly higher than ox-Lp(a)2 and ox-Lp(a)2/Lp(a) in all the studied groups of ACS, stable CAD and control, respectively (Table 2).

Logistic regression was next performed to examine the relationship of ACS and stable CAD with the levels of ox-Lp(a) detected by 2 assays, controlling for plasma lipids, Lp(a) and clinical characteristics, including age, sex, coronary risk factors (hypertension, tobacco use, diabetes mellitus, family history of CAD), medications (statins, other hypocholesterolemic agents, Beta-blockers), and past medical history (MI, congestive heart failure) (Table 3). After controlling for these factors, odds ratios (OR) of ox-Lp(a)1 on ACS and stable CAD were 5.06 [95% confidence interval (95% CI) 1.82–14.04] and 2.20 (0.78–6.22), respectively, compared with controls; those of ox-Lp(a)2 on them were 3.37 (1.07–10.63) and 1.35 (0.41–4.48), respectively.

ROC curve analysis of ox-Lp(a) in ACS and stable CAD

To compare the association of ox-Lp(a), Lp(a) and LDL cholesterol levels with ACS and stable CAD, ROC curve analysis was performed in the ACS and stable CAD, respectively (Fig. 3 and Table 4). ROC curve analysis confirmed that the performance of the association of ox-Lp(a)1 with ACS was significantly superior to those of ox-Lp(a)2, Lp(a) and LDL cholesterol; while the performances of ox-Lp(a)2, Lp(a) and LDL cholesterol with ACS were similar. The performance of the association between ox-Lp(a)1 and stable CAD was significantly superior to that between ox-Lp(a)2 and stable CAD; while the performances of ox-Lp(a)2 detected by 2 assays in identifying stable CAD were similar to those of Lp(a) and LDL cholesterol.

Associations with the extent of angiographically documented disease

Partial correlation analysis was performed to study associations of ox-Lp(a) with the extent of angiographically documented disease. Controlling for plasma lipids, Lp(a) and clinical characteristics, the

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>ACS (n = 161)</th>
<th>Stable CAD (n = 114)</th>
<th>Control (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.5±10.7</td>
<td>61.8±10.2</td>
<td>59.5±10.8</td>
</tr>
<tr>
<td>Male/female</td>
<td>106/55</td>
<td>65/49</td>
<td>59/41</td>
</tr>
<tr>
<td>Coronary risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>109 (68)</td>
<td>84 (74)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>64 (40)</td>
<td>35 (31)</td>
<td>35 (35)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>36 (22)</td>
<td>35 (31)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Family history of coronary artery disease</td>
<td>13 (8)</td>
<td>5 (4)</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Statins</td>
<td>123 (76)</td>
<td>80 (70)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other hypocholesterolemic agents</td>
<td>5 (3)</td>
<td>3 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>117 (73)</td>
<td>67 (59)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Past medical history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>38 (24)</td>
<td>37 (32)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>57 (35)</td>
<td>40 (35)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Lipid levels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.42±1.25</td>
<td>5.09±1.09</td>
<td>4.71±0.83</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>3.28±1.17</td>
<td>2.99±0.97</td>
<td>2.64±0.66</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.23±0.21</td>
<td>1.25±0.28</td>
<td>1.41±0.30</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.96±1.09</td>
<td>1.84±1.10</td>
<td>1.48±0.73</td>
</tr>
</tbody>
</table>

Data are presented as the mean value±SD or number (%) of subjects. Compared with control: *P<0.05, **P<0.01, ***P=0.001. Compared with stable CAD: †P<0.05.
significant correlations of ox-Lp(a)1 (R=0.193, P=0.023) and ox-Lp(a)2 (R=0.186, P=0.028) were found with the extent of CAD in ACS, respectively. No association of the extent of CAD was found with ox-Lp(a)1 (R=0.064, P=0.547) and ox-Lp(a)2 (R=0.064, P=0.547) in stable CAD.

Discussion

This study showed that elevated ox-Lp(a) levels detected by 2 assays were associated with the presence of ACS and stable CAD patients, and with severity of ACS. Though a strong correlation was noted between ox-Lp(a) levels detected by 2 assays, ROC curve and OR analysis confirmed that ox-Lp(a)1 levels represent a better biochemical risk marker than ox-Lp(a)2 as well as Lp(a) for ACS and stable CAD.

Ox-Lp(a)1 has been reported to play more potent role than native Lp(a) in atherosclerosis [5–9]. The degree of oxidized apo(a) or apoB protein of Lp(a) has both been detected to estimate circulating ox-Lp(a) levels [10,11]. We previously have also developed two ELISAs for measuring plasma ox-Lp(a) level, using human autoantibodies against ox-Lp(a) to capture ox-Lp(a) or polyclonal antibodies against ox-LDL to capture oxidized apoB of Lp(a), and then quantitating with monoclonal anti-apo(a) enzyme conjugate. The isolated autoantibody reacted with both ox-Lp(a) and ox-LDL, but not with native Lp(a) and LDL. Furthermore, after being fully absorbed by ox-LDL, the remaining autoantibodies still had strong reactivity with ox-Lp(a), which indicates that human autoantibodies against ox-Lp(a) can recognize both oxidized apo(a) and apoB of Lp(a). Ox-LDL, as well as other lipoproteins or proteins binding related oxidized epitopes, such as albumin, can be captured by both antibodies against ox-Lp(a) or ox-LDL, while they cannot be detected by our 2 ELISAs because of the use of monoclonal antibody against apo(a) as quantitating antibodies. In addition, plasma ox-LDL levels are low and as the samples are diluted, plasma ox-LDL has no influence on 2 assays [18]. In general, only oxidized Lp(a) can trigger an autoimmune response in vivo, and subsequently producing autoantibodies. Thus, autoantibodies isolated from human pooled plasma may accurately reflect the state of Lp(a) oxidation in vivo, and may be useful to keep the remaining antibodies identical from different batches. How to keep the autoantibodies identical remains to be established in future studies.

A significantly positive relationship was found between ox-Lp(a) levels detected by 2 assays, while bias was also found between ox-Lp(a)1 and ox-Lp(a)2. Bland and Altman [21] recommended that mean difference would be the estimated bias, and the systematic difference between methods, and the SD of the differences would measure random fluctuations around this mean. It was estimated that for 95% of subject ox-Lp(a)1 would be between 23.29 μg/mL below ox-Lp(a)2 and 35.51 μg/mL above it. Furthermore, it was found that the bias increased along with increasing magnitude of ox-Lp(a)1.

The present studies shows that ox-Lp(a)1 levels detected by 2 assays increased in stable CAD, and especially in ACS, and might be one of the major contributing factors for the development of atherosclerosis, which is similar to what we previously reported [14]. Though relationship and difference were found between ox-Lp(a)1 and ox-Lp(a)2, it was important that ox-Lp(a)1 and ox-Lp(a)1/Lp(a) were both significantly higher than ox-Lp(a)2 and ox-Lp(a)2/Lp(a) in all the studied groups. The high degree of ox-Lp(a)1 may be caused by the fact that the antibodies recognize both oxidized apo(a) and apoB of Lp(a). ROC curve analysis not only confirmed that ox-Lp(a)1 levels detected by 2 assays, Lp(a) and LDL cholesterol all had performances in identifying ACS and stable CAD, but also confirmed that the performances of ox-Lp(a)1 were significantly superior to those of ox-Lp(a)2. In addition, the performance of ox-Lp(a)1 was significantly superior to those of Lp(a) and LDL cholesterol in ACS. Furthermore, controlling for plasma lipids, Lp(a) and clinical characteristics, OR of ox-Lp(a)1 by 2 assays remained to reach statistical significance on ACS, while OR of ox-Lp(a)1 did not reach statistical significance on stable CAD. The different values of OR also indicated that acuity of ox-Lp(a)1 to identify ACS was superior to that of ox-Lp(a)2. Therefore, plasma ox-Lp(a)1 levels may represent a better biochemical risk marker than ox-Lp(a)2 as well as Lp(a) for ACS and stable CAD. The diagnostic implications of the assay remain to be further established.

Partial correlation analysis found that ox-Lp(a)1 levels were associated with a graded increase in the extent of CAD in the patients with ACS, while not in stable CAD, which is supported by our previous study [14] and other studies about oxidized phospholipids [22–26].

Recently, a series of studies have demonstrated convincingly that a key oxidized phospholipid is preferentially associated with Lp(a) [22] and Lp(a) was recently found to be significantly associated with future incident CAD [27].

![Fig. 3. Receiver-operating characteristic curve analysis of ox-Lp(a) and Lp(a) levels in patients with ACS and stable CAD. Ox-Lp(a)1: detected by anti-ox-Lp(a); ox-Lp(a)2: detected by anti-ox-LDL.](image)

Table 4

<table>
<thead>
<tr>
<th>Variables</th>
<th>Area</th>
<th>SE</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ox-Lp(a)1</td>
<td>0.803</td>
<td>0.028</td>
<td>0.747–0.858</td>
<td>0.000</td>
</tr>
<tr>
<td>Ox-Lp(a)2</td>
<td>0.673</td>
<td>0.037</td>
<td>0.629–0.725</td>
<td>0.000</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>0.704</td>
<td>0.034</td>
<td>0.638–0.770</td>
<td>0.000</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.692</td>
<td>0.032</td>
<td>0.629–0.755</td>
<td>0.000</td>
</tr>
<tr>
<td>Stable CAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ox-Lp(a)1</td>
<td>0.607</td>
<td>0.037</td>
<td>0.597–0.742</td>
<td>0.000</td>
</tr>
<tr>
<td>Ox-Lp(a)2</td>
<td>0.607</td>
<td>0.039</td>
<td>0.531–0.683</td>
<td>0.007</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>0.635</td>
<td>0.039</td>
<td>0.550–0.710</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.614</td>
<td>0.038</td>
<td>0.539–0.689</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Ox-Lp(a)1: detected by anti-ox-Lp(a); Ox-Lp(a)2: detected by anti-ox-LDL.

Compared with Lp(a): §P < 0.05; compared with ox-Lp(a)-1: ‡P < 0.01; compared with LDL cholesterol: †P < 0.01.
and correlates with both the presence and extent of angiographically
documented CAD [23,24], and their levels increase after ACS [25] and
immediately after percutaneous coronary intervention [26]. Increased
ox-Lp(a) level in stable CAD and especially in ACS, and its association
with the extent of angiographically documented CAD suggest that ox-
Lp(a) particles in the blood come from the arterial wall, such as
released from ruptured or permeable plaques. It is also possible that oxidation-specific epitopes generated in the arterial
intima, such as oxidized phospholipids, might have been transported
by some mechanisms to Lp(a) acceptors, or might move between LDL
and Lp(a). Meanwhile, elevated Lp(a) level may result in increased
circulating ox-Lp(a). Ox-Lp(a) was found related with Lp(a), which
shows that more Lp(a) in subjects with high Lp(a) has more chance to
be oxidized in vivo. In addition, Lp(a) is known to act as an acute-
phase reactant in patients with ACS. Our previous study has also found
increased Lp(a) and ox-Lp(a) levels positively related with C-reactive
protein in patients with rheumatoid arthritis [13], which suggests that
inflammation promotes Lp(a) synthesis and its oxidation.

One limitation of this study is that we did not explore the asso-
ciation of inflammation with native and oxidized Lp(a). In addition,
the exact epitopes of ox-Lp(a) detected by the autoantibodies have not been defined, though the human autoantibodies have been shown to
recognize both oxidized apo(a) and apoB of Lp(a).

In conclusion, the present study demonstrates that ox-Lp(a) levels
increased in CAD, especially in ACS. Ox-Lp(a) levels using antibodies
against ox-Lp(a) may represent a better biochemical risk marker than
those using antibodies against ox-LDL, as well as Lp(a) for ACS and
stable CAD. The assay of ox-Lp(a) may provide a new approach to
investigate the causal role of ox-Lp(a) in atherosclerotic cardiovas-
cular disease in a prospective study and to explore the exact pathogenic
role of ox-Lp(a).

Acknowledgments

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