Acute impact of the early application of alirocumab on lipoprotein (a) and interleukin-6 in patients with unstable angina pectoris: a retrospective before-after study

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Research Article

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Abstract

Background Lipoprotein (a) is a determined causal risk factor for residual risks of recurrent ischemic cardiovascular events. Alirocumab has been found to reduce lipoprotein (a) levels. However, its effects on lipoprotein (a) and inflammation marker in a Chinese population with unstable angina remain to be characterized.

Aim We aimed to assess the effect of alirocumab on lipoprotein (a) and inflammatory marker in Chinese subjects with unstable angina.

Method In a retrospective before-after study, lipoprotein (a), interleukin-6 and other lipid profiles were measured before and after 4 weeks of alirocumab treatment in 53 patients with unstable angina (UA) who had already received oral lipid-lowering therapies.

Results The alirocumab significantly lowered the levels of lipoprotein (a) (-11.28 mg/dL; \( p < 0.001 \)) and interleukin-6 (-1.65 pg/mL; \( p < 0.001 \)) after treatment. Moreover, there was a positive linear correlation between lipoprotein (a) and interleukin-6 at baseline (\( R=0.86; p < 0.001 \)). Furthermore, in 11 patients with lipoprotein (a) levels \( \geq 50 \) mg/dL at baseline, lipoprotein (a) (-27.37 mg/dL; \( p < 0.001 \)) and interleukin-6 (-2.97 pg/mL; \( p < 0.001 \)) decreased after treatment. In 42 patients with lipoprotein (a) levels < 50 mg/dL at baseline, lipoprotein (a) (-7.07 mg/dL; \( p = 0.001 \)) and interleukin-6 (-1.31 pg/mL, \( p < 0.001 \)) also decreased after treatment.

Conclusions Early application of alirocumab may be effective in reducing the levels of lipoprotein (a) and interleukin-6 in Chinese patients with unstable angina in the short term, especially in patients with lipoprotein (a) \( \geq 50 \) mg/dL.

Impact Statements

- Early application of alirocumab (one type of proprotein convertase subtilisin/kexin type 9 inhibitors) may be an effective treatment strategy for the management of lipoprotein (a) among Chinese patients with unstable angina, especially in patients with lipoprotein (a) \( \geq 50 \) mg/dL.
- The alirocumab also exerted lowering effects of interleukin-6, especially in patients with lipoprotein (a) \( \geq 50 \) mg/dL. Moreover, there might be a positive linear correlation between lipoprotein (a) and interleukin-6, which indicates that interleukin-6, may be a pro-inflammatory marker of lipoprotein (a).
- The exact efficacies of alirocumab on lipoprotein (a) and interleukin-6 are still not fully established and well-designed randomized controlled trials are required to further exploration.

Introduction

Elevated concentrations of lipoprotein (a) [Lp(a)] and associated inflammation disorder sharply increase the risk of atherosclerotic cardiovascular disease (CVD)-related events [1, 2] and impair the medical efforts in improving CVD prognosis [3] based on the multidimensional findings in pathophysiology [4],
epidemiology [5], Mendelian randomization [6], genome-wide analysis [7], post hoc analysis of randomized controlled clinical trials [8] and meta-analysis [9]. Meanwhile, the available evidence strongly suggests that the pathogenicity of Lp(a) is widespread across ethnic groups [3], owing to its pro-inflammatory and pro-atherosclerotic properties [10]. Moreover, Lp(a), independent of low-density lipoprotein cholesterol (LDL-C), is significantly associated with residual cardiovascular risk in patients with unstable angina (UA) [11–13], especially in certain Chinese populations with high Lp(a) levels [14]. As a result, a trend toward stricter regulation of Lp(a) has been performed recently in the guideline [15, 16]. However, whatever statins or ezetimibe, as common-used lipid-lowering therapies, are largely ineffective for Lp(a) [17, 18]. Accordingly, the effective management of Lp(a) remains in difficulty even after intensive treatment with oral medications [19]. Therefore, new regimes are urgently needed to improve Lp(a) related residual risk and poor prognosis in clinical practice.

As a novel lipid lowering agent, emerging and robust evidence of proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) have been demonstrated with significantly reduction in different types of lipids and cardiovascular events [20]. Although clinical studies have proven that PCSK9i could significantly decrease elevated Lp(a) levels and reduce the increased risk with established cardiovascular disease [21–23], the effects of PCSK9i on Lp(a) in different populations with various clinical phenotypes of cardiovascular diseases are distinct [24]. Furthermore, the effect of PCSK9i for Lp(a) and inflammatory marker in Chinese patients with UA remains unclear and no relevant studies have been reported. Thus, we are interested in attempting to provide an answer to the above question for the first time.

**Aim**

In order to improve the management of Lp(a) in clinical practice, this retrospective before-after study was carried out to evaluate the effects of 4 weeks treatment with alirocumab (one type of PCSK9i) on Lp(a) and inflammatory marker-interleukin-6 (IL6) in Chinese patients with UA who had already received oral lipid-lowering therapies.

**Ethics approval**

The research project was given ethical approval by the Ethics Review Board of Ningbo First Hospital [Approval number: 2022-RS100, dated 26 July 2022]. The study adhered fully to the guidelines outlined in the Declaration of Helsinki.

**Methods**

**Study Population**

This retrospective study preliminarily enrolled patients admitted to Ningbo First Hospital from June 2021 and May 2022 for diagnosis of unstable angina (UA). Then the secondary screening was carried out according to the inclusion and exclusion criteria. The inclusion criteria were the patients met all the following criteria simultaneously: (1) received alirocumab therapy for at least one month; (2) Complete
hospitalization and one-month follow-up data were available. Meanwhile, patients with acute myocardial infarction (AMI), active infection, severe liver or renal failure, autoimmune diseases, neoplastic diseases, and patients with missing data on alirocumab therapy were all excluded from the study. Finally, a total of 53 alirocumab treated patients with UA was consecutively included for further analysis.

**Data analysis**

All data were extracted from the electronic medical records database. All the subjects were received alirocumab (75 mg) on the discharge day due to medication limitations in hospitalized patients. The data collections of clinical characteristics were conducted based on a structured data collection form. According to medication specifications, the injection of alirocumab (75 mg) was repeated 2 weeks interval. The outpatient follow-up was performed approximately 4 weeks after discharge (before the third dose of alirocumab injection), and the blood tests were re-evaluated in the fasting state. All the tests performed in the Central laboratory of Ningbo First Hospital. The parameters measured included: Lp(a), interleukin-6 (IL6), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), LDL-C. We compared the parameters between before and 4 weeks after treatment.

**Subgroup analysis**

Based on the evidence that a significant association between Lp(a) and major adverse cardiovascular events (MACE) was observed at the Lp(a) level of 50 mg/dL or higher [25], subgroup analysis was performed based on an Lp(a) level of 50 mg/dL at baseline: high-Lp(a) subgroup-patients with Lp(a) levels ≥ 50 mg/dL (n = 11); low-Lp(a) subgroup-patients with Lp(a) levels < 50 mg/dL (n = 42). Then, subgroup analyses were further conducted.

**Data Analysis**

Continuous variables were expressed as mean ± SDs, categorical variables as count (percentage). Differences between before-after self was analyzed by paired-t test; differences between 2 groups were analyzed by independent-t test or Fisher's exact test where appropriate. Linear correlation was used to analyze the relationship of 2 independent normality quantitative parameters. All analyzes were conducted by statistical SPSS software 25.0 (IBM Corp., Armonk, NY, USA). The level of significant difference was set as p-value < 0.05 for all tests.

**Results**

**Clinical Characteristics of baseline**

The median age of 53 UA patients treated with alirocumab was 62.49 ± 9.77 years, and 36 out of 53 (67.9%) were male. The median body mass index (BMI) was 24.28 ± 3.10 kg/m². In additional, 24 out of 53 (45.3%) were current smokers, 36 out of 53 (67.9%) had hypertension, 17 out of 53 (32.1%) had diabetes mellitus, 4 out of 53 (7.6%) had hyperlipidemia, and 19 out of 53 (35.8%) were on statins and ezetimibe combination therapy. The median Lp(a) was 35.81 ± 35.75 mg/dL (range of reference value:
0.00–30.00 mg/dL), and the median IL6 was 4.63 ± 1.13 pg/mL (range of reference value: 0.00–20.00 mg/dL). The details of clinical characteristics at baseline were presented in Table 1.

### Table 1
Clinical characteristics of patients at baseline

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Unstable angina patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 53)</td>
</tr>
<tr>
<td><strong>Parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.49 ± 9.77</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>36 (67.9)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.28 ± 3.10</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>24 (45.3)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>36 (67.9)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>17 (32.1)</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>4 (7.6)</td>
</tr>
<tr>
<td>Statin monotherapy, n (%)</td>
<td>28 (52.8)</td>
</tr>
<tr>
<td>Atorvastatin-20mg/d</td>
<td>6 (11.3)</td>
</tr>
<tr>
<td>Rosuvastatin-10mg/d</td>
<td></td>
</tr>
<tr>
<td>Statin + ezetimibe combination, n (%)</td>
<td>15 (28.3)</td>
</tr>
<tr>
<td>Atorvastatin-20mg/d + ezetimibe</td>
<td>4 (7.6)</td>
</tr>
<tr>
<td>Rosuvastatin-10mg/d + ezetimibe</td>
<td>1.80 ± 1.17</td>
</tr>
<tr>
<td>Lipid profiles</td>
<td>4.63 ± 1.13</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.09 ± 0.25</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>2.90 ± 0.79</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>35.81 ± 35.75</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>4.63 ± 1.13</td>
</tr>
<tr>
<td>Lp(a) (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Inflammatory marker</td>
<td></td>
</tr>
<tr>
<td>IL6 (pg/mL)</td>
<td></td>
</tr>
</tbody>
</table>

(BMI: body mass index; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Lp(a): lipoprotein (a); IL6: interleukin-6).

Effect of alirocumab on Lp(a) and IL6
After 4 weeks treatment with alirocumab, as shown in Fig. 1a, Lp(a) significantly decreased by 31.5%, from 35.81 ± 35.75 mg/dL to 24.53 ± 30.40 mg/dL (p < 0.001). Meanwhile, IL6 is an inflammatory marker in clinical evaluation of Lp(a) [26, 27]. Thus, we also detected the effect of alirocumab on circulating IL6 levels and found that IL6 also markedly decreased by 35.6%, changing from 4.63 ± 1.13 pg/mL to 2.98 ± 1.00 pg/mL (p < 0.001) (Fig. 1b). Both Lp(a) and IL6 rapidly declined after 2-times administration of alirocumab in Chinese patients with UA.

Then, linear correlation analysis showed that the distributions of Lp(a) and IL6 from all UA patients at baseline had a positive linear correlation (R = 0.86, p < 0.001). Therefore, IL6 was also taken into consideration for further subgroup analysis.

**Subgroup analysis**

Based on the level of Lp(a) (cutoff value was 50 mg/dL) at baseline, patients were divided into 2 subgroups: high-Lp(a) subgroup (n = 11) and low-Lp(a) subgroup (n = 42). The levels of Lp(a) in high-Lp(a) subgroup (95.10 ± 29.85 mg/dL) were similar to the distribution of Lp(a) found in other Eastern Asian population studies [10, 11], which suggested that patients in high-Lp(a) subgroup exposed to higher residual cardiovascular risk. The details for subgroups were presented in Table 2.
Table 2
Clinical characteristics of patients in subgroups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>high-Lp(a) subgroup (n = 11)</th>
<th>low-Lp(a) subgroup (n = 42)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.45 ± 10.06</td>
<td>63.55 ± 9.53</td>
<td>0.125</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>9 (81.8)</td>
<td>27 (64.3)</td>
<td>0.469</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.62 ± 4.01</td>
<td>24.19 ± 2.86</td>
<td>0.686</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>7 (63.6)</td>
<td>17 (40.5)</td>
<td>0.194</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>5 (45.5)</td>
<td>31 (73.8)</td>
<td>0.143</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>3 (27.3)</td>
<td>14 (33.3)</td>
<td>0.739</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>1 (9.1)</td>
<td>3 (7.1)</td>
<td>0.831</td>
</tr>
<tr>
<td>Statin monotherapy, n (%)</td>
<td>6 (54.5)</td>
<td>28 (66.7)</td>
<td>0.496</td>
</tr>
<tr>
<td>Statin + ezetimibe combination, n (%)</td>
<td>5 (45.5)</td>
<td>14 (33.3)</td>
<td>0.496</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.66 ± 1.35</td>
<td>1.83 ± 1.14</td>
<td>0.669</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>4.52 ± 1.12</td>
<td>4.66 ± 1.14</td>
<td>0.719</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>0.96 ± 0.25</td>
<td>1.12 ± 0.24</td>
<td>0.066</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>2.90 ± 0.82</td>
<td>2.90 ± 0.79</td>
<td>0.992</td>
</tr>
<tr>
<td>Lp(a) (mg/dL)</td>
<td>95.10 ± 29.85</td>
<td>20.28 ± 14.63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL6 (pg/mL)</td>
<td>6.28 ± 0.48</td>
<td>4.20 ± 0.80</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

As shown in Fig. 2a, the difference of Lp(a) in high-Lp(a) subgroup (95.10 ± 29.85 mg/dL) and low-Lp(a) subgroup (20.28 ± 14.63 mg/dL) at baseline was significant (p < 0.001). After 4 weeks alirocumab treatment, Lp(a) decreased from 95.10 ± 29.85 mg/dL to 67.73 ± 31.12 mg/dL in high-Lp(a) subgroup (p < 0.001) and from 20.28 ± 14.63 mg/dL to 13.21 ± 17.44 mg/dL in low-Lp(a) subgroup (p = 0.001). Meanwhile, the difference of IL6 in high-Lp(a) subgroup (6.28 ± 0.48 pg/mL) and low-Lp(a) subgroup (4.20 ± 0.80 pg/mL) in baseline was also significant (p < 0.001). After 4 weeks treatment with alirocumab, IL6 decreased from 6.28 ± 0.48 pg/mL to 3.31 ± 0.97 pg/mL (p < 0.001) in high-Lp(a) subgroup and from 4.20 ± 0.80 pg/mL to 2.89 ± 1.01 pg/mL in low-Lp(a) subgroup (p < 0.001) (Fig. 2b). The results suggested that UA patients with higher Lp(a) levels experienced greater absolute reductions in Lp(a) and IL6 by using 2-times administration of alirocumab.

**Effect of alirocumab on common lipid profiles**
In addition, the changes of common lipid profiles in all UA patients (n = 53) after 4 weeks alirocumab treatment were shown in Table 3, the levels of TG, TC and LDL-C significantly decreased after treatment: TG decreased by 22.8%, from 1.80 ± 1.17 mmol/L to 1.39 ± 0.68 mmol/L (p = 0.003); TC decreased by 35.6%, from 4.63 ± 1.13 mmol/L to 2.98 ± 1.00 mmol/L (p < 0.001); LDL-C decreased by 46.2%, from 2.90 ± 0.79 mmol/L to 1.56 ± 0.72 mmol/L (p < 0.001); however, HDL-C was not significantly different before and after treatment (p = 0.921). Our results showed that the alirocumab had convincing lowering effects of TG, TC and LDL-C in Chinese patients with UA as other clinical studies [28, 29].

Table 3
Effect of 4 weeks treatment with alirocumab on common lipid profiles (n = 53)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Change Mean (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG (mmol/L)</td>
<td>1.80 ± 1.17</td>
<td>1.39 ± 0.68</td>
<td>-0.41 (22.8%)</td>
<td>0.003</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>4.63 ± 1.13</td>
<td>2.98 ± 1.00</td>
<td>-1.65 (35.6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>2.90 ± 0.79</td>
<td>1.56 ± 0.72</td>
<td>-1.34 (46.2%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.09 ± 0.25</td>
<td>1.08 ± 0.26</td>
<td>-0.01 (0.9%)</td>
<td>0.921</td>
</tr>
</tbody>
</table>

Discussion

In the present retrospective study, levels of Lp(a) and IL6 were markedly and quickly decreased with 2-times administration of alirocumab, especially in UA patients with Lp(a) levels ≥ 50 mg/dL. Meanwhile, the LDL-C and TC also significantly decreased as in other clinical studies [29, 30]. Therefore, different from the previous oral lipid-lower medications, the PCSK9i indeed restored our confidence in the management of Lp(a) [31].

Lp(a) is a particle in which apolipoprotein a [Apo(a)] is linked to LDL-like particles via a disulfide bond [32]. The Lp(a) concentration is genetically determined and largely independent of sex, age, and diet [33]. The emergence of pathophysiological and epidemiologic data strongly supports, excluding various stress-induced conditions, that Lp(a) is a causal factor in CVD [34]. For now, Lp(a) disorder has become the most prevalent lipid disorder globally, with elevated levels estimated at > 1.4 billion people [1, 35], especially prevalent among Chinese population with CVD [36, 37]. Elevated level of Lp(a) is related to increasing risk with varied clinical phenotypes, ranging from myocardial infarction, to stroke in individuals [2]. Accordingly, the rationale for managing Lp(a)-mediated atherosclerotic cardiovascular disease risk is stronger than ever before. Meanwhile, Lp(a) level is associated with the residual risk of UA [13], which may be the best single marker in assessing UA [11]. Moreover, studies based on East Asian populations highlight the importance of Lp(a) intervention to improve atherosclerosis and prevent cardiovascular risks [36, 38]. Therefore, a Chinese population with UA is the valuable target to study the effect of PCSK9i on Lp(a).
Meanwhile, Lp(a) associated vascular inflammation plays multiple maladaptive roles, which contribute to the progression and the destabilization of CVD [39]. Lp(a) could penetrate into the intima of arteries and promote macrophage infiltration [40], further activate pro-inflammatory signaling activation, and trigger inflammatory responses in the arterial wall [41]. A large body of evidence has accumulated supporting the use of IL6 as a clinical measure of inflammation [42, 43]. Accordingly, IL6 may be a marker and evaluation indicator of Lp(a)-associated inflammatory progression in CVD [44, 45]. In additional, IL-6 has emerged as a potential factor in individuals at high atherosclerotic risk, but without any systemic inflammatory disorder [46]. However, there are no studies on the relationship between Lp(a) and IL6 in Chinese patients with UA so far. In our results, there was a positive linear correlation between Lp(a) and IL6 at baseline, which suggested that Lp(a) may contribute to the elevated inflammation in patients with UA. Additionally, the alirocumab had an inhibiting impact on IL6 in patients with UA, which was construed as the anti-inflammation effect of alirocumab. Although recent studies have revealed that Lp(a) and chronic inflammation can interact to rapidly promote the progression of CVD [47, 48], the short-time inhibition of IL6 could not influence Lp(a) levels. [49]. Therefore, we speculate that the decrease of IL6 level is caused by the inhibiting action of alirocumab on Lp(a), and more studies are needed to unequivocally assess the impact of alirocumab.

Furthermore, the effects of lipids-lowering therapy with alirocumab or evolocumab on individual clinical efficacy and safety endpoints are always been a hot pot in clinical research [50, 51]. Importantly, the benefits of different types of PCSK9i of lipid-lowering are homogenous. Then, compared with the study based on evolocumab and Korean population with stable angina [52], in our work, we found that alirocumab appeared to have better short-term efficacy in reducing Lp(a) and similarly efficacious in anti-inflammation. Further evidence-based researches are required to determine the different selections between PCSK9i and clinical phenotypes. We believe that our clinical practice will provide useful reference information and clinical guidance for the high-quality management of the UA populations in China, especially for those patients with high Lp(a) level.

Limitation

There were several potential limitations to the study owing to the retrospective study design and availability of data: First, this was a single-center, small sample retrospective study, the statistical power was relatively weak. Second, other information, such as changes in diet and lifestyle, could not be measured precisely. Third, lipid-lowering therapies at baseline were not uniform. Furthermore, it was hardly to derive a concrete clinical outcome of monitoring the lipid-lowering effects for only 4 weeks. The long-term effect of alirocumab in Chinese patients with UA, particularly on Lp(a) and IL6 should also be in-depth investigated in the future.

Conclusion

Taken together, our study found that 2-times administration of alirocumab may effectively reduce levels of Lp(a) and IL6 in Chinese patients with UA in the short term, especially in subjects with Lp(a) ≥ 50
mg/dl. However, due to the limitations of study design, no definitive conclusions can be drawn about the early application of alirocumab in a Chinese population with UA. We recommend that UA patients with high Lp(a) level should be given individualized treatment by weighing the benefits against the risks in until further large-scale clinical studies confirm the exact effect of early application of alirocumab for Lp(a).

Declarations

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Conflicts of Interest The authors declare that there is no conflict of interest.

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**Figures**

**Figure 1**

**Effect of 4 weeks treatment with alirocumab on Lp(a) and IL6.** (a) The Lp(a) decreased by 31.50%, from 35.81 ± 35.75 mg/dL to 24.53 ± 30.40 mg/dL (n=53); (b) the IL6 decreased by 35.6%, from 4.63 ± 1.13 pg/mL to 2.98 ± 1.00 pg/mL (n=53). *p < 0.001.
Effect of alirocumab on Lp(a) and IL6 in subgroup analysis. All 53 patients were divided into two groups at baseline: high-Lp(a) subgroup with Lp(a) levels ≥ 50 mg/dL (n=11); low-Lp(a) subgroup with Lp(a) levels < 50 mg/dL (n=42). (a) There was a significant difference of Lp(a) at baseline between high-Lp(a) subgroup (95.10 ± 29.85 mg/dL) and low-Lp(a) subgroup (20.28 ± 14.63 mg/dL). After 4 weeks alirocumab treatment, Lp(a) significantly decreased from 95.10 ± 29.85 mg/dL to 67.73 ± 31.12 mg/dL in high-Lp(a) subgroup and from 20.28 ± 14.63 mg/dL to 13.21 ± 17.44 mg/dL in low-Lp(a) subgroup. (b) There was a significant difference of IL6 at baseline between high-Lp(a) subgroup (6.28 ± 0.48 pg/mL) and low-Lp(a) subgroup (4.20 ± 0.80 pg/mL). After 4 weeks treatment with alirocumab, IL6 also significantly decreased from 6.28 ± 0.48 pg/mL to 3.31 ± 0.97 pg/mL in high-Lp(a) subgroup and from 4.20 ± 0.80 pg/mL to 2.89 ± 1.01 pg/mL in low-Lp(a) subgroup. * $p < 0.001$, # $p = 0.001$. 