Apolipoprotein B/A-I Ratio Predicts Lesion Severity and Clinical Outcomes in Diabetic Patients With Acute Coronary Syndrome

Yue Liu, MD; Si-da Jia, MD; De-shan Yuan, MD; Na Xu, MD; Lin Jiang, MD; Zhan Gao, MD; Jue Chen, MD; Yue-jin Yang, MD; Run-lin Gao, MD; Bo Xu; Jin-qing Yuan, MD

Background: Dyslipidemia plays a crucial role in acute coronary syndrome (ACS). Paucity of data is available concerning the effect of apolipoprotein (apo) B/A-I ratio on the severity and outcomes in diabetic patients with ACS. This study investigated these associations in a Chinese cohort undergoing percutaneous coronary intervention.

Methods and Results: In 2013, a total of 2,563 diabetic patients concomitant with ACS were included. Patients were divided into 2 groups based on the apoB/apoA-I ratio on admission: <0.63 (n=1,279, 49.9%) and ≥0.63 (n=1,284, 50.1%). Angiographic complexity and severity were determined by SYNTAX score (SS). A higher apo ratio was significantly associated with higher proportions of acute myocardial infarction (MI) and intermediate-high SS. Multivariable logistic regression analysis showed that the apo ratio was an independent factor of complicated lesions (OR 1.341, 95% confidence interval 1.039–1.730, P=0.024). Moreover, consistent results were found in the subgroups of normal concentrations of conventional lipid parameters. During a median follow-up period of 878 days, significant differences were found in periprocedural MI (1.0% vs. 2.2%, P=0.019) and total events of MI (2.0% vs. 3.3%, P=0.028). After adjusting for confounders, a high apo ratio remained independently predictive of MI, the risk of which was doubled during the periprocedural period and in the long term.

Conclusions: The ApoB/apoA-I ratio is an independent predictor for complicated lesions and future MI in patients with diabetes and ACS.

Key Words: Acute coronary syndrome; Apolipoprotein; Recurrent myocardial infarction

Acute coronary syndrome (ACS) is a common disease with high morbidity and mortality. In particular, for patients with concomitant diabetes mellitus, there is 75% of deaths resulting from ischemic events, and therefore secondary prevention is essential.1 Guidelines have recommended that ACS patients receive lipid-lowering treatment and that a low-density lipoprotein cholesterol (LDL-C) reduction of ≥50% from baseline or an LDL-C goal of <1.8 mmol/L is preferable for those at high risk.2-4 In addition to the conventional lipid profile, such as LDL-C, total triglyceride (TG), and total cholesterol (TC), abundant evidence has indicated that apolipoproteins (apo) might be a robust predictor for primary prevention, and the latest guidelines recommend apoB as an alternative to LDL-C for risk assessment.5-8 The large population AMORIS (Apolipoprotein-related Mortality RISK) study found that high apoB/apoA-I ratio increased incidence of acute myocardial infarction (MI) and stroke during a long-term follow up.5,9,10 Other research has shown a close relationship between apo ratio and insulin resistance or diabetes.11,12 However, these findings were derived from participants without established cardiovascular diseases at baseline. In patients with known ACS and diabetes, whether baseline apoB/apoA-I ratio helps identify worsened angiographic characteristics and prognoses has not been fully investigated. Therefore, we conducted this cohort study to evaluate the influence of apoB/apoA-I ratio at admission to determine the complexity and severity of ACS as well as long-term outcomes.

Methods

Study Population
This was a prospective, observational study in a single...
After excluding patients without a history of apo or glycosylated hemoglobin (HbA1c) on admission, 2,563 patients with known diabetes or HbA1c >6.5% were eligible for this study (Figure 1). The Institutional Review Board of our hospital approved the study protocol in accordance with center (Fuwai Hospital, National Center for Cardiovascular Diseases, Beijing, China). Between January and December in 2013, a total of 6,431 patients presenting with ACS (including MI and unstable angina) were consecutively enrolled for percutaneous coronary intervention (PCI). After excluding patients without a history of apo or glycosylated hemoglobin (HbA1c) on admission, 2,563 patients with known diabetes or HbA1c >6.5% were eligible for this study (Figure 1). The Institutional Review Board of our hospital approved the study protocol in accordance with
the Declaration of Helsinki (No. 2013-449), and written informed consent was obtained from all participants before the intervention.

**Measurements of Lipid Indices and Definition of Dyslipidemia**

Blood tests were carried out within 24 h after admission. The concentrations of apo were measured by using an immunoassay analyzer (Hitachi 7150, Tokyo, Japan); other relevant levels were also measured, including serum LDL-C, TC, TG, and high-density lipoprotein cholesterol (HDL-C); the methods used are described in other research. Other related laboratorial indexes were measured according to standard test protocols.

The distribution of lipid indices are described in the Supplementary Figure. We divided subjects into 2 groups according to the median value of the apoB/apoA-I ratio: <0.63 (n=1,279, 50.0%) and ≥0.63 (n=1,284, 50.0%).

Hyperlipidemia was considered when one or more of the following criteria were met: hypercholesterolemia, TC ≥6.2 mmol/L; hypertriglyceridemia, triglyceride ≥2.3 mmol/L; hyper-LDL-cholesterolemia, LDL-C ≥4.1 mmol/L; low-HDL-cholesterolemia, HDL-C <1.04 mmol/L; high-non-HDL-cholesterolemia, non-HDL cholesterol ≥2.7 mmol/L; history of MI or stroke; history of peripheral artery disease; and smoking.

### Table 1. Baseline Characteristics of Patients in the Low and High ApoB/ApoA-I Ratio Groups

|                        | Total (n=2,563) | Low ratio (n=1,279) | High ratio (n=1,284) | P value |
|------------------------|-----------------|---------------------|----------------------|---------|
| Age, years             | 59.6±10.0       | 60.9±9.8            | 58.3±10.2            | <0.001  |
| Male, n (%)            | 1,883 (73.5)    | 923 (72.2)          | 960 (74.8)           | 0.136   |
| BMI, kg/m²             | 26.3±3.1        | 26.1±3.2            | 26.4±3.1             | 0.003   |
| Hypertension           | 1,794 (70.0)    | 930 (72.7)          | 864 (70.2)           | 0.003   |
| Hypertension           | 1,841 (71.8)    | 912 (71.3)          | 929 (72.4)           | 0.556   |
| Hypertriglyceridemia   | 601 (23.4)      | 185 (14.4)          | 416 (32.5)           | <0.001  |
| Low-HDL-cholesterolemia| 262 (10.2)      | 77 (6.0)            | 185 (14.4)           | <0.001  |
| High-non-HDL-cholesterolemia | 258 (10.1) | 22 (1.7)            | 236 (18.4)           | <0.001  |
| Previous MI            | 394 (15.4)      | 208 (16.3)          | 186 (14.5)           | 0.212   |
| Previous stroke        | 330 (12.9)      | 167 (13.1)          | 163 (12.7)           | 0.784   |
| COPD                   | 64 (2.5)        | 37 (2.9)            | 27 (2.1)             | 0.200   |
| PAD                    | 71 (2.8)        | 50 (3.9)            | 21 (1.6)             | <0.001  |
| Smoking                | 1,452 (56.7)    | 685 (53.6)          | 767 (59.7)           | 0.002   |
| Presentation           |                |                     |                     | <0.001  |
| Acute MI               | 738 (28.8)      | 280 (21.9)          | 458 (35.7)           |         |
| Unstable angina        | 1,825 (71.2)    | 999 (78.1)          | 826 (64.3)           |         |
| WBC, ×10⁹/L            | 7.26±2.16       | 7.00±2.07           | 7.52±2.20            | <0.001  |
| Glucose, mmol/L        | 7.62±2.71       | 7.33±2.51           | 7.91±2.86            | <0.001  |
| HbA1c, %               | 7.65±1.37       | 7.5±1.3             | 7.8±1.4              | <0.001  |
| TC, mmol/L             | 4.23±1.08       | 3.74±0.87           | 4.71±1.06            | <0.001  |
| Total triglyceride, mmol/L | 1.92±1.21     | 1.64±1.10           | 2.20±1.25            | <0.001  |
| ApoB, g/L              | 0.86±0.25       | 0.70±0.15           | 1.02±0.23            | <0.001  |
| ApoA-I, g/L            | 1.33±0.25       | 1.41±0.26           | 1.24±0.20            | <0.001  |
| LDL-C, mmol/L          | 2.52±0.90       | 2.05±0.63           | 2.99±0.89            | <0.001  |
| HDL-C, mmol/L          | 1.00±0.28       | 1.08±0.30           | 0.92±0.22            | <0.001  |
| Creatinine, umol/L     | 76.20±17.86     | 75.20±16.81         | 77.20±18.80          | 0.005   |
| eGFR, ml/min/1.73m²    | 90±17           | 89±16               | 90±17                | 0.515   |
| LVEF <40%              | 38 (1.5)        | 14 (1.1)            | 24 (1.9)             | 0.105   |
| Left main disease      | 180 (7.0)       | 85 (6.6)            | 95 (7.4)             | 0.456   |
| Multivessel disease    | 2,039 (79.6)    | 1,011 (79.0)        | 1,028 (80.1)         | 0.524   |
| SYNTAX score           | 12±8            | 12±8                | 13±8                 | 0.008   |
| Number of stents >3    | 546 (21.3)      | 255 (19.9)          | 291 (22.7)           | 0.092   |
| Medicine at discharge  |                |                     |                     |         |
| Aspirin                | 2,530 (98.7)    | 1,261 (98.6)        | 1,269 (98.8)         | 0.591   |
| Clopidogrel            | 2,530 (98.7)    | 1,262 (98.7)        | 1,268 (98.8)         | 0.852   |
| β-blocker              | 2,330 (90.9)    | 1,149 (89.8)        | 1,181 (92.0)         | 0.059   |
| CCB                    | 1,352 (52.8)    | 697 (54.5)          | 655 (51.0)           | 0.077   |
| Statin                 | 2,453 (95.7)    | 1,223 (95.6)        | 1,230 (95.8)         | 0.829   |
| RAS inhibitor          | 1,513 (59.0)    | 754 (59.0)          | 759 (59.1)           | 0.934   |

Values are presented as mean±SD or n (%). Apo, apolipoprotein; BMI, body mass index; CCB, calcium channel blocker; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PAD, peripheral artery disease; RAS, renin-angiotensin system; SYNTAX, Synergy between percutaneous coronary intervention with TAXUS and Cardiac Surgery; TC, total cholesterol; WBC, white blood cell.
If PCI proceeded for longer than 1 h, an additional 1,000 U of heparin sodium was administered. Results of coronary angiography were interpreted by experienced cardiologists. More than 70% stenosis of vessels was an indication for stent implantation.

**SYNTAX score (SS)** was assessed by 2 of the 3 experienced cardiologists in an independent angiographic core laboratory; both cardiologists were blinded to clinical outcomes. A SS $\leq 22$ was considered as a low level, 23–32 as an intermediate level, and $\geq 33$ as a high level.

**Procedure and Medication**

The PCI strategy was left to the attending physicians’ assessments. All patients received aspirin 300 mg and clopidogrel (loading dose of 300 or 600 mg) as soon as possible before interventions. During the procedure, unfractionated heparin (100 U/kg) was administered to all patients, and glycoprotein IIb/IIIa inhibitors were used based on the healthcare practitioner’s discretion. If PCI proceeded for longer than 1 h, an additional 1,000 U of heparin sodium was administered. Results of coronary angiography were interpreted by experienced cardiologists. More than 70% stenosis of vessels was an indication for stent implantation.

**Follow up and Definition of Endpoints**

All patients were evaluated by clinical visit or by phone at 1, 3, 6, and 12 months, and annually thereafter through the

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**Table 2. Independent Predictors of Intermediate-High SYNTAX Score**

|                | OR   | 95% CI          | P value |
|----------------|------|-----------------|---------|
| **ApoB/apoA-I**|      |                 |         |
| Continuous variable | 1.007 | 1.001–1.012 | 0.026  |
| $\geq 0.63$     | 1.341 | 1.039–1.730 | 0.024  |
| Presence of acute MI | 1.442 | 1.105–1.882 | 0.007  |
| eGFR <60 mL/min/1.73 m$^2$ | 2.358 | 1.312–4.239 | 0.004  |

CI, confidence interval; OR, odds ratio. Other abbreviations as in Table 1.

**Table 3. Subgroups Analyses of Association Between ApoB/ApoA-I and SS**

| Subgroups | No. of patients with SS >22 (n, %) | HR (95% CI) | P value for interaction |
|-----------|-----------------------------------|-------------|------------------------|
| **Age (years)** |                                     |             |                        |
| <65       | 66/791 (8.3)                       | 1.511 (1.091–2.094) | 0.946                  |
| $\geq 65$ | 59/444 (13.3)                      | 1.153 (0.757–1.759) |                        |
| **Sex**   |                                     |             |                        |
| Male      | 86/890 (9.7)                       | 1.389 (1.205–1.602) | 0.916                  |
| Female    | 39/345 (11.4)                      | 1.109 (0.842–1.462) |                        |
| **TC (mmol/L)** |                                  |             |                        |
| $\leq 5.98$ | 124/1,216 (10.2)                   | 1.321 (1.016–1.718) | 0.794                  |
| $>5.98$   | 1/19 (5.3)                         | 3.094 (0.360–26.582) |                        |
| **LDL-C (mmol/L)** |                                |             |                        |
| $<1.8$    | 49/470 (10.4)                      | 0.797 (0.314–2.026) | 0.667                  |
| 1.8–2.59  | 51/553 (10.2)                      | 1.863 (1.234–2.814) |                        |
| $\geq 2.6$| 25/212 (12.1)                      | 1.122 (0.685–1.838) |                        |
| **HDL-C (mmol/L)** |                                |             |                        |
| $<0.7$    | 117/1,160 (10.1)                   | 1.312 (1.002–1.719) | 0.534                  |
| $\geq 0.7$| 8/75 (10.7)                        | 1.632 (0.678–3.925) |                        |
| **HbA1c (%)** |                                  |             |                        |
| $<6.5$%   | 15/157 (9.6)                       | 0.553 (0.189–1.617) | 0.138                  |
| $\geq 6.5$%| 110/1,078 (10.2)                   | 1.421 (1.088–1.855) |                        |
| **eGFR (mL/min/1.73 m$^2$)** |                             |             |                        |
| $<60$     | 108/1,167 (9.3)                    | 1.319 (1.006–1.729) | 0.908                  |
| $\geq 60$ | 17/68 (25.0)                       | 1.410 (0.639–3.114) |                        |

SS, SYNTAX score; HR, hazard ratio. Other abbreviations as in Tables 1, 2.

HDL-cholesterolemia, HDL-C $<0.7$ mmol/L (based on the standard of the center laboratory of hospital), or currently taking any lipid-lowering drug. High-non-HDL-cholesterolemia was defined as non-HDL (=TC-LDL-C) $\geq 4.6$ mmol/L.  

Procedure and Medication

The PCI strategy was left to the attending physicians’ assessments. All patients received aspirin 300 mg and clopidogrel (loading dose of 300 or 600 mg) as soon as possible before interventions. During the procedure, unfractionated heparin (100 U/kg) was administered to all patients, and glycoprotein IIb/IIIa inhibitors were used based on the healthcare practitioner’s discretion. If PCI proceeded for longer than 1 h, an additional 1,000 U of heparin sodium was administered. Results of coronary angiography were interpreted by experienced cardiologists. More than 70% stenosis of vessels was an indication for stent implantation.

SYNTAX score (SS) was assessed by 2 of the 3 experienced cardiologists in an independent angiographic core laboratory; both cardiologists were blinded to clinical outcomes. A SS $\leq 22$ was considered as a low level, 23–32 as an intermediate level, and $\geq 33$ as a high level.

Follow up and Definition of Endpoints

All patients were evaluated by clinical visit or by phone at 1, 3, 6, and 12 months, and annually thereafter through the
follow-up center of Fuwai Hospital. The endpoints were all-cause death and MI.5,6 MI was defined by the Third Universal Definition of myocardial infarction.

**Statistical Analyses**

Continuous variables were summarized as mean±standard deviation or median (P25, P75) and were compared using the Student’s t-test or ANOVA. Categorical variables were expressed as percentages (%) and were compared using chi-squared statistics or Fisher’s exact test as indicated. Spearman’s correlation was used when one or both of the indices were not normally distributed. Independent predictors for intermediate-high SS were determined by using multivariable logistic regression analysis. Kaplan-Meier curves and proportional regression analysis was used to compare long-term outcomes between the groups. Note that a 2-stage process instead of a log-rank test was valid to examine the difference between 2 crossing curves.17 Age, gender, body mass index, and confounders that were statistically significant in the univariate Cox analysis were incorporated in the multivariate Cox model, and results were shown as a hazard ratio and corresponding 95% confidence intervals. A 2-tailed P value of <0.05 was considered to be statistically significant. All of the analyses were performed with the SPSS Statistics version 20.0 (SPSS Inc., Chicago, IL, USA) and R software version 3.4.3 (R Core Team, Vienna, Austria).

**Results**

A total of 2,563 consecutive diabetic patients with ACS were evaluated in the present study. The average age was 60±10 years; 1,883 (73.5%) patients were male and 738 (28.8%) were presented with acute MI. Of 1,773 self-reported diabetic patients, 902 (50.9%) had taken antidiabetic medicine and 684 (38.6%) underwent insulin treatment. Figure 2 showed that apoB/apoA-I was moderately or strongly related with other lipid indices, and the strongest one was found between it and LDL/HDL (Spearman r=0.842, P<0.001).

Patients were divided into low and high ratio groups, as described above. Detailed baseline characteristics (e.g., demographic, clinical, laboratorial, and angiographical indices and medication) are presented in Table 1. Patients with high apoB/apoA-I were younger, had fewer hypertension and peripheral vascular diseases, but more commonly had disturbed lipid and glucose metabolism. Regarding angiographic characteristics, the high ratio group was associated with an increased presence of acute MI and intermediate-high SS. No difference was found in the medication taken between the groups.

None of the traditional lipid parameters or their ratios (non-HDL-C, LDL-C/HDL-C) were eligible for predicting SS in univariate logistic regression analysis (all P>0.05). A multivariate model showed that apoB/apoA-I ratio (as a categorical or a continuous variable), admission of acute MI, and estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m²) were independent factors of intermediate-high SS (Table 2). Moreover, subgroup analyses further revealed that there was no significant interaction of other covariates (age, sex, TC, LDL-C, HDL-C, HbA1c or eGFR) for apoB/apoA-I in the prediction of SS. The predictive ability of the apoB/apoA-I ratio was consistent in the subgroup with normal HDL-C, LDL-C or and TC levels (Table 3).

The median follow-up period was 878 (IQR 807, 939) days, and all subjects achieved at least 1-year follow up and 99.2% completed 2-year follow up. Overall, 43 (1.7%) patients died and 68 (2.7%) patients had MI, of which 41 occurred during the periprocedural period. Occurrences of periprocedural MI (1.0% vs. 2.2%, P=0.019) and total events of MI (2.0% vs. 3.3%, P=0.028) were significantly different between the low and the high ratio group, while all-cause deaths were comparable. Kaplan-Meier curves also supported the ongoing difference in MI between the groups (Figure 3). Moreover, a multivariable Cox proportional regression model showed that a high apoB/apoA-I ratio remained independently predictive of MI, the risks of which were increased by 1.4- and 1.2-fold during the periprocedural period and in the long term (Table 4). Of note, SS, apoA-I, apoB, and other traditional lipid parameters were not contributable to MI (all P values >0.05 in the univariate analyses).

**Discussion**

In the present study, we evaluated the predictive ability of baseline apoB/apoA-I ratio for the characteristics of coronary artery lesions, as well as long-term outcomes in a large cohort of diabetic patients admitted with ACS. The major findings of this study are as follows: (1) the apoB/apoA-I ratio was positively associated with complicated...
angiographical changes and shown to be an independent factor of intermediate-high SS; (2) predictions of lesion severity remained significant in patients with a low level of LDL-C; and (3) multivariable Cox regression model indicated that the apo ratio could predict recurrences of MI during the periprocedural period and in the long term.

It is well established that both diabetes mellitus and hyperlipidemia serve as major risk factors for atherosclerotic cardiovascular diseases.1,2,18,19 And these 2 comorbidities further worsen prognosis when following up patients diagnosed with ACS (e.g., death, MI, or other ischemic events). For this population at high ischemic risk, life-long, lipid-lowering therapy is commonly required to achieve a stricter LDL-C control.1,2,4 Nevertheless, the precise target level of lipid-lowering treatment is still inconclusive. Various studies have shown that even some patients with a LDL-C below 1.8 mmol/L had so-called residual risk for cardiovascular events, and it might be explained, in part, by the effects of TG and HDL-C or inflammatory status.20,21 Some studies thus considered other promising parameters for risk stratification and apo was acknowledged as an informative one.

Apo regulates the synthesis and metabolism of lipoprotein particles and stabilizes their structures. ApoB is present in very low-density lipoproteins, intermediate-density lipoproteins, large buoyant LDL and small dense LDL, which all have atherogenic potential.22 A growing body of research suggests that the retention of cholesterol-rich and triglyceride-rich apoB-containing remnant lipoproteins within the artery wall drives the process of atherosclerosis.24,25 ApoA-I is the primary functional component of HDL and can remove excess cholesterol from plaque.25,26 So, the ratio of apoB/apoA-I indicates the balance between pro-atherogenic and anti-atherogenic sides. A higher apo ratio means a higher level of circulating cholesterol and a higher chance of its deposition in the vessel wall.

The distribution of apo ratio varied markedly among diseases, ethnic groups and areas. In the AMORIS study, the mean apoB/apoA-I was 0.99 in men and 0.82 in women.5 Likewise, in the multinational INTERHEART study, the median value of apoB/apoA-I was 0.75, whereas it was 0.65 in the Chinese subgroup, which is similar to our data.6 It is important to note that the previous study tested the role of apo ratio in primary prevention whereas this one estimated secondary prevention in established ACS subjects. For now, the cut-off value is not uniform and confirmed. Some studies adopted the cut-off value of 0.9 for males and 0.8 for females.27–29 Considering a relatively lower lipid profile in the Chinese cohort, we simply used the median value of 0.63 as a threshold and also found significant disparity between low and high apo ratio groups. Therefore, the present study hinted that a stricter standard should be set for patients with established ACS and diabetes.

In agreement with several case-control studies, our results found that apo has greater predictive ability than the other traditional lipid parameters for MI, despite an apparently close correlation within them.6,7,30 The INTERHEART study demonstrated that the apoB/apoA-I ratio accounted for a 54% population-attributable risk of acute MI;6 however, only a few studies have mentioned the relativity with disease severity. Patel et al found apoA-I could discriminate atherosclerosis shown by coronary atheroma scores in stable coronary artery disease (CAD).31 Ohwada et al commented that both apoA-I and apoB were significantly associated with necrotic core volume.32 A study including 792 patients with angiographically defined CAD

| Table 4. Independent Predictors of Outcomes in Multivariate Cox Regression Analysis |
|---------------------------------------------|-----------|-----------|-----------|
| Death                                      | HR   | 95% CI    | P value   |
| Age                                        | 1.093 | 1.055–1.133| <0.001    |
| LVEF <40%                                  | 3.259 | 1.154–9.784| 0.026     |
| WBC                                        | 1.169 | 1.043–1.311| 0.007     |
| MI                                         |       |           |           |
| High apoB/apoA-I                           | 2.219 | 1.144–4.304| 0.018     |
| Number of stents                           | 1.232 | 1.040–1.460| 0.016     |
| Fasting glucose                            | 1.086 | 1.010–1.168| 0.025     |
| eGFR <60 mL/min/1.73 m²                    | 2.599 | 1.215–5.560| 0.014     |
| Periprocedural MI                          |       |           |           |
| High apoB/apoA-I                           | 2.410 | 1.015–5.725| 0.046     |
| Number of stents                           | 1.317 | 1.074–1.616| 0.008     |

Abbreviations as in Tables 1–3.
showed that the apoB100/apoA-I ratio was the only independent lipid marker for the Gensini scores and the number of stenotic vessels. SS is an anatomical risk score used to calculate the degree, extension, complexity, and severity of coronary artery lesions. It has been recommended for treatment decision and risk prediction, particularly in patients with complicated characteristics (e.g., left main coronary artery involvement, multivessel diseases or diabetes). To the best of our knowledge, this study was the first to explain the correlation between apo ratio and SS in ACS, and also finding evidence about the involvement of apo in the atherosclerotic progression in the context of plaque instability. Moreover, subgroup analyses further demonstrated the indicative value of the apoB/apoA-I ratio for severe angiographic findings, mostly because of its prominent effect in patients without abnormality of other lipid indices. These observations might result from different scenarios: (1) apoB exists in atherogenic particles, not just LDL alone. And apo-A-I accounts for ~70% of total HDL, indicating functionality of HDL. Consequently, the apo ratio appears to be associated more with lipoprotein abnormalities. (2) A standardized, direct test of apo values with no requirement of fasting blood samples favors it from a methodological aspect. Furthermore, it gave a glimpse into the complex mechanistic interactions within inflammation, lipid and glucose metabolism, even under normal cholesterol levels, as depicted by a conventional lipid profile; this will require further investigation.

Previous studies have specified the relationship of on-treatment levels of apo or its ratio with outcomes in patients receiving statin therapy. We provided additional evidence that baseline apoB/apoA-I ratio could also strongly associated with both short- and long-term MI recurrences; while other lipid parameters could not. As described above, apo elements have an effect on MI initiation and aggravation. Therefore, a high apo ratio suggests ongoing and unstable atherosclerotic progression and this might be superior for providing comprehensive information of lipid status in the long term.

Recently, CSL112, a recombinant apoA-I, has been assessed for its safety and efficacy in MI management. Whether apo or its ratio can be introduced or even replace LDL-C as the pivotal treating target for the secondary prevention of ACS is still yet to be clarified. Future research of novel medication directly for apo mediation, especially in well-organized randomized controlled trials, might extend the knowledge of the lipid profile.

Study Limitations

There are several limitations of our study that need to be considered. First, we conducted a retrospective analysis based on a prospective, single-center observational study. Some inherent biases therefore affected the statistical power, although some deviations related to different centers’ and operators’ experience were reduced in the results from other studies. Second, the fact that the rate of future events was relatively lower requires cautious interpretation. Various explanations are possible, and include: (1) drug-eluting stents and other procedural advancement; (2) a rather “low risk” profile of subjects (namely, lower prevalence of severe comorbidities, cardiac arrest, and SS >32); and (3) under-reported MI resulting from insufficient medical records. Finally, a lack of records of pre-hospital statin or fibrates use in those with dyslipidemia, and long-term compliance after discharge might affect the results.

Conclusions

Baseline apoB/apoA-I ratio could contribute to differentiating high-risk patients with complicated and severe lesions as well as MI during short- and long-term follow-up periods, particularly when LDL-C is at a normal level.

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Conflicts of Interest

None.

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Supplementary Files

Please find supplementary file(s): http://dx.doi.org/10.1253/circj.C3-19-1097