



# Is the ratio of apoB/apoA-1 the best predictor for the severity of coronary artery lesions in Chinese diabetics with stable angina pectoris? An assessment based on Gensini scores

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## Abstract

**Background** There is a paucity of data about the best lipid ratio predicting the severity of coronary artery disease (CAD) in patients with diabetes mellitus. We determined the relationship between five conventional lipid ratios and the extent of coronary artery lesions in Chinese Type 2 diabetics with stable angina pectoris (SAP). **Methods** A prospective cohort study within 373 type 2 diabetic patients diagnosed with stable CAD by coronary angiography was performed. All patients were classified into three groups according to the tertiles of Gensini scores (GS, low group < 8 points  $n = 143$ ; intermediate group 8–28 points,  $n = 109$ ; high group > 28 points,  $n = 121$ ). Association between the ratios of apolipoprotein (apo) B and apoA-1, total cholesterol and high density lipoprotein cholesterol (TC/HDL-C), triglycerides and HDL-C (TG/HDL-C), low density lipoprotein cholesterol and HDL-C (LDL-C/HDL-C), Non-HDL-C/HDL-C and GS were evaluated using the receivers operating characteristic (ROC) curves and multivariate logistic regression models. **Results** The ratio of apoB/apoA-1, TC/HDL-C, LDL-C/HDL-C, and Non-HDL-C/HDL-C were correlated with Gensini scores. Area under the ROC curves for predicting high Gensini scores in the ratios of apoB/apoA-1, TC/HDL-C, LDL-C/HDL-C and Non-HDL-C/HDL-C were 0.62, 0.60, 0.59 and 0.60, respectively ( $P < 0.005$  for all). According to multivariate logistic regression analysis after adjusted with demographic characteristic and other lipid parameters, the ratio of apoB/apoA-1 is qualified as an independent discriminator for the severity of CAD. However, after further adjusting different baseline variables, such as left ventricular ejective fraction, hemoglobin A1c, leukocytes count and serum creatinine, none of the above lipid ratios remained. **Conclusions** Compared with other lipid parameters, the ratio of apoB/apoA-1 appears to be more significantly correlated with the extent of coronary artery lesions in Chinese diabetics, but it was not an independent predictor in these settings.

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**Keywords:** Coronary artery disease; Diabetic mellitus; Gensini scores; Lipid disorder

## 1 Introduction

Abundant evidence has shown that dyslipidemia participates in both initiation and perpetuation of atherosclerotic disease and coronary artery disease (CAD).<sup>[1–4]</sup> And Type 2 diabetic mellitus (DM) is widely regarded as a risk equivalent of CAD.<sup>[5]</sup> Therefore, it is important to screen a distinguishing complex of lipid parameters or lipid ratios which can best identify high risk populations simultaneously experiencing CAD and Type 2 DM.<sup>[6]</sup> Several prospective observations provided striking evidence about the clinical

significance of lipid ratios such as the ratio of apolipoprotein (apo) B and apoA-1 (apoB/apoA-1); total cholesterol and high density lipoprotein cholesterol (TC/HDL-C); low density lipoprotein cholesterol and HDL-C (LDL-C/HDL-C); triglycerides and HDL-C (TG/HDL-C); non-HDL-C and HDL-C.<sup>[7–13]</sup> Among these lipid ratios, the ratio of apoB and apoA-1, an indicator for the balance between atherogenic and atheroprotective cholesterol transport, as well as insulin resistance, was superior to any other lipid parameters for accurately and effectively predicting the cardiovascular risk, or adverse cardiac events. Moreover, combined use of high sensitivity C-reactive protein (hs-CRP) and ratio was regarded as a stronger predictor of the severity of CAD and abnormal glucose metabolism than its individual components in patients with normal fasting glucose.<sup>[14]</sup> Although TC, LDL-C, and apoB levels were comparable between some ethnic population such as African-Americans

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and Caucasians, the associations of these parameters with allele specific apoA levels, or ratios of apoB and apoA might be different across ethnicities.<sup>[15,16]</sup>

Nonetheless, whether and which ratio of lipids is the best and independent indicator for the extent of CAD in Chinese population with DM remains unknown. Therefore, the aim of the current study is to prospectively examine the association of lipid ratios and severity of CAD by the Gensini Scoring system in these settings.

## 2 Methods

### 2.1 Study design and population

The study complied with the Declaration of Helsinki and was approved by the hospital ethnic review board. Written informed consent was obtained from all of the patients included in this study.

Between June 2011 and March 2012, we consecutively enrolled 373 women and men (70.2%) aged from 31 to 79 years (average age 58.7 years) at our institute. All of the patients were diagnosed with type 2 DM and typical stable angina pectoris (SAP). Patients with type 1 DM, acute coronary artery syndrome (ACS), significant hematologic disorders (leukocytes count  $3.5 \times 10^9/L$  or  $\geq 20 \times 10^9/L$ ), infectious or inflammatory disease, and severe liver and/or renal insufficiency were excluded from the study. All subjects enrolled in the study underwent detailed clinical, hematologic and angiographic examination for assessment of the cardiac status and were asked for their present and past history about traditional risk factors of CAD, such as smoking habits, hypertension, hyperlipidemia, obesity, DM, previous stroke, peripheral vascular disease, family history of CAD and non-cardiovascular diseases.

Hypertension was defined as repeated (at least two times in different circumstances) blood pressure measurements  $\geq 140/90$  mmHg and was assumed to be present in patients taking anti-hypertensive drugs. Diagnosis of DM and differential diagnosis of type 1 and type 2 DM were based on ADA guidelines.<sup>[17]</sup> DM was diagnosed in patients with fasting serum glucose levels of 7.0 mmol/L in multiple determinations, or under active treatment with insulin or oral hypoglycemic agents. The differentiation of type 1 and type 2 DM was carried out by multiple elements, such as the age of onset, history of ketosis, concentration of insulin, curves of insulin release, and clinical manifestation. Hyperlipidemia was defined as TC concentrations of  $\geq 5.2$  mmol/L or TG concentrations of  $\geq 1.7$  mmol/L.

The angina pectoris conformed to Canadian Cardiovascular Society of grade I-III and excluded from ACS was diagnosed as SAP. The indications for coronary angiography are in accordance with the ACC/AHA guidelines for

CAG.<sup>[18]</sup> CAD was defined as the presence of significant obstructive stenosis, at least 50% of the vessel lumen diameter, in any of the main coronary arteries by at least two independent senior interventional cardiologists based on quantity coronary angiography (QCA). The severity of CAD was represented by the Gensini Scoring system.<sup>[19]</sup> In general, the extent of stenosis and the values of Gensini scores (GS) by QCA are conducted at least twice by the cardiologists and the average values are taken in order to avoid the inter-observer variability as much as possible. The left ventricular ejection fraction (LVEF) was evaluated by an echocardiographer using the area-length methods with modified Simpson's rule.

### 2.2 Measurements of biomarkers

Venous blood samples were obtained from each patient at baseline upon admission. TC and TG were measured by enzymatic methods and HDL-C by a direct method (Roche Diagnostics, Basel, Switzerland). LDL-C was obtained by Friedewald's formula (if fasting, triglycerides  $< 3.39$  mmol/L), or by ultracentrifugation. ApoB and apoA-1 were measured using an immunoturbidimetric method (Tinaquant; Roche Diagnostics) calibrated against the World Health Organization/International Federation of Clinical Chemistry reference standard SP3-07. Hemoglobin A1c (HbA1c) concentrations were measured using a Tosoh G7 Automate HPLC Analyzer (TOSOH Bioscience, Japan). All other included biomarkers were analyzed by standard hematological and biochemical tests.

### 2.3 Statistical analysis

Quantitative variables were expressed as mean  $\pm$  SD, and qualitative variables were expressed as numbers and percentages. Continuous variables and categorical variables were analyzed by the Kruskal-Wallis test, Chi-squared statistical tests, or Student's *t*-test when appropriate. The association between variables was examined using Spearman and Pearson correlation coefficient, when appropriate. Receiver operating characteristic (ROC) curves were constructed at the most discriminating cut-off values aimed to document the predictive power of the studied ratios of various lipid parameters for high GS. Based on the tertiles of GS, the enrolled patients were classified into three groups (low group  $< 8$  points,  $n = 143$ ; intermediate group 8-28 points,  $n = 109$ ; high group 28 points,  $n = 121$ ). The Kruskal-Wallis tests, or one-way analysis of variance tests, were used to compare three groups. Predictive ability for the studied ratios of lipid parameters for high GS was carried out by binary logistic regression models using forward stepwise selection process. A *P* value of less than 0.05 was considered as statistical significance. Statistical studies were

carried out with the SPSS program (version 19.0, SPSS, Chicago, Illinois, USA).

### 3 Results

#### 3.1 Baseline characteristics

The study consisted of 373 type 2 diabetic patients of

Chinese Han referred to CAG with an average age of  $58.7 \pm 9.6$  years (range: 31 to 79) due to typical SAP. The baseline characteristics and laboratory findings of the population by the tertiles of GS (low group < 8 points,  $n = 143$ ; intermediate group 8-28 points,  $n = 109$ ; high group > 28 points,  $n = 121$ ) were summarized in Table 1. In brief, patients with higher GS were accompanied with lower HDL-C and LVEF,

**Table 1. Baseline characteristics according to the tertiles of Gensini scores**

Variables	Low (< 8; $n = 143$ )	Intermediate (8-28; $n = 109$ )	High (> 28; $n = 121$ )	<sup>a</sup> <i>P</i> -value for trend	<sup>b</sup> <i>P</i> -value
<b>Risk factors</b>					
Age, yr	56.7 ± 9.9	60.0 ± 9.4	59.8 ± 8.9	0.008	0.121
Male gender	94 (65.7)	78 (71.6)	90 (74.4)	0.291	0.226
BMI (kg/m <sup>2</sup> )	25.7 ± 3.3	24.9 ± 2.8	25.7 ± 3.0	0.120	0.447
Current smoking	68 (47.6)	59 (54.1)	70 (57.9)	0.235	0.121
Hypertension	85 (59.4)	77 (70.6)	82 (67.8)	0.145	0.508
Hyperlipidemia	100 (69.9)	88 (80.7)	99 (81.8)	0.039	0.177
PVD	3 (2.1)	3 (2.8)	2 (1.7)	0.847	0.650
Prior stroke	6 (4.2)	3 (2.8)	6 (5.0)	0.690	0.523
Family history of CAD	7 (4.9)	13 (11.9)	17 (14.0)	0.033	0.064
<b>Laboratory test</b>					
LVEF (%)	62.8 ± 7.7	63.1 ± 7.4	60.2 ± 9.5	0.014	0.003
Leukocyte (10 <sup>9</sup> /L)	6.3 ± 1.5	6.2 ± 1.6	6.8 ± 1.5	0.003	0.001
Platelet count (10 <sup>9</sup> /L)	204.5 ± 60.4	192.0 ± 45.8	206.5 ± 55.4	0.098	0.224
Hemoglobin (g/L)	139.4 ± 15.2	138.3 ± 15.6	137.1 ± 15.6	0.505	0.305
HbA1c (%)	6.4 ± 1.2	6.9 ± 1.6	7.0 ± 1.3	0.000	0.004
FBG	5.6 ± 1.6	6.4 ± 2.7	6.2 ± 1.9	0.009	0.253
AST (IU/L)	19.4 ± 13.3	18.5 ± 9.2	17.4 ± 10.0	0.342	0.185
ALT (IU/L)	31.2 ± 33.3	29.7 ± 21.9	28.7 ± 25.1	0.772	0.554
Creatinine	73.8 ± 15.0	75.6 ± 16.4	78.6 ± 14.9	0.041	0.019
<b>Lipid profile</b>					
TG (mmol/L)	1.7 ± 1.0	1.7 ± 0.8	1.8 ± 1.1	0.434	0.230
TC (mmol/L)	4.0 ± 1.0	4.0 ± 0.9	4.1 ± 1.1	0.572	0.360
LDL-C (mmol/L)	2.3 ± 0.9	2.4 ± 0.8	2.5 ± 0.9	0.292	0.121
HDL-C (mmol/L)	1.1 ± 0.3	1.1 ± 0.3	1.0 ± 0.2	0.011	0.009
Lipoprotein (a) (mg/L)	237.7 ± 217.5	190.9 ± 211.2	289.7 ± 283.6	0.008	0.007
ApoA (g/L)	1.4 ± 0.3	1.5 ± 0.3	1.4 ± 0.3	0.012	0.057
ApoB (g/L)	1.0 ± 0.3	1.0 ± 0.3	1.1 ± 0.3	0.045	0.015
ApoB/apoA	0.7 ± 0.2	0.7 ± 0.2	0.8 ± 0.2	0.006	0.002
TC/HDL-C	3.8 ± 1.1	3.7 ± 1.0	4.1 ± 1.1	0.023	0.009
TG/HDL-C	1.7 ± 1.5	1.7 ± 1.0	1.9 ± 1.5	0.300	0.133
LDL-C/HDL-C	2.2 ± 0.9	2.2 ± 0.8	2.4 ± 0.8	0.029	0.009
Non-HDL-C/HDL-C	2.8 ± 1.1	2.7 ± 1.0	3.0 ± 1.1	0.023	0.009
<b>Prior treatment</b>					
Aspirin	136 (95.1)	106 (97.2)	118 (97.5)	0.501	0.463
Beta-blocker	103 (72.0)	87 (79.8)	109 (90.1)	0.001	0.001
ACE-I/ARB	27 (18.9)	22 (20.2)	44 (36.4)	0.002	0.000
Statin	125 (87.4)	109 (100)	116 (95.9)	0.000	0.258

Data are presented as mean ± SD or  $n$  (%). <sup>a</sup>*P*-value obtained from analysis of variance, Kruskal-Wallis test, or chi-squared test; <sup>b</sup>*P*-value for high GS versus non-high (low and intermediate) GS. ACE-I: angiotensin converting enzyme inhibitors; ALT: alanine aminotransferase; ApoA-1: apolipoprotein A-1; ApoB: apolipoprotein B; ARB: angiotensin receptor blocker; AST: aspartate aminotransferase; BMI: body mass index; CAD: coronary artery disease; FBG: fasting blood glucose; GS: Gensini score; HbA1c: hemoglobinA1c; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; Non-HDL-C: TC subtracted to HDL-C; PVD: peripheral vascular disease; TC: total cholesterol; TC/HDL-C: ratio of TC to HDL-C; TG: triglycerides.

but higher values of lipoprotein (a), HbA1c, leukocytes and serum creatinine. Specifically, the ratios of apoB/apoA-1, TC/HDL-C, LDL-C/HDL-C and Non-HDL-C/HDL-C were unbalanced both by trend analysis of the three groups and comparison tested for the groups of high GS and low-intermediate GS.

### 3.2 Correlation between the lipid ratios and GS

To explore the relationship of the studied lipid ratios and GS system in diabetic patients, correlation analysis was performed by Pearson analysis (or Spearman's correlation when appropriate) in the present study (Figure 1). According to Pearson's correlation, the ratios of apoB/apoA-1, TC/HDL-C, LDL-C/HDL-C and Non-HDL-C/HDL-C were correlated with GS [correlation coefficient ( $r$ ) was 0.16, 0.14, 0.14 and 0.14, respectively,  $P < 0.005$  for all]. Meanwhile, as shown in Figure 2, there were significant differences between lipid ratios (including the apoB/apoA-1, TC/HDL-C, LDL-C/HDL-C, Non-HDL-C/HDL-C) and the tertiles of GS (test for trend,  $P = 0.006, 0.023, 0.029,$  and  $0.023,$  respectively).

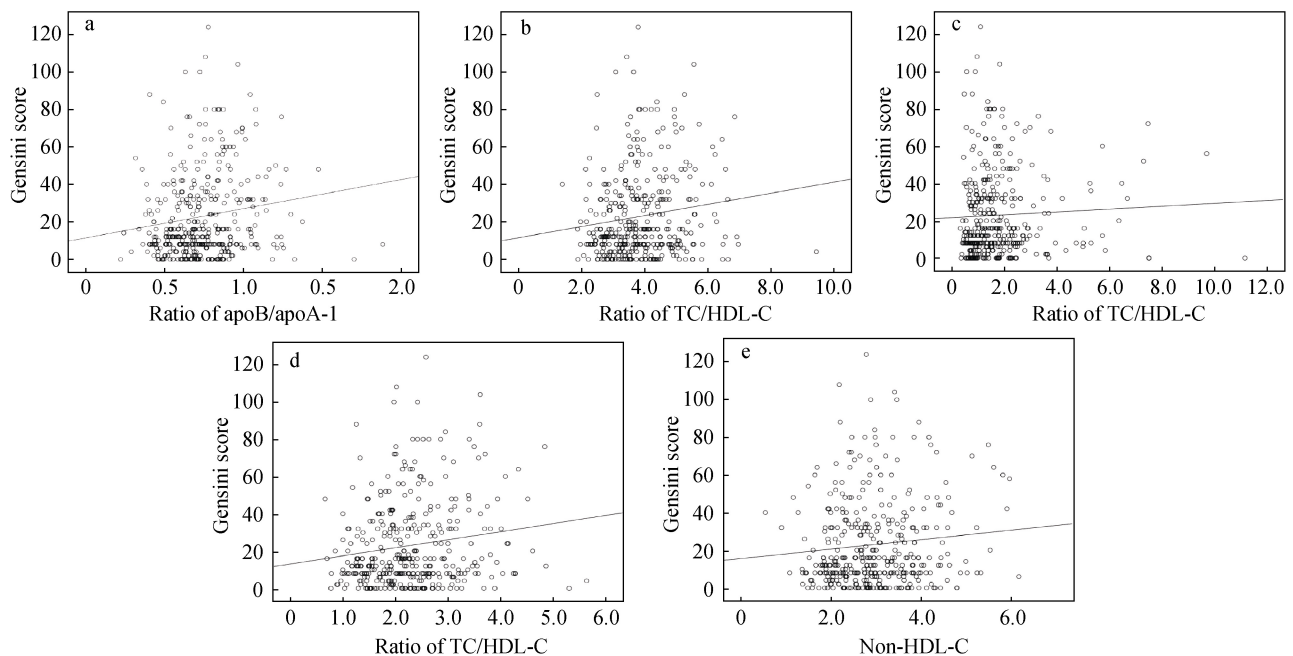
### 3.3 Utility of lipid ratios for predicting the presence and severity of CAD

Area under the ROC curves (AUC) also indicated robust discriminatory power of the ratios of apoB/apoA-1, TC/HDL-C, LDL-C/HDL-C and Non-HDL-C/HDL-C

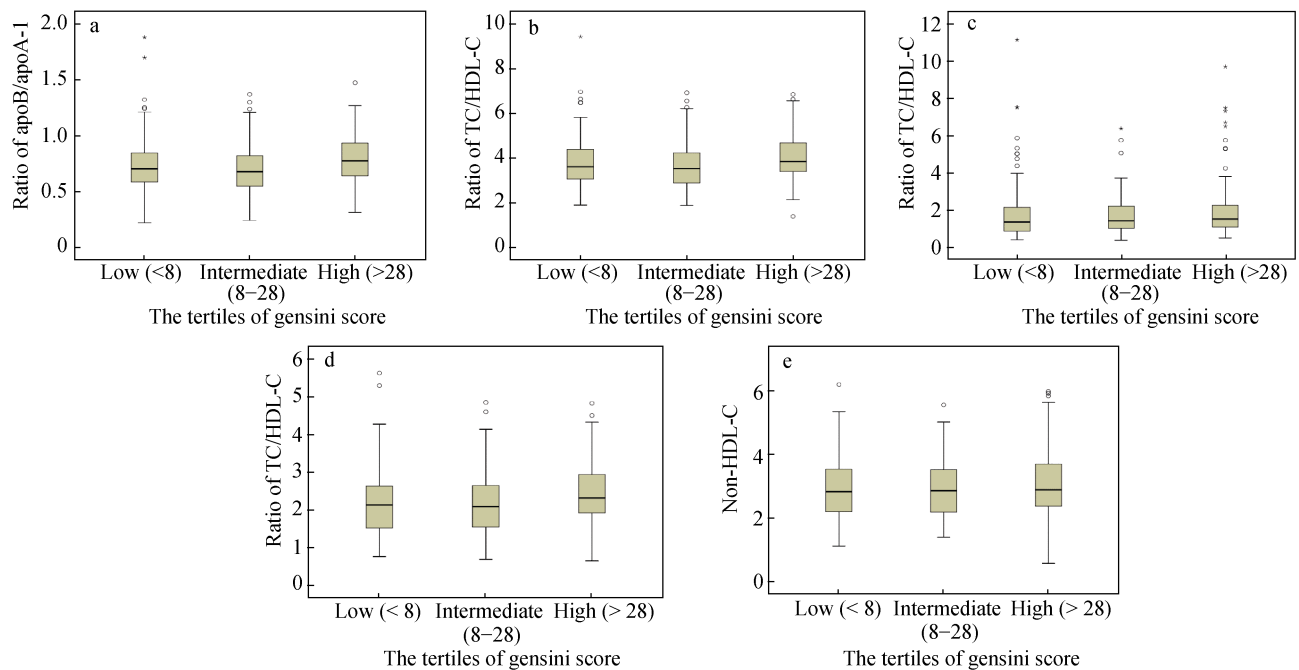
(AUC = 0.62, 0.60, 0.59 and 0.60, respectively,  $P < 0.005$  for all) for high GS ( $> 28$  points) in type 2 diabetics (Table 2 and Figure 3). As showed in Table 3, after adjusting with gender, age, BMI, TC, TG, LDL-C, HDL-C, ratio of TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, and non-HDL-C/HDL-C, multivariate logistic regression Model 1 suggested that the ratio of apoB/apoA-1 was an independent indicator for high GS in Chinese diabetics (OR = 4.05, 95% CI: 1.52-10.82,  $P = 0.005$ ). However, as shown in Model 2, none of the studied lipid ratios were an independent predictor for the extent of CAD after further adjusted with potential confounding variables in baseline characteristics, such as LV-EF, HbA1c, leukocytes count, and serum creatinine.

## 4 Discussion

According to prior investigations, some of lipid ratios might be better than routinely used lipid parameters and associated with an increased risk of CAD, or adverse outcome in CAD patients, or apparently healthy person with and without DM.<sup>[2,7,12,20-22]</sup> A case in point is the evidence from Japanese diabetic patients which indicated that the ratio of TC/HDL-C and non-HDL-C was the best lipid predictor for the presence of CAD. Although there is somewhat heterogeneity about race and gender, several studies have demonstrated that concurrence of high levels of fasting TG



**Figure 1.** Scatter diagrams indicated the correlation of studied lipid ratios and Gensini scores. ApoA-1: apolipoprotein A-1; apoB: apolipoprotein B; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.



**Figure 2.** The studied lipid ratios according to the tertiles of Gensini scores. ApoA-1: apolipoprotein A-1; apoB: apolipoprotein B; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.

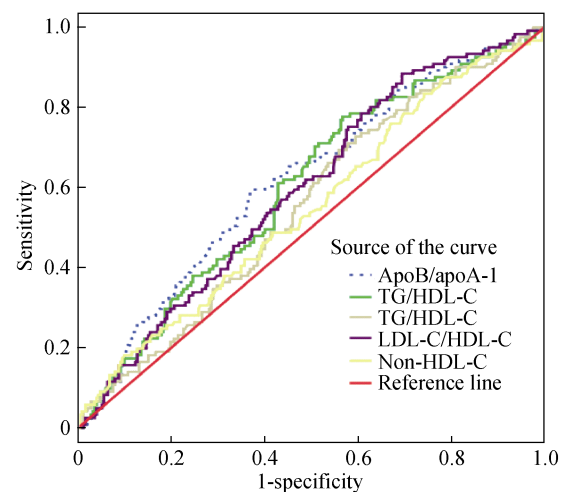
**Table 2.** Comparison of AUC among lipid profiles for predicting the severity of coronary artery lesions in the study population.

Variables	AUC	95% CI	P-value
TG	0.53	0.46–0.59	0.403
TC	0.52	0.46–0.58	0.539
LDL-C	0.55	0.48–0.61	0.142
HDL-C	0.41	0.34–0.47	0.003
Lipoprotein (a)	0.57	0.51–0.63	0.024
ApoA	0.42	0.36–0.49	0.017
ApoB	0.57	0.51–0.64	0.022
ApoB/apoA	0.62	0.56–0.68	0.000
TC/HDL-C	0.60	0.54–0.66	0.002
TG/HDL-C	0.56	0.49–0.62	0.083
LDL-C/HDL-C	0.59	0.54–0.66	0.003
Non-HDL-C/HDL-C	0.60	0.54–0.66	0.002

ApoA-1: apolipoprotein A-1; apoB: apolipoprotein B; AUC: area of receivers operating characteristic curves; HDL-C: high density lipoprotein cholesterol; hs-CRP: high sensitivity C-reactive protein; LDL-C: low density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.

and low levels of HDL-C, generally expressed as the TG/HDL-C index, are associated with insulin resistance (IR), or glucose metabolic intolerance.<sup>[23,24]</sup> Similarly, a large sample size of retrospective cohort from Asia recently suggested that non-HDL-C/HDL-C was a better predictor for metabolic syndrome and IR, when directly compared with the

ratio of apoB/apoA-1.<sup>[25]</sup> However, evidence also showed that the apoB/apoA-1 ratio was better than other cholesterol-related ratios to estimate the balance between proatherogenic and antiatherogenic lipoproteins, and to assess the coronary risk, or the adequacy of statin therapy.<sup>[26]</sup> Besides, previous studies suggested that the apoB/apoA-1 ratio



**Figure 3.** ROC curves show the discriminatory power of the studied lipid ratio on high Gensini scores. ApoA-1: apolipoprotein A-1; apoB: apolipoprotein B; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; ROC curves: receiver operating characteristic curves; TG: triglycerides.

**Table 3. Univariate and multivariate logistic regression analysis to determine the independent predictor for high Gensini scores.**

Variables	Univariate		Multivariate	
	OR (95%CI)	P-value	OR (95% CI)	P-value
Model 1				
ApoB/apoA	4.41 (1.67–11.7)	0.003	4.05 (1.52–10.82)	0.005
Lipoprotein (a)	1.00 (1.00–1.00)	0.008	1.00 (1.00–1.00)	0.015
Model 2				
LVEF	0.96 (0.94–0.99)	0.004	0.97 (0.94–0.99)	0.010
HDL-C	0.32 (0.13–0.76)	0.010	0.38 (0.15–0.94)	0.036
Lipoprotein (a)	1.00 (1.00–1.00)	0.008	1.00 (1.00–1.00)	0.011
HbA1c	1.24 (1.07–1.44)	0.005	1.23 (1.05–1.44)	0.011
Leukocytes	1.28 (1.10–1.47)	0.001	1.19 (1.02–1.38)	0.023

Model 1 adjusted for gender, age, BMI, TC, TG, LDL-C, HDL-C, TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, and non-HDL-C/HDL-C. Model 2 adjusted for gender, age, BMI, apoB/apoA, TC/HDL-C, LDL-C/HDL-C, non-HDL-C/HDL-C, and serum creatinine. ApoA-1: apolipoprotein A-1; ApoB: apolipoprotein B; BMI: body mass index; CI: confidential interval. HbA1c: hemoglobinA1c; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; OR: odds ratio; TC: total cholesterol; TG: triglycerides.

was an independent risk factor for CAD and superior to any of the lipid ratios.<sup>[27]</sup> For instance, data from Indian patients of acute myocardial infarction (AMI) demonstrated that the ratio of apoB/apoA-1 was a discriminator for CAD risk better than other conventional lipid ratios, including the ratio of TC/HDL-C, Non-HDL-C/HDL-C and LDL-C/HDL-C.<sup>[13]</sup> Meanwhile, the Apoprotein-related Mortality Risk (AMORIS) cohort with 94,667 men and 75,675 women directly compared the ratio of TC/HDL-C and apoB/apoA-1 to estimate the lipoprotein-related risk of vascular disease. The authors concluded that the apoB/apoA-1 ratio, both in men and women, was better than any of the conventional lipid ratios in these settings.<sup>[28]</sup> Thus, the ratio of apoB/apoA has been widely utilized as a marker to predict the risk of CAD with and without DM.

The current analysis focused on the role of lipid ratio in predicting the severity of CAD in Chinese Han with type 2 diabetics and provided the following vital information. First, according to baseline characteristics, diabetic patients with high GS (> 28 points) showed with lower LVEF and HDL-C, but higher HbA1c, serum creatinine, and leukocytes count, conforming with the features simultaneously accompanied with DM and CAD. Second, admission information also indicated that the absolute ratios of apoB/apoA-1 for the study population (involved in totally Chinese Han) were significantly lower than Americans, Indians, Iranians, and Canadians, but higher in the at-risk cutoff values of 0.64.<sup>[13,20,27–30]</sup> Third, we compared the association of the apoB/apoA-1 and other lipid ratios with GS. In partially agreement with previous studies, as shown in ROC curves and box graphs, our data further demonstrated that the ratio of apoB/apoA-1 might confer as the best discriminator for the severity of CAD in diabetic patients.<sup>[13,31]</sup> However, inconsistent with early investigations and after

adjusting potential confounders, none of the included lipid ratios remained as an independent predictor for high GS.<sup>[13,32]</sup> Apparently, the present study not only confirmed the previous studies, but also provided valid information concerning the role of lipid ratios on predicting the extent of CAD in diabetics.

Patient-based studies and case-controlled trials have suggested that the ratio of apoB/apoA-1 predicts cardiovascular risk more accurately and effectively than the use of either apoB or apoA alone, or any other of the lipid indexes.<sup>[7, 33–35]</sup> Regarding the basic data of our study, the higher ratios of apoB/apoA-1 were associated with, more severe the CAD would be when assessed with GS. This might indicate that occurrences of DM combined with elevated apoB/apoA ratios synergistically increased the risk for CAD.<sup>[33]</sup> Subsequently, the diagnostic analysis by ROC curves suggested that the ratio of apoB/apoA-1 surpassed all other ratios including TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, and Non-HDL-C/HDL-C, and qualified as a most powerful discriminator for the high degree of CAD in these settings. A study of India diabetic patients also suggested that the ratio of apoB and apoA provided better information regarding the risk of CAD in diabetic patients.<sup>[34]</sup> Besides, data from high risk CAD of South Korea indicated that apoB/apoA-1 ratio was the only variable that differentiated the patients with CAD from those without CAD and provides additional information supplied by traditional lipid risk factors.<sup>[9]</sup> Rasouli and his colleagues initially assessed the clinical significance of apoB/apoA-1 in patient with stable CAD. The results demonstrated that the ratio of apoB/apoA-1 was an independent risk factor for CAD and superior to any of the cholesterol-related ratios (AUC = 0.71,  $P = 0.0001$ ).<sup>[27]</sup> Furthermore, evidence from epidemiological studies suggested that the apoB/apoA-1 ratio was an

independent predictor for high risk of AMI in the future.<sup>[33,35]</sup> A large, standardized case-control study of AMI in 12,461 cases and 14,637 age-matched, and gender-matched controls in 52 countries confirmed that the non-fasting apoB/apoA-1 ratio was superior to any of the cholesterol-related ratios for estimated risk of AMI in all ethnic groups, both sexes, and all ages. Thus, the authors recommended that the ratio of apoB/apoA-1 should be introduced into worldwide clinical practice.<sup>[33]</sup> Apparently, current data from Chinese patients with type 2 DM supported the hypothesis that the apoB/apoA-1 ratio might be better than any of the other lipid ratios.

Despite the fact that the apoB/apoA-1 ratio qualified as an independent discriminator for the severity of CAD in diabetic patients after adjusting with basic demographic characteristic and other lipid parameters, the ratio failed to be an independent predictor after further adjusting with other potent variables, such as HbA1c, leukocytes count and serum creatinine. The underlying hypothesis of the results most likely consisted in three aspects. First of all, the ethnic difference and sample size of the present study might have some potential impacts on it. More importantly, the apoB/apoA-1 ratio yielded to traditional risk factors and confounding factors in this ethnic setting, as well as the extensive and intensive administration of statins in the study population.<sup>[3,7,13]</sup> Finally, evidence from the AIM-HIGH (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglyceride and Impact on Global Health Outcomes) trial suggested that the decreased ratios of apoB/apoA-1 to 19% and one year on potent medicine treatment did not lead to a reduction of adverse cardiac events.<sup>[34]</sup> Nonetheless, a high ratio of apoB/apoA-1 stands for an increased risk of CAD in diabetics of the current population and thus, it was important to bring it into clinical therapeutic targets.<sup>[35]</sup>

Although this was the first study on type 2 diabetic patients of Chinese Han to determine whether and which lipid ratios could be the best predictor for the severity of CAD, limitations of the present study were obvious. Above all, this was a relatively small sample size from an observational, and single center study, and thus it was subjected to various unaccounted confounders inherent in such an analysis. Moreover, as sample size is limited, the current cohort population might be unable to represent Chinese Han diabetics totally. Besides, we failed to directly compare the usefulness of all lipid ratios for predicting the severity of CAD with diabetic patients in different races and genders in Chinese native population.

In conclusion, compared with other lipid parameters, the ratio of apoB/apoA-1 appeared to be more significantly

correlated with the extent of coronary artery lesions in Chinese diabetics, but it was not an independent predictor in these settings.

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