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The atherogenic index of plasma is a strong and independent predictor for coronary artery disease in the Chinese Han population

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Abstract

Dyslipidemia is one of the most important factors for coronary artery disease (CAD). The atherogenic index of plasma (AIP), a new comprehensive lipid index, might be a strong marker for predicting the risk of CAD.

A hospital-based case-control study including 2936 CAD patients and 2451 controls was conducted in a Chinese population. Traditional lipid parameters were detected, and nontraditional lipid comprehensive indexes were calculated.

Compared with controls, CAD patients had higher levels of total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C). By contrast, the level of high-density lipoprotein cholesterol (HDL-C) was lower in CAD patients. The values of nontraditional lipid profiles, including non-HDL-C, TC/HDL-C, LDL-C/HDL-C, non-HDL-C/HDL-C (atherogenic index, AI), TC*TG*LDL/HDL-C (lipoprotein combine index, LCI), and Ig (TG/HDL-C) (AIP), were all significantly higher in the cases than in the controls. The results of Pearson correlation analyses indicated that AIP was positively and significantly correlated with TC (r=0.125, P<.001), TG (r=0.810, P<.001), LDL-C (r=0.035, P<.001), non-HDL-C (r=0.322, P<.001), TC/HDL-C (r=0.669, P<.001), LDL-C/HDL-C (r=0.647, P<.001), AI (r=0.669, P<.001), and LCI (r=0.688, P<.001) and was negatively correlated with age (r=-0.122, P<.001) and HDL-C (r=-0.632, P<.001). In the univariate logistic regression analysis, AIP was the lipid parameter that was most strongly associated with CAD, with an unadjusted odds ratio of 1.782 (95% confidence interval: 1.490–2.131, P<.001), for an increase of 1-SD. Multivariate logistic regression analyses revealed that AIP was an independent risk factor for CAD.

AIP might be a strong and independent predictor for CAD in the Chinese Han population.

Abbreviations: Al = atherosclerosis index, AIP = atherogenic index of plasma, CAD = coronary artery disease, DM = diabetes mellitus, EH = essential hypertension, HDL-C = high-density lipoprotein cholesterol, LCI = lipoprotein combined index, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

Keywords: atherogenic index of plasma, coronary artery disease, lipids

1. Introduction

Coronary artery disease (CAD) is the leading cause of mortality and morbidity worldwide, a fact that has been widely accepted.^[1] According to a report on cardiovascular diseases in China, the

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prevalence of CAD is continuously increasing; about 1 in 5 Chinese adults is afflicted by CAD.^[2] CAD is recognized as a multifactorial disease that is influenced by environmental and genetic factors.^[3] Dyslipidemia is one of the most important factors for CAD. A growing body of evidence indicates that decreases in high-density lipoprotein cholesterol (HDL-C) and increases in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) may contribute to the progression of atherosclerosis.^[4,5] Among them, LDL-C is considered to be the primary target for therapy. However, after reducing LDL-C to the recommended levels, an ~50% remnant cardiovascular risk remains, thus encouraging researchers to find new CAD predictors.^[6] Compared with single lipid parameters, the comprehensive lipid indexes, such as non-HDL-C (TC minus HDL-C), TC/HDL-C, LDL-C/HDL-C, non-HLD-C/HDL-C (atherogenic index, AI), and TC*TG*LDL/HDL-C (lipoprotein combine index, LCI), are considered to be better predictors for CAD.^[7,8]

In recent years, researchers have focused on a new comprehensive lipid index, the atherogenic index of plasma (AIP), which might comprehensively reflect the balance between atherogenic and anti-atherogenic factors. Recently, AIP has been shown to be a strong marker for predicting the risk of CAD.^[9–11] In a crosssectional study conducted in Iran, the value of AIP was positively associated with waist circumference and body mass index and was inversely associated with physical activity.^[9] In another prospective study, AIP predicted CAD independently in a Turkish population. However, the results were inconsistent. Nansseu et al^[12] revealed that AIP was not an independent factor

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determining the impact of the risk of cardiovascular disease in Cameroonian postmenopausal women. In a prospective cohort study, Hartopo et al^[13] investigated the relationship between the AIP value and major adverse cardiovascular events during intensive hospitalization in patients with acute myocardial infarction (AMI). According to the value of AIP, patients were divided into a low AIP group (AIP <0.24) and high AIP group (AIP \geq 0.24). They found that a low AIP value, in contrast with a high AIP value, was an independent predictor for all-cause mortality in patients with AMI who were undergoing intensive hospitalization.

Whether the AIP level is related to the risk of CAD in the Chinese Han population remains unknown. Therefore, the purpose of this study was to evaluate the relationship between AIP and the risk of CAD in a Chinese population undergoing coronary angiography (CAG).

2. Methods

2.1. Study population

A total of 5387 consecutive unrelated adult patients undergoing CAG for suspected CAD in Wujin Hospital affiliated with Jiangsu University were enrolled in this study between January 2006 and December 2015.

The exclusion criteria were the following: patients who did not undergo a CAG examination or had repeated CAG examinations; incomplete data for traditional lipid profiles; patients who were taking lipid-lowering medication for more than 6 months; and patients with hypothyroidism or nephrotic syndrome.

The study protocol was approved by the Ethics Committee of our hospital. Because this retrospective case–control study was based on data from patient medical records, written informed consent was not obtained from the participants.

2.2. Diagnostic criteria

CAD was defined in accordance with the 1979 WHO diagnostic criteria, ^[14] and all of the patients underwent a CAG examination. The CAG examinations were performed using Judkin technique via the radial or femoral artery. Angiograms were analyzed by 2 experienced doctors who were blinded to this study. Control subjects were defined as those lacking typical angina pectoris symptoms and those in whom stenosis of the major coronary arteries was less than 50%. Essential hypertension (EH) and diabetes mellitus (DM) were defined according to features described in our previous report.^[15] Briefly, EH was defined as systolic pressure \geq 140 mm Hg and/or diastolic pressure \geq 90 mm Hg and/or use of anti-hypertensive drugs. DM was defined as fasting glucose levels \geq 7.0 mmol/L and/or use of antidiabetic drugs. Smoking was defined as daily cigarette smoking.

2.3. Statistical analysis

Continuous variables are presented as the mean \pm standard deviation (SD) and were compared using an independent samples t test. Categorical variables are expressed as frequencies and percentages and were compared using a Chi-square test. The correlation between the AIP value and other variables was calculated by a Pearson correlation analysis. Both univariate and multivariate logistic regression analyses were performed to explore the relationship between the lipid parameters and risk of

CAD. The adjusted odds ratio (OR) per 1 SD increase in the corresponding lipid variable and 95% confidence intervals (95% CIs) were calculated. All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL) 17.0. A value of P < .05 in a 2-sided test was considered significant.

3. Results

3.1. Baseline characteristics of CAD patients and controls

Table 1 lists the baseline characteristics of the population. A total of 5387 subjects were included in our study, including 2935 (54.50%) CAD patients and 2452 (45.50%) controls. The mean age of patients was 62.16 ± 9.28 (age range: 34–39) years; 60.18% (3, 242) of them were male. The patients in the CAD group were older than those in the control group. The rate of smoking as well as histories of EH and DM were significantly higher in the CAD group.

Compared with the controls, CAD patients had higher levels of TC, TG, and LDL-C. By contrast, the level of HDL-C was lower in CAD patients. The values of nontraditional lipid profiles, including non-HDL-C, TC/HDL-C, LDL-C/HDL-C, AI, LCI, and AIP, were all significantly higher in the CAD group than in the control group. In subgroup analyses that were stratified by gender, we found that all of the lipid profiles were associated with CAD risk in both males and females except for TG (Fig. 1).

3.2. Correlation analysis of AIP with other variables

Pearson correlation analysis was performed to investigate the correlation of AIP with other continuous variables. As summarized in Table 2, AIP was positively and significantly correlated with TC (r=0.125, P<.001), TG (r=0.810, P<.001), LDL-C (r=0.035, P<.001), non-HDL-C (r=0.322, P<.001), TC/HDL-C (r=0.669, P<.001), LDL-C/HDL-C (r=0.447, P<.001), AI (r=0.669, P<.001), and LCI (r=0.688, P<.001) and was negatively correlated with age (r=-0.122, P<.001) and HDL-C (r=0.632, P<.001).

3.3. Logistic regression analyses for AIP with CAD risk

In the univariate logistic regression analysis, AIP was the lipid parameter that was most strongly associated with CAD with an unadjusted OR of 1.782 (95% CI: 1.490–2.131, P < .001) for an increase of 1-SD (Table 3). This association persisted after adjustments for some CAD risk factors (age, sex, smoking, EH, and DM) (Table 4).

4. Discussion

The present study explored the relationship between AIP and CAD risk in the Chinese Han population. Our results revealed that AIP was a significant and independent predictor for CAD risk and might be better than traditional lipid parameters and other lipid ratios.

Studies have shown that dyslipidemia is one of the known risk factors for CAD.^[4] The association between traditional lipid measures, including TC, LDL-C, and TG, has been well documented in their association with the incidence of CAD. In addition, lipid ratios, such as TC/HDL-C, LDL-C/HDL-C, AI and LCI, were also considered to be predictors for CAD. Because of the small particle size, small density LDL (sdLDL) more easily invades and deposits on the arterial wall compared with LDL and

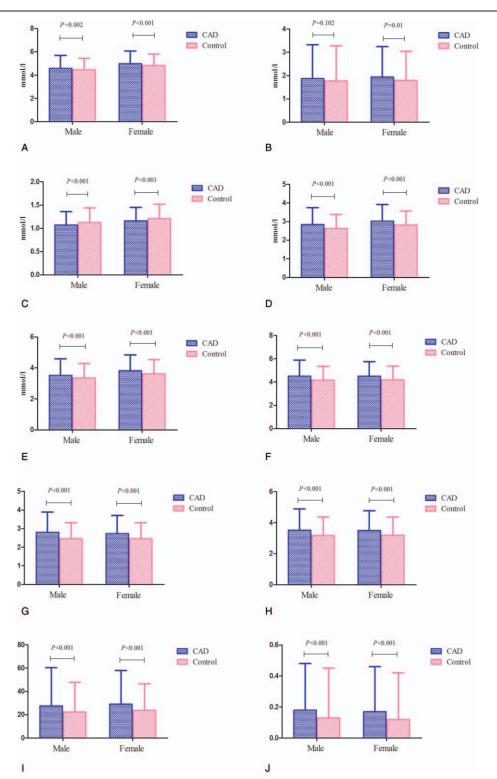


Figure 1. Associations between lipid parameters and CAD risk by gender (A: TC; B: TG; C: HDL-C; D: LDL-C; E: non-HDL-C; F: TC/HDL-C: G: LDL-C/HDL-C; H: AI; I: LCI; J: AIP).

is easily oxidized to oxLDL. When oxLDL is phagocytized by macrophages, macrophages are converted to foam cells, further causing arteriosclerosis and cardiovascular disease. In recent years, several studies have found that sdLDL is an important marker for predicting arteriosclerosis, and its clinical use was recommended.^[16] However, because of the complicated detection method and expensive costs, the detection of sdLDL is limited in clinical applications.

AIP, the logarithm of the molar ratio of TG to HDL-C, was first described by Dobiášová and Frohlich^[17] in 2001; AIP has a

Variables	CAD patients (n = 2936)	Controls (n=2451)	t (χ²)	Р	
Age, y	63.59 ± 9.56	60.44 ± 9.54	12.05	<.001	
Male [n (%)]	2007 (68.36%)	1235 (50.39%)	180.03	<.001	
Smoker [n (%)]	907 (30.89%)	440 (17.95%)	119.29	<.001	
EH [n (%)]	2066 (70.37%)	1416 (57.77%)	92.72	<.001	
DM [n (%)]	728 (24.80%)	322 (13.14%)	115.70	<.001	
Traditional lipid profiles					
TC, mmol/L	4.72±1.10	4.66 ± 0.99	2.29	.022	
TG mmol/L	1.89 ± 1.40	1.79 ± 1.38	2.65	.008	
HDL-C, mmol/L	1.10 ± 0.29	1.17±0.31	-8.47	<.001	
LDL-C, mmol/L	2.90 ± 0.91	2.72 ± 0.76	7.74	<.001	
Nontraditional lipid profiles					
Non-HDL-C	3.62 ± 1.06	3.49 ± 0.93	4.95	<.001	
TC/HDL-C	4.51 ± 1.34	4.19 ± 1.17	9.36	<.001	
LDL-C/HDL-C	2.79 ± 1.04	2.46 ± 0.85	12.29	<.001	
AI	3.51 ± 1.34	3.19 ± 1.17	9.36	<.001	
LCI	28.10 ± 31.63	23.10±24.17	6.42	<.001	
AIP	0.17 ± 0.30	0.12 ± 0.31	6.378	<.001	

AI = atherosclerosis index, AIP = atherogenic index of plasma, CAD = coronary artery disease, DM = diabetes mellitus, EH = essential hypertension, HDL-C = high-density lipoprotein cholesterol, LCI = lipoprotein combined index, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

stronger sensitivity that reflects the interaction between atherogenic and protective lipoprotein. A previous study showed that the value of AIP was inversely associated with the diameter of LDL-C particles and indicated the sdLDL particle size.^[18] Therefore, AIP could be considered to be an economic and reliable indicator of CAD. There are some advantages in using AIP in clinical applications. First, after logarithmical transformation, AIP can correct for the lack of a normal distribution. Second, the value of AIP can be obtained by direct calculation and requires no extra cost. Third, AIP may indirectly serve as a surrogate of the particle size of LDL.

Several studies have demonstrated that AIP is associated with metabolic syndrome and increased with body weight.^[19,20] In 2015, Zhu et al^[21] conducted a meta-analysis to explore the relationship between lipid parameters and DM risk. They demonstrated that AIP was positively associated with DM and that the standardized mean difference was 1.78 (95% CI: 1.04–2.52); this was higher than traditional lipid parameters.^[21] Other studies revealed that AIP was positively associated with blood uric acid and C-reaction protein and was strongly associated with oxidative stress.^[22,23] In recent years, a growing

Correlation between AIP and other variables.					
Variable	R	Р			
Age	-0.122	<.001			
TC	0.125	<.001			
TG	0.810	<.001			
HDL-C	-0.632	<.001			
LDL-C	0.035	.011			
Non-HDL-C	0.322	<.001			
TC/HDL-C	0.669	<.001			
LDL-C/HDL-C	0.447	<.001			
AI	0.669	<.001			
LCI	0.688	<.001			

Al=atherosclerosis index, HDL-C=high-density lipoprotein cholesterol, LCl=lipoprotein combined index, LDL-C=low-density lipoprotein cholesterol, TC=total cholesterol, TG=triglyceride.

body of evidence has indicated that AIP is a strong marker to predict the risk of CAD.

The value of AIP varies greatly in different ethnic populations.^[24] In our study, the mean AIP level was 0.15 ± 0.34 (-1.7 to 1.55) in the overall population; this level was higher than that in a 40-year-old Slovak population (0.064 ± 0.310 in males and -0.150 ± 0.306 in females). Even in the same ethnic population, AIP also varied greatly. In another study conducted in a middleaged Chinese population, the value of AIP was 0.092 ± 0.325 in the total population; this value was lower than our results.^[20]

Our study found that AIP was inversely correlated with age, which was in agreement the results described by Hartopo et al.^[13] Interestingly, a previous study conducted in a normal Chinese population suggested that AIP was associated with gender and increased with age.^[25] Nansseu et al^[12] also concluded that AIP was not associated with age. This discrepancy might partly be the result of the different selected populations. In our study, all participants were hospitalized and underwent a CAG

Table 3

Univariate logistic regression analyses for lipid parameters with CAD risk.

Variables	OR	95% CI	Р
Traditional lipid profiles			
TC, mmol/L	1.062	1.009-1.118	.022
TG, mmol/L	1.055	1.014-1.098	.009
HDL-C, mmol/L	0.462	0.385-0.554	<.001
LDL-C, mmol/L	1.302	1.217-1.393	<.001
Nontraditional lipid profile	S		
Non-HDL-C	1.149	1.087-1.214	<.001
TC/HDL-C	1.235	1.181-1.292	<.001
LDL-C/HDL-C	1.460	1.372-1.554	<.001
Al	1.235	1.181-1.292	<.001
LCI	1.007	1.005-1.009	<.001
AIP	1.782	1.490-2.131	<.001

Al=atherosclerosis index, AIP=atherogenic index of plasma, HDL-C=high-density lipoprotein cholesterol, LCI=lipoprotein combined index, LDL-C=low-density lipoprotein cholesterol, TC=total cholesterol, TG=triglyceride.

Table 4

Multivariate logist	c regression	analyses fo	r lipid	parameters	with CAD	risk.
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Variables	Model 1 [*]		Model 2^{\dagger}		Model 3 [‡]	
	Adjusted OR (95% CI)	Р	Adjusted OR (95% CI)	Р	Adjusted OR (95% CI)	Р
TC, mmol/L	1.173 (1.110–1.239)	<.001	1.160 (1.097-1.227)	<.001	1.152 (1.089–1.218)	<.001
TG, mmol/L	1.101 (1.056-1.149)	<.001	1.078 (1.033-1.125)	.001	1.049 (1.005-1.095)	.029
HDL-C, mmol/L	0.511 (0.423-0.618)	<.001	0.535 (0.443-0.648)	<.001	0.572 (0.472-0.693)	<.001
LDL-C, mmol/L	1.425 (1.326-1.531)	<.001	1.417 (1.318–1.523)	<.001	1.408 (1.309-1.515)	<.001
Non-HDLC	1.127 (1.198-1.349)	<.001	1.252 (1.179–1.329)	<.001	1.234 (1.162-1.310)	<.001
TC/HDL-C	1.277 (1.218-1.339)	<.001	1.257 (1.199–1.318)	<.001	1.233 (1.176–1.293)	<.001
LDL-C/HDL-C	1.499 (1.405-1.599)	<.001	1.479 (1.385–1.578)	<.001	1.448 (1.357-1.546)	<.001
AI	1.277 (1.218-1.339)	<.001	1.257 (1.149–1.318)	<.001	1.233 (1.176–1.293)	<.001
LCI	1.010 (1.008–1.013)	<.001	1.009 (1.007-1.012)	<.001	1.008 (1.005-1.010)	<.001
AIP	2.095 (1.735-2.529)	<.001	1.523 (1.350–1.718)	<.001	1.660 (1.367-2.016)	<.001

AI = atherosclerosis index; AIP = atherogenic index of plasma; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; LCI = lipoprotein combine index; TC = total cholesterol; TG = trialyceride.

* Adjusted for age, sex, and smoking.

[†] Adjusted for age, sex, smoking, and hypertension.

* Additionally adjusted for DM.

examination. The average age was 62.16 ± 9.28 years in our study, different from the previous study. In China, older people pay more attention to lifestyle changes and actively control the intake of cholesterol; this may be another reason for the difference.

In 2016, Zhan et al^[11] found that AIP was higher in Chinese patients with acute coronary syndrome than in controls, reflecting the lipid-driven inflammatory state in acute coronary syndrome. Compared with the study by Zhan et al,^[11] our study has several advantages. First, the sample size in our study is larger (5378 vs 754). Second, we not only compared the relationship between the value of AIP and the risk of CAD but also compared the risk difference to CAD between AIP and other lipid parameters. In our study, we found that the value of AIP in the CAD group was higher than in controls $(0.17 \pm 0.30 \text{ vs } 0.12 \pm$ 0.31). The univariate logistic regression analysis revealed that AIP was the lipid parameter that was most strongly associated with CAD, with an unadjusted OR of 1.782 (95% CI: 1.490–2.131, P < .001), for an increase of 1-SD. Further, the multivariate logistic analysis models demonstrated that AIP was the most powerful predictor for CAD. In the correlation analysis, we found that AIP was most positively correlated with TG (r =0.810, P < .001) and was negatively correlated with HDL-C (r = -0.632, P < .001). These findings were in agreement with previous studies.^[9,25] Third, AIP might vary by gender.^[26] In our study, we carried out subgroup analysis by gender and found that AIP was correlated with CAD risk either in males or in females.

Several limitations should be mentioned. First, the present study was a retrospective study. We could not obtain some useful data, such as waist circumference, body mass index, and physical activity. These data are associated with AIP and might affect the interpretation of the results. A prospective study with a good design should be carried out in the future. Second, the population of the study was from hospitalized patients undergoing a CAG examination; this population does not represent the general population.

Despite the limitations, our study concluded that AIP might be a strong and independent predictor for CAD in the Chinese Han population.

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