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Risk Factors, Coronary Severity, Outcome and ABO Blood Group

A Large Chinese Han Cohort Study

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Abstract: ABO blood type locus has been reported to have ethnic difference and to be a pivotal genetic determinant of cardiovascular risk, whereas few prospective data regarding the impact on cardiovascular outcomes are available in a large cohort of patients with angiography-proven coronary artery disease, especially from the Chinese population. The objective of this study was to assess the prognostic role of blood type in future cardiovascular events (CVEs) in Chinese Han patients undergoing coronary angiography.

The population of this prospective cohort study consisted of 3823 eligible patients, and followed annually to capture all CVEs. Baseline characteristics and ABO blood type were obtained. Cox proportional hazards models were used to evaluate the risk of ABO blood type on CVEs.

New CVEs occurred in 348 patients [263 (10.3%) non-O and 85 (7.8%) O] during a median period of 24.6 months follow-up. Significantly, non-O blood group was related to the presence and severity of coronary atherosclerosis and several risk factors including inflammatory markers. The log-rank test revealed that there was a significant difference between non-O and O blood groups in event-free survival analysis ($P = 0.026$). In particular, the Cox proportional hazards models revealed that non-O blood type was associated with increased CVEs risk [hazard ratio (95% confidence interval) 1.320 (1.033–1.685)], even after adjusting for potential confounders [adjusted hazard ratio (95% confidence interval) non-O: 1.289 (1.003–1.656); A: 1.083 (0.797–1.472); B: 1.481 (1.122–1.955); AB: 1.249 (0.852–1.831), respectively].

Non-O blood type is associated with future CVEs in Chinese Han patients undergoing coronary angiography.

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INTRODUCTION

After its first description in 1901, the ABO blood group system has been of immense interest more than a century. The ABO gene locus has been mapped to chromosome 9 at locus 9q34.[1] The antigens (A, B, and H determinants) have been shown to consist of complex carbohydrate molecules, which are traditionally regarded as placed on the extracellular surface of the red blood cell membranes, are actually expressed on a variety of human tissues, including epithelium, sensory neurons, platelets, and vascular endothelium.[2] The ABO blood group system was the first genetic polymorphism discovered in humans.[3] Thus, research on ABO group system has been of great interest, because of its medical importance in different diseases.[4,5]

ABO blood groups, in particular non-O blood groups, have been suggested to be associated with several cardiovascular risk factors,[6] and even a higher risk of ischemic heart disease (IHD), cerebral ischemia of arterial origin, and of developing severe manifestations of atherosclerosis.[7] Although several cross-sectional studies including the data from our group have revealed the relation between non-O blood group and an increased coronary artery disease (CAD) risk,[8–10] prospective data remain controversial.[11–14] The evidences based on large-scale general population supported that non-O blood type have higher risk of developing CAD[11] and increased cardiovascular mortality.[12] A study involving patients from the Netherlands who underwent major vascular surgery, however, did not find any relationship between ABO blood groups and cardiovascular mortality during 4 years follow-up.[13] Moreover, a 10 years follow-up study from Italy proved that non-O blood group increased the risk for cardiac death in non-elderly patients undergoing coronary angiography.[14] In addition, it has been well accepted that the distribution of ABO blood groups are distinct in different ethnic population.[15] Thus, the possible reasons for the discrepancy may be because of the diversity of enrolled population and ethnic difference of these studies.

In this follow-up investigation regarding a large cohort of Chinese Han patients who underwent coronary angiography (n = 3823), we sought to address the relationship of ABO blood group with cardiovascular risk factors, the association between

ABO blood group and the CAD incidence and severity, and the value of ABO blood group in predicting future cardiovascular events (CVEs).

METHODS

Patients

The study protocol was approved by the hospital's ethical review board (Fuwai Hospital and National Center for Cardiovascular Diseases, Beijing, China) and complied with the Declaration of Helsinki. The informed written consent was obtained from each patient. In the current cohort study, a total of 3823 Chinese Han patients were enrolled through March 2011 to April 2014. Patients newly referred to our institution with clinically suspected or known coronary atherosclerosis scheduled for selective coronary angiography were prospectively recruited and enrolled. All the enrolled patients have a detailed clinical, laboratory data, and well-documented traditional cardiovascular risk factors. Exclusion criteria included active cardiopulmonary diseases and serious systematic diseases, such as serious acute left heart failure, severe trauma, significant hematologic disorders, infectious or systematic inflammatory disease within 1 month, severe liver (aspartate aminotransferase or alanine aminotransferase 3 times more than the upper normal limits) and/or renal insufficiency (blood creatinine >132 μmol/L), and malignant disease on the baseline. The flowchart of our sample enrollment is shown in Supplemental Figure 1 http://links.lww.com/MD/A479.

TABLE 1. Baseline Characteristics of the Study Population According to the Occurrence of Events

	Events (n = 348)	No Events (n = 3306)	*P* Value
Demographic Characteristics			
Age (years)	59.4 (9.8)	57.7 (9.9)	0.003
Male sex, n (%)	252 (72.4)	2321 (70.2)	0.422
Body mass index, (kg/m^2)	25.7(3.1)	25.7 (3.2)	0.620
Current smoking status, n (%)	187 (53.8)	1732 (52.4)	0.651
Current alcohol intake, n (%)	101 (28.9)	843 (25.5)	0.175
Medical History, n (%)			
History of hypertension	250 (71.8)	2023 (61.2)	<0.001
History of diabetes	114 (32.7)	840 (25.4)	0.005
History of dyslipidemia	271 (78.0)	2446 (74.0)	0.120
Previous PCI or CABG	86 (24.7)	691 (20.9)	0.099
Family history of CAD	51 (14.7)	522 (15.8)	0.759
Incident CAD, n (%)	341 (98.0)	2845 (86.1)	<0.001
LM diseased	53 (15.7)	269 (8.3)	<0.001
1 vessel diseased	67 (19.5)	861 (26.3)	0.006
2 vessels diseased	104 (30.2)	925 (28.2)	0.437
3 vessels diseased	166 (48.3)	1007 (30.7)	<0.001
Cardiac Parameters			
Resting heart rate (bpm)	70 (9)	70 (8)	0.270
Systolic blood pressure (mm Hg)	125 (15)	125 (16)	0.741
Diastolic blood pressure (mm Hg)	76 (10)	76 (10)	0.201
Fasting glucose (mmol/L)	5.90 (1.97)	5.59 (1.61)	0.001
TC (mmol/L)	4.25 (1.14)	4.19 (1.11)	0.373
TG (mmol/L)	1.94 (1.91)	1.78 (1.12)	0.112
LDL-C (mmol/L)	2.53 (0.91)	2.53 (0.97)	0.967
HDL-C (mmol/L)	1.07 (0.28)	1.08 (0.29)	0.480
ABO type, n (%)			0.017
O	85 (7.8)	1010 (92.2)	
A	86 (8.9)	883 (91.1)	
B	138 (11.5)	1057 (88.5)	
AB	39 (9.9)	356 (90.1)	
O/non-O group, n (%)			0.019
O	85 (7.8)	1010 (92.2)	
non-O	263 (10.3)	2296 (89.7)	
Cardiovascular Medication Use, n (%)			
ACEI	50 (14.5)	364 (11.0)	0.228
ARB	54 (15.4)	410 (12.4)	0.385
β-blockers	183 (52.5)	1689 (51.1)	0.775
Statins	221 (63.5)	2205 (66.7)	0.321

Data are expressed as mean (standard deviation) or n (%). ACEI = angiotensin-converting enzyme inhibitors, ARB = angiotensin-receptor blocker, CABG = coronary artery bypass grafting, CAD = coronary artery disease, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, LM = left main coronary artery, PCI = percutaneous coronary intervention; TC = total cholesterol, TG = triglyceride.

TABLE 2. ABO Groups, Risk Factors, and Severity of Coronary Atherosclerosis

	ABO Blood Group		
	O (n = 1139)	Non-O (n = 2684)	*P* Value
Risk Factors, n (%)			
History of hypertension	706 (62.0)	1675 (62.4)	0.826
History of diabetes	303 (26.6)	698 (26.0)	0.717
History of dyslipidemia	823 (72.3)	2018 (75.2)	0.062
Previous PCI or CABG	244 (21.4)	561 (20.9)	0.729
Family history of CAD	179 (15.7)	416 (15.5)	0.857
Lipid Profiles (mmol/L)			
TC	4.17 (1.12)	4.22 (1.10)	0.187
TG	1.81 (1.37)	1.79 (1.15)	0.740
LDL-C	2.52 (1.07)	2.54 (0.91)	0.629
HDL-C	1.07 (0.28)	1.08 (0.28)	0.353
Inflammatory Markers			
HS-CRP (mg/L)	2.39 (2.94)	2.71 (3.24)	0.003
Fibrinogen (g/L)	3.16 (0.71)	3.20 (0.76)	0.103
WBCC (10^9/L)	6.30 (1.65)	6.29 (1.62)	0.908
ESR (mm/h)	9.51 (10.30)	10.59 (10.81)	0.003
Gensini score	18 (4−43)	20 (6−43)	0.032

Data are expressed as n (%) or mean (standard deviation). CABG = coronary artery bypass grafting, CAD = coronary artery disease, ESR = erythrocyte sedimentation rate, HDL-C = high-density lipoprotein cholesterol, hs-CRP = high-sensitivity C-reactive protein, LDL-C = low-density lipoprotein cholesterol, PCI = percutaneous coronary intervention, TC = total cholesterol, TG = triglyceride, WBCC = white blood cell count.

FIGURE 1. The incidence of coronary artery disease and myocardial infarction (A) and the severity of coronary atherosclerosis (B). NS = not significant.

The definitions of traditional cardiovascular risk factors have been described in our previous studies.[16] Dyslipidemia was defined as fasting total cholesterol ≥5.1 mmol/L or triglyceride ≥1.70 mmol/L or the use of lipid-modulating medications. Hypertension was defined as repeated blood pressure measurements ≥140/90 mm Hg (at least 2 times in different environments) or currently taking antihypertensive drugs. The definition of diabetes mellitus (DM) was fasting serum glucose level ≥7.0 mmol/L in multiple determinations, or the currently use of medications. Patients with a reported smoking habit of at least 1 cigarette per day were classified as current smokers.

Biochemical Analyses

At baseline, fasting whole blood samples were obtained from a vein in the antecubital fossa and were collected in precooled ethylenediaminetetraacetic acid tubes from each patient. The ABO blood groups were determined by standard procedures using agglutination techniques as we previously indicated.[8] The concentrations of low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were analyzed by selective solubilization method (LD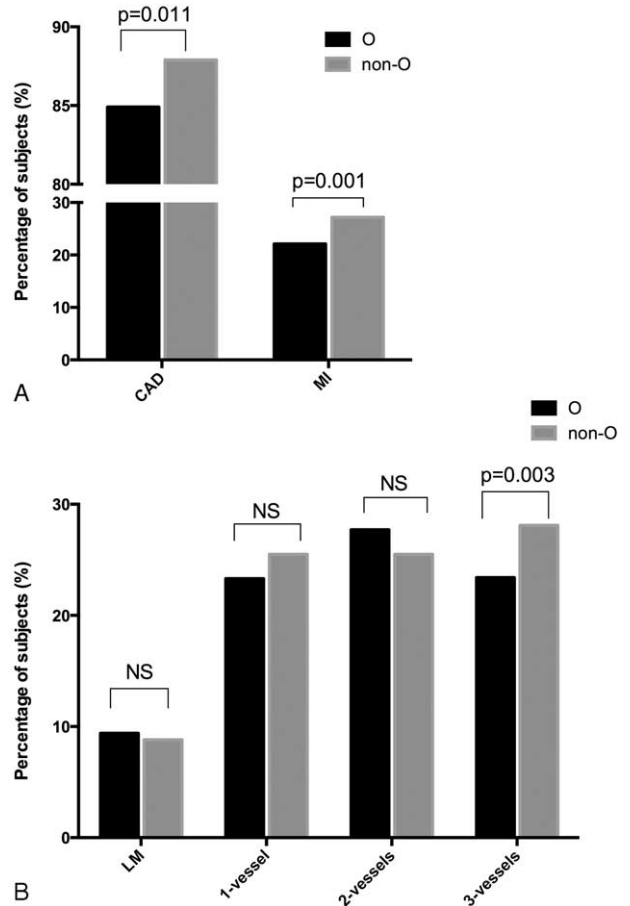L-C or HDL-C kit, Kyowa Medex, Tokyo). All of the lipid profiles were determined by automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan). The high sensitivity-C reactive protein (hs-CRP) concentrations were determined by immunoturbidimetry (Beckmann Assay, Bera, CA). The erythrocyte sedimentation rate (ESR) was analyzed by Westergren method. The fibrinogen levels were measured by the Stago auto analyzer using Clauss method (Diagnostic Stago, Taverny, France). White blood cell counts were determined by the automated hematology analyzer (Sysmex XE-1200, Kobe, Japan).

Gensini Score Calculation

All the angiographic data were collected for each patient, and the severity of coronary atherosclerosis was calculated by the Gensini score system by assigning a severity score to each coronary stenosis according to the degree of luminal narrowing (the score was given from 1 to 32) and its geographic importance (the score was given from 0.5 to 5).[17] A detailed description of the calculation method has been published previously.[8,18]

Outcome Measurement

Follow-up data were obtained via standardized telephone interviews conducted by study nurses who were blinded to the aim of this study, after 6, 12, 24, 36, 48, and 60 months. If
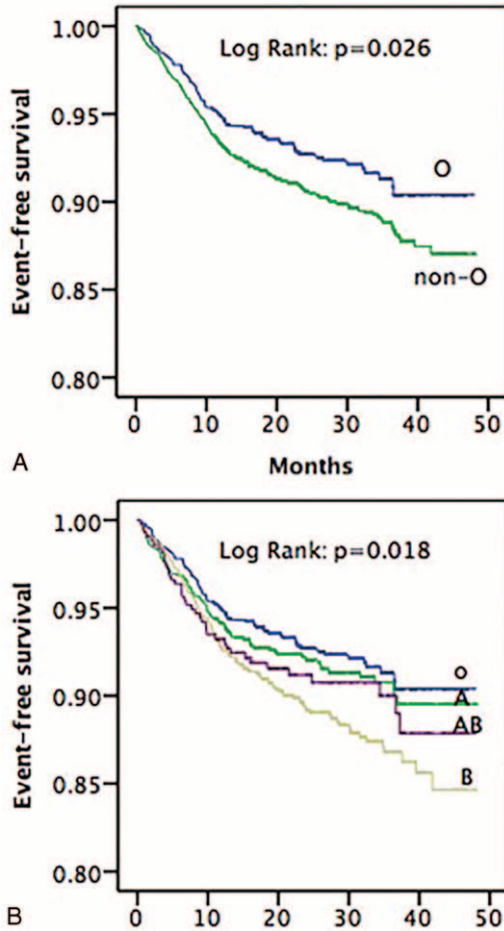
FIGURE 2. The event-free survival analysis between O and non-O (A) or A, B, and AB groups (B).

TABLE 4. Multivariate Cox Proportional Regression Analyses

	ABO Blood Group		
	O	**Non-O**	**P Value**
No. of events	85 (7.8%)	263 (10.3%)	
Median follow-up time, months	24.4	24.6	
Age-adjusted HR (95% CI)	1	1.313 (1.028−1.677)	0.029
Multivariated model 1 HR (95% CI)	1	1.318 (1.030−1.685)	0.028
Multivariated model 2 HR (95% CI)	1	1.304 (1.019−1.668)	0.035
Multivariated model 3 HR (95% CI)	1	1.291 (1.005−1.659)	0.046

Multivariate Cox proportional regression analyses were applied. Model 1: adjusted for age + history of hypertension, diabetes mellitus; Model 2:Model 1 + hs-CRP; Model 3:Model 2 + Gensini score. CI = confidence interval, HR = hazard ratio, hs-CRP = high-sensitivity C-reactive protein.

and unexpected coronary revascularization [including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG)] because of clinical deterioration. All available relevant data from any reported possible event were collected. Death of a patient was reported by relatives or the general practitioners who treated the patient. Three experienced physicians who were masked to any of the study data independently classified the events.

Statistical Analysis

The values are expressed as the mean (standard deviation) for the continuous variables and as the number (percentage) for the categorical variables. Continuous variables and categorical variables were analyzed by the Student t test or χ^2 statistic test when appropriate.

To investigate the relation of ABO blood type to traditional cardiovascular risk factors (such as lipid profiles and inflammatory markers) as well as the presence and severity of CAD, Student t test or χ^2 statistic test was performed in the current study.

The event-free survival rates between O and non-O blood groups were estimated by the Kaplan–Meier method and compared by the log-rank test. The effect of ABO blood type on the occurrence of CVEs was evaluated using Cox proportional hazards models. Hazard ratio (HR) and 95% confidence interval (CI) were calculated for non-O (A, B, and AB) versus O blood type. The HR were adjusted for age in model 1, with additional adjustment for history of hypertension and DM in model 2, with additional adjustment for hs-CRP in model 3, and further excluded the potential influence of the severity of coronary atherosclerosis in model 4, all of which may confound the relationship between ABO blood type and CVEs. Patients were censored if they were lost to follow-up (4.4%).

The statistical analysis was performed with SPSS version 19.0 software (SPSS Inc., Chicago, IL). For all analyses, $P < 0.05$ was considered significant.

patients reported that they had been hospitalized, appropriate hospital records were consulted. The primary endpoints were the composite of death, nonfatal acute myocardial infarction, unstable angina need for hospitalization, stroke, heart failure,

TABLE 3. Univariate Cox Proportional Regression Analyses

	Hazard Ratio	**95% CI**	**P Value**
Age	1.016	1.005−1.027	0.004
Sex	1.097	0.867−1.388	0.441
BMI	0.994	0.962−1.028	0.730
Hypertension	1.593	1.259−2.015	<0.001
Diabetes mellitus	1.389	1.110−1.739	0.004
Dyslipidemia	1.203	0.933−1.552	0.155
hs-CRP	1.027	0.997−1.059	0.082
Gensini score	1.011	1.008−1.013	<0.001
Non-O	1.320	1.033−1.685	0.026

Univariate Cox proportional regression analyses were performed. BMI = body mass index, CI = confidence interval, hs-CRP = high-sensitivity C-reactive protein.
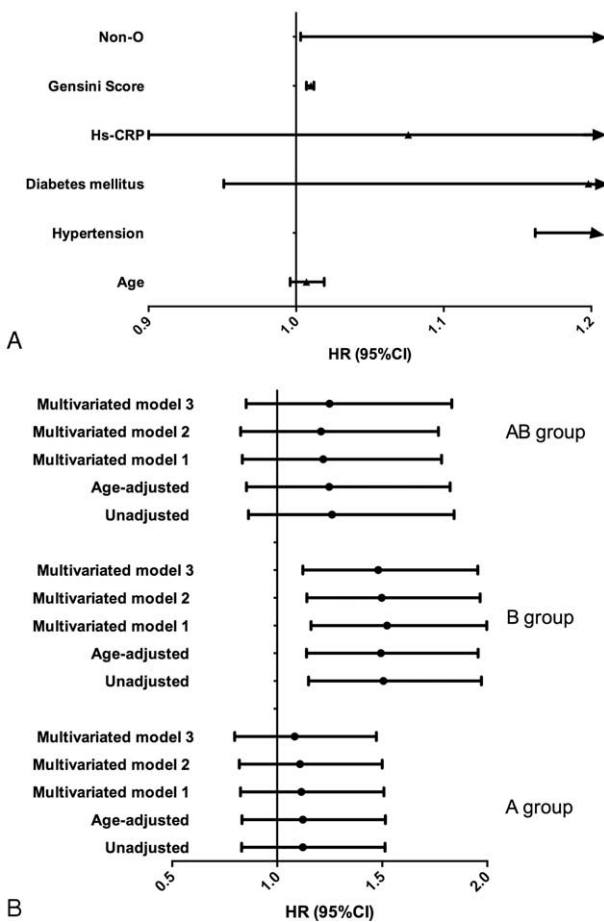
FIGURE 3. Multivariate Cox proportional models to reveal the association of non-O blood group (A) or A, B, and AB groups (B) with future cardiovascular events. Model 1: adjusted for age + his-history of hypertension, diabetes mellitus; Model 2:Model 1 + high-sensitivity C-reactive protein; Model 3:Model 2 + Gensini score.

RESULTS

Baseline Characteristics

We initially recruited 3823 consecutive patients who underwent selective coronary angiography. Follow-up data were not obtained in 169 patients (4.4%) for several reasons (declined to participate, wrong addresses, etc.). ABO blood group distribution in this analysis showed that 1139 (29.8%) were from group O, 1015 (26.5%) group A, 1255 (32.8%) group B, and 414 (10.8%) group AB. Baseline characteristics according to the occurrence of CVEs were shown in Table 1. There was a trend toward older, higher percentage of hypertension, DM, CAD (especially higher proportion of left main artery and 3 vessels disease), and higher levels of fasting blood glucose in patients who have CVEs. Meanwhile, the use of cardiovascular medications, such as angiotensin-converting enzyme inhibitors, angiotensin-receptor blocker, β-blockers, and statins was similar between groups. Significantly, the patients in the CVEs group tended to have higher prevalence of non-O blood group.

Cardiac Events During Follow-Up

The median period of follow-up was 24.6 months (interquartile range: 16.5–34.5 months). A total of 348 patients (9.1%) presented with CVEs during the follow-up period. Of these, 69 (19.8%) developed unstable angina pectoris, 32 (9.2%) suffered nonfatal myocardial infarction, 10 (2.9%) developed heart failure, 170 (48.9%) underwent myocardial revascularization procedures (PCI or CABG) because of clinical deterioration, 43 (12.4%) had strokes, and 24 (6.9%) died (18 cardiac death). Patients who suffered acute coronary syndrome (ACS) and underwent revascularization procedures were assigned once in the group with revascularization. As indicated in Supplemental Figure 2 http://links.lww.com/MD/A479, the non-O group had significant higher prevalence of unstable angina pectoris (2.1% versus 1.1%, $P = 0.035$), slightly higher cardiac death (0.6% versus 0.2%, $P = 0.080$), and total death (0.8% versus 0.3%, $P = 0.061$), whereas had similar percentage of nonfatal myocardial infarction ($P = 0.874$), heart failure ($P = 0.998$), revascularization ($P = 0.234$), and stroke ($P = 0.970$). More importantly, the percentage of total CVEs was significantly higher in the non-O blood group (10.3% versus 7.8%, $P = 0.019$).

Relation of ABO With Risk Factors, Incidence, and Severity of Coronary Artery Disease

We next made this analysis to verify the relationship of non-O blood types with traditional risk factors as well as with CAD or myocardial infarction susceptibility and severity. In the current study, the traditional risk factors, such as the percentage of hypertension, DM, previous PCI or CABG, and family history of CAD were not statistically different between O and non-O groups (all $P > 0.05$). Meanwhile, the prevalence of dyslipidemia was slightly higher in the non-O blood group ($P = 0.062$). Given that lipid and inflammation were the established major contributors to cardiovascular disease, we further analyzed the link between ABO and lipid and inflammatory markers. Dramatically, we observed that the inflammatory markers including hs-CRP and ESR were higher in the non-O versus O blood groups ($P = 0.003$, both, Table 2). No significant differences, however, were found regarding the lipid profiles in the current analysis ($P > 0.05$, all, Table 2).

As indicated in Figure 1, the presence of CAD, myocardial infarction, and 3 vessels coronary disease was dramatically increased in the non-O blood groups ($P = 0.011$, $P = 0.001$, and $P = 0.003$, respectively). In addition, the non-O blood group had markedly higher Gensini score than the O group ($P = 0.032$).

Non-O Blood Type and the Risk of Cardiovascular Events

As shown in Figure 2, patients with non-O blood groups had an increased risk of CVEs compared with those with O blood group (Fig. 2A). The Kaplan–Meier analysis demonstrated a significant difference in the event-free survival rate between non-O and O blood group ($P = 0.026$). Among the 4 blood groups, the log-rank test for equality revealed that the event-free survival was statistically and significantly different (P for trend $= 0.018$, Fig. 2B).

In the Cox proportional hazard regression analysis, compared with patients with blood group O, those with blood group non-O were more likely to develop CVEs (HR $= 1.320$, 95% CI:

TABLE 5. Reported ABO Blood Groups for Cardiovascular Risk

Study	Study Design	Study Patients	Follow-Up Time	Endpoints	Summary Cardiovascular Risk of Non-O Blood Group-Associated (Adjusted HR or OR, 95% CI)
For Risk of Cardiovascular Events					
Carpeggiani et al[14]	Prospective	N = 4901, receiving coronary angiography	10 years	All-cause and cardiac mortality	1.53 (1.06−2.21) (in <65 years)
Januszkiewicz et al[28]	Prospective	N = 418, with ACS	69 months	All-cause mortality	NS
Etemadi et al[12]	Prospective	N = 50,045, general population based	6.9 years	All-cause and cardiac mortality	1.15 (1.03−1.27)
Bakker et al[13]	Retrospective	N = 4679, with major vascular surgery	4 years	Mortality	NS
Roest et al[24]	Prospective	N = 200 (IHD)/1732 (control), women	NA	MI	1.8 (1.0−3.0)
Jager et al[25]	Prospective	N = 631, population based	5 years	All-cause and cardiac mortality	2.08 (0.85−5.07)
Reilly et al[26]	Case-control (GWAS)	N = 5783 (CAD + MI) /3644 (CAD but no MI)	NA	MI	1.62 (1.23−2.13)
For Risk of Coronary Artery Disease					
Amirzadegan et al[6]	Cross-sectional	N = 2026, underwent CABG	NA	CAD	NS
Lopez-Mejias et al[29]	Cross-sectional	N = 2140, with rheumatoid arthritis	NA	Subclinical and CVD	NS
Gong et al[8]	Cross-sectional	N = 2919, receiving coronary angiography	NA	Severity of CAD	A:1.44 (1.16−1.80)
He et al[11]	Prospective	N = 89,501, general population based	>20 years	CAD	A:1.06 (0.99−1.15);
B:1.15 (1.04−1.26); AB:1.23 (1.11−1.36)					
Sode et al[27]	Prospective	N = 66,010, general population based	NA	VTE, MI	1.1 (1.0−1.1)

CAD = coronary artery disease, CI = confidence interval, CVD = cardiovascular disease, GWAS = genome-wide association studies, HR = hazard ratio, MI = myocardial infarction, NA = not available, NS = not significant, OR = odds ratio, VTE = venous thromboembolism.

1.033−1.685, Table 3). Simultaneously, we observed that age, hypertension, DM, hs-CRP, and Gensini score were all significant predictors of CVEs occurrence (HR = 1.016, 95% CI: 1.005−1.027; HR = 1.593, 95% CI: 1.259−2.015; HR = 1.389, 95% CI: 1.110−1.739; HR = 1.222, 95% CI: 1.000−1.493; and HR = 1.011, 95% CI: 1.008−1.013). Consequently, we further performed the multivariate adjustment for these potential risk factors. The data indicated that the associations between non-O blood groups and CVEs were not substantially altered in this analysis (multivariate-adjusted model 3, HR = 1.291, 95% CI: 1.005−1.659, Table 4). In addition, history of hypertension and Gensini score were both associated with significantly increased CVEs in the fully adjusted multivariate Cox regression analysis (Fig. 3A). In the next analysis, we additionally examined the risk

of CAD by comparing the A, B, and AB with the O blood type. Compared with patients reporting blood group O, those with A, B, and AB blood type had fully adjusted HR (95% CI) of 1.083 (0.797−1.472), 1.481 (1.122−1.955), and 1.249 (0.852−1.831), respectively (Fig. 3B).

DISCUSSION

The current prospective study assessed the relation of ABO to risk factors and coronary severity, and more importantly, to future CVEs in 3823 Chinese Han patients with suspected or documented CAD who underwent elective coronary angiography. To the best of our knowledge, it is the first study deriving from a large cohort of Chinese Han population. As a result, we

observed that non-O blood group was associated with higher inflammatory markers, CAD susceptibility, and severity. Moreover, we found a significantly elevated risk of CVEs occurrence for patients with blood group non-O. The highest risk was observed for blood group B, followed by blood groups AB and A. The prognostic value of non-O blood group for future CVEs was not significantly modified by other known risk factors, including the baseline severity of coronary atherosclerosis. Our study adds to the current literature for providing further evidence for suggesting the pivotal role of non-O blood group in CVEs occurrence.

The association of non-O blood groups with the increased risk of cardiovascular disease has been recognized for some time.[7,12] These observations have led a number of studies to investigate the relationship between ABO blood group and traditional risk factors and further postulate a mechanism whereby some of these associations with ABO operate through these risk factors. There is growing evidence that the ABO blood group is the major determinant of plasma VIII, von Willebrand factor, and thrombomodulin,[19] which lead to increased thrombotic tendency. Recently, a series of genome-wide association studies have linked the ABO locus to the serum levels of soluble intercellular adhesion molecule-1, tumor necrosis factor α, and P-selectin,[20,21] which are implicated in the atherosclerotic procession. Consistently, we also found that the non-O blood type had significantly higher inflammatory markers, such as hs-CRP and ESR levels in the current study, and may suggest the potential link between non-O and inflammation in promoting atherosclerosis. Furthermore, the non-O blood group has long been shown to correlate with higher total cholesterol and LDL-C levels,[22] and the recent study proposed that approximately 10% of the effect of ABO blood group on CAD susceptibility was mediated by plasma cholesterol levels.[23] Nonetheless, in our analysis, the plasma cholesterol levels were not statistically different between O and non-O groups although the percentage of dyslipidemia was slightly higher in the non-O group. This discrepancy was properly because of the influence of statin treatment. Besides that, we found that the non-O blood type was related to significantly higher presence of CAD and myocardial infarction, higher percentage of 3 vessels disease, and higher Gensini score, all of which were strong CVEs predictors.

The current data, however, were inconsistent regarding the association between non-O blood groups and increased cardiovascular risk because of the paucity of information from these studies (as shown in Table 5). A large-scale study combined the Nurses' Health Study and the Health Professionals Follow-up Study cohort including a meta-analysis, non-O blood group had higher risk of CAD and 6.27% of the CAD patients were attributable to non-O blood groups.[11] Nevertheless, this study was based on the general population and did not report all the CVEs. The recent published Golestan Cohort Study reported an increased mortality, particularly because of cardiovascular diseases in non-O blood groups,[12] but the primary design of this study did not specific to cardiovascular disease. Although several cross-sectional as well as prospective studies have reported a higher cardiovascular risk in patients with blood group non-O,[8,14,24–27] some others did not support this viewpoint.[6,13,28,29] In light of the preceding discussion and the ethnic difference of ABO blood distribution, we performed this large-scale follow-up study in Chinese Han patients who underwent coronary angiography. Our study provided additional evidence for investigating the relationship between ABO and cardiovascular disease outcomes.

One limitation of our study is the observational and single-center design, whether the data can be used in more populations needs further investigations. Second, there was not enough cardiovascular mortality in this study to allow direct survival analysis. Third, the mechanism was not explored in the current study.

In summary, we observed higher inflammatory level and more severe coronary atherosclerosis in patients have non-O blood group. Specifically, our data for the first time suggested that non-O blood group was related to a higher CVEs occurrence. More importantly, this relationship remained significant even after adjusting for traditional and potential risk factors, including the inflammatory marker, hs-CRP, and the baseline severity of coronary atherosclerosis assessed by Gensini score.

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