Sex-based difference in influence of A blood group on increased risk of coronary artery disease among Chinese adults: a propensity score matching analysis

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Research

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Abstract

Background ABO blood group is a risk factor for coronary artery disease (CAD), but whether it is more strongly associated with CAD in Chinese individuals is less clear. The aim of this current study was therefore to investigate the association among patients hospitalized for primary coronary angiography and to explore the potential mediator of plasma lipids. Methods A total of 1079 patients, including 698 with- and 381 without newly diagnosed CAD, were retrospectively enrolled from November 2012 to December 2018. Clinical characteristics, plasma lipid levels and ABO blood groups were recorded and analyzed. Characteristics of the patients with and without CAD were compared after propensity score matching analysis (346 vs. 346). Correlation analysis was performed to assess the relationship between ABO types and clinical variables. Logistic regression analysis was constructed to determine the association of ABO blood group with CAD. Results There was not significant difference in the distribution of ABO types between CAD and non-CAD group in overall population. However, propensity-matched analysis showed that CAD in the women subgroup presented more frequently with blood group A, but not non-CAD (60.2% versus 44.1%, P =0.014). The statistically significant difference was not observed among men (37.5% versus 30.3%, P =0.157). When compared with non-A blood group, the A blood group had not a greater difference in lipid profiles among women (P all>0.05). Correlation analysis performed in women revealed that CAD was significantly correlated with A type (r= 0.171, P = 0.003). After adjustment for age, hypertension, cigarette smoking, drinking and lipid profiles, logistic regression analysis showed that blood group A was an significant predictor for CAD in women (OR=2.152, 95% CI 1.285~3.605, P =0.004) . Conclusion Cumulatively, the present study indicated that blood group A was a significantly risk factor for coronary artery disease in Chinese women.

Introduction

There is robust evidence that coronary artery disease (CAD) is common and is associated with substantial risk for cardiac or all-cause mortality and major adverse cardiac eventa [1, 2]. Studies to date have recognized multiple causes of CAD, including diabetes mellitus (DM) and dyslipidemia[3, 4]. A number of researches conducted in European, Asia and Africa have suggested that non-O blood groups are considered as strong risk factors for developing CAD and cardiovascular mortality, and the blood group O has emerged as a protective factor of CAD among whole adults [5–10]. Therefore, attention should be given to the ABO blood group when evaluating and assessing patients with CAD to determine the risk for cardiovascular disease. It is clinically important to understand the distribution of ABO types among patients with CAD.

Moreover, cardiovascular risk factors often co-occur and may act synergistically to impact one's overall risk of cardiovascular events [11]. It is a widely believed paradigm that dyslipidemia contributes to plaque instability and development of CAD. And it is important to note that individuals with non-O type have higher cholesterol absorption rates [12]. Thus, several papers put forward to explain the association between ABO groups and CAD by lipid levels [13, 14]. The underlying mechanism of such an association between ABO type and CAD remains to be clarified. Whereas, there is insufficient information available

about the certain correlation between distribution of ABO groups and CAD among patients underwent coronary angiography in China using propensity score matching analysis.

The purpose of this study was to explore the precise influence of ABO blood groups on the risk of CAD in both sexes in Chinese patients by propensity-matched analysis on the data from participants enrolled in this observational study consisting of 1079 patients in China.

Methods

Study participants

Patients with suspected symptoms of CAD (chest pain, chest distress, ECG changes, syncope, heart failure, multiple risk factors) were eligible for inclusion in department of cardiology of the Wujin Hospital Affiliated with Jiangsu University spanning from November 2012 to December 2018. Of 2028 patents, 1079 cases were included in the final study population. The study participants without previous history of CAD at baseline received primary coronary angiography (CAG). DM was defined according to the American Diabetes Association guidelines [15]. Exclusion criteria included patients lack of information about ABO blood groups (n=935)and lipid profiles (n=14).

Two and more experienced interventional cardiology physicians assessed the results after the CAG procedure. CAD was defined as stenosis of 50% or more of the diameter of the major coronary blood vessels [16]. According to the coronary angiography results, 698 patients were assigned to the CAD group, and 381 to the non-CAD group. The study was approved by the ethics committee of Wujin Hospital Affiliated with Jiangsu University, China. Because the data were retrospectively collected from electric record, written informed consent was not obtained from the participants.

Clinical characteristics and biochemical parameters analysis

In this cross-sectional study, clinical characteristics relevant to CAD regarding gender, age, smoking, drinking, high blood pressure (HBP), DM, systolic blood pressure(SBP), diastolic blood pressure (DBP) and heart rate (HR) gathered throughout history and basic clinical examination. Venous blood samples were obtained from all the patients in a fasting state on the morning following the admission day. Laboratory investigations were done for study patients. ABO blood groups and plasma lipid parameters including total cholesterol (TC), total cholesterol (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), apolipoprotein A-1 (Apo A-1) and apolipoprotein (Apo B) were evaluated using standard techniques. Baseline clinical and biochemical characteristics were collected and evaluated retrospectively by investigators for all study patients.

Statistic analysis

All statistical analysis were performed with SPSS version 25.0. Continuous variables were expressed as mean ± standard deviations. Categorical variables were described as frequencies and percentages. The comparisons in continuous variables were analyzed by the Student *t* test, One-Way ANOVA or non-

parametric Mann-Whitney test, as approprite. Differences between two groups were tested with the Chi-square for categorical variables. Logistic regression analysis was used to identify the impact of ABO blood groups on CAD. Odds ratio (OR) and 95% confidence interval (95% CI) were computed. Propensity score matching was performed to balance patients characteristics. The variables used in the model were: gender, smoking, drinking, HBP, DM, TC, TG, LDL-C, HDL-C, Apo A-1) and Apo B. One-to-one nearest-neighbor matching was conducted using a match tolerance of 0.02. All *P* values were two sided. *P* value less than 0.05 was considered as statistically significant.

Results

The baseline characteristics of involved participants before and after propensity score matching analysis

Baseline characteristics comparing those developed CAD and those remained CAD-free were described in Table 1. In CAD group composed of 698 patients, the mean age at baseline was 63.69±10.01 years, while in non-CAD group composed of 381 participants, the mean age was 61.17±9.01 years. Among the study sample, participants with CAD were significantly older than those with non-CAD (*P*=0.000). Those with CAD were more likely to be men, had a higher prevalence of smoking status, hypertension and DM history, higher SBP. Participants with CAD had generally higher levels of TG, LDL-C and Apo B, and lower concentrations of HDL-C and Apo A1. This observational study also revealed that all patients with A type were not more to be in CAD group, and there was statistical no significance in both sexes.

After propensity score matching analysis, distribution of A blood group were siginificantly higher in overall patients with CAD (37.9% versus 27.7% , *P*=0.006). In the women subgroup, CAD presented more frequently with blood group A, but not non-CAD (60.2% versus 44.1% , *P*=0.014). The statistically significant difference was not observed in the men subgroup (37.5% versus 30.3% , *P*=0.157).

Table 1. Baseline characteristics of the study patients with or without CAD

Characteristic	Before matching			After matching		
	CAD group (n=698)	Non-CAD group (n=381)	*P*value	CAD group (n=346)	Non-CAD group(n=346)	*P*value
Men, n (%)	469 (67.2)	205 (53.8)	0.000	200 (57.8)	195 (56.4)	0.759
Smoking, n (%)	288 (41.3)	93 (24.4)	0.000	98 (28.3)	91 (26.3)	0.609
Drinking, n (%)	85 (12.2)	35 (9.2)	0.164	37 (10.7)	34 (9.8)	0.802
Age, y	63.69±10.01	61.17±9.01	0.000	64.59±9.60	61.03±9.07	0.000
DM, n (%)	212 (30.4)	66 (17.3)	0.000	71 (20.5)	63 (18.2)	0.501
HBP,n (%)	521 (74.6)	248 (65.1)	0.001	233 (67.3)	237 (68.5)	0.807
SBP, mmHg	136.17±22.07	132.70±17.99	0.001	136.46±21.96	133.43±18.33	0.021
DBP, mmHg	82.11±13.86	81.84±11.14	0.951	82.26±13.64	82.22±11.39	0.536
HR,beats/min	74.44±13.49	73.65±13.91	0.047	74.01±13.15	73.58±14.09	0.160
TC, mmol/L	4.56±1.13	4.50±0.96	0.836	4.42±1.07	4.49±0.97	0.222
TG, mmol/L	1.91±1.46	1.70±1.13	0.002	1.72±1.13	1.75±1.16	0.859
HDL-C,mmol/L	1.08±0.27	1.18±0.31	0.000	1.15±0.30	1.16±0.30	0.656
LDL-C, mmol/L	2.83±0.96	2.63±0.75	0.005	2.59±0.85	2.65±0.75	0.224
Apo A-1, g/L	1.24±0.24	1.30±0.25	0.000	1.27±0.25	1.28±0.25	0.757
Apo B, g/L	0.97±0.29	0.90±0.23	0.002	0.90±0.27	0.91±0.24	0.286
A blood group, n (%) Total	252 (36.1)	124 (32.5)	0.269	131 (37.9)	96 (27.7)	0.006
Women	82 (35.8)	56 (31.8)	0.463	56 (60.2)	90 (44.1)	0.014

Men	170 (36.2)	68 (33.2)	0.496	75 (37.5)	59 (30.3)	0.157

CAD: coronary artery disease, SBP: systolic blood pressure, DBP: diastolic blood pressure; HBP: high blood pressure; DM: diabetes mellitus; HR: heart rate; TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; Apo A-1: apolipoprotein A-1; Apo B: apolipoprotein B

Association between blood ABO types and lipid levels

No significant difference was obtained in lipid profiles among different ABO blood groups in all of the 692 patients (Supplementary Table 1). Furthermore, the concentrations of TC, TG, HDL-C, LDL-C, Apo A-1 and Apo B were similar for women with A group, versus non-A group. Similar lipid profiles were observed among diabetic women with A and non-A types (P 0.05 for all,Table 2).

Table 2. Lipid levels in study patients with A and non-A blood types in both sexes

Variable	Male			Female		
	A type(n=134)	Non-A type(n=261)	*P*value	A type(n=93)	Non-A type(n=204)	*P*value
TC, mmol/L	4.42±1.05	4.27±0.93	0.305	4.75±1.16	4.58±1.00	0.192
TG, mmol/L	1.67±1.01	1.77±1.29	0.938	1.87±1.30	1.66±0.94	0.069
HDL-C,mmol/L	1.16±0.30	1.11±0.29	0.160	1.20±0.32	1.19±0.28	0.882
LDL-C,mmol/L	2.61±0.84	2.49±0.73	0.146	2.84±0.89	2.69±0.80	0.161
Apo A-1, g/L	1.26±0.22	1.23±0.25	0.393	1.35±0.27	1.32±0.24	0.307
Apo B, g/L	0.89±0.25	0.88±0.25	0.612	0.96±0.31	0.91±0.24	0.271

TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; Apo A-1: apolipoprotein A-1; Apo B: apolipoprotein B

Correlation between A type and clinical variables in women

We next investigated the relationship between A type and a cluster of demographic parameters and biochemical indices, the results of correlation analysis were shown in Table 3. Notably, A type was positively correlated with CAD in women. However, there were no relationships between A type and age, smoking, HBP, DM, SBP, HR, TG, HDL-C, LDL-C, Apo A-1 and Apo B. After adjustment for age, CAD remained significantly correlated with A type (r= 0.171, P= 0.003).

Table 3. Partial correlations analysis of variables associated with A type in women

Variable	A type		A type (age adjusted)	
	r	*p* value	r	*p* value
Age	-0.089	0.128		
Smoking	-0.039	0.500	-0.036	0.536
HBP	-0.070	0.229	-0.059	0.311
DM	-0.003	0.961	0.002	0.977
SBP	0.008	0.894	0.007	0.903
HR	-0.004	0.944	-0.035	0.547
TG	0.106	0.069	0.090	0.124
HDL-C	-0.009	0.882	0.022	0.712
LDL-C	0.062	0.285	0.083	0.156
Apo A-1	0.014	0.810	0.061	0.293
Apo B	0.064	0.272	0.089	0.125
CAD	0.149	0.010	0.171	0.003

Logistic regression analysis of relationship between A type and CAD in women

Binary logistic regression was conducted to establish the association between ABO types and CAD. The regression model was established using forward Wald method. The inclusion level was set as 0.05 and the exclusion level was 0.1. After adjustment for common cardiovascular risk factors such as age, hypertension, cigarette smoking, drinking and lipid profiles, analysis showed that blood group A was independently associated with an increased CAD risk compared to non-A types (OR=2.152, 95% CI 1.285~3.605, *P*=0.004) in women (Table 4).

Table 4. Logistic regression analysis for CAD in women

Variables	B	S.E	Wald	Sig.	Exp(B)	95%CI
Type A	0.766	0.263	8.483	0.004	2.152	1.285~3.605
Age	0.047	0.015	10.306	0.001	1.048	1.018~1.078

Discussion

To our knowledge, this is the first observational investigation of sex difference in ABO blood group distribution among Chinese adults by propensity-matched analysis. There are several key findings: first, prevalence of A blood group was different between these with and without CAD in overall adults. Second, in our study, positive relationship between blood group A and increased risk of CAD was obtained among women, but not among men. Third, we observed that blood group A was significantly correlated with CAD independent from lipid profiles.

Prior studies have demonstrated that blood group A is more closely aligned with a higher risk of CAD compared with non-A blood groups. Furthermore, second coronary angiography indicates that in-stent restenosis is significantly more prevalent in individuals with blood group A than those with other blood groups [17]. In the meanwhile, several studies reveal that ABO blood groups are not associated with CAD in

general population [18, 19]. The results of these studies have been inconsistent or conflicting in different countries or races. Although an increased CAD risk has been demonstrated in Chinese Han patients with non-O type [20], the exact role of ABO type for predicting CAD events in Chinese individuals has not been addressed. Thus, it is now clinically important to understand ABO group to identify or exclude CAD risk among participants. For all the study subjects, this study revealed that patients with A type were not more to be in CAD group, and there was statistical no significance in both sexes. As we all known that cardiovascular risk factors often co-occur and may act synergistically to impact one's overall risk of cardiovascular events. Thus, one-to-one nearest-neighbor matching was performed to balance the cardiovascular risk factors in our study. After propensity score matching analysis, distribution of A blood group were siginificantly higher in the patients with CAD (37.9% versus 27.7%, P = 0.006).

Recently, a case-control study was introduced for the difference, and it has demonstrated that AB blood group has a higher odd ratio for the development of CAD and can be considered as a risk factor for the development of CAD in females with DM [21]. We believed that the association between ABO types and CAD risk might have sex-based difference in subjects. Therefore, participants were subsequently evaluated for sex-based difference in the association between ABO types and CAD. As shown in Table 1, in the women subgroup, CAD presented more frequently with blood group A, but not non-CAD (60.2% versus 44.1%, P = 0.014). Nervertheless, the statistically significant difference was not observed in the men subgroup (37.5% versus 30.3%, P = 0.157). After adjustment for conventional risk factors, logistic regression analysis suggested that women with blood group A had a significantly increased risk of developing CAD than those with non-A blood groups. Among Chinese women, blood group A was associated with a approximate 2.2-fold greater odds of CAD. Overall, the finding had coincided with other reports from the general population. And it was key to find sex-based difference in influence of A blood group on increased risk of coronary artery disease. Further investigations are required to validate these findings.

There are extensive evidences suggesting that ABO blood group information is not only expressed in red blood cells, but also in platelets and vascular endothelial cells. Thus, the mechanism underlying the association between ABO blood groups and CAD may be complex, and remains to be determined. Several pathways such as dyslipidemia, coagulopathy, inflammatory response (such as IL10, IL-6, and C-reactive protein), platelet aggregation and PCSK9 probably may contribute to the effect of ABO types on CAD[13, 14, 21–25]. Mediation analysis indicates that around 10.5% of the effect of A blood group on CAD is mediated by TC levels [26]. Moreover, LDL-C level is thought to be a mediator of the effect of non-O type on coronary artery disease and myocardial infarction [27]. Overall, it is still unclear whether there is any interaction between ABO types and lipid profiles in regard to development of CAD. Our results showed that patients with CAD had significantly higher levels of TG, LDL-C and Apo B, but statistically lower levels of HDL-C and Apo A-1. However, the concentrations of TC, TG, HDL-C, LDL-C, Apo A-1 and Apo B were similar for women with A group, versus non-A group. In our study, the results of correlation analysis showed that, among Chinese women, A type was correlated positively with CAD. And there were no relationships between A type and age, smoking, DM, HBP, SBP, HR, TG, HDL-C, LDL-C, Apo A-1 and Apo B. After adjustment for age, CAD remained significantly correlated with A type (r = 0.171, P = 0.003). The results

highlighted our findings that the effect of ABO blood groups on development of CAD in Chinese women was not mediated by lipid levels.

Several limitations to this study need to be considered. First, the optical coherence tomography (OCT) examination indicates that the plaques of blood group O are exhibited more stably compared with non-O blood groups. And the non-O groups have more serious coronary artery stenosis than O blood group [28]. For lack of OCT, assessment for plaques in CAD patients particularly those with blood group A was absent in our study. Second, it was a single-center, retrospective, observational study, baseline data such as body mass index, physical activity and socioeconomic status was incomplete. Our results could be biased for small sample size. Furthermore, nutraceuticals can influence lipids metabolism and act on lipids metabolism. However, the information was absent.Therefore, multicenter, large-scale and prospective studies will be required to clarify the association of ABO blood group distribution with CAD and cardiovascular risk factors in Chinese patients.

Conclusions

In summary, our data supported a positive association between A blood group and risk of CAD in Chinese women. Results of the present study demonstrated that among Chinese women, A blood group led to a significantly higher risk of CAD than other blood groups. However, this higher association was not due to lipid levels. The report may help in identifying those adults at high risk, who could receive further attention and preventative treatment.

Abbreviations

CAD
coronary artery disease, SBP:systolic blood pressure HBP:high blood pressure
DBP
diastolic blood pressure, TC:total cholesterol,TG:triglyceride
LDL-C
low-density lipoprotein cholesterol, HDL-C:high-density lipoprotein cholesterol
Apo A-I
apolipoprotein A-I, Apo B:apolipoprotein B

Additional Files

Supplementary Table 1 Lipid levels in study patients with A and non-A blood types

Declarations

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author.

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Contributions

Y.B.Song researched the data and wrote the manuscript. G.J.Cai reviewed the manuscript. All authors collected the data.

Ethics declarations

The study was approved by the ethics committee of Wujin Hospital Affiliated with Jiangsu University, Changzhou, China.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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