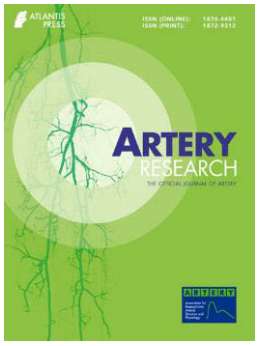

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ABO blood group differences relationship with coronary atherosclerotic markers

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KEYWORDS
ABO blood;
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Abstract *Background:* The mechanisms linking ABO blood group to coronary atherosclerosis is inconsistent and not fully understood.
Objectives: To investigate the relationship between ABO blood groups with coronary atherosclerotic markers (coronary artery calcification (CAC), coronary plaque presence and coronary luminal stenosis (CAD)) and pericardial fat volume (PFV) in patients with suspected coronary artery disease assessed by Multidetector CT angiography (MDCT).
Patients and methods: Two hundred twenty consecutive patients who underwent 64-slice MDCT angiography for assessment of coronary artery disease were recruited. Of these, 180 patients (97 females (54%) and 83 males (46%) with a mean age of 51.7 ± 12 years) were found to be eligible and were enrolled in the study.
Results: We classified the blood groups into O blood group (51.6%) and non O blood group (38%). There were no significant differences in the distribution of CAC, CAD, PFV and coronary plaque presence between different blood groups ($P > 0.05$). The distribution of major cardiovascular risk factors did not differ significantly among the ABO blood groups, except for a significant association between O blood group and smoking ($P = 0.04$).

Adjustment for age and sex showed no significant associations between blood groups with coronary atherosclerotic markers or PFV ($P > 0.05$). Non O blood group were significantly correlated with CAC ($P = 0.01$), coronary plaque ($P = 0.04$) and PFV ($P = 0.03$) after adjustment for CAD and CAC.

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Conclusion: No significant relationship were observed between ABO blood groups with coronary atherosclerotic markers and PFV. Non O blood group showed a significant correlation with CAC and PFV after adjustment for CAC and CAD.

Introduction

ABO blood group antigens are glycoproteins and glycolipids expressed on the surface of red cells, platelets and endothelial cells acting as a principle agents for endothelial cell proliferation and their expression is partially dependent on racial origin.[1,2]

In the last two decades, several studies have been reported that ABO blood groups are linked with a risk of coronary artery disease and ABO blood groups could play a role in the coronary atherosclerosis process through a modulation in the vascular endothelial hemostasis.[2–5]

However, the potential mechanism linking ABO groups with coronary artery disease remains unclear and little is known regarding the association of blood groups with subclinical atherosclerosis and cardiac fat deposits.

Recently, the important role of coronary artery calcification (CAC) and pericardial fat volume (PFV) as an imaging markers of subclinical coronary atherosclerosis assessed by multidetector CT (MDCT) have been reported in several large follow-up studies for assessing the extent and early coronary endothelial dysfunction that may precede the development of mature atherosclerotic changes of coronary artery disease.[6–9]

The main aim of our study was to investigate the relationship between ABO blood groups with coronary atherosclerotic markers (CAC, coronary plaque presence and coronary luminal stenosis) and PFV in patients with suspected coronary artery disease.

Patients and methods

This cross-sectional study was carried out at the Cardiology Center at Al-Sader Teaching Hospital. Informed consent was obtained from all individual participants included in the study. The study was approved by our institution. Two hundred twenty consecutive Iraqi patients with intermediate pretest probability of ischemic heart disease based on their age, sex and cardiac symptoms who underwent 64-slice MDCT angiography for assessment of coronary artery disease (CAD) were recruited between January 2014 and June 2015. Of these, 180 patients were found to be eligible and were enrolled in the study.

Forty patients were excluded because of a poor examination technique or motion artifact ($n = 6$), aortic root anomalies or dissection ($n = 2$), difficulty in accurate pericardial fat volume calculation or segmentation of fat ($n = 10$), or data were missing ($n = 22$).

Using standard physician-based questionnaires, a history of conventional cardiac risk factors for CAD was obtained from each patient at the time of coronary MDCT angiography examination including a positive family history of premature CAD (occurring before the age of 55 years in men and before 65 years in women), current smoking history (more than 10 cigarettes per day in the last year), a history of hypertension or use of anti-hypertension medications, hyperlipidemia was defined as total cholesterol $\geq$200 mg/dl or triglyceride levels $\geq$150 mg/dl or use of lipid lowering drugs, a history of diabetes mellitus or use of insulin or diabetic lowering drugs and obesity with a body mass index $\geq$30. Patients were asked to report their blood type (A, B, AB, O, or unknown) in the questionnaires.

CT scan protocol

CT coronary angiography was performed with a 64-slice scanner (Aquilon 64, v. 4.51 ER 010; Toshiba Medical Systems, Tochigi, Japan). Before multi-slice CT angiography was performed, a non-contrast CT was obtained to calculate the calcium score according to the Agatston for total heart calcium (summed across all lesions identified within coronary arteries) using a sequence scan with a slice thickness of 3 mm.

Coronary calcification area was defined as at least three contiguous voxels with a CT density >130 Hounsfield units. When the patient's heart rate was more than 65 beat per minute, a β-blocker (metoprolol; 20—120 mg orally) was given before the scan. A bolus of 80 ml contrast medium (Omnipaque; 350 mg/ml iodine) was injected intravenously at a rate 5 ml/s, followed by 30 ml of normal saline. The scan was obtained from the aortic arch to the level of the diaphragm during a single breath hold. Using retrospective ECG-gating and ECG-dependent tube current modulation, the following parameters were performed: collimation, width 32.5 × 32.5 cm; slice thickness, 0.5 mm; rotation time, 0.35 s; tube voltage, 120 kV; maximum effective tube current, 890 mA; and table feed, 0.3 mm/rotation at 75% of R—R cardiac cycle. Examination time took ~10 s. MDCT images were rearranged using a smooth kernel (B25f) with a slice thickness of 0.5 mm (increment of 0.3 mm). CT data sets were transferred to a dedicated workstation (Vitrea 2 Workstation; Vital Image, Plymouth, MN, USA) for image analysis.

For the analysis of coronary atherosclerotic markers detected by MDCT, severity of coronary artery stenosis was visually graded as normal (normally appearing lumen), non-obstructive with a mean lumen diameter reduction of <50% or obstructive with a mean lumen diameter reduction of $\geq$50% in a single vessel by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment in two orthogonal projections and multiple if there was non-obstructive and obstructive

lesions in the same patient. A calcified plaque was defined as a structure of >1 mm within and/or adjacent to a coronary vessel lumen consisting of calcium only. The calcium score was categorized as CAC = 0 (zero), 1–99 (mild), 100–399 (moderate) and ≥400 (extensive calcification).

For coronary computed tomography (CT) analysis, a calcified plaque was defined as a structure of >1 mm within and/or adjacent to a coronary vessel lumen consisting of calcium only. The severity of coronary artery stenosis was visually graded as either normal (normally appearing lumen), non-significant stenosis (with a mean lumen diameter reduction of <50%), or significant stenosis (with a mean lumen diameter reduction of ≥50% in a single vessel) by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment in two orthogonal projections.

CAD was defined when patients had one significant coronary stenosis and more. The calcium score was categorized as <10 (no or minimal calcification), 10–99 (mild), 100–400 (moderate) and >400 (extensive calcification).

PFV was defined as any fatty tissue located within the pericardial sac and measured three-dimensionally with the contrast-enhanced phase. PFV measured three-dimensionally with the contrast-enhanced phase. The layer of the pericardium was manually traced and a three-dimensional image of the heart was constructed. Then the PFV was quantified by calculating the total volume of the tissue whose CT density ranged from −250 to −20 HU within the pericardium by using three D workstation.[10] All MDCT images were assessed by two independent radiologists with more than 5 years' experience in coronary MDCT angiography interpretation.

Statistical analysis

Data are presented as mean ± standard deviation or as numbers with percentages, as appropriate. Categorical data are expressed as frequencies and group comparisons were performed using Pearson's chi-square test. Continuous variables are presented as mean ± standard deviation and were compared using the Student's *t*-test or analysis of variance, as appropriate. A *P*-value of less than 0.05 was considered statistically significant. The statistical analysis was processed using SPSS ver.13.

Results

This study comprised 180 patients (97 females (54%) and 83 males (46%) with a mean age of 51.7 ± 12 years and range from 34 to 71 years) with a prior history of chest pain ($n = 130$), dyspnea ($n = 30$), an equivocal exercise tolerance test ($n = 12$), syncope ($n = 3$) and other ($n = 5$) who underwent 64-slice MDCT angiography examinations for assessment of CAD. PFV mean was 91.6 ± 57.5 cm^3 and mean coronary calcium score was 79 ± 200 with CAC (coronary calcium score >0) percentage of 42.7% in the whole sample. The frequency for blood group A, B, AB, O and unknown was 32(17.7), 22(12.5%),14(7.7)93 (51.6%) and 19 (10.5%) respectively. The prevalence of the ABO groups in our study was similar to that reported in Saudi Arabia as both Iraq and Saudi Arabia in general share the same ethnicity.[11]

Patient characteristics are summarized in Table 1.

For statistical analysis, we classified the blood groups into O blood group (51.6%) and non O blood group (38%).

There were no significant differences in the distribution of CAC, CAD, PFV and coronary plaque presence between different blood groups ($P > 0.05$; Table 2).

The distribution of major cardiovascular risk factors (hypertension, diabetes, hyperlipidemia, BMI, family history, age and male) did not differ significantly among the ABO blood groups, except for a significant association between O blood group and smoking ($P = 0.04$).

Adjustment for age and sex showed no significant associations between blood groups with coronary atherosclerotic markers or PFV.

O blood group: The mean coronary calcium score was 75 ± 193 and PFV mean was 92 ± 62 cm^3.

No significant correlations had been observed between O blood group and coronary atherosclerotic markers even after adjustment for CAD, CAC, age and sex.

Non O blood group: The mean coronary calcium score was 74 ± 155 and PFV mean was 95 ± 59 cm^3.

After adjustment for coronary calcium score grades, non O blood group were significantly correlated with PFV in

Table 1 Patients characteristics.

Parameter	No. (%) or mean ± SD
Age (years)	53 ± 11
Male	83(46)
Female	97(54)
Risk factors	
Hypertension	77(43)
obesity	67(37)
Family history	35(19)
Diabetes mellitus	37(21)
Hyperlipidemia	34(19)
Smoking	15(8)
Coronary atherosclerotic markers	
Coronary plaque	
Present	71(40)
Absent	108(60)
Coronary artery disease	
Normal arteries	109(61)
Non-obstructive lesion	17(9)
Obstructive lesion	25(14)
Multiple lesions	29(16)
Coronary calcification groups	
Zero	103(57)
Mild calcification	46(26)
Moderate calcification	16(9)
Extensive calcification	15(8)
Pericardial fat volume	91.6 ± 57 cm^3
Blood group frequency	
O	93(52)
A	32(18)
B	22(12)
AB	14(8)
Unknown	19(10)

Table 2 Distribution of coronary atherosclerotic markers and PFV between O and non O blood groups.

	O Blood group	Non O blood group	P Value
Coronary artery disease (CAD)			
Normal coronaries	57(61%)	42(62%)	0.9
Non-obstructive lesion	7(8%)	7(10%)	0.5
Obstructive lesion	11(12%)	11(16%)	0.4
Multiple lesions	18(19%)	8(12%)	0.1
CAC			
Zero	56(60%)	36(53%)	0.3
>0	37(40%)	32(47%)	0.3
PFV	92 ± 62 cm^3	95 ± 59 cm^3	0.5

patients with moderate CAC ($P = 0.03$) and coronary plaque presence ($P = 0.04$) in mild CAC group (CAC = 1–99). Non O blood group patients tended to have a higher CAC level compared to patients with O blood group after adjustment for CAD ($P = 0.01$).

Discussion

In the present study, no significant relationship were observed between ABO blood groups with coronary atherosclerotic markers and PFV in patients with suspected coronary artery disease.

To the best of the authors' knowledge, there is no study highlights the potential relationship between ABO groups with CAC and PFV using MDCT in patients with suspected CAD.

The results of studies regarding the association between ABO blood groups and coronary atherosclerosis have been inconsistent.

Several epidemiological studies in different populations, including American, Norwegian, British and Hungarian populations have been showed an association between non O blood group and CAD.[3,4,12,13]

On the other hand, other studies reported no significant relationship between ABO blood group and the risk of CAD.[1,14,15]

Furthermore, Asian studies also showed inconsistent relationship between ABO blood groups and CAD.[16–18]

Biswas S et al. studied the relationship of ABO blood group in 250 individuals from Asian Indian Bengali population of India and they found that AB blood group decreases the risk of CAD in healthy controls while the O blood group increases the risk of CAD.[16]

The role of variations in the distribution of blood groups in various parts of the world as a possible cause for these inconsistent results has been suggested by the results of an Iranian prospective study of 10,621 patients enlisted for CABG reported that the prevalence of CAD is markedly higher in blood group O patients than in all other ABO blood groups, which is in contrast with other studies done in Europe and the United States.[17]

A Turkish cohort study conducted in 470 patients with acute ST elevation myocardial infarction showed that ABO blood groups were not be significantly correlated with the risk and development of acute myocardial infarction and the prevalence and of ABO blood groups was similar between patients with acute myocardial infarction and control group.[18]

The inconsistencies in the association between ABO blood group and cardiovascular disease may be attributed to the difference in racial and ethnic background of population who have been enrolled in the studies and selection criteria for inclusion in the study design.

Another result of our study was that non O blood group was significantly correlated with PFV, coronary plaque presence and had a higher level of CAC compared to patients with O blood group after adjustment for CAC and CAD respectively.

Evidences from conventional coronary angiography based studies have been reported the role of increased prothrombotic state and levels of systemic inflammatory response as a possible cause for the significant correlation between ABO blood group and the risk of coronary artery disease.[1,5]

However, the links that explains the complex role of ABO blood groups to CAD pathogenesis remains unclear.

The role of inflammatory markers and LDL-C metabolism associated with ABO blood groups variants has been suggested by a meta-analysis study that showed a significant CAD risk in non-O blood group individuals compared to O blood group individuals.[19]

A genome-wide association studies reported that Blood group non O genotypes had greater odds of myocardial infarction in patients with angiographic CAD than did blood group O suggesting that a specific genetic loci may be implicated in the process of coronary atherosclerosis whereas others predispose to subsequent acute myocardial infarction through plaque rupture.[20]

The significant association between non O blood group with PFV and CAC in our study might be less conclusive due to the small size of our sample after adjustment.

However, this association could highlight the complex role of ABO in the pathogenesis of coronary atherosclerosis.

There were several limitations in this study. First, the study was a single center investigation, and the population was not randomly selected, as it involved only patients with intermediate pretest probability of ischemic heart disease based on physician referral. There is, therefore, the possibility of selection bias. Second, the number of patients was relatively small, especially when the study population was divided into subgroups. Third, a causal relationship between ABO blood groups with coronary atherosclerotic markers and PFV cannot be established because of the cross-sectional nature of our study. Fourth, estimation error may occur as the blood group in our study was self-reported and not rely on molecular techniques.

Conclusion, the findings of our study suggest no significant relationship between different ABO blood groups with coronary atherosclerotic markers and PFV. The relationship between non O blood group with PFV, CAC and coronary plaque presence should be tested in larger follow ups studies to clarify its significance and role in coronary atherosclerosis.

Compliance with ethical standards: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional

and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Conflict of interest

All authors declare that they have no conflict of interest.

References

1. Karabuva S, Carević V, Radić M, Fabijanić D. The association of ABO blood groups with extent of coronary atherosclerosis in Croatian patients suffering from chronic coronary artery disease. *Biochem Med Zagreb* 2013;**23**(3):351—9.
2. Zhou S, Welsby I. Is ABO blood group truly a risk factor for thrombosis and adverse outcomes? *World J Cardiol* 2014 Sep 26;**6**(9):985—92.
3. Garrison RJ, Havlik RJ, Harris RB, Feinleib M, Kannel WB, Padgett SJ. ABO blood group and cardiovascular disease: the Framingham study. *Atherosclerosis* 1976 Nov-Dec;**25**(2—3): 311—8.
4. Erikssen J, Thaulow E, Stormorken H, Brendemoen O, Hellem A. ABO blood groups and coronary heart disease (CHD). A study in subjects with severe and latent CHD. *Thromb Haemost* 1980;**43**:137—40.
5. Lee HF, Lin YC, Lin CP, Wang CL, Chang CJ, Hsu LA. Association of blood group A with coronary artery disease in young adults in Taiwan. *Intern Med* 2012;**51**:1815—20.
6. Silverman MG, Blaha MJ, Krumholz HM, Budoff MJ, Blankstein R, Sibley CT, et al. Impact of coronary artery calcium on coronary heart disease events in individuals at the extremes of traditional risk factor burden: the Multi-ethnic study of atherosclerosis. *Eur Heart J* 2014 Sep 1;**35**(33): 2232—41.
7. Nafakhi H, Al-Nafakh HA, Al-Mosawi AA, Al Garaty F. Correlations between aortic root calcification and coronary artery atherosclerotic markers assessed using multidetector computed tomography. *Acad Radiol* 2015;**22**(3):357—62.
8. Iozzo P. Myocardial, perivascular, and epicardial fat. *Diabetes Care* 2011;**34**(Suppl. 2):S371—9.
9. Nafakhi H, Al-Mosawi A, Al-Nafakh H, Tawfeeq N. Association of pericardial fat volume with coronary atherosclerotic disease assessed by CT angiography. *Br J Radiol* 2014 Jun;**87**(1038). 20130713.
10. Ito T, Nasu K, Terashima M, Ehara M, Kinoshita Y, Ito T, et al. The impact of epicardial fat volume on coronary plaque vulnerability: insight from optical coherence tomography analysis. *Eur Heart J Cardiovasc Imagin* 2012 May;**13**(5): 408—15.
11. Jaff MS. ABO and rhesus blood group distribution in Kurds. *J Blood Med* 2010;**1**:143—6.
12. Whincup PH, Cook DG, Phillips AN, Shaper AG. ABO blood group and ischaemic heart disease in British men. *BMJ* 1980;**300**: 1679—82.
13. TarjJn Z, Tonelli M, Duba J, ZorJndi A. Correlation between ABO and Rh blood groups, serum cholesterol and ischemic heart disease in patients undergoing coronarography. *Orv Hetil* 1995;**136**:767—9 [in Hungarian].
14. Jukic I, Bingulac-Popovic J, Dogic V, Babic I, Culej J, Tomicic M, et al. ABO blood groups and genetic risk factors for thrombosis in Croatian population. *Croat Med J* 2009;**50**:550—8.
15. Amirzadegan A, Salarifar M, Sadeghian S, Davoodi G, Darabian C, Goodarzynejad H. Correlation between ABO blood groups, major risk factors, and coronary artery disease. *Int J Cardiol* 2006;**110**:256—8.
16. Biswas S, Ghoshal PK, Halder B, Mandal N. Distribution of ABO blood group and major cardiovascular risk factors with coronary heart disease. *Biomed Res Int* 2013;**2013**. 782941.
17. Anvari MS, Boroumand MA, Emami B, Karimi A, Soleymanzadeh M, Abbasi S, et al. ABO blood group and coronary artery diseases in Iranian patients awaiting coronary artery bypass graft surgery: a review of 10,641 cases. *Lab Med* 2009;**40**:528—30.
18. Sari I, Ozer O, Davutoglu V, Gorgulu S, Eren M, Aksoy M. ABO blood group distribution and major cardiovascular risk factors in patients with acute myocardial infarction. *Blood Coagul Fibrinolysis* 2008;**19**(3):231—4.
19. He M, Wolpin B, Rexrode K, Manson JE, Rimm E, Hu FB, et al. ABO blood group and risk of coronary heart disease in two prospective cohort studies. *Arterioscler Thromb Vasc Biol* 2012 Sep;**32**(9):2314—20.
20. Reilly MP, Li M, He J, Ferguson JF, Stylianou IM, Mehta NN, et al. Identification of ADAMTS7 as a novel locus for coronary atherosclerosis and association of ABO with myocardial infarction in the presence of coronary atherosclerosis: two genome-wide association studies. *Lancet* 2011;**377**(9763): 383—92.