

# Relationship between ABO Blood Group and Coronary Artery Disease in Patients Undergoing Elective Coronary Angiography

Ramin Eskandari<sup>#1</sup>, Zahra Hosseinzadeh<sup>r</sup>, Yousef Rezaei<sup>r</sup>, Sepideh Emami<sup>r</sup>

Received 25 Jan 2021, Accepted for publication 14 Apr 2021

## Abstract

**Background & Aims:** The ABO blood group antigens have been associated with coronary artery disease (CAD) and cardiovascular mortality. However, there are some controversies in this regard. We sought to determine the association between the ABO blood group and the severity of CAD among patients undergoing elective diagnostic coronary angiography (CAG).

**Materials & Methods:** In this retrospective study, patients undergoing elective CAG were recruited during a year, from January to December 2019. The diagnosis of CAD was based on the narrowing of coronary artery lumen (<50% as mild CAD, 50-70% as moderate CAD, and >70% as severe CAD). Subsequently, the number of involved coronary arteries was also defined. The ABO blood group and Rh status were also identified.

**Results:** A total of 192 patients undergoing elective CAG were assessed. The patients' mean age was  $59.6 \pm 10.7$  years, and 113 (58.9%) subjects were male. After categorization into the O and the non-O blood groups, the number of involved coronary arteries and the severity of lumen narrowing were not significantly different between groups. Those values were also comparable between the A, B, AB, and O blood groups. Irrespective of blood group, patients with negative Rh had a higher prevalence of coronary artery narrowing (50-70%) compared to patients with positive Rh ( $p=0.043$ ).

**Conclusion:** This study showed no association between the ABO blood group and the severity of CAD among patients undergoing elective CAG. Moreover, negative Rh was associated with the lower degrees of coronary artery narrowing compared to positive Rh.

**Keywords:** ABO blood group, Rhesus antigen, coronary artery disease, coronary angiography

**Address:** Firoozgar Hospital, Tehran, Iran. Postal Code: 1593747811

**Tel:** +9821 8214 1201

**Email:** Eskandari.r@iums.ac.ir

## Introduction

The ABO blood group antigens, as carbohydrate molecules, are expressed on the variety of human cells, including red blood cells, platelets, vascular endothelium, and epithelial cells; therefore, those may

be considered as potential factors involved in the pathophysiology of cardiovascular diseases and malignancies (1,2). It has been demonstrated that the ABO blood groups, particularly non-O blood type, are predisposing factors for developing coronary artery

<sup>1</sup> Department of Cardiology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

<sup>2</sup> Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

<sup>3</sup> Heart Valve Disease Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

<sup>4</sup> Department of Cardiology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

disease (CAD) and cardiovascular mortality (1,3-6). However, given prior findings and recent meta-analyses, there are controversies in terms of the association between the ABO blood groups and the development of cardiovascular disease and clinical outcomes (5,7,8)

The Nurses' Health Study and the Health Professionals Follow-up Study, two prospective cohort studies, have demonstrated that ABO blood group was associated with CAD risk. Compared with non-O blood groups, those with the blood type O had lower risk of developing CAD (5). Several cross-sectional studies have also found a relationship between ABO blood group and myocardial infarction (MI) (9-11). Therefore, in this cross-sectional study we sought to determine the association between the ABO blood group status and the presence of CAD and its severity in patients undergoing elective diagnostic coronary angiography (CAG).

## Materials & Methods

In a retrospective study conducted in Firoozgar hospital, Tehran, Iran, patients undergoing diagnostic CAG were recruited based on inclusion and exclusion criteria. Inclusion criteria included individuals with a suspicious CAD who underwent diagnostic CAG. The exclusion criteria included those with acute myocardial infarction, elevated troponin levels, familial hypercholesterolemia, chronic inflammatory status as well as the lack of data on the status of conventional risk factors for CAD and the ABO blood group/Rh status. Baseline characteristics and the details of procedure were collected using an investigator-designed questionnaire. The study protocol was approved by the local ethics committee of our institution, Iran University of Medical Sciences, Tehran, Iran.

All diagnostic CAGs were performed based on the American College of Cardiology Foundation and the American Heart Association (ACCF/AHA) practical guidelines (12). Accordingly, the CAG was performed through femoral or radial artery using Judkins' method

(Siemens, Forcheim, Germany). Low osmolar or iso-osmolar contrast media were used in all cases. The diagnosis of CAD was based on the narrowing of coronary artery lumen, including 50-70% and >70% narrowing of the coronary artery lumen based on the atherosclerotic plaque burden. Subsequently, the number of involved coronary arteries was also identified.

Given our hospital routine care, the blood samples were taken from all patients at least 6 hours before CAG so as to measure the complete blood counts. The samples were collected into tubes containing EDTA and were analyzed. The prior medical histories were obtained via medical charts. Hypertension was defined as systolic and diastolic blood pressures above 140 and 90 mm Hg, respectively, and/or taking antihypertensive drugs.<sup>13</sup> The familial history of CAD was defined as patients had a first-degree male or a female relative less than 55 and 65 years old with CAD, respectively. Diabetes mellitus was also considered when patients met one of these criteria: 1) the symptoms of diabetes in addition to plasma glucose >200 mg/dL; 2) a fasting plasma glucose  $\geq 126$  mg/dL; 3) a 2-hour post-load glucose  $\geq 200$  mg/dL during a glucose tolerance test; and/or 4) taking anti-diabetic medicines (14).

## Statistical analysis:

Based on the variables' distribution normality, continuous variables were analyzed using the t-test or Mann-Whitney U test as appropriate. Categorical variables were compared using chi-squared test. All analyses were performed using Statistical Package for the Social Sciences (SPSS) version of 21.0 (IBM, Armonk, NY, USA). Two-tailed p-values were reported for comparisons.

## Results

A total of 192 patients undergoing elective CAG were assessed. The patients' mean age was  $59.6 \pm 10.7$

years, and 113 (58.9%) subjects were male. The frequency of patients with diabetes mellitus, hypertension, and dyslipidemia was 71 (33.3%), 85 (44.3%), and 26 (13.5%), respectively. The prevalence of A, B, AB, and O blood groups was 68 (35.4%), 39 (20.3%), 14 (7.3%), and 71 (37%), respectively. Fifty patients (26%) had severe stenosis of coronary artery defined as >70% luminal narrowing and forty-six patients (24%) had three-vessel involvement of

coronary arteries.

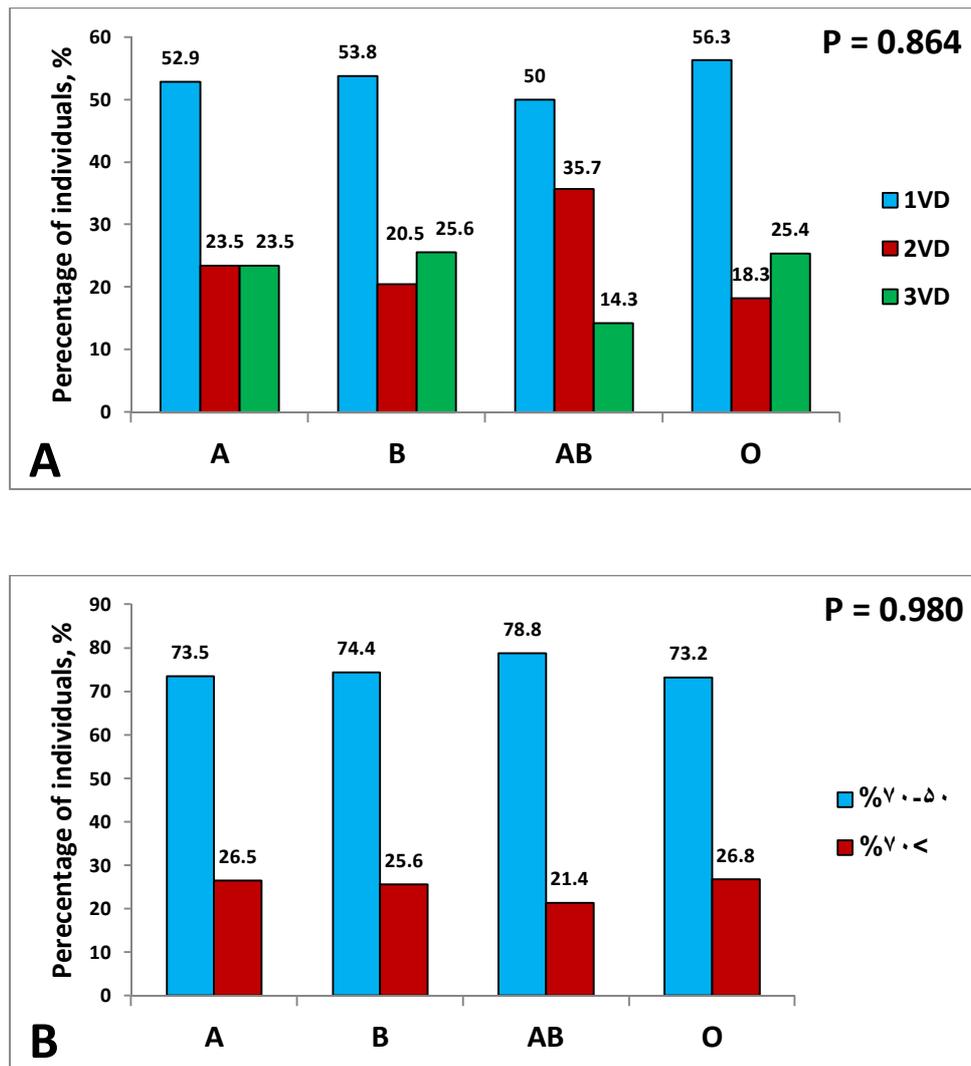
After categorization of patients into the O and the non-O blood groups, the mean age was comparable between groups ( $p = 0.125$ ). The frequency of conventional cardiovascular risk factors was also comparable between groups (all had  $p > 0.05$ ). The number of CAD involvement and CAD severity was not significantly different between groups. Other details are summarized in Table 1.

**Table 1.** Baseline characteristics and angiographic findings in study patients

	O blood group n = 71	Non-O blood group n = 121	P value
Age, year	61.2 ± 9.8	58.7 ± 11.1	0.125
Male, n	45 (63.4)	68 (56.2)	0.329
Diabetes mellitus, n	42 (34.7)	22 (31)	0.597
Hypertension, n	50 (41.3)	35 (49.3)	0.283
Dyslipidemia, n	16 (13.2)	10 (14.1)	0.866
Smoking, n	13 (10.7)	7 (9.9)	0.846
Familial history of CAD, n	11 (9.1)	4 (5.6)	0.389
Rhesus antigen positivity, n	65 (91.5)	105 (86.8)	0.316
Number of involved coronary artery, n			0.656
1VD	40 (56.3)	64 (52.9)	
2VD	13 (18.3)	29 (24)	
3VD	18 (25.4)	28 (23.1)	
Degree of coronary artery involvement, n			0.862
50-70%	52 (36.6)	90 (63.4)	
>70%	19 (38)	31 (62)	

All values are presented as number (%) and mean ± SD

CAD, coronary artery disease; VD, vessel disease



**Fig 1.** The distribution of coronary artery involved (A) and the degrees of coronary artery lumen narrowing (B) among the ABO blood groups

We also compared the distribution of CAD involvement and the degree of stenosis of coronary artery lumen among blood groups and the Rh status. The prevalence of 1-vessel disease, 2-vessel disease, and 3-vessel disease was not significantly different between A, B, AB, and O blood groups ( $p = 0.864$ ). The frequency of coronary artery stenosis was also comparable between the ABO blood groups, too (Figure 1). Irrespective of the ABO blood group, the prevalence of CAD involvement was comparable between groups by the Rh status ( $p = 0.549$ ); however, patients with

negative Rh had lower degrees of coronary artery narrowing compared to those with positive Rh ( $p=0.043$ ; Figure 2).

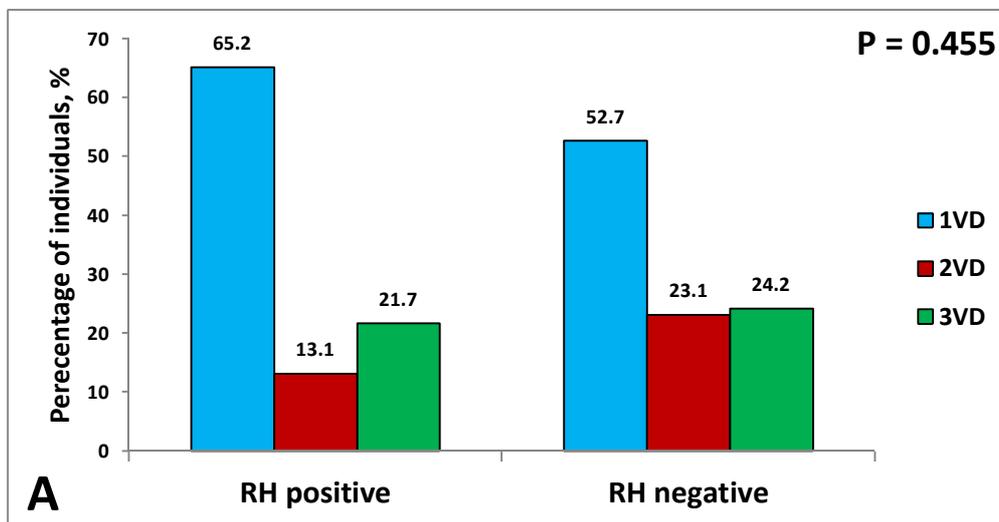
Moreover, we compared patients based on the type of the ABO blood groups, including A, B, AB, and O. The number of patients with a prior history of conventional cardiovascular risk factors was comparable between ABO blood groups (all  $p > 0.05$ ). The severity of CAD defined as the narrowing severity of coronary artery and number of involved coronary arteries were also comparable between ABO blood groups. Other details are summarized in Table 2.

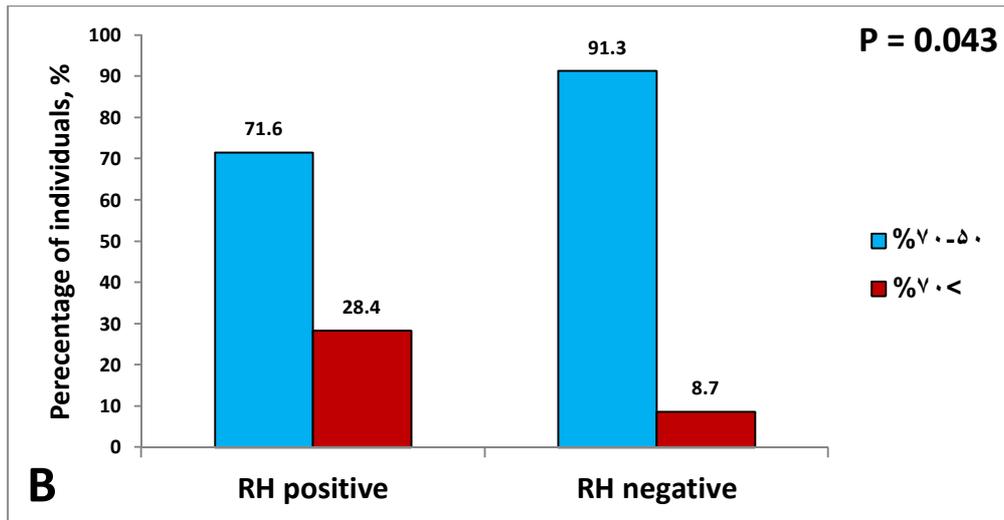
**Table 2.** Baseline characteristics of patients based on ABO blood groups

	A n = 68	B n = 39	AB n = 14	O n = 71	P value
Age					
Male	33 (48.5)	24 (61.5)	11 (78.6)	45 (63.4)	0.114
Diabetes mellitus	26 (38.2)	12 (30.8)	4 (28.6)	22 (31)	0.760
Hypertension	30 (44.1)	14 (35.9)	6 (42.9)	35 (49.3)	0.605
Dyslipidemia	8 (11.8)	8 (20.5)	0	10 (14.1)	0.260
Current smoking	7 (10.3)	5 (12.8)	1 (7.1)	7 (9.9)	0.935
Familial history of CAD	4 (5.9)	6 (15.4)	1 (7.1)	4 (5.6)	0.269
Coronary artery narrowing groups					0.762
<5%	21 (30.9)	14 (35.9)	2 (14.3)	21 (29.6)	
50-70%	29 (42.6)	15 (38.5)	9 (64.3)	31 (43.7)	
>70%	18 (26.5)	10 (25.6)	3 (21.4)	19 (26.8)	
Number of involved coronary artery					0.864
1VD	36 (52.9)	21 (53.8)	7 (50)	40 (56.3)	
2VD	16 (23.5)	8 (20.5)	5 (35.7)	13 (18.3)	
3VD	16 (23.5)	10 (25.6)	2 (14.3)	18 (25.4)	

Values are presented as mean ± SD and number (%)

CAD = coronary artery disease; VD = vessel disease





**Fig 2.** The distribution of coronary artery involved (A) and the degrees of coronary artery lumen narrowing (B) among the Rh status group

## Discussion

In this retrospective study, we found that the distribution of CAD involvement confirmed by diagnostic CAG was comparable between ABO blood groups. On the other hand, irrespective of the ABO blood group, patients with the Rh-negative had lower degrees of coronary artery narrowing compared to patients with the Rh-positive.

The relationship between the ABO blood groups and the risk of CAD has long been recognized, although this association is inconsistent among studies. Wiggins et al.'s study about the association of ABO genotypes with cardiovascular disease has shown an increased risk for MI in patients with A allele carriers compared with O allele homozygotes (15). In another study, Reilly et al (16). Argued that ABO locus was associated with the presence of CAD, but it did not correlate with MI in known CAD patients, indicating different genetic potentials between the development of atherosclerosis and the presence of MI in individuals diagnosed with CAD. He et al (5). in a study consisting of two large cohort studies have shown that the non-O blood group was associated with an increased risk for the development of CAD. In addition, Etemadi et al (1). In

another large cohort study with 7 years follow-up have found that the non-O blood group was significantly associated with mortality in particular due to cardiovascular diseases. In contrast, some reports have shown that O blood group was significantly frequent among individuals with CAD (17,18). Amirzadegan et al (19). Showed that among CAD patients undergoing coronary artery bypass graft surgery there was no association between the ABO blood group and cardiovascular risk factors. Moreover, they found that the prevalence of major risk factors was similar in patients with different ABO blood groups, and ABO blood groups did not affect the development of premature CAD. In another study by Bakker et al (20) among patients undergoing vascular surgeries, no increased hazard of long-term mortality was observed among the non-O blood group patients. The development of cardiovascular events within 30 days after surgery was found to be 4.9% in the non-O blood group and 5.5% in the O blood group patients ( $p = 0.42$ ). In addition, antiplatelet and anticoagulant agents did not interact with such findings. A meta-analysis regarding the impact of ABO blood types on arterial thrombotic events has found a weak association between the non-O

blood group and MI (7). In the present study we showed that there was no significant difference between ABO blood groups and CAD involvement among patients undergoing diagnostic CAG.

The severity of CAD was assessed among individuals with different ABO blood groups. A total of 1152 patients undergoing primary on-pump coronary artery bypass surgery were evaluated in Finland (21). The study showed that patients with blood group B had higher CAG score values, indicating more severe CAD among them compared to other blood groups. In another study, Omidi et al (22) found that the patients with O blood group had more severe CAD compared to non-O blood group. In a cross-sectional study among Chinese population undergoing diagnostic CAG, the Gensini score was significantly higher among the blood group A compared to non-A blood group (10). Among Turkish population with stable CAD, the number of patients with non-O blood group was higher among upper tertiles of SYNTAX score compared to O blood group (23). Moreover, Gong et al (24) found a direct association between the presence of blood group A and the severity of CAS measured by Gensini score. In contrast, among Croatian patients with chronic CAD, there was no association between ABO blood groups and extent of CAD quantified by number of involved coronary artery disease, Gensini score, and the number of segments narrowed >50% in CAG (25). We divided patients into three groups based on coronary artery narrowing, of which there were no significant differences between ABO blood groups, but patients with Rh-negative status had higher degrees of coronary artery narrowing compared to Rh-positive individuals. Moradi et al (26) in a case-control study showed that patients with myocardial infarction had more negative Rh compared to controls. In contrast, in another Iranian-based population, the Rh status was comparable between patients with or without CAD (27). Further studies with

clinical follow-up are required to explore the association between Rh status and CAD severity.

#### **Study Limitations:**

This study suffers from some limitations that need to be addressed in future studies. First, the small sample size of study precludes us from providing more definite conclusion regarding the association between blood group and CAD status. Second, it was a retrospective study without clinical follow-up to show the long-term effects of ABO blood groups and Rh status on prognosis. The large-scale prospective studies are deemed to show the prognostic value of ABO blood group among CAD patients in order to help us with the development of risk stratification of CAD patients.

#### **Conclusion**

The current study showed that there was no association between the ABO blood group and the severity of CAD among patients undergoing diagnostic CAG. Moreover, negative Rh was associated with a higher prevalence of coronary artery stenosis (50-70%). Further large-scale prospective studies are required to explore the prognostic value of the ABO blood group and the Rh status among the Iranian population.

#### **Conflicts of interest**

The authors have none to declare.

#### **References**

1. Etemadi A, Kamangar F, Islami F, Poustchi H, Pourshams A, Brennan P, et al. Mortality and cancer in relation to ABO blood group phenotypes in the Golestan Cohort Study. *BMC medicine* 2015;13:8.
2. Franchini M, Capra F, Targher G, Montagnana M, Lippi G. Relationship between ABO blood group and von Willebrand factor levels: from biology to clinical implications. *Thrombosis journal* 2007;5:14.

3. Carpeggiani C, Coceani M, Landi P, Michelassi C, L'Abbate A. ABO blood group alleles: A risk factor for coronary artery disease. An angiographic study. *Atherosclerosis* 2010;211:461-6.
4. Chen Y, Chen C, Ke X, Xiong L, Shi Y, Li J, et al. Analysis of circulating cholesterol levels as a mediator of an association between ABO blood group and coronary heart disease. *Circulation Cardiovascular genetics* 2014;7:43-8.
5. 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;32:2314-20.
6. Wu O, Bayoumi N, Vickers MA, Clark P. ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. *J Thromb Haemost* 2008;6:62-9.
7. Dentali F, Sironi AP, Ageno W, Crestani S, Franchini M. ABO blood group and vascular disease: an update. *Semin Thromb Hemost* 2014;40:49-59.
8. Askin L, Cetin M, Turkmen S. Absence of a correlation between the ABO blood group and thrombus burden in patients with ST-segment elevation myocardial infarction. *Coron Artery Dis* 2018;29:145-50.
9. von Beckerath N, Koch W, Mehilli J, Gorchakova O, Braun S, Schömig A, et al. ABO locus O1 allele and risk of myocardial infarction. *Blood Coagul Fibrinolysis* 2004;15:61-7.
10. Hong XL, Li Y, Fu GS, Wu H, Wang Y, Gu CX, et al. Association of ABO blood groups with the severity of coronary artery disease: a cross-sectional study. *J Geriatr Cardiol* 2019;16:701-5.
11. Nydegger UE, Wuillemin WA, Julmy F, Meyer BJ, Carrel TP. Association of ABO histo-blood group B allele with myocardial infarction. *Eur J Immunogenet* 2003;30:201-6.
12. Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2014;64:1929-49.
13. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo J, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure The JNC 7 Report. *JAMA* 2003;289:2560-71.
14. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2011;34:S62-9.
15. Wiggins KL, Smith NL, Glazer NL, Rosendaal FR, Heckbert SR, Psaty BM, Rice KM, Lumley T. ABO genotype and risk of thrombotic events and hemorrhagic stroke. *J Thromb Haemost* 2009;7:263-9.
16. 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;377:383-92.
17. Anvari MS, Boroumand MA, Emami B, Karimi A, Soleymanzadeh M, Abbasi SH, 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 Medicine* 2009;40:528-30.
18. Mitchell JR. An association between abo blood-group distribution and geographical differences in death-rates. *Lancet* 1977;1:295-7.
19. 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.
20. Bakker EJ, Valentijn TM, Hoeks SE, van de Luitgaarden KM, Leebeek FW, Verhagen HJ, et al. ABO blood type

- does not influence the risk of cardiovascular complications and mortality after vascular surgery. *Eur J Vasc Endovasc Surg* 2013;45:256-60.
21. Biancari F, Satta J, Pokela R, Juvonen T. ABO blood group distribution and severity of coronary artery disease among patients undergoing coronary artery bypass surgery in Northern Finland. *Thromb Res* 2002;108:195-6.
22. Omidi N, Khorgami MR, Effatpanah M, Khatami F, Mashhadizadeh M, Jalali A, et al. Association between ABO blood group and severity of coronary artery disease in unstable angina. *ARYA Atheroscler* 2017;13:4.
23. Kaya A, Tanboğa İ H, Kurt M, Işık T, Kaya Y, Günaydın ZY, et al. Relation of ABO blood groups to coronary lesion complexity in patients with stable coronary artery disease. *Anadolu Kardiyol Derg* 2014;14:55-60.
24. Gong P, Luo SH, Li XL, Guo YL, Zhu CG, Xu RX, et al. Relation of ABO blood groups to the severity of coronary atherosclerosis: an Gensini score assessment. *Atherosclerosis* 2014;237:748-53.
25. 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. *Biochemia medica* 2013;23:351-9.
26. Moradi M, Alaoddolehei H, Farajpour M, Sadighian F, Naghipour M, Jafari pour I. The association between ABO/Rh blood group and myocardial infarction. *Sci J Iran Blood Transfus Organ* 2018;15:144-8.
27. langari SH, Bahar A, Asadian L, Abediankenai S, Namazi SS, Kashi Z. Coronary Heart Disease and ABO Blood Group in Diabetic Women: A Case-Control Study. *Sci Rep* 2019;9:7441.