ORIGINAL ARTICLE

Blood group types and clinical, procedural, and adverse outcomes in ST-elevated myocardial infarction patients: A 3-year cohort in Iran

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Background: The objectives of this study were to assess the relation of blood groups and the rate of successful angioplasty in patients with ST-elevated myocardial infarction (STEMI) and also to investigate long-term adverse outcomes follow-up. **Materials and Methods:** In this study, 500 eligible patients with definitive diagnosis of STEMI who underwent primary percutaneous coronary intervention (PCI) were followed up for 3 years. The patient's angiography images were examined and thrombolysis in myocardial infarction (TIMI) flow rate and coronary artery patency rate were evaluated in different ABO blood groups. All patients were followed up after 3 years based on major adverse cardiovascular events. **Results:** There was no significant difference in coronary artery patency rate between the patients of the different blood types with respect to TIMI flow before (P = 0.19) and after revascularization (P = 0.69). The incidence of atrial fibrillation (AF) in blood Group A was the highest. Death in the blood Groups AB and O was significantly higher than the other groups. No significant differences were seen in different blood groups in the frequency of mortality (P = 0.13), myocardial infarction (P = 0.46), heart failure (P = 0.83), re-hospitalization, angiography (P = 0.90), PCI (P = 0.94), coronary artery bypass graft (P = 0.26), implantable cardioverter defibrillator (ICD) implantation (P = 0.26), and mitral regurgitation (P = 0.88). **Conclusion:** The incidence of AF in blood Group A and inhospital mortality in blood Groups AB and O were the highest. The blood group may be considered in assessment of clinical risk in STEMI patients.

Key words: Blood group antigens, coronary vessels, myocardial revascularizations, ST-elevated myocardial infarction

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INTRODUCTION

Coronary artery disease (CAD), considering the most important cause of death in the world, is a multifactorial disease and atherosclerosis is one of the most common causes of CAD.[1,2] Although obesity, hypertension (HTN), cigarette smoking, family history, and diabetes mellitus (DM) are known traditional risk factors for CAD, sometimes patients with myocardial infarction (MI) have no risk factors. Genetic factors also play a role in CAD and inheritance of ABO groups could have an important effect in this context.[3,4] Previous studies have shown that blood groups other than O are associated with a higher rate of CAD risk or increased severity of vascular involvement in CAD. In fact, they have stated that blood type O can be considered a protective factor.[5-7]

The association of ABO blood group with plasma lipid levels has been shown previously; the A blood group has been focused on particularly due to higher levels of serum total cholesterol and low-density lipoprotein cholesterol.[3,8,9] The ABO gene encoding

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glycosyltransferases with different substrate specificities to determine blood type is located on chromosome 9q34 with three variant alleles (A, B, and O).[10]

The Framingham study demonstrated a higher rate of ischemic events in the individuals with blood Group A than the other blood groups, but Northwick Park has been reported a significant increase in CAD risk for blood Group AB.[11]

The thrombolysis in MI (TIMI) flow rate is known as a well-studied grading system for coronary reperfusion on angiogram. More survival has been related to earlier TIMI Grade 3 flow with reperfusions thrombolysis or primary percutaneous coronary intervention (PCI).[12] However, there is not enough contemporary data to predict affects of suboptimal TIMI flow as well as the effective management approaches.[13] Even so, it has not been clearly defined if there is any real relation between blood group and CAD or not.

The objectives of this study were to detect the association of blood groups and the rate of vascular patency in the angiography of patients with ST-elevated MI (STEMI) and also to evaluate long-term adverse outcomes.

METHODS

In this study, 500 eligible patients with definitive diagnosis of STEMI who underwent primary PCI, from January 1, 2016, to December 31, 2017, in Chamran Cardiovascular Medical and Research Center in Isfahan, were followed up for 3 years. Patients were excluded from the study if they received treatments other than PCI, i.e., fibrinolytic therapy only.

The research protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1398.718), and all the subjects were asked to fill out the written informed consent in case of death from their families.

Demographic and clinical information of the patients including body mass index (BMI), age, weight, sex, height, and cardiovascular risk factors, such as HTN, DM, cigarette smoking, family history, and history of MI, was extracted from the patients' medical records. After accepting the patient to participate in the study, laboratory assessments including blood group were performed.

The patient's angiography images were examined by two expert interventional cardiologists and TIMI flow and coronary artery patency rate were calculated. All patients were followed up after 3 years based on major adverse cardiovascular events (MACEs). By medical file reviewing and telephone interview, data were gathered.

Cases in the 3-year follow-up that were part of MACE were as follows:

- Nonfatal MI: Experiencing chest pain related to MT, changes in the electrocardiographic (ECG) related to MI, or more than 20% increase in level of baseline troponin I
- Stent thrombosis: Thrombosis originating from the stent or a thrombus 5 mm proximal or distal to the stent leading to partial or complete occlusion of the lumen
- Mortality: Cardiac deaths caused by arrhythmia, MI, decompensated heart failure (HF) (cardiovascular death)
- HF: HF diagnosed with echocardiography.

Statistical analysis was performed by SPSS software (version 25; SPSS Inc., Chicago, Ill., USA). The data were expressed as mean ± standard deviation or n (%). In addition, the Chi-square test was used to compare the frequency distribution of the qualitative data. Furthermore, both the one-way analysis of variance and the Kruskal–Wallis test were used to compare the mean of quantitative data between different blood groups. In all analyzes, a significance level of <0.05 was considered.

RESULTS

Of 500 patients with STEMI, there were 442 (88.4%) males and 58 (11.6%) females with a mean age of 58.24 ± 11.84 years. Among the patients with STEMI, 168 (33.6%) had blood Group A, 103 (20.6%) were with blood Group B, 55 (11%) had AB blood group, and 174 (34.8%) had blood Group O. There was a significant difference in the frequency distribution of the different blood groups in terms of sex ($P < 0.05$), as 90% of patients in blood Groups A and B were male. No significant differences were found between the patients of the different blood groups with respect to age, weight, height, BMI, and past medical history and drug history [$P > 0.05$, Table 1].

In addition, the assessment of the hospital variables showed no significant differences between the patients of different blood types in terms of the ECG and the first ECG for revascularization, type of treatment (PCI or thrombolysis), left main stenosis >50%, number of epicardial coronary artery territories with stenosis >50%, staging PCI, coronary artery bypass graft (CABG), and stent thrombosis ($P > 0.05$).

Furthermore, the evaluation of coronary artery patency rate showed that no significant difference was observed between the patients of the different blood types with respect to TIMI flow rate before and after revascularization ($P > 0.05$). However, a significant difference was found between the patients of the different blood types in terms of

the incidence of atrial fibrillation (AF) and inhospital mortality ($P < 0.05$). The incidence of AF in patients with O blood group was 0, and those with A blood group had the highest incidence of AF. Of 25 deaths, 7 and 12 cases were in the patients with blood Groups AB and O, respectively, which were significantly higher than the other two blood groups [Table 2].

Finally, the assessment of 3-year major adverse cardiovascular effects in patients showed no significant differences between the patients with different blood groups respecting the frequency of mortality, MI, HF, mitral regurgitation, re-hospitalization, angiography, PCI, CABG, and ICD implantation ($P > 0.05$). Furthermore, the incidence rate of stroke was 3.6% (2 cases) and 0.6% (1 case) in the two blood Groups AB and O, respectively, with no stroke in the other blood groups [$P < 0.05$, Table 3].

DISCUSSION

The present study, which included 500 STEMI cases from a cohort of STEMI patients in a major central province of Iran, showed that the presentation, clinical and procedural outcomes of STEMI does not differ between ABO blood groups except for in hospital new AF and in hospital death that was higher in blood Group A, more prevalent in blood Groups AB and O. The incidence of stroke at 3-year follow-up was higher in AB and B blood groups (not clinically meaningful due to small number of events).

Although it has been for several decades that the association of ABO blood groups and CAD risk is investigated, the results have been conflicting and the mechanisms of associations remain unclear.[14] The importance of the ABO blood groups' role in CAD patients' prognosis has been reported in some previous studies,[15] and some of them had not been confirmed this association.[16-19] A significant correlation between blood Group A and the higher risk of postacute M heart rupture has been reported in Fu *et al.*'s study in univariate as well as multivariate analyses that was the first study considering the blood group as an independent risk factor for heart rupture in Chinese subjects with acute *myocardial infarction*.[18]

Biswas's study showed that the AB blood group is associated with lower risk of CAD, while the O blood group is more frequent in atherosclerotic patients.[19] Lee *et al.* proposed that blood Group A is accompanied with an increased risk of CAD and MI than the other blood groups.[20] While they have suggested that blood Group O is significantly associated with a decreased risk of CAD which is not consistent with our study. Omidi *et al.* evaluated 309 patients of moderate- to high-risk unstable angina based on the TIMI risk score. This study showed more prevalent severe CAD in blood Group O compared with the other groups.[21] Chen *et al.* found that there is a significantly higher CAD risk in blood Group A and lower in blood Group O, indicating that both blood Groups A and non-O were the risk factors for CAD.[22] In the patients with uncontrolled blood pressure, the A blood group was suggested as an independent risk factor for CAD presence and severity.[23] Regarding the results of a meta-analysis of ABO blood groups, the risk of MI in non-O blood group increased by 25%; however, it was not confirmed when only the prospective studies

Table 1: Patient characteristics based on blood group

Characteristics	Total	A	B	AB	O	*P*
Age	58.24±11.84	57.55±11.50	57.62±12.95	58±11.72	59.36±11.54	0.49[a]
Weight	77.70±13.31	76.93±12.79	80.72±14.79	76.28±11.38	77.12±13.32	0.14[b]
Height	170.37±8.28	170.17±7.61	171.02±9.87	169.16±8.15	170.55±7.94	0.65[a]
BMI	26.78±4.10	26.66±3.25	27.58±4.50	26.66±3.25	26.47±4.38	0.28[b]
Male	442 (88.4)	153 (91.1)	93 (90.3)	42 (76.4)	154 (88.5)	0.025[c]
Smoker	218 (43.6)	84 (50)	38 (36.9)	22 (40)	74 (42.5)	0.17[c]
DM	136 (27.2)	48 (28.6)	28 (27.2)	15 (27.3)	45 (25.9)	0.96[c]
HTN	163 (32.6)	52 (31)	33 (32)	19 (34.5)	59 (33.9)	0.93[c]
History of hypercholesteromia	151 (30.2)	49 (29.2)	34 (33)	16 (29.1)	52 (29.9)	0.92[c]
History of stroke	20 (4)	6 (3.6)	5 (4.9)	2 (3.6)	7 (4)	0.98[d]
History of MI	54 (10.8)	24 (14.3)	13 (12.6)	4 (7.3)	13 (7.5)	0.16[c]
History of CABG	12 (2.4)	2 (1.2)	4 (3.9)	1 (1.8)	5 (2.9)	0.52[d]
History of AF	7 (1.4)	3 (1.8)	3 (2.9)	1 (1.8)	0 (0)	0.13[d]
History of CHF	56 (11.8)	18 (11.2)	9 (9.3)	4 (7.8)	25 (15)	0.39[c]
History of angina	81 (16.2)	34 (20.2)	18 (17.5)	6 (10.9)	23 (13.2)	0.22[c]
History of PCI	57 (11.4)	21 (12.5)	13 (12.6)	1 (1.8)	22 (12.6)	0.13[c]
History of peripheral vascular disease	12 (2.4)	6 (3.6)	2 (1.9)	2 (3.6)	2 (1.1)	0.37[d]
Sleep apnoea	21 (4.2)	7 (4.2)	6 (5.8)	3 (5.5)	5 (2.9)	0.57[d]
Drug history Antiplatelet	81 (16.2)	32 (19.04)	16 (15.05)	7 (10.9)	26 (14.9)	0.33[c]
Drug history Statin drugs	145 (29)	53 (31.6)	36 (34.8)	13 (23.6)	43 (24.6)	0.83[c]

[b]Kruskal-Wallis. [c]Chi-Square. [d]Fisher's Exact test

Table 2: In-hospital characteristics of AMI based on blood group

Variables	Total	A	B	AB	O	*P*
Time of call to first ECG (hour)	2.01±3.11	2.03±2.95	2.46±4.24	1.68±2.96	1.83±2.43	0.57[a]
Time of first ECG to revascularization (hour)	2.63±4.29	2.46±3.96	2.28±4.13	2.38±3.10	3.07±4.95	0.25[a]
Qualifying ECG						0.89[b]
Anterior STEMI	255 (51)	87 (51.8)	53 (51.5)	30 (54.5)	85 (48.9)	
Others	245 (49)	81 (48.2)	50 (48.5)	25 (45.5)	89 (51.1)	
Treatment						0.23[b]
PCI	205 (44.1)	62 (39)	39 (41.5)	26 (52)	78 (48.1)	
Thrombolysis	260 (55.9)	97 (61)	55 (58.5)	24 (48)	84 (51.9)	
LMS stenosis>50%						o. 46[c]
No	377 (99)	125 (98.4)	75 (98.7)	36 (100)	141 (99.3)	
Protected by CABG	2 (0.5)	0	1 (1.3)	0	1 (0.7)	
Unprotected	2 (0.5)	2 (1.6)	0	0	0	
Number of epicardial territories with stenoses>50%						0.28[b]
0	120 (24)	41 (24.4)	27 (26.2)	19 (34.5)	33 (19)	
1	180 (36)	59 (35.1)	39 (37.9)	21 (38.2)	61 (35.1)	
2	130 (26)	47 (28)	21 (20.4)	11 (20)	51 (29.3)	
3	70 (14)	21 (12.5)	16 (15.5)	4 (7.3)	29 (16.7)	
TIMI flow before						0.19[b]
0	183 (48.7)	67 (52.8)	39 (52)	21 (60)	56 (40.3)	
1	30 (8)	6 (4.7)	4 (5.3)	4 (11.4)	16 (11.5)	
2	69 (18.4)	24 (18.9)	15 (20)	5 (14.3)	25 (18)	
3	94 (25)	30 (23.6)	17 (22.7)	5 (14.3)	42 (30.2)	
TIMI flow post						0.69[c]
0	2 (0.5)	0	0	0	2 (1.4)	
1	8 (2.1)	4 (3.2)	2 (2.7)	0	2 (1.4)	
2	92 (24.6)	33 (26.2)	22 (29.7)	7 (20)	30 (21.6)	
3	272 (72.7)	89 (70.6)	50 (67.6)	28 (80)	105 (75.5)	
Staging PCI						0.14[c]
No	473 (94.8)	161 (96.4)	100 (97.1)	54 (98.2)	158 (90.8)	
Performed	12 (2.4)	4 (2.4)	1 (1)	1 (1.8)	6 (3.4)	
Planned to be performed	14 (2.8)	2 (1.2)	2 (1.9)	0	10 (5.7)	
CABG	3 (0.6)	1 (0.6)	0	0	2 (1.1)	0.86[c]
Stent thrombosis	1 (0.2)	0	0	0	1 (0.6)	1[c]
AF	8 (1.6)	6 (3.6%)	1 (1)	1 (1.8)	0	0.039[c]
Hospital Death	25 (5)	3 (1.8)	3 (2.9)	7 (12.7)	12 (6.9)	0.006

[a]Kruskal-Wallis. [b]Chi-Square. [c]Fisher's Exact test

were included.[24] In acute MI patients, Lin *et al.* showed that blood Type O is related to spontaneous reperfusion of the occluded coronary artery.[13] This report was in contrast to our findings with more inhospital mortality in O blood group. Another study that was done during 4 years of postvascular surgery follow-up in The Netherlands indicated no correlation between ABO blood groups and long-term mortality or cardiovascular side events.[25] It has been also well accepted that ABO blood group distribution is distinct in different ethnics.[26] Thus, these discrepancies may be resulted from the different population and ethnics as well as the various lifestyles.

It has been shown that ABO groups other than O are associated with thrombosis.[27] Furthermore, it is suggested that Factor VIII plasma concentration relation with ABO blood groups can be mediated via *von Willebrand factor*.[28] In a study by Separham *et al.*, the association of a better answer to thrombolytic treatment with A or B blood group antigens in patients with acute STEMI has been reported.[29] In the current study, the baseline TIMI flow as well as procedural successfulness was not different between blood group types. In fact, the degree of coronary patency before and after revascularization did not differ between blood groups.

Not be able to achieve normal TIMI-3 flow has been proposed to be associated with patient-related factors (age, traditional risk markers) as well as other potentially modifiable clinical and procedural risk factors (admission systolic blood pressure, baseline TIMI flow thrombus, and burden total stent length). The lack of final TIMI-3 flow resulted in worse clinical short-term outcomes.[15] High thrombus burden is supposed to be more associated with impaired epicardial and myocardial perfusion as well as percentage of no-reflow.[30]

Table 3: Out of hospital characteristics of AMI based on blood group

Variables	Total	A	B	AB	O	*P*
Mortality	38 (7.6)	7 (4.2)	8 (7.8)	7 (12.7)	16 (9.2)	0.13[a]
MI	14 (2.8)	7 (4.2)	3 (2.9)	0	4 (2.3)	0.46[b]
Stroke	3 (0.6)	0	0	2 (3.6)	1 (0.6)	0.038[b]
HF (EF <55%)	23 (4.6)	9 (5.4)	5 (4.9)	1 (1.8)	8 (4.6)	0.83[b]
Mitral regurgitation	60 (12)	15 (8.9)	11((10.06)	9 (16.3)	25 (14.3)	0.88[a]
RV dysfunction(TAPSE <17mm)	10 (2)	2 (1.1)	2 (1.9)	2.5 (4.5)	3.5 (2.1)	0.43[b]
Rehospitalization	109 (21.8)	36 (21.4)	21 (20.4)	11 (20)	41 (23.6)	0.90[a]
Angiography	70 (14)	24 (14.3)	13 (12.6)	6 (10.9)	27 (15.5)	0.80[a]
PCI	71 (14.2)	23 (13.7)	14 (13.6)	7 (12.7)	27 (15.5)	0.94[a]
CABG	21 (4.2)	9 (5.4)	6 (5.8)	0	6 (3.4)	0.26[b]
ICD	19 (3.8)	6 (3.6)	1 (1)	3 (5.5)	9 (5.2)	0.26[b]

[a]Chi-Square. [b]Fisher's Exact test

Evaluation of coronary artery patency using TIMI flow in STEMI patients regarding blood groups can be considered one of the strong points of this study that, to the best of our knowledge, is not concerned in other cohorts. Larger sample size of STEMI patients in a tertiary referral PCI-capable hospital in central province of Iran as well as valid follow-up data made this study more valuable.

Confounding factors such as ethnics, lifestyle, genetics, and adherence to prescribed drugs made limitations for definite interpretation of results. Regarding the performance of proneness matching and appropriate statistical adjustments for controlling these limitations, it is not possible to eliminate the impact of some unmeasured confounders completely.

In the 3-year follow-up of MACEs, it has been shown in the current study that blood type was not associated with patient mortality. It should be noted that the patients in this study were similar in terms of age, sex, BMI, smoking, and history of underlying diseases, but the evaluation of the other confounding factors such as eating habits, and physical activity adherence to treatment and lifestyle and hereditary factors have not been possible. Therefore, it is not possible to give preference to any of the blood groups in the incidence of long-term mortality of patients. On the other hand, among the MACEs studied for 3 years, only the incidence of stroke was different between blood groups, no stroke in the patients with blood Group A or B, one in O blood group, and two in AB group. The rarity of stroke made any interpretation about stroke difficult. Other complications had the same distribution among different blood groups.

CONCLUSION

This study, on 500 STEMI cases from a cohort of STEMI patients in a major central province of Iran, showed no significant difference between the patients of the different blood types with respect to TIMI flow before and after revascularization. The results of the present study revealed that the incidence of AF in blood Group A and hospital mortality in blood Groups AB and O were the highest. Other clinical and procedural outcomes did not differ between blood types. Furthermore, only the incidence of stroke in the 3-year follow-up of MACEs had a difference between blood groups without valuable interpretable result due to the few event rates. Therefore, given various confounding factors, it can be said that achieving a valuable relationship between blood groups and the occurrence of cardiovascular complications is a very complex task, and this study only considers blood type as a point of reflection for experts and recommends to continue research in this field.

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Conflicts of interest

There are no conflicts of interest.

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