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Blood group as a novel predictor of postoperative atrial fibrillation after off-pump coronary artery bypass grafting

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SUMMARY

OBJECTIVE: The objective of this study was to reveal whether there was a possible relationship between the blood group and postoperative atrial fibrillation after off-pump coronary artery bypass grafting.

METHODS: Between January 2020 and January 2022, 452 patients undergoing off-pump coronary artery bypass grafting surgery consisted of the research population. Patients were divided into two groups based on the occurrence of new-onset atrial fibrillation from the time of operation until discharge. Group 1 (atrial fibrillation group) had 122 patients, whereas group 2 (non-atrial fibrillation group) contained 350 patients. Patients' baseline clinical characteristics and operative and postoperative data were recorded and then compared between the groups. Moreover, a multivariate logistic regression analysis was also conducted to identify the predictors of postoperative atrial fibrillation.

RESULTS: Non-O blood groups were substantially more common in the atrial fibrillation group than in the non-atrial fibrillation group. Patient age differences between the atrial fibrillation and non-atrial fibrillation groups were statistically significant, and patients in the atrial fibrillation group were detected to be older. Mean left atrial diameter, rates of obesity and prior percutaneous coronary intervention history, and perioperative intraaortic balloon pump requirement were significantly greater in the atrial fibrillation group than in the non-atrial fibrillation group. According to logistic regression analysis, blood group, age, left atrial diameter, obesity, and prior percutaneous coronary intervention were identified as predictors of postoperative atrial fibrillation.

CONCLUSION: We demonstrated for the first time in the literature that ABO blood type was a novel and significant predictor of new-onset atrial fibrillation after off-pump coronary artery bypass grafting.

KEYWORDS: Atrial fibrillation. Blood group. Coronary artery bypass grafting.

INTRODUCTION

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia caused by irregular atrioventricular activity, which is characterized by atrial mechanical functional loss[1]. Depending on the atrioventricular node's conduction function, the ventricular rate is variable and irregular. Instead of P waves, an electrocardiogram shows rapid, irregular fibrillation waves of various shapes and sizes[2]. AF is the most common arrhythmia after coronary artery bypass grafting (CABG). It occurs most frequently on the second and third days after the operation[3]. Previously, cardiac surgery-related postoperative atrial fibrillation (POAF) was considered a minor complication. However, in recent research, POAF has been shown to increase early and late mortality and morbidity. POAF is associated with lower left ventricular hemodynamic performance and an increased risk of heart failure and cerebrovascular events, resulting in more extended hospital stays, higher costs, and higher mortality[3]. As a result, it causes problems for both patients and medical professionals and increases the expense of healthcare[4]. Therefore, identifying individuals at risk of POAF and taking appropriate precautions during the perioperative phase is critical.

The presence of A and B antigens on the surface membranes of red blood cells determines the ABO blood group. In addition to red blood cells, the corresponding antigens are expressed on platelets, vascular endothelium, and epithelium. Furthermore, they are found in saliva and body fluids[5]. According to the current literature, there appears to be a link between the ABO blood groups and several autoimmune diseases including Crohn's disease (CD), psoriasis, multiple sclerosis (MS), lupus erythematosus, and type 1 diabetes mellitus (DM)[6-10]. In addition, according to a recent review, many studies have demonstrated the links between ABO blood groups and thromboembolic diseases. Myocardial infarction, atherosclerotic vascular disease, venous thromboembolism, and cardiovascular ischemic events have all been connected, and those with non-O blood groups were shown to be at a higher

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risk than those with O blood groups in all cases[11]. Moreover, a recent study also showed a significant relationship between blood groups and idiopathic high-degree atrioventricular block associated with myocardial fibrosis and sclerosis[12].

To the best of our knowledge, there is no study in the literature examining a possible relationship between the blood group and POAF, which is associated with inflammatory, thrombogenic, and fibrotic processes. Therefore, we designed this study to reveal whether there was a relationship between the blood group and new-onset POAF after off-pump CABG.

METHODS

Ethical considerations

The study obtained approval from the local ethics committee (Decision No: 2022/97, Date: 12/04/2022). All patients were informed about the operation and perioperative process, and their verbal and written consent was taken before the operation. The study was conducted in accordance to the ethical principles of the Declaration of Helsinki.

Study design and population

This cross-sectional study population included 452 patients who underwent off-pump beating-heart CABG surgery in our institution between January 2020 and January 2022. The patients' medical data were gathered from the hospital records and then evaluated retrospectively. The patients were divided into two groups according to the development of new-onset AF during the postoperative period until discharge. There were 122 patients in group 1 (AF group) and 350 individuals in group 2 (non-AF group). Both groups were compared in terms of the baseline clinical parameters, intraoperative data, and postoperative results.

For this study, POAF was defined as new-onset AF of any duration that required pharmacological treatment (i.e., beta-blockers, calcium channel blockers, amiodarone, anticoagulants, etc.).

Exclusion criteria of the study were as follows: a history of paroxysmal, persistent or permanent AF prior to surgery, conventional on-pump CABG surgery, emergency surgery, re-operative surgery, concomitant valve surgery, and surgical techniques other than isolated off-pump CABG.

Surgical procedure

All patients were operated under general anesthesia. Internal thoracic artery and vena saphena magna were the most common harvested bypass grafts. Following the standard median sternotomy and pericardiotomy, coronary arteries and ascending aorta were examined. Coronary anastomoses were initiated following an intravenous heparin administration of 200 IU/kg and obtaining a target-activated clotting time of above 300 s. Distal anastomoses were performed first, followed by proximal anastomoses. Octopus tissue stabilizer was used for providing the proper position of the beating heart. Bulldog clamp and air blowing were used providing a blood-free space during distal anastomosis. The effect of unfractionated heparin was neutralized by protamine infusion after the anastomoses were completed, and the procedure was terminated in the standard fashion.

Arrhythmia monitoring

After the operation, all patients were transferred to the intensive care unit (ICU) and were continuously monitored with a cardiac rhythm monitor during ICU follow-up. All patients had standard 12-lead ECG recordings taken before the operation, immediately after the operation, and then twice a day during their postoperative hospital stay in both the ICU and the acute inpatient ward. Additional ECG recordings were obtained when there was a clinical suspicion of arrhythmia.

Laboratory analysis

The AB0-Rh blood groups were identified using the lam agglutination technique with a blood grouping reagent (Dia-Gast, Loos, France), the microplate agglutination procedure with the Galileo System (Stratec, Frankfurt, Germany), or the gel centrifugation assay with the IH-1000 Fully Automated System (DiaMed, Cressier, Switzerland).

Statistical analysis

Data were collected, tabulated, and statistically analyzed. Before statistical analysis, the distributional properties of the data were evaluated using the Shapiro-Wilk test. For normally distributed data, continuous variables were expressed as mean±standard deviation, and group comparison was performed using an independent two samples t-test. Non-normally distributed data were expressed as median (min.–max.), and group comparison was performed using the Mann-Whitney U test. Categorical variables were presented as the frequency and percentage, and the ^{2} test was used for bivariate comparison. The single and multiple explanatory variable(s) logistic regression (LR) analysis methods were employed. In the single explanatory variable LR analysis, we estimated the odds ratios with 95% confidence intervals of SSI for each study variable, and the significance level of each factor/covariate was determined. In the multiple explanatory variable LR analysis, the initial model was fit including all significant independent variables. Then, a backward-elimination

approach in a multiple explanatory variable LR model was conducted to evaluate the model for potential confounding effects. In this model, the factors/covariates were removed one at a time, starting with the factor/covariate that had the largest p-value, until all remaining factors had a two-sided p-value<0.05. The goodness of fit was tested using the Hosmer-Lemeshow test. The result was considered significant when the P-value was less than 0.05. The statistical software package 21.0 SPSS was used.

RESULTS

The study comprised 122 subjects with POAF and 330 subjects without POAF, and the frequency of POAF was 27% (122/452). When the blood types of the patients were analyzed, the O blood group (23.9%) and the non-O blood group (i.e., A, B, and AB blood group) were detected (73.9%). The majority of patients (86.2%) were Rh (D) positive, whereas 13.7% were Rh (D) negative. The AF and non-AF groups' preoperative demographic and clinical features, as well as intraoperative and postoperative data, were compared (Tables 1 and 2).

Patients in the AF group were significantly older than those in the non-AF group (67.9±7.7 vs. 63.5±10.5 years, p<0.001). A non-O blood group (p<0.004) was significantly more prevalent in the AF group than in the non-AF group. Additionally, mean left atrial (LA) diameter, incidences of obesity, previous percutaneous coronary intervention (PCI) history, and intraaortic balloon pump requirement (IABP) requirement were found to be significantly higher in the AF group than in the non-AF group. Other preoperative demographics and clinical characteristics, as well as all intraoperative

Table 1. Preoperative baseline characteristics of the study groups.

Variables	Non-AF group (n=330)	AF group (n=122)	p-value
Demographic			
Age (years)	63.53 (±10.55)	67.93 (±7.76)	<0.001
Gender, female/male	80/250	32/90	0.664
Blood group type			
0/Non-0 group	98/232	20/102	0.004
Rh positive	284 (86.0%)	102 (83.6%)	0.512
Medical history			
Hypertension	164 (49.0%)	62 (50.8%)	0.888
Diabetes mellitus	136 (41.2%)	42 (34.4%)	0.122
Hyperlipidemia	82 (24.8%)	38 (31.1%)	0.178
Obesity	80 (24.2%)	50 (41.0%)	0.002
Smoking	164 (49.7%)	38 (31.1%)	<0.001
Heart failure	98 (29.6%)	30 (24.6%)	0.225
LVEF level (%)	51.5 (±9.32)	51.26 (±8.82)	0.996
LA diameter (cm)	3.79 (±0.51)	4.39 (±0.85)	<0.001
Peripheral arterial disease	30 (9.1%)	16 (13.1%)	0.209
Myocardial infarction	150 (45.4%)	56 (45.9%)	0.932
Chronic renal dysfunction	38 (11.5%)	18 (14.7%)	0.321
Chronic liver disease	2 (0.06%)	0 (0.0%)	0.389
Chronic pulmonary disease	20 (6.1%)	8 (6.6%)	0.846
Previous CVE	54 (16.4%)	20 (16.4%)	0.994
Previous PCI	52 (15.8%)	34 (27.9%)	0.004
Beta-blocker usage	132 (40.0%)	50 (41.0%)	0.850
LMCA disease	46 (13.9%)	14 (11.5%)	0.193

AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LA: left atrium; CVE: cerebrovascular event; PCI: percutaneous coronary intervention; LMCA: left main coronary artery. p-value<0.05 is considered as statistically significant.

and postoperative variables, revealed no significant differences between the groups.

The independent effects of probable demographic and perioperative parameters associated with POAF were evaluated by univariate and multivariate LR analysis. After applying the univariate analysis, six parameters were found as statistically significant for POAF (i.e., age, non-O blood groups, obesity, LA diameter, previous PCI, and IABP requirement), and then these variables were included in the multivariate analysis. The multivariate analysis revealed that age, non-O blood groups, obesity, LA diameter, and previous PCI were independently linked with POAF (Table 3).

DISCUSSION

This study was designed to examine whether there was a potential predictive relationship between blood groups and the development of new-onset POAF after off-pump CABG. Our findings suggested that patients with non-O blood group types had a higher risk for developing POAF than O blood group patients, as expected. According to multivariate regression analysis, age, LA diameter, obesity, and previous PCI history also caused a higher risk of developing POAF, which is consistent with the literature. The most intriguing and significant finding of our study was that blood group types independently predicted the development of POAF, for the first time in the literature.

The pathophysiology of POAF after CABG is still being researched. According to current evidence, POAF is thought to be caused by a combination of factors. Increased inflammation, Ischemia, oxidative stress, atrial fibrosis, excessive catecholamine delivery to the systemic circulation, autonomic tonus imbalance, and changes in connexin expression all contribute to forming a predisposing anatomic substrate[3].

Previous research has found a link between blood type and diseases caused by inflammation, thromboembolism, and fibrosis. Rumley et al. described that patients with non-O blood groups have lower plasma levels of factor VIIIc and von Willebrand factors than those with blood group O, so their

Table 2. Intraoperative and postoperative variables.

Variables	Non-AF group (n=330)	AF group (n=122)	p-value
LIMA usage	288 (87.3%)	106 (86.9%)	0.193
Complete revascularization	308 (93.3%)	110 (90.2%)	0.257
Inotrope requirement	72 (21.8%)	38 (31.1%)	0.056
In-hospital mortality	8 (2.4%)	2 (1.6%)	0.615
Number of distal bypasses	3.64 (±1.19)	3.72 (±1.17)	0.528
IABP requirement	16 (4.8%)	12 (9.8%)	0.045

AF: atrial fibrillation; LIMA: left internal mammary artery; IABP: intraaortic balloon pump. p-value<0.05 is considered as statistically significant.

Table 3. Results of multivariate logistic regression analysis for the prediction of atrial fibrillation.

Variables	Univariate	p-value	Multivariate	p-value
	OR (95%CI)		OR (95%CI)	
Non-O blood group	0.464 (0.272–0.792)	0.005	0.421 (0.216–0.820)	0.011
Rh positive	1.211 (0.683–2.144)	0.512		
Age	1.047 (1.024–1.071)	0.001	1.039 (0.008–1.071)	0.015
Hypertension	1.031 (0.679–1.565)	0.888		
Obesity	0.468 (0.308–0.773)	0.002	0.535 (0.311–0.922)	0.024
Smoking	2.294 (1.476–3.567)	0.001	1.904 (1.051–3.448)	0.034
Heart Failure	0.745 (0.463–1.199)	0.226		
LA diameter	3.927 (2.712–5.688)	0.001	4.049 (2.630–6.236)	0.001
Previous PCI	0.484 (0.295–0.794)	0.004	0.289 (0.151–0.554)	0.001
IABP requirement	0.459 (0.210–1.000)	0.049		

CI: confidence interval; AF: atrial fibrillation; LA: left atrium; PCI: percutaneous coronary intervention; IABP: intraaortic balloon pump. p-value<0.05 is considered as statistically significant.

risk of thrombosis differs[13]. In a population-based meta-analysis, Kole et al. reported an association between ABO blood groups and cardiovascular disease risk profiles[14]. Astarcıoğlu et al. found that non-O blood type was an independent risk factor for prosthetic valve thrombosis in research that included patients with mechanical prosthetic valve thrombosis[15]. According to Clark et al., the ABO blood group altered the pathogenesis and prognosis in individuals with cerebral Ischemia of arterial origin[16]. In the Framingham study population, peripheral vascular disease was also more prevalent in people with non-O blood types[17].

According to a previous study, there appears to be a link between the ABO blood types and a number of autoimmune illnesses. Studies have shown that ABO blood type significantly impacts circulating glycoprotein levels, which are essential for endothelial function and inflammation[18]. Type A blood was linked to high-sensitivity C-reactive protein levels and the number of antibiotic purchases yearly in prospective cohort research by Parente et al., which looked at ischemic heart disease occurrences in 4531 type 1 DM patients[10]. Furthermore, according to Oner et al., type A blood was the most prevalent genotype in all diabetes groups in both genders. However, type AB was substantially more common among type 1 DM patients[19]. This points to an inflammatory/infectious mediator in diabetes individuals that connects the non-O blood association to specific outcomes. The AB0 antigens have been related to the fructosyltransferase 2 (FUT2) gene, which is also a recognized CD locus. A study on CD patients found that individuals who lacked the FUT2 gene and were non-O blood-type carriers were less protected than type O blood group carriers[6].

Similarly, another study showed that non-O blood type was linked to an increased risk of complications such as invasive illness and structures[20]. Several studies have also shown a link between MS and the ABO blood group. In Basque research, blood group 0 was protective against MS compared with blood groups A, B, or Rh(+)[8]. As a result, evidence indicates that ABO blood types can alter the prognosis of various diseases by influencing the inflammatory status. Most research indicates type 0 as a protective factor and a risk factor for people who do not have type 0.

Furthermore, some research suggests that the AB0 gene may have a role in the fibrotic/sclerotic process. According to Hakyemez et al., blood types may be a hereditary risk factor for progression to severe hepatic fibrosis and cirrhosis.[21] Again, some links between blood types and cancer fibrosis have been discovered[22]. A significant association was found between blood types and the cardiac conduction system related to myocardial fibrosis and sclerosis in a recent study by Acar et al., with the non-O blood group being associated with increased risk[12].

The findings of our research are relevant and useful in clinical practice. Due to the rise in hospitalization and complications, POAF is now highly significant. Before the procedure, it is critical to identify high-risk individuals. According to this research, POAF is linked to fibrosis and inflammation. Fibrosis and inflammation are more likely in people with blood group 0 than those with other blood groups. Consequently, by looking at blood group values that are regularly evaluated during pre-operative evaluation, we may anticipate individuals at risk for POAF.

Limitations

Our study has the following limitations. First, the major limitations of the study were retrospective design and a limited number of cases which included reflection of the experience of a single institution. The second limitation was that due to the need for mid- and long-term data from the research population, it was unable to establish a link between POAF and mid- and long-term survival. Finally, postoperative cardiac rhythm monitoring was not performed constantly after the ICU stay. It is possible to miss the asymptomatic short and silent attacks of POAF.

CONCLUSION

This research demonstrated for the first time in the literature that the ABO blood group was a novel and independent predictor of new-onset AF after CABG surgery. The blood group determination is an inexpensive and easily applicable test routinely performed in the preoperative period, and it may help us predict the new-onset AF after CABG surgery based on the results of our study. Nevertheless, further prospective, large-scale, well-designed studies are required to support our findings and obtain stronger scientific evidence.

AUTHORS' CONTRIBUTIONS

ID: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft. **AM:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing.

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