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Impact of ABO Blood Group on Prosthetic Valve Thrombosis: A Single Center Study

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Abstract

Objective: Prosthetic valve thrombosis (PVT) is an obstruction of a valve prosthesis by non-infective thrombotic material. A number of studies have reported an association between ABO blood groups and thromboembolic events. Little is known about impact of ABO groups on prosthetic valve thrombosis. Therefore, we studied the distribution of ABO blood groups in patients with PVT.

Material and Methods: This was a single center retrospective cohort of patients with PVT during ten years period in the northwest of Iran. All patients received intensified anticoagulation or thrombolysis or redo surgery according to physician decision. Then, all patients divided into two blood group: O and non-O group, and in-hospital adverse events and mortality were compared between groups.

Results: During 10-year period, there were 85 episodes of PVT in 80 patients. Number of patients who developed PVT according to ABO group were: 23 (27%) in group A, 23 (27%) in group B, 12 (14.1%) in group AB and 27 (31.7%) in group O. Overall, 58 (68.2%) patients had non-O blood group. There was no significant difference in distribution of ABO group between general cohort and patients with PVT ($P=0.81$). Failed thrombolysis occurred only in group non-O patients ($P=0.0001$). Also 4 (14.8%) patients in group O and 13(22.4%) in group non-O died ($P=0.4$).

Conclusion: There was no association between ABO blood group and PVT. Complication were more in non-O blood group. Failed thrombolysis was developed only in non-O patients. Larger studies are needed to better define this issue.

Keywords: Prosthetic valve thrombosis, ABO group, Non-O blood group

Introduction

Prosthetic valve thrombosis (PVT) is a rare but serious complication of heart valve replacement. It is an obstruction of a valve prosthesis caused by non-infective thrombotic materials. The interaction of a variety of prosthesis- and patient-related are risk factor for PVT. Indeed, valve thrombosis is a subcategory of thromboembolic events. Thrombus presents acutely with overt congestive symptoms (1).

The ABO blood types introduced by Dr. Landsteiner in 1901. The clinical significance of blood type ABO extends beyond the blood transfusion and organs transplantation. There has been a lot of research into the relationship between blood groups as a cause of various disease or effective factor for prognosis or treatment of disease and cancers (2,3). Although the explanation for the relationship between ABO blood groups and some of the diseases has not yet been fully known, several reports have suggested that there is a relationship between ABO blood types and atherosclerotic cardiovascular diseases (4,5).

Also numbers of studies have reported an association between ABO blood groups and thromboembolic events (6-8).

Some studies also have shown the O blood group can protects against venous thromboembolism in individuals with the factor V Leiden (9).

Increased risk of arterial and venous thrombotic events including myocardial infarction and pulmonary thromboembolism have been seen in non-O blood group subjects (8,10,11). A large study showed in normal and healthy population, non-O blood groups explain >30% of venous thromboembolic events (8). Therefore ABO blood groups may potentially be used for identifying at-risk individuals, but its clinical utility requires further comparison with other risk markers.

The precise mechanism for this increased thrombogenicity may be related to higher level of plasma thrombogen factors. In fact, increased levels of factor VIII (9,12), von Willebrand factor (vWF) (10,12,13), prothrombin fragment (14), and a low a PTT (12) have been found in non-O blood types.

Little is known about impact of ABO groups on prosthetic valve thrombosis. Although blood type cannot be modified as a risk factor, but having the knowledge of the relationship between blood groups and prosthetic valve thrombosis can help to improve control of INR and other

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factors of thrombogenicity. There are conflicting results about the relationship between blood groups and prosthetic valve thrombosis based on research areas.
Therefore, the aim of this study was to study the distribution of ABO blood groups in patients with PVT in a tertiary center.

Materials and Methods

Details of present study has been reported previously (15). Briefly, this was a single center retrospective cohort of patients with PVT during ten years period in the north west of Iran. Diagnosis of PVT was based on clinical presentation and diagnostic modality including echocardiography and or fluoroscopy. Patients with high trans prosthetic gradient in echo study or reduced or fixed leaflet excursion were enrolled in this study. Patients with inadequate imaging data or suspicious to infective endocarditis were excluded. Therapeutic approach was based on physician decision and included 1) Intensified heparin and continuing warfarin, 2) Thrombolysis with streptokinase with following dose: loading dose 250 000 IU in 30 minutes then 100 000 IU per hour for 48-72 hours or 3) Redo surgery including re-replacement or thrombus/pannus excision.
Then, all patients divided to two blood group: O and non-O group, and in-hospital adverse events including death, Intra cranial hemorrhage, Ischemic stroke, major or minor bleeding were recorded in each group.
Continuous variables were expressed as mean ± SD and categorical variables as frequencies and percentages. Comparison of continuous variables was performed by student's *t* test and categorical variables by Fisher exact test. SPSS version 16 was used for statistical analysis and *P* value <0.05 was considered statistically significant.

Results

During ten years, there was 2327 cases of valve replacement in our center. Distribution of blood group in general cohort was as follow: 779 in group A(33.4%), 553 in group B (22.9%), 232 in group AB (9.9%) and 767 in group O (32.9%). During 10-year period, there were 85 episodes of PVT in 80 patients. Number of patients who had developed PVT according to ABO group were: 23 (27%) in group A, 23 (27%) in group B, 12 (14.1%) in group AB and 27 (31.7%) in group O. Overall, 58 (68.2%) patients had non-O blood group.
There was no significant difference in distribution of ABO group between general cohort and patients with PVT ($P=0.81$).When compared to the reported distribution of the ABO group (O 33%, A 33%, AB 10%, B 23%) in Azari population in north west of Iran (8). we observed nearly similar results in patients with PVT.
On the other hand, 4 (14.8%) patients in group O and 13 (22.4%) in group non-O died ($P=0.4$). The distribution of dead patients in non-O group was as follow: 6 (70.3%) in group A, 5 (8.6%) in group B and 2 (3.4%) in group AB.
Table 1 shows the baseline clinical characteristics by blood group. There was no significant difference in clinical, demographic, position and type of involved valves between blood group O and non-O. Mean INR level in group O was slightly elevated than group non-O (3.6 ± 1.7 vs 2.09 ± 1.5 respectively, $P=0.7$). Platelet count was higher in O group than non-O group but this difference was not statistically significant (186300 ± 15873 vs 170880 ± 83701, $P=0.6$). Other laboratory values was similar between group O and non-O (Table 2). With respect to complication of management strategies, main findings were as below. All major complications in thrombolytic group was seen in group non-O and were as follow: Intracranial hemorrhage (ICH) was seen in 2 patients with group B and 1 with group A, ischemic stroke was seen in 2 patients with group B and minor bleeding in 1 with group AB.
Failed thrombolysis occurred only in group non-O patients ($P=0.0001$): Three patients had group AB, 2 had group B and 2 had group A.
All but one complications in surgical group occurred in patients with non-O blood type. One patient with AB blood group developed ICH, one patient with A group had ischemic stroke, one patient with A group and other with B group had minor bleeding and only one patient with O group had major bleeding.
All died patients in thrombolytic group and surgical group had non-O blood type. Two had A blood group, three had B blood group, and two had AB blood group. Considering all complication of patients, there was no significant difference between group O and non-O (Table 3).

Discussion

This study showed there was no significant association between ABO blood group and prosthetic valve thrombosis. But there was more bleeding events in non-O group (albeit statistically nonsignificant). Another main finding of our study was that failed thrombolysis occurred only in

Table 1. Baseline Clinical Parameters According to Blood Group Type

Parameter	O Group (n = 27)	Non-O Group (n = 58)	*P*
Mean age (year)	51.7 ± 12.5	48.0 ± 13.2	0.2
Female (%)	15 (65.2)	34 (56.7)	0.6
Mean time since surgery (year)	6.6 ± 5.3	5.5 ± 5.03	0.4
Position of prosthetic valve, (%)			
Mitral	16 (59.2)	37 (63.7)	0.6
Aorta	8 (29.6)	13 (22.4)	0.2
Tricuspid	2 (7.4)	4 (6.8)	0.6
Mitral + aorta	1 (3.7)	4 (6.8)	0.4
Type of prosthetic valve, (%)			
Bileaflet	21 (77.7)	53 (91.3)	0.2
Cage-ball	2 (7.4)	2 (3.4)	0.3
Tilting disc	1 (3.7)	3 (5.1)	0.7
NYHA class (%)			
I-II	11 (40.7)	25 (43.1)	0.3
III	9 (33.3)	22 (37.9)	0.3
IV	7 (25.9)	11 (18.9)	0.3
Subtherapeutic INR (less than 2.5)	18 (66.6)	40 (68.9)	0.3

Abbreviation: NYHA, New York Heart Association.

Table 2. Baseline Laboratory and Hemodynamic Values According to Blood Type

Parameter	O Group n = 27	Non-O Group n = 58	*P*
Hemoglobin (g/ dL)	12.7 ± 2.2	12.3 ± 2.9	0.5
Creatinine (mg/dL)	1.06 ± 0.3	1.9 ± 0.6	0.3
White blood cells	14513 ± 4882	12350 ± 2082	0.6
Systolic BP (mm Hg)	109.09 ± 4.06	107.69 ± 2.9	0.7
Diastolic BP (mm Hg)	66.52 ± 2.1	68.67 ± 1.5	0.4
Heart rate (bpm)	79.5 ± 5.3	84.9 ± 4.1	0.4
Mortality	4 (14.8%)	13 (22.4%)	0.4

Abbreviation: BP, blood pressure.

Table 3. Complications of Patients According to Blood Group

Complication	O Group n = 27	Non-O Group n = 58	*P*
ICH (%)	0 (0)	4 (6.8)	0.3
Major bleeding (%)	1 (3.7)	0 (0)	0.3
CVA (%)	0 (0)	3 (5.2)	0.5
Minor bleeding (%)	0 (0)	3 (5.2)	0.5
Death (%)	4 (14.8)	13 (22.4)	0.5
Total complication (%)	5 (18.5)	23 (39.6)	0.08

Abbreviation: CVA, Cerebrovascular accident; ICH, Intracranial hemorrhage.

non-O blood group.

There is not any study about impact of ABO blood groups in patients with prosthetic valve thrombosis. In recent years many studies have reported an elevated risk of venous and arterial thrombosis in patients with non-O blood group (17).

Several previous studies reported that peoples with non-0 blood groups had higher risk of all thrombotic events (venous thromboembolism, pulmonary thromboembolism, peripheral or cerebral vascular thromboembolism) compared with group 0 peoples (7-9). Also some study showed higher rates of atherothrombotic coronary events (4,5). But some failed to find such relation (19,20). In contrast, blood group 0 individuals are consistently over-represented in patients with inherited bleeding tendency with the factor V Leiden (9).

The increased risk of thromboembolism may be associated with higher plasma levels of vWF and FVIII factors in the non-0 blood groups persons, as showed vWF levels can be up to 25% higher in non-0 blood groups than 0 blood group individuals (10,12,13).

We did not find such association between non-O blood group and increased risk of PVT. Our results was similar to the study by Hanson et al (18) which did not elucidate any association ABO groups and ischemic stroke. Different pathophysiological mechanism and factors like level of anticoagulation and warfarin metabolism may responsible for these conflicting data. Unlike many previous studies, bleeding events was more seen in non-O blood group. Many arterial and venous thrombotic syndromes have an indolent course, but PVT usually occurs in an acute setting with under coagulation as a major predisposing factor (in our series nearly 70% had inadequate anticoagulation) (15).

This may be responsible for negative results of present study regarding ABO group association with PVT. Apart from this reason there may be another explanation for our results. Recent studies about relation of non-O group with thrombotic disease in Iran have failed to show such association (19,20). This is probably related to ethnical issue and needs further study. Another finding in present study was lack of response to thrombolysis only in non-O group patients. Higher plasma level of vWF may be the cause but again warrants further study.

We found there is not significantly higher PVT rate in non-O blood groups patients with compared with O blood group. Then it was not an independent predictor factor for PVT in patients with mechanical prosthesis.

Study Limitations

Our study has major limitations: Single center, none randomized retrospective nature of this study under powers its finding. Also, we had not enough data regarding details of ABO antigens and genes metabolizing warfarin.

Conclusion

In this study there was no association between ABO blood group and PVT. More complication was seen in non-O blood group. Failed thrombolysis was developed only in non-O patients. Larger studies are needed to better define this issue.

Ethical Issues

Written informed consent was obtained from patients and study approved by ethical committee of our center

Conflict of Interests

The authors declare no conflict of interests.

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None to be declared.

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