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The relationship between the ABO blood group and chronic venous disease in deep vein thrombosis

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ABSTRACT

Aims: This study aims to investigate the relationship between the ABO blood group and chronic venous disease in terms of deep vein thrombosis (DVT).

Methods: This study was planned as a retrospective case-control study in which 1031 patients were included between February 1, 2022, and July 1, 2022. After systematic sampling, the case group (88) and the control group (113) were analyzed in terms of blood groups. Then the patients were divided into 3 groups. group 1: patients with non-O blood group and chronic venous disease (CVD) (n=75), group 2: patients with non-O blood group and non-CVD (n=73), and group 3: patients with O blood group and CVD patients (n=28). It was analyzed whether there was a difference between these 3 groups and from which group and in what form.

Results: The non-O blood group was significantly higher in the DVT group than the control group (p=0.001). There was no significant difference between the A, B, and AB blood groups (p=0.21, p=0.51, p=0.08, respectively). When group 1, group 2, and group 3 were compared, a significant difference was found (p=0.006). In the posthoc analysis, no difference was found between group 1 and group 2 (p=0.99), a difference was found between group 3 and group 1-group 2, and it was found to be lower (p=0.34, p=0.46, respectively).

Conclusion: We found the non-O blood group was higher in the DVT group compared to the control group. We found that the non-O blood group alone was higher in patients with DVT than CVD alone. While non-O blood type and CVD are important risk factors for DVT, non-O blood type can increase the risk of DVT more than CVD. However, this finding needs to be discussed in future studies.

Keywords: Deep vein thrombosis, ABO blood group, chronic venous disease

INTRODUCTION

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a chronic disease that affects approximately 10 million people every year and is an important health problem.[1]

Commonly known risk factors for VTE include increasing age, inactivity, malignancy, major surgery, and heart failure.[2] A close association has been shown between VTE and the non-O blood group, whereas there is less certainty about the relationship between the non-O blood group and arterial thrombosis, especially myocardial infarction.[3]

There are many studies investigating the relationship between ABO blood group or varicose veins and DVT. However, there are not many studies examining these two risk factors separately and investigating which risk factor alone poses a higher risk for DVT. Therefore, we planned this case-control study. We aimed to investigate the relationship between the ABO blood group and varicose veins in terms of DVT.

METHODS

The study was approved by the Kırıkkale University Faculty of Medicine Ethics Committee (Date: 28.09.2022, Decision No: 2022.09.07). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. This study was planned as a retrospective case-control study in which all patients who applied to Kırıkkale Yüksek İhtisas Hospital Cardiovascular Surgery outpatient clinic between February 1, 2022, and July 1, 2022, were examined and a total of 1031 patients were included. Those younger than 18 years of age, patients who have previously been diagnosed with DVT but no DVT was found in their examinations, those with a history of cardiac surgery, patients who underwent surgery for chronic venous disease or peripheral artery disease, those who had thrombophlebitis, those who use direct oral anticoagulants (DOAC), for reasons other than DVT, those with chronic kidney disease, those with cancer, patients with a central catheter, pregnant women, and patients with a genetically proven predisposition to thrombosis were excluded.

The basic demographic characteristics, medical histories, laboratory findings, venous clinical severity scores (VCSS), Villalta scores, Clinical, Etiological, Anatomical, and Pathophysiological (CEAP) scores of the patients, drugs administered, and complications were recorded. The patients

were followed up routinely at 1, 3, and 6 months. The medical treatments of the patients were planned by analyzing the risk group, and low molecular weight heparin (LMWH), vitamin K antagonist (VKA), or DOAC were started.

Firstly, the patients were divided into two groups. Case group: patients with DVT detected in color Doppler ultrasonography (DUS) performed during the first examination (n=88), control group: patients without DVT as a result of DUS (n=653). The diagnosis of CVD disease was made with the examination performed in the outpatient clinic and DUS findings. After that, randomized sampling from the control group was performed and 113 patients were evaluated. In the first stage of the study, it was analyzed whether there was a difference between these two groups. Then, to examine the relationship between blood group and CVD in terms of DVT, all patients included in the study were divided into 3 groups as follows; group 1: Those with non-O blood group CVD (n=75), group 2: Those with non-O blood group without CVD (n=73), and group 3: Those with O blood group with CVD (n=73) n=28) (Figure). In the next stage, it was analyzed whether there was a difference between these 3 groups and from which group and in what form.

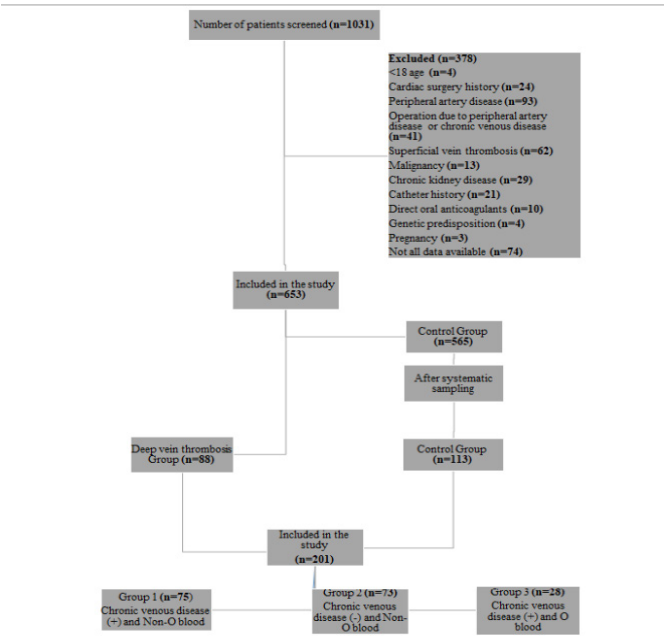

Figure. Flow chart for patient selection

Statistical Analysis

IBM (SPSS) Statistics v.22.0 was used to analyze the data. In descriptive statistics, continuous variables were expressed as min-max, median, and interquartile range and categorical variables were expressed as frequency (n) and percent (%). The normality of the distribution was evaluated with the Kolmogorov-Smirnov test. Student's t-test was used for numerical variables and parametric data, and the Mann-Whitney U test was used for non-parametric data. Pearson $\chi 2$ test and Fisher exact test were used for categorical variables and parametric and non-parametric data. Wilcoxon sign rank test was used to compare scores. The Kruskal-Wallis test was used to make comparisons between groups. Then, post hoc analysis was performed using the Tamhane test. The statistical significance level was accepted as $p<0.05$.

RESULTS

When the basic demographic characteristics of the patients were examined, it was found that chronic obstructive pulmonary disease and cerebrovascular accident were found to be higher in the case group, and female gender in the control group (p=0.001, p=0.02, p=0.001 respectively) (Table 1). There was a similar rate of CVD in both groups (p=0.55). There was no statistical difference between DVT and control groups in terms of CEAP scores among patients with CVD. When compared in terms of blood group, the non-O blood group was found to be significantly higher in the DVT group compared to the control group (n=75, 85.2% and n=73, 64.6%, p=0.001, respectively). There was no significant difference between A, B, and AB blood groups (p=0.21, p=0.51, p=0.08, respectively. Of the patients in the case group, 42 (47.7%) were acute and 44 (50%) were chronic. In the control group, the history of having COVID-19 was lower, and the history of the COVID-19 vaccine was higher (p=0.4, p=0.02, respectively). Although the basic laboratory parameters were similar between the groups, aspartate aminotransferase, and c-reactive protein (CRP) were found to be higher in the DVT group (p=0.03, and p<0.001, respectively). VCSS and Villalta scores decreased significantly in the first month after treatment compared to the first diagnosis (p<0.001, p<0.001, respectively).

To examine the relationship between the non-O blood group and CVD for DVT, the patients were divided into 3 groups and the results of the analysis are shown in Table 2. A statistical difference was found between the groups according to the results of the Kruskal-Wallis test (p=0.006). In the post hoc analysis performed to examine which group the difference originated from, no difference was found between group 1 and group 2 (p=1), a difference was found between group 3 and group 1-group 2, and it was found to be lower (p=0.003, p=0.003, respectively).

Complications observed in the case group during the study period are shown in Table 3. One (1.1%) patient died due to acute massive PE. PE developed in 2 (2.2%) patients, minor bleeding in 1 (1.1%), and residual vein thrombosis in 10 (11.3%) patients. VKA was started in 51 (57.9%) patients, LMWH in 10 (11.3%), and DOAC in 26 (29.5%) patients as initial treatment.

DISCUSSION

DVT is an important cause of morbidity and mortality. Many genetic and acquired risk factors for DVT have been identified so far.[2] The fact that genetic factors cannot be changed is important for patients in this risk group. Many studies have been conducted so far regarding blood type, one of the genetic factors that increase the risk of DVT. Varicose veins, one of the acquired risk factors, have also been shown to have a causal effect on DVT.[4] Yet, as far as we know, there is no study comparing the relationship between these risk factors. Therefore, we planned this case-control study.

As the first result of our study, we found that the non-O blood group was significantly higher in patients with DVT compared to the control group. However, there was no significant difference between A, B, and AB blood groups. These findings support other studies in the literature. Having a non-O blood type has been associated with an increased

Table 1. Patient demographics. clinical characteristics. and laboratory parameters

	Deep vein thrombosis (n=88)			Control (n=113)			
	Min-max or n (%)	Median	IQR	Min-max or n (%)	Median	IQR	p
Gender female	52 (59.09)			74(65.4)			0.001*
Age (years)	20-99	60	26	21-88	50	23	0.09
Height (cm)	144-189	170	12	150-186	168	11	0.057
Weight (kg)	40-130	78	16	38-110	75	18	0.1
Body surface area (kg/m^2)	1.26-2.36	1.9	0.24	1.32-2.31	1.87	0.99	0.04*
Body mass index (m^2)	17.1-48.2	26.6	6.3	15.2-44.4	26.9	6.4	0.25
Coronary artery disease	5 (5.7)			8 (7.1)			0.69
Heart failure	3 (3.4)			1 (0.9)			0.20
Diabetes mellitus	11 (12.5)			11 (9.7)			0.53
Hypertension	23 (26.1)			20 (17.9)			0.14
Chronic obstructive pulmonary disease	10 (11.4)			1 (0.9)			0.001*
Cerebrovascular accident	6 (6.8)			1 (0.9)			0.02*
Smoking	34 (38.6)			38 (33.6)			0.65
0 blood group	13 (14.8)			40 (35.4)			0.001*
Non-0 blood group	75 (85.2)			73 (64.6)			0.001*
A blood group	42 (47.7)			44 (38.9)			0.21
B blood group	18 (20.5)			19 (16.8)			0.51
AB blood group	15 (17)			10 (8.8)			0.08
Chronic venous disease	43 (48.9)			60 (53.1)			0.55
CEAP 1	23 (26.1)			35 (31)			0.45
CEAP 2	17 (19.3)			20 (17.6)			0.64
CEAP 3	3 (3.4)			5 (4.4)			0.41
COVID-19 vaccination	68 (77.3)			101 (89.4)			0.02*
COVID-19 history	44 (50)			50 (44.2)			0.4
Leukocyte (10^9/L)	1.5-14.6	7.8	4.1	3.2-14.0	7.3	2.2	0.001*
Hemoglobin (g/dl)	8.0-16.9	12.0	3.0	9.0-17.0	12.00	1.00	0.002*
Platelet (10^9/L)	101.0-534.0	254.5	93.8	129.0-423.0	262.00	102.5	0.21
Creatinine (mg/dl)	0.2-2.1	0.7	0.4	0.3-8.7	0.6	0.3	0.8
Aspartate aminotransferase (IU/L)	8-522	20	10.4	7-118	18	7	0.03*
Alanine aminotransferase (IU/L)	4-269	17	9.8	5-198	15	8	0.21
C-reactive protein (mg/dl)	0.02-17	0.59	2.0	0.01-11	0.3	0.5	<0.001*
D-Dimer (ng/mL)	52-3864	358	345				
Fibrinogen (mg/dl)	20-45	24	7				
International normalization ratio	0.8-3.8	1.1	3				
Deep vein thrombosis side							
Right	42 (47.7)						
Left	53 (60.2)						
Bilateral	12 (13.6)						
Deep vein thrombosis time							
Acute	35 (39.7)						
Subacute	16 (18.1)						
Chronic	44 (50)						
Deep vein thrombosis localization							
Common iliac vein	3 (3.4)						
External iliac vein	14 (15.9)						
Common femoral vein	46 (52.2)						
Superficial femoral vein	64 (72.7)						
Popliteal vein	70 (79.5)						
Crural	30 (26.4)						
	Admission			First month			
Venous Clinical Severity Score	2-23	7	4	1-21	4	3	<0.001*
Villalta Score	3-24	9	5	1-22	5	4	<0.001*

CEAP: Clinical. Etiology. Anatomy. and Pathological. IQR: Interquartile range

Table 2. Comparison of groups with the Kruskal-Wallis test in terms of DVT

	N	Mean Rank	χ2	p
Group 1	75	93.09		
Group 2	73	93.10	10,17	0,006
Group 3	28	64.21		

Table 3. Complications in the case group, initial and maintenance treatments

Complications	n=88 (%)
Mortality	1(1.1)
Postoperative pulmonary thromboembolism	2(2.2)
Minor bleeding	1(1.1)
Residual vein thrombosis	10(11.3)
Initial therapy	
Warfarin	52(59)
Low molecular weight heparin	10(11.3)
Rivaroxaban	26(29.5)
Maintenance therapy	
Acetylsalicylic acid	7(7.9)
Warfarin	35(39.7)
Low molecular weight heparin	3(3.4)
Rivaroxaban	42(47.7)
Apixaban	1(1.1)

risk of proximal DVT in the lower extremities.[5] Spavor et al.[6] showed that non-O blood type is associated with the risk of DVT. People with non-O blood type have higher levels of factor VIII (FVIII) and von Willebrand factor (vWF) compared to people with blood type O.[7] Elevated FVIII and vWF are moderate risk factors for VTE.8 Larsen et al.[9] showed that women with blood group A or AB had a 2-fold higher risk of VTE during pregnancy and puerperium than women with blood group O, while women with blood group B did not show an increased risk. Jukić et al.[10] also showed that people with non-OO blood type are at twice the risk of thrombosis than those with non-OO blood type. In addition, carriers of AB and A2 B genotypes showed the highest risk of thrombosis, followed by BB/O1 B/O2 B genotypes and O1 A1/O2 A1 genotypes. Dentali et al.[11] reported that non-O blood type may be associated with residual vein occlusion. It is also reported that O-blood group patients have higher fibrinolytic activity compared to non-O patients. These results and the findings of our study overlap with each other. Blood group, which is a simple and easily accessible genetic risk factor that cannot be changed, can be a guide in determining the patient groups in the risk group for DVT.

Because many factors may pose a risk for DVT and these may affect the results of the study, we had to exclude a significant number of patients from the entire patient cohort to reduce the impact of other risk factors. As a result of our study, no significant difference was found between patients with the non-O blood group and CVD and patients with only the non-O blood group in terms of DVT. However, patients with only CVD were associated with DVT at a significantly lower rate than the other two groups. However, in our study, although there was no difference in CVD rates and CEAP stages in patients in the DVT and control groups, it was observed that the majority of CEAP stages were stages 1 and 2. Since patients who underwent interventional procedures for CVD were excluded from the study, the data of many advanced-stage patients were not analyzed. According to the results of this study, it was found that the non-O blood group poses a higher risk for DVT compared to varicose veins, but future studies with a higher number of patients are required to generalize these results.

DVT is a serious complication of COVID-19.[12] Günertem et al.[13] reported that VTE may adversely affect the prognosis of COVID-19 patients and therefore it is important to conduct a risk analysis for DVT. In the control group, the history of having COVID-19 was lower, and the history of the COVID-19 vaccine was higher. Although we matched patient groups for risk factors as much as possible, this difference may have partially affected the results of the study.

It is important to know beforehand about patients at high risk of DVT. When it comes to the long-term treatment phase after DVT treatment, it is useful to pay attention to the blood group while evaluating the risk status of the patient. This simple information can be helpful in counseling, further testing, and identifying patients at risk. However, future studies with larger numbers of patients are needed to clarify these findings.

Limitations

This study was retrospective. At first, there was a significant difference between the number of patients in the case group and the control group. Therefore, we conducted a completely randomized systematic sampling without appropriate patient selection into groups. Patients in the case group included acute and chronic patients and were not homogeneously distributed. Similarly, the CEAP stages were heterogeneous and most of the advanced CVD patients were excluded because of the interventional procedure. The difference in the rates of COVID-19 between the groups may also have affected the result in terms of DVT risk. In addition, we were not able to analyze the FVIII and vWF levels in our hospital. Although we made a detailed comparison for the case and control groups and found no critical differences in terms of baseline characteristics, we were unable to make an additional comparison for Groups 1, 2, and 3 in the second stage due to small numbers. Finally, we could not perform subgroup analysis for the blood group. By analyzing these, more useful results can be found in the future.

CONCLUSION

The non-O blood group was higher in the DVT group compared to the control group. When the non-O blood group and CVD were evaluated together, we found that the non-O blood group alone was higher in patients with DVT than in CVD alone. While the non-O blood type and CVD are important risk factors for DVT, non-O blood type can increase the risk of DVT more than CVD. However, this finding needs to be discussed in future studies.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Kırıkkale University Faculty of Medicine Ethics Committee (Date: 28.09.2022, Decision No: 2022.09.07).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Khan F, Tritschler T, Kahn SR, Rodger MA. Venous thromboembolism. *Lancet*. 2021;398(10294):64-77.
2. Anderson Jr FA, Spencer FA. Risk factors for venous thromboembolism. *Circulation*. 2003;107(23 Suppl 1):I9-I16.
3. Franchini M, Mannucci PM. ABO blood group and thrombotic vascular disease. *Thromb Haemost*. 2014;112(6):1103-9.
4. Li R, Chen Z, Gui L, et al. Varicose veins and risk of venous thromboembolic diseases: a two-sample-based mendelian randomization study. *Front Cardiovasc Med*. 2022;9:849027.
5. Spiezia L, Campello E, Bon M, et al. ABO blood groups and the risk of venous thrombosis in patients with inherited thrombophilia. *Blood Transfus*. 2013;11(2):250-253.
6. Spavor M, Halton J, Dietrich K, et al. Age at cancer diagnosis, non-O blood group and asparaginase therapy are independently associated with deep venous thrombosis in pediatric oncology patients: a risk model. *Thromb Res*. 2016;144:27-31.
7. Schleef M, Strobel E, Dick A, Frank J, Schramm W, Spannagl M. Relationship between ABO and Secretor genotype with plasma levels of factor VIII and von Willebrand factor in thrombosis patients and control individuals. *Br J Haematol*. 2005;128(1):100-107.
8. Martinelli I. von Willebrand factor and factor VIII as risk factors for arterial and venous thrombosis. *Semin Hematol*. 2005;42(1):49-55.
9. Larsen TB, Johnsen SP, Gislum M, Moller CA, Larsen H, Sorensen HT. ABO blood groups and risk of venous thromboembolism during pregnancy and the puerperium. A population-based, nested case-control study. *J Thromb Haemost*. 2005;3(2):300-304.
10. Jukic I, Bingulac-Popovic J, Dogic V, et al. ABO blood groups and genetic risk factors for thrombosis in Croatian population. *Croat Med J*. 2009;50(6):550-558.
11. Dentali F, Di Minno MN, Turato S, et al. Role of ABO blood group and of other risk factors on the presence of residual vein obstruction after deep-vein thrombosis. *Thromb Res*. 2014;134(2):264-267.
12. Cai C, Guo Y, You Y, et al. Deep venous thrombosis in COVID-19 patients: a cohort analysis. clin appl thromb hemost. 2020;26:1076029620982669.
13. Günertem E, Akay T, Aliyev A, et al. Treatment and prophylaxis strategies for deep vein thrombosis during COVID-19 outbreak. *Turk J Vasc Surg*. 2020;29(3):203-207.