

Effect of ABO Blood Groups, Age and Gender on Coagulation Assays in Patients With Acute Deep Vein Thrombosis

Zeliang Chen

Shantou University Medical College

Jinhua Deng

Mianyang Central Hospital

Qingna Hu

Shantou University Medical College

Jing Cao

Shantou University Medical College

Lishan Wu

Shantou University Medical College

Xuerui Tan

Shantou University Medical College

Min Yu (✉ 717146@sina.com)

Shantou University Medical College <https://orcid.org/0000-0003-1135-5088>

Research

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Abstract

Background: Genetic polymorphisms, age, gender and body weight are major determinants of warfarin dose requirements. Our previous study showed that patients with non-O blood groups required higher doses of warfarin than those with O blood groups. However, the underlying mechanism was not well known.

Objectives: The study aimed to investigate the influence of ABO blood group, age and gender on the values of coagulation tests in patients with acute deep vein thrombosis in Chinese Han population.

Methods: A retrospective study was conducted in the First Affiliated Hospital of Shantou University Medical College in Southern China. Two hundreds and 35 patients with confirmed diagnosis of acute deep vein thrombosis were included. Coagulation tests were determined.

Results: Of 235 patients with acute deep vein thrombosis of lower extremities, 70 patients had blood group A (29.79%), 71 patients had blood group B (30.21%), 30 patients had blood group AB (12.77%), and 64 patients had blood group O (27.23%). The study showed no difference about coagulation tests among the patients with different blood groups. Coagulation tests were not affected by age and gender.

Conclusion: Our study showed that ABO blood group, age and gender had no effects on coagulation tests in patients with acute deep vein thrombosis

1. Introduction

Deep vein thrombosis (DVT) is a major health problem worldwide, which can affect more than one out of 1000 people every year [1]. Endothelial injury, hypercoagulability and stasis are three main predisposing factors that favor thrombosis. The common risk factors for DVT included increasing age, obesity, previous venous thromboembolism, surgery, trauma and immobility [2].

ABO blood groups, an inherited characteristic, consist of four types: A, B, AB, and O blood group. The relations between ABO blood groups and human disorder have long been recognized. The potential roles of ABO blood groups in DVT have also been addressed. There is a higher risk for DVT in patients with non-O blood groups than in patients with blood group O [3–5]. More recently, we found that the patients in the O blood group had lower warfarin dose requirements than those in the A, B and AB blood groups [6]. However the underlying mechanism was not well known.

The ABO blood type is long known to have a profound influence on haemostasis, which was mainly associated with factor VIII and VIII levels [7, 8]. It is notable that plasma vWF levels are approximately 25 ~ 30% lower in O type than non-O type individuals [9]. Therefore, ABO blood type likely affects coagulation assays such as activated partial thromboplastin time (APTT) and thrombin generation assay (TGA) values. It was reported that there is a higher APTT value in healthy volunteers with O blood group than that with non-O blood group [10, 11]. Furthermore APTT were affected by age and sex [10].

Coagulation tests such as fibrinogen, fibrin degradation products and tissue plasminogen activator antigen are higher in patients with DVT [12]. However the effects of ABO blood group, age and gender on coagulation tests in DVT remind to be determined. The present study is to investigate the influence of ABO blood group, age and gender on the values of coagulation tests in patients with acute DVT.

2. Methods

A retrospective descriptive study was carried out in the First Affiliated Hospital of Shantou University Medical College in Southern China. Patients diagnosed with acute DVT between January 2015 and April 2020 were reviewed to detect data of patients. The diagnosis of DVT was done based on typical clinical symptoms and the ultrasonograph findings. The patients with severe hepatic or renal insufficiency were excluded. Coagulation assays included prothrombin time (PT), international normalised ratio (INR), APTT, thrombin time (TT), and fibrinogen (Fib). The study profile is shown in Fig. 1. The study was approved by the ethics committee of Shantou University Medical College.

Data are presented as the number of patients or mean \pm SD. Differences between groups were assessed by Chi-square tests or by ANOVA for multiple comparisons using SPSS 16.0. P value < 0.05 was considered significant.

3. Results

As shown in the Table S1 (shown in the supplemental data), there are 235 patients in this study. 93 patients (39.57%) were male and 142 patients (60.43%) were female, with an age of 57.88 ± 16.01 and 57.36 ± 16.86 years old, respectively. 178 patients had thrombosis in the left lower extremity. 46 patients in the right lower extremity and 11 patients in the both lower extremity. The frequency of ABO blood group in patients was as follows: 70 patients had blood group A (29.79%), 71 patients had blood group B (30.21%), 30 patients had blood group AB (12.77%), and 64 patients had blood group O (27.23%). Age, gender, weight, white blood cell (WBC), hemoglobin (HGB), red blood cell (RBC), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), serum creatinine (Scr), uric acid (UA), cholesterol (Chol), triglyceride (TRIG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) between patients with different ABO blood groups were not significant. There was significant difference about platelet among the four groups. Primary clinical characteristics of patients with ABO blood groups are summarized in Table 1. There are no differences of coagulation assays including PT, APTT and INR among A, B, AB and O blood group (shown in Table 2). Considering the sample of group AB patients was small, we compared coagulation assays in blood group O and non-O patients. It was reported that the individuals with type O had prolonged APTT than those with type non-O [10, 11]. However, as shown in Table S2, there was no difference about APTT between the patients with blood group O and non-O (no difference about the clinical characteristics of patients, shown in Table S3). APTT were significantly affected by age and sex, with lower APTT values in females than in males and negative correlation between age and APTT [10], but in present study significant effects of age (shown in Table

S4) and sex (shown in Table S5) on APTT were not observed (clinical characteristics of patients shown in Table S6 and S7 respectively).

Table 1
Primary characteristics of patients with ABO blood groups

Blood group	A	B	AB	O	P-Value
Total number	70	71	30	64	
Age (years, mean \pm SD)	57.38 \pm 16.46	55.08 \pm 17.05	60.00 \pm 14.37	59.39 \pm 16.82	0.386
Sex					0.841
Male	25	30	13	25	
Female	45	41	17	39	
Weight (kg, n = 172)	60.22 \pm 9.94	63.46 \pm 14.31	59.00 \pm 11.48	61.65 \pm 10.34	0.382
WBC ($\times 10^9/L$)	9.06 \pm 3.68	8.38 \pm 2.62	9.01 \pm 3.01	9.02 \pm 2.76	0.523
HGB (g/L)	117.52 \pm 18.75	119.71 \pm 24.75	117.10 \pm 24.42	117.42 \pm 22.59	0.912
RBC ($\times 10^9/L$)	3.97 \pm 0.59	4.14 \pm 0.69	4.04 \pm 0.79	4.01 \pm 0.71	0.501
PLT ($\times 10^9/L$)	198.20 \pm 69.99	228.71 \pm 91.37	263.76 \pm 86.78*	211.51 \pm 72.84	0.002
ALT (U/L)	25.62 \pm 22.20	23.15 \pm 18.59	26.50 \pm 40.62	24.94 \pm 25.78	0.916
AST (U/L)	24.52 \pm 13.03	23.71 \pm 11.09	32.04 \pm 53.60	27.24 \pm 17.71	0.363
BUN (mmol/L)	5.44 \pm 2.74	5.72 \pm 4.39	7.46 \pm 8.53	5.47 \pm 2.60	0.168
Scr (μ mol/L)	92.78 \pm 53.47	105.04 \pm 123.03	127.15 \pm 187.82	84.82 \pm 19.86	0.247
UA (μ mol/L, n = 224)	326.50 \pm 107.49	348.89 \pm 123.61	356.33 \pm 127.12	324.22 \pm 117.63	0.459
Chol (mmol/L, n = 187)	5.07 \pm 1.14	5.00 \pm 1.00	5.51 \pm 1.76	4.85 \pm 1.00	0.161
TRIG (mmol/L, n = 187)	1.26 \pm 0.59	1.39 \pm 0.83	1.30 \pm 0.62	1.18 \pm 0.49	0.427
HDL (mmol/L, n = 187)	1.23 \pm 0.42	1.17 \pm 0.30	1.29 \pm 0.45	1.19 \pm 0.27	0.547

* AB blood group vs A, B and O blood group P < 0.05.

WBC, white blood cell; HGB, hemoglobin; RBC, red blood cell; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Scr, serum creatinine; UA, uric acid; Chol, cholesterol; TRIG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Blood group	A	B	AB	O	P-Value
LDL (mmol/L, n = 187)	3.31 ± 0.84	3.27 ± 0.70	3.53 ± 1.09	3.14 ± 0.77	0.325
* AB blood group vs A, B and O blood group P < 0.05.					
WBC, white blood cell; HGB, hemoglobin; RBC, red blood cell; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Scr, serum creatinine; UA, uric acid; Chol, cholesterol; TRIG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein.					

Table 2
Coagulation assays of patients with ABO blood groups

Blood group	A	B	AB	O	P-Value
Total number	70	71	30	64	
PT (s)	11.64 ± 1.20	11.84 ± 1.61	11.16 ± 0.81	11.57 ± 2.01	0.745
PT% (%)	91.71 ± 19.20	90.23 ± 20.53	97.72 ± 14.02	95.15 ± 19.67	0.222
INR	1.01 ± 0.10	1.02 ± 0.13	0.97 ± 0.07	1.00 ± 0.17	0.302
APTT (s) (n = 103)	29.98 ± 6.76	28.75 ± 5.80	25.69 ± 3.91	28.26 ± 4.85	0.101
PTR	1.01 ± 0.10	1.03 ± 0.14	0.97 ± 0.07	1.00 ± 0.17	0.282
TT (s) (n = 82)	16.63 ± 1.46	18.28 ± 4.32	17.56 ± 1.83	17.02 ± 1.41	0.207
Fib (g/L) (n = 230)	3.27 ± 1.14	3.45 ± 1.18	3.47 ± 0.94	3.16 ± 0.99	0.399
PT, prothrombin time; INR, international normalised ratio; APTT, activated partial thromboplastin time; TT, thrombin time; Fib, fibrinogen.					

4. Discussion

Normal hemostasis is a state of fine balance between procoagulant and anticoagulant factors in circulating blood. DVT is a condition with blood clot developed in the veins. The standard treatment for patients with acute DVT is anticoagulant therapy. Though new oral anticoagulants such as dabigatran, rivaroxaban, apixaban and edoxaban are as safe and effective as vitamin K antagonists (VKAs) [13], warfarin is still the most widely-used anticoagulant in the world and remains a viable oral anticoagulant for many patients because of its availability and cost [14]. However, the anticoagulant activity of warfarin was affected by various factors, such as age, sex, body weight and genetic polymorphisms [15–18], it is not easy to maintain the target INR range. In previous study, we found that there is a higher dose of warfarin requirement in patients with non-O blood groups than O blood groups, the underlying mechanism

was not well known. Whether ABO blood type influences coagulation assays in patients with acute DVT remain to be determined.

Coagulation tests are widely used in clinic to detect abnormalities of hemostasis. The PT, APTT, TT, INR and fibrinogen are commonly performed coagulation tests. The reference intervals had minor variation with sex and age in healthy individuals [19] while. Blood lipids influence the values of PT but not APTT. Individuals with high triglyceride levels ($\geq 200\text{mg/dl}$) had shorter PT values than those with lower triglyceride levels [20]. APTT was significantly prolonged in healthy with type O than those with type non-O while PT was not affected [10, 11]. A shortened APTT is associated with the risk of venous thromboembolism [21]. However, in the present study, there are no differences about APTT among the A, B, AB and O blood groups. Furthermore the difference about APTT between blood group O and non-O was not significant, which suggested that the effect of ABO blood group on APTT varied with race.

PT is used to evaluate the extrinsic and final common pathways of coagulation, which is commonly used to monitor warfarin anticoagulant therapy. However, PT varied with the thromboplastin reagents and the instrument used in the laboratory, it is difficult to monitor warfarin anticoagulation and evaluate the anticoagulation effect of warfarin by PT. To correct for these differences, the INR was introduced. Initial INR before anticoagulation might have an influence on warfarin dose requirements. A lower value of initial INR would need more doses of warfarin when attaining the target INR. In the present study differences in INR between patients with different ABO blood groups were not significant, which suggested that the patients in the O blood group had lower warfarin dose requirements than those in non-O blood groups [6] was not associated with the initial INR.

Fibrinogen plays a key role in the blood coagulation system. Elevated plasma fibrinogen level is a risk factor for cardiovascular disease [22, 23]. Though fibrinogen was higher in patients with DVT than in controls [24], there were no significant differences in fibrinogen in patients with DVT for group O compared with group non-O blood group [25]. In the present study, no differences were also found in patients among A, B, AB and O blood group. Moreover the difference about APTT between blood group O and non-O was not significant, which confirmed the previous report [25].

Apart from ABO blood group, the effects of sex and age on APTT have also been reported [10], with a significant higher APTT value in males than in females and negative correlation with age. However there was no significant difference about the influence of age and sex on APTT, suggesting the effect of age and sex on APTT also varied with race.

There were a few limitations in the present study. First, it was a retrospective study, unknown factors affecting coagulation tests can not be excluded. Second, the population of the study is small, large sample would be needed to verify the relations between APTT and ABO blood groups, sex and age in patients with acute DVT. Last, APTT varied with race [26], the association between ABO blood groups, sex, age and APTT in the Chinese Han population from the Chaoshan region may be different from that in populations from other races in China.

In summary, the present study demonstrated that coagulation tests were not affected by ABO blood group, age and gender in patients with acute deep vein thrombosis in the Chinese Han population from the Chaoshan region.

List Of Abbreviations

Deep vein thrombosis (DVT); Activated partial thromboplastin time (APTT); Prothrombin time (PT); International normalised ratio (INR)

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of Shantou University Medical College. The need for consent was waived because of the retrospective data.

Availability of data and materials

Raw data supporting the obtained results are available at the corresponding author.

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Authors' Contributions:

ZLC and JHD drafted the manuscript. QNH, JC, LSW and XRT were involved in data collection and statistical analysis. MY conceived of the study. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Figures

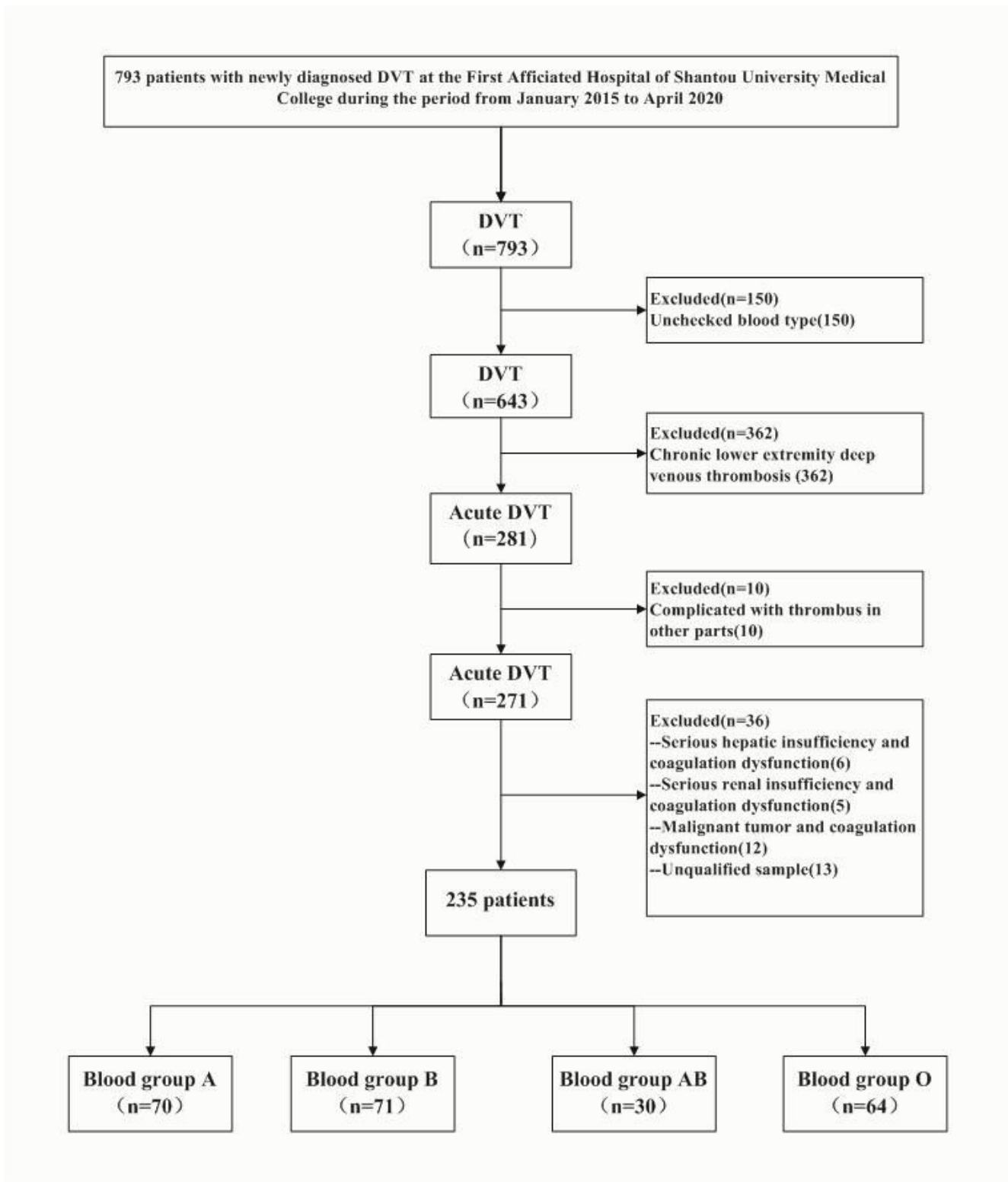


Figure 1

Study profile DVT, deep vein thrombosis;

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