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332.THROMBOSIS AND ANTICOAGULATION: CLINICAL AND EPIDEMIOLOGICAL

Risk Factors, Clinical Manifestations, Anticoagulation Duration, and Outcomes in Carriers of Severe Inherited Thrombophilia

Zina Ibrahim, BS [1], *Jessica Kim, MS* [2], *Maria T DeSancho, MDMSc* [3]

[1] Weill Cornell Medical College, New York, NY
[2] Weill Cornell Medicine, New York, NY
[3] Division of Hematology and Medical Oncology, Department of Medicine, Weill Cornell Medicine/New York Presbyterian Hospital, New York, NY

Severe Inherited thrombophilia comprises deficiencies of antithrombin (AT), protein C (PC), and protein S (PS), while gain-of-function (GoF) variants include homozygosity for factor V Leiden (FVL) or prothrombin gene G20210A mutation (PGM), or double-heterozygosity. Persons with AT, Protein C, or S deficiencies have a heightened risk of developing thrombosis from a young age. Several family members are usually affected, and thrombosis may occur in unusual locations.Homozygote or double heterozygous of GoF variants may not have a family history of thrombosis, and the first thrombotic event may present later in life. The optimal duration and type of anticoagulation and their long-term outcomes for persons with severe thrombophilia require further investigation. This study aimed to compare risk factors, clinical manifestations, type and duration of anticoagulation and clinical outcomes between persons with AT, protein C, and S deficiencies and homozygote or double heterozygous persons with GoF variants.

Retrospective evaluation of electronic medical records of persons with severe inherited thrombophilia referred to the Center for Blood Disorders at Weill Cornell Medicine-New York Presbyterian Hospital between January 2009 and December 2022. Severe deficiencies of AT, PC and PS were defined as (AT $\leq$ 60%, PC $\leq$ 50% and PS $\leq$ 40%). Results needed to be confmed in second testing in one month interval. Statistical analysis was performed using descriptive statistics, and chi-square test and Fisher's exact test were applied to compare variables between persons with AC deficiencies and GoF variants.

795 persons with inherited thrombophilia were identified, of those 671 were excluded as they had mild thrombophilia. Of the remaining 124 persons, 17 were eliminated due to absence of confirmatory results. A total of 107 persons were analyzed. There were 47 (44%) persons with anticoagulant deficiencies (AT, PC, and PS) and 60 (56%) homozygotes for FVL, PGM or double heterozygote. Mean age (SD) was 48 (13.6) and 49 (12.2) for anticoagulation deficiency and GoF mutation, respectively (Table 1).

Overall risk factors for thrombosis were similar in both groups. A positive family history of thrombosis in a first-degree family member was higher in the anticoagulant deficient group (68%) compared to the GoF mutation (42%) (p=0.008). In addition, persons with anticoagulant deficiency had higher rates of thrombosis before 40 years of age compared to the GoF mutation group, 68% and 26%, respectively (p=0.031). The most frequent anticoagulant prescribed was a DOAC in both groups, with 38% and 30% used for the anticoagulation deficient group and GoF mutation group, respectively. The duration of anticoagulation was similar in both groups with most patients remaining on anticoagulation for more than one year (79% anticoagulant deficient group, 65% GoF mutation group) (p=0.3). Patients with AC deficiency had more recurrent thrombotic events while on anticoagulation compared to GoF variants (17% vs 6.7%) (Table 2). Our results indicate that patients with severe inherited thrombophilia either due to anticoagulant deficiencies or GoF mutations are likely to remain on anticoagulation for long durations and may have recurrent thrombosis despite therapeutic anticoagulation.

Disclosures No relevant conflicts of interest to declare.

Table 1

Baseline Characteristics	Anticoagulant Deficiency, N = 47	Gain of Function Mutation, N = 60	P value
Race/Ethnicity			
American Indian	0 (0%)	2 (3.3%)	
Asian	6 (13%)	0 (0%)	
Black/African American	6 (13%)	0 (0%)	
Hispanic/Latino	2 (4.3%)	0 (0%)	
Multiracial	0 (0%)	3 (5.0%)	
Unknown	2 (4.3%)	3 (5.0%)	
White	31 (66%)	52 (87%)	
Sex			
Female	31 (66%)	45 (75%)	
Male	16 (34%)	15 (25%)	
Age			
Mean (SD)	48.0 (13.6)	49.0 (12.2)	
Median (IQR)	47.0 (39.0, 52.5)	48.0 (41.0, 55.2)	
BMI			
Mean (SD)	26.2 (4.4)	26.2 (4.2)	
Median (IQR)	25.9 (22.8, 28.7)	25.5 (23.5, 28.9)	
Unknown	4	2	
Family History of Thrombosis			0.008
Yes	32 (68%)	25 (42%)	

Table 2

	Anticoagulant Deficiency (n=47)	Gain of Function Mutation (n=60)	p value
Age at First Thrombosis			0.031
< 40 years old	32 (68%)	26 (43%)	
> 40 years old	5 (11%)	15 (25%)	
Asymptomatic/Unknown	10 (21%)	19 (32%)	
Treatment			0.8
ASA	8 (17%)	8 (13%)	
DOAC	18 (38%)	18 (30%)	
LMWH	6 (13%)	8 (13%)	
VKA	6 (13%)	11 (18%)	
None	9 (19%)	15 (25%)	
Duration of Treatment			0.3
< 1 year	2 (4.3%)	3 (5.0%)	
> 1 year	37 (79%)	39 (65%)	
Unknown/Lost to follow-up	8 (17%)	18 (30%)	
Outcomes			0.3
Residual thrombosis	7 (15%)	5 (8.3%)	
Recurrent thrombosis off anticoagulation or on subtherapeutic anticoagulation	7 (15%)	13 (22%)	
Recurrent thrombosis on anticoagulation	8 (17%)	4 (6.7%)	
Resolution of thrombosis	5 (11%)	11 (18%)	
Major bleeding	1 (2.1%)	0 (0%)	
Unknown/Lost to follow-up	8 (17%)	8 (13%)	

Figure 1

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