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The Association Between Thromboembolic Complications and Blood Group in Patients With Atrial Fibrillation

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Abstract

Objective: To determine whether blood type affects the risk of thromboembolic complications in patients with atrial fibrillation (AF).

Patients and Methods: The Mayo Clinic electronic medical record was searched (between January 1, 2004, and December 31, 2010) to identify all patients with AF with blood group assessment. Records were analyzed for stroke, transient ischemic attack, left atrium appendage thrombus, cerebral or peripheral embolism, and hemorrhagic stroke. All events were adjusted for Congestive heart failure, Hypertension, Age >75 Years, Diabetes mellitus, and Stroke/transient ischemic attack score.

Results: Of the 47,816 patients with AF, 14,462 had blood group type available (40% women; mean age, 73±12 years). These included 12,363 patients with nonvalvular atrial fibrillation (NVAF) (40% women; mean age, 73±12 years) and 2099 patients with valvular AF (41% women, mean age, 73±12 years). Within patients with NVAF, the rate of peripheral embolization was significantly lower in those with blood type O (2.0%) than in those with other blood types (3.0%; odds ratio, 0.66; 95% CI, 0.52-0.84; $P<.001$). Neither cerebral thromboembolic (8.1% for "O" vs 8.2% for "non-O" blood group for NVAF and 7.29% vs 7.76% for valvular AF) nor cerebral hemorrhage (2.0% each group) events rates differed by blood group.

Conclusion: Blood group O may be protective against peripheral cardioembolic complications of NVAF, which may relate, in part, to reduced circulating von Willebrand factor levels. Cerebral thromboembolic event rates did not differ by blood group.

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The ABO blood group system is categorized into blood groups A, B, AB, and O on the basis of differing red cell membrane antigens. Beyond relevance to transfusion medicine, blood groups have been shown to exhibit differing bleeding and thromboembolic propensity.[1,2] Indeed, a meta-analysis of studies on blood group type and the risk of cardiovascular complications revealed a significant association between non-O blood groups and the risk of myocardial infarction (pooled odds ratio [OR], 1.25; 95% CI, 1.14-1.36; $P=.00001$) and ischemic stroke (pooled OR, 1.14; 95% CI, 1.01-1.27; $P=.03$).[2] Multiple previous studies have reported a close relationship between blood group type and von Willebrand factor (VWF) level.[3-7] In fact, 30% of the genetic determinant of the VWF level is related to the effect of ABO blood group. N-Linked oligosaccharide side chains on VWF molecules contain A and/or B blood group antigens that are encoded by the blood group gene (*ABO*), and the presence of these antigens decreases VWF clearance.[8,9] Consequently, individuals with A, B, or AB blood group have increased circulating VWF and factor VIII levels relative to those with group O. Patients with blood group O have 25% lower levels of VWF than do patients with non-O blood groups.[5]

Atrial fibrillation (AF) increases the risk of thromboembolism 5-fold.[10] Although stroke is the most common complication of this dysrhythmia, peripheral emboli account for 4% to 6% of embolic events.[11,12] Annual thromboembolic rates in AF, however, vary over a 40-fold range.[13] Despite a growing list of individual patient risk factors, the individual propensity for thromboembolism in AF remains poorly understood. Clearly, additional risk factors important

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in AF-associated thrombogenesis remain to be elucidated.[10-13] Although previous studies have identified the VWF level and activity as independent predictors of thromboembolic complications in nonvalvular atrial fibrillation (NVAF),[14-16] the association between blood groups and the risk of AF-related thromboembolic complications has not been evaluated.

To determine whether blood group type affects the risk of thromboembolic complications in patients with AF, event rates in patients with blood group O were compared with those with other blood groups.

PATIENTS AND METHODS

The Mayo Clinic electronic medical record was searched (between January 1, 2004, and December 31, 2010) to identify all patients with AF. Subsequently, all patients with the diagnosis of AF and blood group assessment were identified. Patients were considered to have the diagnosis of AF if this arrhythmia was confirmed by either electrocardiography or Holter monitoring. Patients were divided into valvular atrial fibrillation (VAF) and nonvalvular atrial fibrillation (NVAF) groups on the basis of the presence of heart valve prostheses (mechanical or biological), more than moderate native valve disease, and other organic heart diseases. All patients gave written consent to use their clinical data and biological specimens for research purposes. This protocol was approved by the Institutional Review Board of the Mayo Foundation (IRB 10-005963), and all research was conducted according to the Declaration of Helsinki.

Congestive heart failure, Hypertension, Age >75 years, Diabetes mellitus, and Stroke/transient ischemic attack (TIA) ($CHADS_2$) scores were calculated for each patient.[17] *International Classification of Diseases* codes were used to identify all AF-related events including cerebrovascular accident (codes 438.0-438.9), transient cerebral ischemia or TIA (codes 435, 435.8, and 435.9), cardioembolism of cerebral arteries (codes 434.1, 434.10, and 434.11), cardioembolism of peripheral arteries (codes 444.0-444.9), and hemorrhagic cerebrovascular accident (codes 430-432.9). Only those events occurring after the confirmation of AF were included in the analysis. Mayo Clinic Echocardiography Laboratory and Cardioversion Unit databases were used to identify all patients with AF and established blood group type who had undergone transesophageal echocardiography (TEE) and those with documented left atrium appendage thrombus (LAAT).[18,19] A patient was considered to be treated with warfarin if clinical records indicated an international normalized ratio (INR) of 1.5 or more and no evidence of liver disease.

Statistical Analyses

The study design was a retrospective cross-sectional analysis. Patient characteristics were tested for statistical significance using 1-way analysis of variance for continuous variables and Pearson chi-square test for categorical variables. The effect of blood group type on cardioembolic or hemorrhagic event rates was tested using logistic regression after adjustment for $CHADS_2$ scores. Results are presented as ORs with corresponding 95% CIs. The cutoff for significance was set at a P value of .05.

Results

Between January 1, 2004, and December 31, 2010, 47,816 patients with AF (18,299 women; mean age, 74±12 years; 29,517 men; mean age, 71±12 years) were evaluated at Mayo Clinic's campus in Rochester, Minnesota (Figure 1). Of these, 14,462 (30%) patients with AF (5815 women; mean age, 74±12 years; 8647 men; mean age, 72±11 years) had blood group testing. Patients were divided into NVAF or VAF on the basis of their valvular status. NVAF was diagnosed in 12,363 (85%) patients (4950 women; mean age, 74±12 years; 7413 men; mean age, 72±11 years) and VAF in 2099 (15%) patients (865 women; mean age, 74±12 years; 1234 men; mean age, 72±11 years). Sex, age, distribution of each $CHADS_2$ element, and final $CHADS_2$ scores were evenly distributed by blood group types for NVAF (Table 1) and VAF (Table 2) groups. $CHADS_2$ scores were not reported for patients in the VAF group because this stroke risk score system was designed and validated for NVAF only.[17]

The ABO blood group distribution of the study participants and that of the US population[20] was very similar (Figure 2).

The percentage of patients with NVAF treated with warfarin did not vary by blood group (P=.58): group A, 70%; AB, 63%; B, 77%; and O, 67%. Similarly, the percentage of patients with VAF treated with warfarin