The Factor V Leiden, Prothrombin Gene 20210GA, Methylenetetrahydrofolate Reductase 677CT and Platelet Glycoprotein IIIa 1565TC Mutations in Patients With Acute Ischemic Stroke and Atrial Fibrillation

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Background and Purpose—We wanted to investigate whether common prothrombotic mutations are more prevalent in patients with atrial fibrillation who have had a stroke than in healthy controls. We also wanted to assess whether early recurrent ischemic cerebrovascular events were more frequent among carriers of the factor V Leiden or the prothrombin gene mutations than among others.

Methods—We used a case-control design with 367 patients with acute ischemic stroke and atrial fibrillation (cases) and 482 healthy blood donors (controls). All mutations were detected with conventional polymerase-chain reaction protocols.

Results—The odds ratios for carriers of the factor V Leiden, prothrombin gene 20210GA, methylenetetrahydrofolate reductase 677CT, or platelet glycoprotein IIIa 1565TC (PlA2) mutation were 0.91, (95% CI, 0.51 to 1.59), 2.25 (95% CI, 0.61 to 8.90), 0.83 (0.61 to 1.13), and 0.79 (0.57 to 1.10), respectively. Early recurrent ischemic stroke and total recurrent ischemic cerebrovascular events were slightly more frequent among carriers of the factor V Leiden mutation than among noncarriers: odds ratio 1.45 (95% CI, 0.41 to 5.1), and 1.59 (0.61 to 4.1), respectively. None of the patients with recurrent ischemic cerebrovascular events had the prothrombin gene mutation.

Conclusion—These mutations are not important risk factors for thromboembolic stroke associated with atrial fibrillation. Carriers of the factor V Leiden mutation had a small, nonsignificantly higher risk of early recurrent ischemic cerebrovascular events. (Stroke. 2007;38:1069-1071.)

Key Words: atrial fibrillation ■ ischemic stroke ■ prothrombotic gene mutations
Results

Table 1 shows the prevalence of the mutations in patients and controls. No patients were homozygous for the factor V Leiden or the prothrombin gene mutation. The odds ratio for carriers of the factor V Leiden, the prothrombin gene, the MTHFR (homo- and heterozygotes) and the GPIIIa mutations were 0.91 (95% CI, 0.51 to 1.59), 2.25 (0.61 to 8.90), 0.83 (0.61 to 1.13) and 0.79 (0.57 to 1.10), respectively. Early recurrent ischemic stroke and total recurrent ischemic cerebrovascular events were slightly more frequent among carriers of the factor V Leiden mutation than among noncarriers: odds ratio 1.45 (95% CI, 0.41 to 5.1) and 1.59 (0.61 to 4.1), respectively. Of the 54 patients who had an early recurrent ischemic cerebrovascular event, none had the prothrombin gene mutation, compared with 8 of 301 (2.7%) among carriers of this mutation. Unfortunately, HAEST was too small for a subgroup analysis of patients with the factor V Leiden mutation to be informative.

Discussion

Our results indicate that none of these prothrombotic gene mutations are important risk factors for ischemic stroke in patients with atrial fibrillation. This means that these mutations cannot be used to identify patients with atrial fibrillation who are at particularly high risk of ischemic stroke, or to select patients for oral anticoagulant treatment. These results are consistent with previous findings in unselected patients with ischemic stroke.1-3,11,12

We cannot completely rule out the possibility of an association. First, although this is a relatively large study of these mutations in this high-risk population, the sample size is still limited and the confidence intervals relatively wide. Secondly, confounding from other prognostic variables may have played a role. Although we performed a number of stratification analyses, we may not have been able to control for all variables of prognostic significance.

To our knowledge no other studies have investigated whether the factor V Leiden or prothrombin gene mutations are risk factors for recurrent ischemic cerebrovascular events in the acute phase of stroke. We found a small, nonsignificant trend toward a higher risk of recurrent ischemic cerebrovascular events among patients who were carriers of the factor V Leiden mutation. If this is true, more intensive antithrombotic therapy may be warranted in acute stroke patients who are carriers of this mutation. Unfortunately, HAEST was too small for a subgroup analysis of patients with the factor V Leiden mutation to be informative.

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Disclosures

None.

References


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