Dear Sir,

Whether the Marburg I variant of factor VII-activating protease (FSAP Marburg I) is associated with an increased risk of venous thromboembolism (VTE) is still an open question. Until now, this topic has been addressed only by two small case-control studies showing differing results (1, 2). This could possibly be due to different characteristics of the patients included in both studies. In the first study, patients with VTE were examined irrespective of whether they presented with a first event of VTE or VTE recurrences (1). In the second study, only patients with a first event of deep vein thrombosis had been included (2). Thus, additional larger studies are needed to give a definite answer on this question. If an association of this variant with idiopathic VTE – as initially described by our group (1, 3) – would be confirmed, studies on the influence of FSAP Marburg I on the recurrence risk of VTE would be indicated, because this clinically defined subgroup of VTE is known to be at a high risk for recurrence (4).

In the January 2006 issue of this Journal, Gulesserian et al. reported on the influence of FSAP Marburg I on the recurrence risk of VTE (5). They analysed the FSAP genotype distribution in a cohort of patients with a first episode of unprovoked VTE, and performed statistical analyses on the probability of and the relative risk (RR) for recurrence. Comparing patients with different FSAP genotypes, there were differences in the cumulative probabilities of recurrence over three years (FSAP Marburg I: 20% vs. wild-type: 12.2%) and the RRs (with/without adjustment for confounding factors: 1.5/1.3), which, however, did not reach statistical significance. They concluded that, if at all, FSAP Marburg I only can be considered a mild risk factor for recurrent VTE.

However, the described study is underpowered for the determination of an association with VTE recurrence of a realistic order of magnitude. The main conclusion of this study is that there is no significant influence of FSAP genotype on VTE re-

Marburg I polymorphism of factor VII-activating protease and risk of recurrent venous thromboembolism

Berthold Hoppe, Thomas Dörner, Holger Kiesewetter, Abdulgabar Salama
Institute of Transfusion Medicine, Campus Benjamin Franklin, Charité – Universitätsmedizin Berlin, Berlin, Germany

Correspondence to:
Dr. Berthold Hoppe
Institute of Transfusion Medicine
Campus Benjamin Franklin, Charité – Universitätsmedizin Berlin
Hindenburgdamm 30
12203 Berlin, Germany
Tel.: +49 30 450553089, Fax: +49 30 450553988
E-mail: berthold.hoppe@charite.de

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currence rates (*FSAP Marburg I*: 7 of 41 patients, recurrence rate: 17%; *FSAP wild-type*: 106 of 813 patients, recurrence rate: 13%). However, the statistical power of this conclusion – calculated by GraphPad StatMate 2.00 (GraphPad Software, USA) – is only about 15%. This is mainly due to the relatively low frequency of *FSAP Marburg I* in the collective studied. When considering the conditions of the present study [N (*FSAP Marburg I*): 41; N (*FSAP wild-type*): 813; recurrence rate (*FSAP wild-type*): 13%] the relative VTE recurrence risk for carriers of *FSAP Marburg I* would have to be as high as 2.8 to reach a statistical power of 80% at a type I error of 0.05. The expectation of such a pronounced influence of *FSAP Marburg I* on the RR of VTE recurrence seems to be inadequate. Depending on the study regarded, even coagulation inhibitor deficiencies [overall: RR: 1.44, (6) – protein C: RR: 1.84, (7) – antithrombin: RR: 2.59, (7)] do not attain a relative risk of this order of magnitude.

References