Importance of Family History as a Risk Factor for Venous Thromboembolism

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Venous thromboembolism (VTE) is a multifactorial disease with many known genetic and acquired risk factors. A positive family history is an independent risk factor for VTE that may reflect the presence of a hereditary thrombophilic disorder. However, the predictive value of a positive family history for detection of known heritable causes of VTE is low, suggesting that there are as-yet undiscovered genetic or environmental risk factors that account for the familial clustering of this disorder.

The most striking findings of the study by Zöller et al was rigorously conducted and is the largest population-based study to date that explores the importance of family history as a risk factor for VTE. The study provides robust evidence of the strength of the association and the influence of age and sex on this association. A potential limitation of the study is that it was restricted to hospitalized cases of VTE, thereby excluding information on siblings who were treated as outpatients. One method to explore the impact of excluding outpatients would be to examine the consistency of the results over the 21-year study period because the shift from inpatient to outpatient management of VTE gained increasing popularity over the years. Although this was not done, outpatient management of VTE is unlikely to have had much impact on the standardized incidence ratios because there is no reason to suspect that patients with a familial sibling VTE history would be affected differently by outpatient treatment than those without such a history. Another potential limitation of this study is the lack of information about known risk factors for VTE. The absence of this information precludes exploration into the extent to which genetic and environmental VTE risk factors contribute to the familial clustering of cases.

The findings of this study have implications for clinical practice. Family history is a powerful risk factor for VTE, particularly in those who have >1 sibling with a history of VTE. Known genetic thrombophilic disorders account for only a fraction of the risk conferred by a positive family history, indicating that testing family members does little to improve risk prediction. In families in which >1 sibling has a history of VTE, the high risk of VTE mandates vigilance for early detection of recurrent disease, avoidance of recognized environmental risk factors such as estrogen-containing compounds, and vigorous thromboprophylaxis during periods of...
The pathogenesis of VTE reflects a complex interplay between inherited and acquired risk factors. The study by Zöller et al highlights the importance of a family history of VTE over the life cycle. For younger patients, a positive family history is a major risk factor for VTE that trumps known thrombophilic disorders. What are the genetic defects responsible for this association? This is an area that deserves further study.

### Disclosures

None.

### References


### Keywords

- Editorial
- Epidemiology
- Risk factors
- Thrombosis
- Venous thrombosis
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Circulation. 2011;124:996-997
doi: 10.1161/CIRCULATIONAHA.111.048868
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/124/9/996

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