Q/ Does hypercoagulopathy testing benefit patients with DVT?

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No evidence suggests that hypercoagulopathy testing benefits most patients with DVT or predicts recurrence better than clinical risk assessment.

EVIDENCE-BASED ANSWER

A/ **NO.** There is no evidence to suggest that testing for hypercoagulopathy benefits most patients with deep venous thrombosis (DVT). Nor has research established that thrombophilia test results improve the ability to predict recurrence better than clinical risk assessment alone (strength of recommendation [SOR]: **B,** multiple cohort studies).

Testing may be warranted in patients younger than 50 years with idiopathic DVT or patients with recurrent episodes of thromboembolism to assess risk in other family members (SOR: **C,** expert opinion).

A theoretical cost-benefit analysis demonstrates that testing for antiphospholipid antibody syndrome and homozygous factor V Leiden may be cost effective when comparing quality-adjusted life years in patients with idiopathic DVT (SOR: **B,** single cost-benefit analysis).

Evidence summary

For thrombophilia testing to be of clinical value in patients with DVT, it must be superior to clinical history alone in determining who is at risk for recurrence; changing therapy based on a positive test must improve clinical outcomes.

Testing doesn't predict risk more accurately than clinical history

Several thombophilic conditions are associated with increased risk for both first and recurrent DVT (**TABLE**).[1-3] Certain clinical characteristics also markedly increase the risk of recurrence, including breast cancer (when the patient is on chemotherapy), lung, pancreatic and other gastrointestinal cancers, some major surgeries, and a history of previous DVT.[1,4] Three cohort studies show that thrombophilia test results don't assess recurrence risk more accurately than these historical factors alone for most patients.[5-7]

Testing may be cost effective for patients with idiopathic DVT

Auerbach and colleagues developed a mathematical model of cost effectiveness and concluded that thrombophilia testing may be cost effective for patients with idiopathic DVT.[8] Their analysis was based on theoretical assumptions that might oversimplify the complexities of practice, however. No clinical trials compare different treatment regimens based on the results of thrombophilia tests.

Prolonged anticoagulation may benefit high-risk patients

Few studies have compared various durations of warfarin treatment for patients with DVT. The risk of recurrence is highest in the first 6 to 12 months after an initial episode.[4] After 12 months the risk decreases, but never to the risk level of people who have never had a DVT.

A Cochrane meta-analysis of 8 RCTs, totaling 2994 patients, evaluated duration of treatment with vitamin K antagonists in DVT. It concluded that although prolonged treatment with vitamin K antagonists reduces the risk of DVT, substantial ongoing risk of bleeding complications remains.[9] Prolonged or even lifelong treatment may be considered for high-risk patients with multiple episodes of DVT or pulmonary embolism.

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TABLE
Thrombophilic conditions that increase the risk of DVT

Thrombophilic condition	Prevalence in patients with first DVT[1]	Relative risk of DVT compared with noncarriers[1-3]
Antithrombin deficiency	1%	5
Protein C	3%	3.1-3.4
Protein S	1%-2%	2
Factor V Leiden	20%	1.14-2.12 (heterozygous) 1.2-6.0 (homozygous)
Prothrombin G20210A	6%	1.9-2.8
Elevated anticardiolipin antibodies	14%	1.6-3.2
Lupus anticoagulant	5%-15%	9-11
Hyperhomocystinemia	10%-25%	2.7

DVT, deep vein thrombosis.

Testing may be warranted in patients younger than 50 years with idiopathic DVT or patients with recurrent episodes of thromboembolism to assess risk in family members.

Cost-effectiveness analysis suggests that prolonged warfarin therapy for patients with the highest risk thrombophilic conditions (homozygous factor V Leiden and antiphospholipid antibody syndrome) also may be warranted.[8]

Recommendations

A consensus opinion from the British Society for Haematology concludes that:

- thrombophilia testing of unselected patients is inappropriate
- initial management of DVT or pulmonary embolism in patients with heritable thrombophilia is no different from that in other patients
- identification of the most prevalent forms of heritable thrombophilia, heterozygous factor V Leiden or prothrombin G20210A, shouldn't influence decisions about duration of anticoagulation therapy.[10]

The consensus statement suggests indefinite anticoagulation for patients with 2 or more spontaneous venous thrombotic events. **JFP**

References

1. Deitcher SR, Gomes MP. Hypercoagulable state testing and malignancy screening following venous thromboembolic events. *Vasc Med*. 2003;8:33-46.
2. Cushman M. Epidemiology and risk factors for venous thrombosis. *Semin Hematol*. 2007;44:62-69.
3. Segal JB, Brotman DJ, Necochea AJ, et al. Predictive value of factor V Leiden and prothrombin G20210A in adults with venous thromboembolism and in family members of those with a mutation: a systematic review. *JAMA*. 2009;301:2472-2485.
4. Bates SM, Ginsberg JS. Clinical practice. Treatment of deep-vein thrombosis. *N Engl J Med*. 2004;351:268-277.
5. Baglin T, Luddington R, Brown K, et al. Incidence of recurrent venous thromboembolism in relation to clinical and thrombophilic risk factors: prospective cohort study. *Lancet*. 2003;362:523-526.
6. Eichinger S, Weltermann A, Mannhalter C, et al. The risk of recurrent venous thromboembolism in heterozygous carriers of factor V Leiden and a first spontaneous venous thromboembolism. *Arch Intern Med*. 2002;162:2357-2360.
7. Laczkovics C, Grafenhofer H, Kaider A, et al. Risk of recurrence after a first venous thromboembolic event in young women. *Haematologica*. 2007;92:1201-1207.
8. Auerbach AD, Sanders GD, Hambleton J. Cost-effectiveness of testing for hypercoagulability and effects on treatment strategies in patients with deep vein thrombosis. *Am J Med*. 2004;116:816-828.
9. Hutten BA, Prins MH. Duration of treatment with vitamin K antagonists in symptomatic venous thromboembolism. *Cochrane Database Syst Rev*. 2006;(1):CD001367.
10. Haemostasis and Thrombosis Task Force, British Committee for Standards in Haematology. Investigation and management of heritable thrombophilia. *Br J Haematol*. 2001;114:512-528.