The High Value Care
One Minute Guide to:

Thrombophilia Testing

Q: Should I test my patient with a provoked deep vein thrombosis (DVT) for hereditary thrombophilia?

Context: The Centers for Disease Control and Prevention estimates that between 300,000 and 600,000 Americans are affected by venous thromboembolism (VTE) yearly. Of these, roughly 60,000 – 100,000 Americans die of VTE yearly, with 25% of deaths occurring within the first month of diagnosis. One third of patients with previous VTE will have a recurrence within 10 years. Approximately 5 – 8% of the United States population has at least one of the several heritable genetic risk factors for thrombophilia.

The Data: A British group from Cambridge prospectively followed a cohort of 570 patients after their first episode of VTE for 2 years to evaluate for the rate recurrence and predictive risk factors[1]. Notably, the study excluded patients with malignancy, antiphospholipid antibody syndrome (APS), anticoagulant use at the time of first occurrence, and cerebral vein thromboses. At two years of follow-up, researchers found an 11% cumulative incidence of recurrent VTE, with mean duration of anticoagulation after the primary episode of 24-27 weeks. None of the 98 patients with a provoked initial VTE (i.e., post-surgical and pregnancy-associated clot up to 2 months post-partum) had a recurrence of VTE during the observation period. Notably, 487 (85%) of patients were tested for one or more heritable thombophilic conditions (factor V Leiden mutation, factor II G20210A mutation, and anti-thrombin III concentrations were tested most frequently, followed by proteins C and S levels). One hundred and thirty-seven (28%) were found to have an inherited thrombophilia; however, no significant difference in rate of VTE recurrence was found between patients with and without a thrombophilic condition (HR 1.5 [95% CI 0.82 – 2.77] p=0.187).

In a separate study, Italian researchers prospectively followed 1,626 patients after their first VTE episode for recurrence over a minimum 10-year period for recurrence of VTE[2]. This study reported a recurrence of VTE in 373 (23%) patients. Previous unprovoked VTE (unadjusted HR 2.3 [95% CI 1.82 – 2.90]) and thrombophilia (unadjusted HR 2.02 [95% CI 1.52 – 2.69]) were significantly associated with risk of recurrence. Of note, patients with APS were included in this analysis and grouped with patients with inherited forms of thrombophilia.

Conclusion: Both studies demonstrate a higher risk of recurrent VTE among patients who originally presented with an unprovoked thrombosis. Surgery and pregnancy were conditions associated with high incidence of primary VTE with significantly lower rates of recurrent VTE. The effect of an underlying thrombophilic condition varied in the two studies, though the exclusion or inclusion of APS—a very thrombophilic condition—may explain the increased risk of recurrence observed in the second study.

The Bottom Line: You should not routinely test patients with a first occurrence of provoke VTE for hereditary thrombophilia. Testing patients with unprovoked VTE for hereditary thrombophilia (i.e., not including APS testing) is of questionable utility and should only be performed when testing will change management[3].

1. Lancet. 2003 Aug 16;362(9383):523-6 **PMID: 12932383**
2. Haematologica. 2007 Feb;92(2):199-205 **PMID: 17296569**
3. NICE Clinical Guidelines, No. 144 **PMID: NBK132796**