Comment on “Venous thrombosis: who should be screened for thrombophilia in 2014?”

To the Editor We read the review article by Paul A. Kyrle with great interest.1 We fully agree with the author that systematic indiscriminate laboratory thrombophilia screening in all patients with the first unprovoked venous thromboembolic episode (VTE) is unwarranted and should be discouraged. However, there is still one important and unanswered question: who should be screened for thrombophilia? We would all probably agree that owing to age dependency of VTE, elder patients should not be screened. However, those aged from 45 to 50 years (or even younger) with unprovoked episodes certainly require our attention. At this point, some differences regarding inherited and acquired thrombophilia may be of issue.

The utility of laboratory investigation for inherited thrombophilia in patients with VTE and their asymptomatic relatives has been largely debated, leading to the production of several guidelines by scientific societies and various working groups. As the risk largely depends on the family history of VTE, the identification of asymptomatic carrier among relatives of the probands with VTE and thrombophilia could reduce cases of provoked VTE by offering them primary antithrombotic prophylaxis during risk situations. In most guidelines, this is considered justified only for relatives of probands with a deficiency of natural anticoagulants or multiple abnormalities. Counselling asymptomatic female relatives of individuals with VTE and/or thrombophilia before planned conception or treatment with hormonal preparations should also be recommended depending on the risk driven by the type of thrombophilia and the family history of VTE.

Acquired thrombophilia mainly involves testing for antiphospholipid antibodies necessary to establish the diagnosis of antiphospholipid syndrome. Even if evidence on the risk of recurrent thrombosis in patients with antiphospholipid antibodies is low or available data are of poor quality, we still believe the testing may be warranted. The tested group should include: younger patients (<50 years), patients with a systemic autoimmune disease and any VTE episode in history, patients with accidentally found prolonged activated partial thromboplastin time (after exclusion of clotting factor deficiency, mainly FXII), and women with recurrent spontaneous pregnancy loss.2 The latest clinical guidelines of the National Institute for Health and Care Excellence also recommend testing for antiphospholipid antibodies: in patients who have had unprovoked deep vein thrombosis (DVT) or pulmonary embolism (PE; if withdrawal of anticoagulation treatment is planned); and in patients who have had unprovoked DVT or PE and have a first-degree relative with previous DVT or PE.

In addition, we would not lightly discard the option to treat positive (especially so-called “triple positive”) patients indefinitely in the light of recent data showing that, in patients diagnosed with antiphospholipid syndrome during the 10-year period, 36.5% of the fatal cases were related to severe thrombosis.

We hope this additional information will help readers of the Polish Archives of Internal Medicine decide whether thrombophilia testing may be of value for primary and secondary VTE prophylaxis in their patients.

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Author’s reply I am delighted about our mutual agreement that systematic laboratory thrombophilia screening in all patients with a first unprovoked venous thromboembolic episode (VTE) is unwarranted and should be discouraged. This does not necessarily mean that specific testing in selected patients is unjustified, but I am very reluctant to call this procedure “screening”.

I agree that young patients with unprovoked VTE episodes or a positive family history of VTE require our attention. Current guideline panels even suggest indefinite anticoagulant treatment for all patients with an unprovoked proximal deep vein thrombosis and/or pulmonary embolism regardless of the presence or absence of laboratory thrombophilia. Regarding the risk of recurrent VTE, it is important to appreciate that the risk does not differ between older and younger patients and exceeds 30% 5 years after discontinuation of anticoagulation in patients younger than 47 years.

My article focused on the impact of certain abnormalities detected by laboratory screening on the risk of recurrent VTE rather than on the risk of a first VTE. Also in the setting of primary VTE prevention, thrombophilia screening (defined as systematic rather than individual testing to identify an abnormality that indicates the presence of a disease [that potentially necessitates treatment] or that is predictive for the course of an ongoing disease [that potentially requires a specific treatment or a treatment modification]) is not reasonable. As regards specific (rather than systematic) testing, 2 clinical scenarios come to my mind: 1) women from families with a known antithrombin deficiency (who may benefit from primary thromboprophylaxis during pregnancy and peripartal antithrombin supplementation); 2) women with recurrent pregnancy loss to detect antiphospholipid antibodies (in which case, they may benefit from low-molecular-weight heparin together with aspirin during their next pregnancy).

As regards antiphospholipid antibodies, testing patients with VTE and a generalized autoimmune disease or a prolonged activated partial thromboplastin time is part of the diagnostic algorithm to detect secondary or primary phospholipid antibody syndrome but does not necessarily alter management strategies. Testing for antiphospholipid antibodies in patients who have had unprovoked VTE if it is planned to stop anticoagulation treatment is not meaningful because guidelines suggest indefinite anticoagulation in these high-risk patients, and the impact of phospholipid antibodies on the recurrence risk is still uncertain. The study by Cervera et al. clearly shows that patients with an antiphospholipid antibody syndrome are at high risk of dying from thrombotic events. However, this study does not provide evidence that long-term anticoagulant treatment improves the prognosis of these patients, of which 10.7% died from hemorrhage.

In conclusion, scientific evidence indicating that laboratory thrombophilia testing is of assistance for managing patients with VTE or of their unaffected relatives is very limited. This is the reason why I once more emphasize that, at present, laboratory thrombophilia screening should be abandoned.

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