The authors respond to "Thrombophilia testing in venous thromboembolism"

We thank Dr. Rehman[1] for his interest in our article on deciding the optimal duration of anticoagulation in patients with acute unprovoked venous thromboembolism,[2] and his comments pertaining to the controversial topic of testing for thrombophilia in the management of venous thromboembolism.

Dr. Rehman refers to a narrative review published in the *New England Journal of Medicine* by Dr. Jean Connors,[3] to suggest that our advice regarding thrombophilia testing to decide duration of anticoagulation is not based on current evidence. However, in Dr. Connors' article, the table summarizing the recommendations regarding testing for thrombophilia states that for unprovoked venous thromboembolism, physicians should "test after treatment for acute event if cessation of anticoagulant therapy is contemplated and test results might change management strategy."[3] The advice in our article reiterates this recommendation.

Dr. Rehman recommends that "patients with unprovoked venous thromboembolism should continue anticoagulation for the rest of their lives, irrespective of whether they have thrombophilia or not." This is not based on current evidence. As we showed in our article,[2] using the prospectively validated "HERDOO2" clinical decision rule[4] allows clinicians to identify women with unprovoked venous thromboembolism at low risk of recurrence who can safely discontinue anticoagulants, and that about 50% of women can be spared the burdens, risks and costs of lifelong anticoagulation. It is important to note that both the derivation[5] and validation[4] studies of the HERDOO2 rule excluded patients with unprovoked venous thromboembolism who have "known high-risk" thrombophilia, because most consider it standard of care to continue anticoagulants in these patients. The American College of Chest Physicians guideline[6] states the following: "Other factors predict risk of recurrence, but not strongly or consistently enough to influence recommendations on duration of therapy once the primary and secondary factors noted previously have been considered. These factors, which have mostly been evaluated in patients with unprovoked venous thromboembolism, include … antiphospholipid antibody (risk ratio [RR] ~2), hereditary thrombophilia (RR ~1.5) …"

Dr. Rehman states, "These recommendations are based on available data that show no substantial difference in rates of recurrent venous thromboembolism between patients with and without thrombophilia."[1] However, the study[7] cited to support his claim is a retrospective case–control study conducted in The Netherlands, comprising 197 venous thromboembolism cases (of which 106 were unprovoked) and 324 controls (of which 130 were unprovoked), which was underpowered to show a difference between these two groups. Because the study was designed to test the hypothesis that testing for inherited thrombophilia in patients with any acute venous thromboembolism would be associated with a lower incidence of subsequent recurrence of venous thromboembolism, it provides very limited evidence to conclude that testing for inherited thrombophilia does not reduce the risk of recurrence in patients with acute unprovoked venous thromboembolism.

Overall, in the absence of high-quality data, we believe it is evident that patients with high-risk thrombophilia should continue anticoagulants indefinitely, and the only way to know whether a patient has high-risk thrombophilia is to test for thrombophilia. We also believe that many patients with unprovoked venous thromboembolism want to know the underlying cause of the condition; it is paternalistic to not offer patients this knowledge. Thus, we suggest testing for thrombophilia in patients who have unprovoked venous thromboembolism and who are potentially going to stop anticoagulation.

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Competing interests: Grégoire Le Gal reports acting as a co-investigator on clinical trials on behalf of Portola Pharmaceuticals, Boehringer Ingelheim, Pfizer, GlaxoSmithKline, Bristol-Myers Squibb, LEO Pharma, Daiichi Sankyo and Bayer; he also reports receiving honorariums from Bayer, Pfizer, GlaxoSmithKline, LEO Pharma, Sanofi and bioMérieux, outside the submitted work. Marc Rodger reports receiving investigator-initiated grants from Programme hospitalier de recherché clinique and bioMérieux for a project validating the HERDOO2 clinical decision rule. No other competing interests were declared.