Letters

COMMENT & RESPONSE

In Reply In our recent research article regarding clinical and genetic determinants associated with venous thromboembolism (VTE) among community-dwelling patients with COVID-19,1 we reported a marked increase of 30-day VTE and identified older age, male sex, obesity, no or partial vaccination, and inherited thrombophilia as key risk factors. We appreciate the insightful comments from Prof Kollias and colleagues and their support of our call for targeted VTE thromboprophylaxis for outpatients with COVID-19.

Hospitalization is the recommended indicator for initiating antithrombotic therapy for patients with COVID-19. However, we argue that the likelihood of post–COVID-19 VTE should be conceptually seen as a continuum, with some outpatients treated for COVID-19 at an even higher risk of VTE than some hospitalized patients. Also, given that VTE hazard peaks substantially and shortly after SARS-COV-2 infection,2 individuals with COVID-19 would likely benefit from earlier interventions for primary prophylaxis. Our study1 identified several independent risk factors that can be used to stratify patients with different risk profiles for post–COVID-19 VTE. We should highlight that although existing trials (eg, ETHIC, ACTIV-4B) did not generally support routine pharmacologic thromboprophylaxis for outpatients with COVID-19, the results should be interpreted as inconclusive given the great statistical uncertainty and underrepresentation of older patients, and consequently, the low event rates. Therefore, the results do not preclude the use of thromboprophylaxis in selected outpatient subpopulations, particularly among those with a high baseline risk of VTE.3 Further trials targeting high-risk infected outpatients and more real-world studies with larger sample sizes and longer follow-up are warranted to supplement the existing evidence.4

Admittedly, the net benefits of antithrombotic therapy should always be weighed against potential harms5–eg, for those at high risk of VTE, risk of bleeding should be considered when prescribing antithrombotic therapy.6 Of note, genetic risk owing to monogenic thrombophilia or polygenic risk score, as evidenced in our study,1 was exclusively associated with venous but not arterial thromboembolism, which may be promising for identifying individuals susceptible to VTE but resistant to bleeding. Finally, we agree with the proposal from Prof Kollias and colleagues to investigate whether the risk factors persist in fully vaccinated people and what potential value disease symptoms may have for VTE prediction. However, our available data are insufficient for answering this question given the limited sample size: only 6 VTE events among the breakthrough infection cohort.

As the number of COVID-19 outpatient cases continues to increase, personalized prophylactic anticoagulation in this large population may prevent a substantial number of individuals with COVID-19 from developing severe thrombotic complications that require hospitalization and/or intensive care. The clinical and genetic risk factors identified by our study1 should inform the identification of participants for new research to bridge the knowledge gaps on the risk vs benefit of pharmacologic thromboprophylaxis.

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