Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Response

To the Editor:

We agree with Porres-Aguilar and colleagues that therapeutic-dose anticoagulation should not be the standard of care for all noncritically ill, hospitalized patients with COVID-19 and, therefore, we provided several specifications to our recommendation in the recent update to the CHEST guideline and expert panel report.[1] We specifically suggest that heparin be used, because its benefits do not appear to extend to other anticoagulants, and that therapeutic dosing be considered only in patients who are at low risk of bleeding.[1,2]

We also agree that the reduction in VTE may be offset by the increased risk of bleeding when using therapeutic-dose heparin in hospitalized patients with COVID-19. However, we disagree about the clinical importance of observed differences in organ support among the more recent randomized controlled trials (RCTs). One trial reported that therapeutic-dose heparin was associated with a 4% absolute increase in organ support-free days and a 4.5% absolute increase in survival without organ support in noncritically ill, hospitalized patients with COVID-19.[3] We believe that these differences are clinically important, relevant to patients and physicians, and reduce resource use.

Some misinterpretation of data in the letter from Porres-Aguilar and colleagues also needs to be highlighted. Although the meta-analysis by Jiménez and colleagues[4] included more than 18,000 patients, the risk of major bleeding was reported only in five of 47 studies (n = 1,411 patients). The risk of major bleeding ranged from 2.2% to 11.3% in the four retrospective studies and was 2.7% in the only prospective cohort study. Furthermore, the meta-analysis did not report major bleeding risk by disease severity. Because admission to the ICU is associated with an increased risk of bleeding, comparing bleeding risks of observational studies that included both critically and noncritically ill patients with bleeding risk in RCTs including only noncritically ill patients is not meaningful. Last, in the prospective cohort study, the risk of major bleeding while receiving intermediate- or therapeutic-dose anticoagulation was significantly lower in noncritically ill compared with critically ill patients [28 of 1,176 (2.4%) vs 84 of 789 (10.6%)].[5] Interestingly, the estimate in noncritically ill patients is similar to the major bleeding risk observed in RCTs (range, 0.9%-2.4%).[2,3,6,7]

Overall, the risk of major bleeding in patients with COVID-19 who receive therapeutic-dose anticoagulation is underreported in observational studies but appears to be similar to the risks observed in RCTs. As detailed in the recent update of the *CHEST* guideline and expert panel report,[1] it is critical to assess bleeding risk before the use of anticoagulation, and therapeutic-dose heparin should be considered only for noncritically ill, hospitalized patients with COVID-19 who have a low risk of bleeding. We would also like to highlight broader issues related to the potential benefits of therapeutic heparin that are discussed in a recent Point-Counterpoint editorial submitted by several of the guideline's authors.[8]

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