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respondents might use the midpoint as a *dumping ground*, allowing many respondents to essentially avoid answering challenging questions. We purposefully eliminated midpoints to compel participants to make a choice. Unwillingness differs from both unreadiness to address a topic and sensitivity regarding taboo subjects; respondents can expend effort to overcome their unwillingness. To assess readiness, we qualitatively analyzed respondents' free descriptions, rather than use quantitative analysis, and we were careful in our conclusions to avoid definitive statements regarding readiness.

Finally, we do not believe that the timing of the survey led to significant social-desirability bias. First, the survey was anonymous and did not use interviews. Second, respondents answered the questionnaire in the context of resource shortages during or just after the first COVID-19 wave, which rather increased survey validity and reliability for these topics. We also presented short scenario examples for each principle in the questionnaire, as also recommended by Masuda et al.

We again thank Masuda and colleagues for suggesting caution in interpreting our results and for providing useful advice for future studies.

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High-Dose Prophylactic Anticoagulation in Severe COVID-19 Pneumonia



To the Editor:

We read with great interest the article by Tacquard et al¹ published in *CHEST* (June 2021). Authors showed that high-dose prophylactic anticoagulation therapy is associated with reduced thrombotic complications in critically ill patients with COVID-19 without increasing bleeding risk. We want to raise a few points that may be important for authors and readers of the article.

This is a retrospective multi-hospital study that compared thrombotic complications in patients treated with high-dose prophylactic anticoagulation (HPAC) to usual dose prophylactic anticoagulation (UPAC). The study started on March 21, 2020, and ended April 10, 2020, which is a noticeably short time. The study compares the practice of anticoagulation before and after guidelines [French Working Group on Perioperative Hemostasis] published on April 3, 2020. We believe the study may have overestimated thrombotic complications in the UPAC group and underestimated bleeding complications in the HPAC group. Patients treated with UPAC may have received higher number of CT chest scans for suspicion of

pulmonary embolism than patients with HPAC. Clinicians using HPAC are less likely to consider CT chest scans for a diagnosis of pulmonary embolism because the patient was already on HPAC. The authors may clarify this issue by reporting the number of CT scans performed for both groups. The practice of anticoagulation is highly variable and dynamic. We documented this practice and this practice's impact on clinical outcome.² Tacquard et al¹ divided data into five time points and captured only the first or last timeframe to define groups (UPAC or HPAC). They did not include data from the middle timeframes in their study, which might have affected results. Moreover, cumulative doses would likely be higher for the UPAC group because they started earlier, while cumulative doses for HPAC would be lower because they started later. Therefore, thrombotic complications may not be accurate and possibly overestimated in UPAC group.

Bleeding complications may have been under estimated because the follow-up time to detect bleeding complications was truly short; for 38% of the sample, bleeding complications dates were not available. The number and nature of bleeding complications, if available, can improve our understanding of the issue.

In fact, high thrombotic complications in the UPAC group in their study may be a result of higher severity of illness, prolonged mechanical ventilation (extended use of sedatives and muscular paralytics), higher usage of continuous renal replacement therapy, and extracorporeal membrane oxygenation. Adjustment for all confounding factors by appropriate statistical modeling would allow a true estimate of thrombotic complications.

Global improvement in the provision of ICU beds, ventilators, and society guidelines occurred at approximately the last week of March 2020. Subsequently patients might have received better care in terms of location and trained staff. This could improve the occurrence of thrombotic complications in the HPAC group. We have observed that continuous renal replacement therapy circuits clot more often when care is provided outside the ICU by staff who are not trained for critical care.

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Response



To the Editor:

We thank Nadeem et al for taking interest in our study that reports the benefit of high-dose prophylactic anticoagulation (HPA) on thrombotic complications in critically ill patients with COVID-19.¹

Nadeem et al hypothesized that patients treated with standard thromboprophylaxis were more severe and had more chest scans, thus more thrombotic complications. This possibility calls for several comments: (1) To evaluate the effect of cumulative individual exposure specifically to HPA on thrombotic complications, we used an original method based on a dedicated time-varying exposure model. Cumulative individual exposure was used as a surrogate for “time within the therapeutic range” and allowed a more appropriate evaluation of the anticoagulation regimen, exposed to frequent changes of doses in ICU. (2) According to the Groupe d'Intérêt en Hémostase Périopératoire guidance document,² the anticoagulant dose increased with the severity of COVID-19 pneumonia. (3) The benefit of HPA on thrombotic complications remained significant after adjustment for severity markers that included SOFA score, PaO₂/FiO₂ ratio, renal replacement therapy, and extracorporeal membrane oxygenation status. In our study, renal replacement therapy was performed in the ICU with trained staff, and renal replacement therapy filter clotting was recorded as an event only when it appeared unusual to experienced physicians.

We agree with Nadeem et al that we may have underestimated the complications of bleeding, and this point is addressed in the discussion.

The current challenge is to identify accurately the patients who are at particularly high thrombotic risk who could benefit from HPA and then determine when