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COVID-19 in the Critically Ill

Too Risky for High-Dose Anticoagulation?

To the Editor:

Tacquard et al[1] endorse increased anticoagulation dosing in critically ill COVID-19 patients in an article published in *CHEST* (June 2021). In this novel and timely study, the authors found a lower rate of thrombosis (hazard ratio, 0.79 [0.65-0.95]) in patients receiving higher than usual heparin doses, with no increase in bleeding. Despite the merits of the study, we must warn against this approach, considering the drawbacks we are experiencing and the confronting evidence.

The first of our concerns is the bleeding risk, which should not be undermined because it causes significant morbidity, especially in the critically ill. In a multicenter study, 7.6% of critically ill COVID-19 patients had bleeding events, and 5.6% had major bleeding.[2] Similarly, a meta-analysis has found an incidence of bleeding of 7.8%,[3] being higher with intermediate and therapeutic doses of anticoagulation, like those studied by Tacquard et al.[1] Concern has also been raised for a subgroup of patients with enhanced bleeding tendency and a prolonged clot lysis time in the critically ill,[4] which suggests complex hematological variations.

Regarding methods, high and intermediate doses should have been distinguished to ease the hands-on of data. Also, we believe the authors should have analyzed non-vessel thrombotic complications separately. The complications studied were derived from extracorporeal circuits, which cause benign thrombosis events[2] and anticoagulation-associated bleedings, which are often serious in our experience. This reminds us of the categorizing of complications by severity, which we believe was missing.

The authors report a 5% and 12% incidence of deep venous thrombosis and pulmonary embolism, respectively, whereas others report VTE in 7.6%.[2] These rates appear comparable to those typical in the ICU, which raises doubt over the burden of thrombosis in this setting. The prevalence of thrombotic complications in COVID-19 has been variable and highly dependent on assessing methods and the type of event studied.[3]

We also need to remark on the finding of immunothrombosis, which was not possible to ponder in this work. Autopsy studies have found thrombosis in the lungs of 57% of patients with SARS-CoV-2 infection.[5] We hypothesize that these phenomena hold a key in the concerning analysis and could dictate whether high doses of anticoagulation are futile at this advanced stage.

Finally, we agree on the usefulness of biomarkers to guide therapy. They are needed to stratify both thrombotic and hemorrhagic risk,[4] bringing a more individualized treatment, preferably at earlier disease stages with fewer dangers present.

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