Optimizing the Risk-Benefit Balance of Thromboprophylaxis in Critically Ill Patients With Coronavirus Disease 2019

To the Editor:

We read with interest the narrative review by Iba et al (1) about the state of knowledge on coagulopathy in patients with coronavirus disease 2019 (COVID-19), published recently in *Critical Care Medicine*. We appreciate the important work provided by the authors on a rapidly evolving subject depending on the several studies already published (2–5). As mentioned by the authors (1), activation of the coagulation pathway seems to be a key point in the clinical picture of patients COVID-19 admitted to ICU. D-dimer level and fibrinogen concentration have been reported as markers that can help the clinician for the patient's prognosis but also in the research for venous thromboembolism (VTE), that can also contribute to the degradation of pulmonary function (2–5). Indeed, several recent studies reported higher rate of VTE compared with non-COVID-19 acute respiratory distress syndrome patients despite thromboprophylaxis (3, 4) probably due to the association of endotheliitis (5), cytokine storm (2) and the enhanced platelet-vessel wall interaction described in these patients in addition to the main independent risk factors already reported in mechanically ventilated ICU: male gender, high body mass index (BMI), and use of neuromuscular blockers. For all of these reasons, optimal thromboprophylaxis is crucial in ICU patients with COVID-19. In their article, Iba et al (1) summarize these current recommendations. Nevertheless, we completely disagree with the dosing recommendations for low molecular weight heparin (LMWH), especially with a dose of 40 mg of enoxaparin once daily as thromboprophylaxis in ICU patients with COVID-19. Indeed, if the optimal dose for thromboprophylaxis remains unclear in ICU patients, the dose of at least 50 international units/kg body weight agrees with some guidelines, especially in COVID-19 patients where overweight is frequently reported. Therefore, the dose suggested by the authors seems very suboptimal. Furthermore, dose of 40 mg of enoxaparin was also the dose reported for thromboprophylaxis in two studies reporting a very high rate of VTE (3, 4). It therefore, seems to us that the risk of VTE greatly exceeds the benefit of treatment. We rather suggest adapting the doses of LMWH according to BMI: 60 mg for BMI greater than or equal to 30 kg/m^2 and 80 mg for BMI greater than or equal to 40 kg/m^2, respectively. Doses could be adapted by the measure of peak anti-Xa and if the risk exceeds the benefit by the risk of bleeding due to the higher frequency of acute renal failure in these patients, trough anti-Xa activity could be measured or unfractionated heparin could be preferred.

As thrombotic complications were frequently reported and associated with higher mortality in ICU patients with COVID-19, higher dose of LMWH guided by anti-Xa activity are probably necessary. We need studies to optimize thromboprophylaxis in these patients.

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