

that, since then, it has frequently been suggested that higher doses of LMWH be given to Covid-19 patients to prevent venous thromboembolism. However, there is no demonstration that standard prophylactic doses are insufficient to prevent it. Pulmonary vessel occlusions that are observed in severe Covid-19 patients are caused by pulmonary thrombi, whose pathogenesis is unclear but likely to be associated with the severe pulmonary inflammation. Concerning the type of heparin, we cannot be certain that one type is better than the other; in other words, it is difficult to say UFH is better than LMWH. LMWH was chosen in the guidance because of the ease of use, no need for laboratory monitoring, and familiarity among the spectrum of doctors with varying experience. The question of whether *therapeutic* doses of either UFH or LMWH should be considered for all patients is currently unknown and the authors would currently reserve such a dose for those who have confirmed thrombosis including filter thrombosis. We are aware however that therapeutic dose is being administered in some centers where there is very high suspicion of pulmonary embolism and imaging is impractical. Although these approaches are reasonable, we stress that these approaches are undertaken in a trial setting.

#### CONFLICT OF INTEREST

Dr. Thachil has received honoraria from Bayer, BMS-Pfizer, Daichii-Sankyo, Boehringer, Mitsubishi, Novo Nordisk, Octapharma, Novartis, Amgen, Norgine, Alexion, Sobi, and CSL-Behring. All other authors declare no conflicts of interest.

#### AUTHOR CONTRIBUTIONS

Jecko Thachil and Marco Cattaneo wrote the response. Ning Tang, Satoshi Gando, Anna Falanga, Marcel Levi, Cary Clark, and Tsohiaki Iba gave comments. All authors approved the final submission.

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## Lupus anticoagulant is frequent in patients with Covid-19

Patients hospitalized for Covid-19 severe infection are more prone to excessive coagulation activation leading to thrombotic events.

Tang et al<sup>1</sup> discussed the importance of high D-dimer and fibrin degradation product level to determine the patient prognostic and the risk of thrombosis. However, they did not look at lupus anticoagulant (LAC). Zhang et al described three cases of thrombosis associated with antiphospholipid antibodies represented by

anticardiolipin (aCL) and anti- $\beta$ 2-glycoprotein I (a $\beta$ 2GPI).<sup>2</sup> No lupus anticoagulant was detected in any of the patients. During the recent Covid-19 outbreak in Mulhouse, France, we have studied 56 patients diagnosed for Covid-19 using polymerase chain reaction (n = 50) or chest computed tomography scan (n = 6), for the presence of LAC with dilute Russell's viper venom time and sensitive activated partial thromboplastin time tests. Twenty-five cases (45%) were LAC positive, whereas aCL or a $\beta$ 2GPI were detected in only five of 50 tested patients (10%, three associated to LAC) using immunoglobulin G and immunoglobulin M detection. Acute infections are known to be sometimes associated with transient LAC, and anticoagulant therapy is usually not needed.<sup>3</sup> Detection of LAC with or without aCL or a $\beta$ 2GPI, in these critically patients, which are characterized by having many thrombosis risk factors, highlight the importance of an early anticoagulant therapy.

#### CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

#### AUTHOR CONTRIBUTIONS

Inès Harzallah and Bernard Drénou collected the data and processed statistics. Inès Harzallah wrote the manuscript and Bernard Drénou and Agathe Debliquis revised the manuscript.

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## Response to “Lupus anticoagulant is frequent in patients with Covid-19” (JTH-2020-00483)

We appreciate the opportunity to respond to the letter from Dr. Inès Harzallah et al. I have also performed antiphospholipid antibody assays including lupus anticoagulant (LAC), anticardiolipin, and anti- $\beta$ 2-glycoprotein I in dozens of our patients; however, very few of them got positive results. We do not believe that antiphospholipid antibody exists universally in COVID-19 patients. In addition, two of the three reported cases with antiphospholipid antibodies mentioned in the letter<sup>1</sup> also seem to meet the International Society on Haemostasis and Thrombosis criteria of disseminated intravascular coagulation,<sup>2</sup> the causality between antiphospholipid antibodies and thrombosis in these cases is still uncertain.

Both the International Society on Haemostasis and Thrombosis and the Clinical and Laboratory Standards Institute guidelines have

urged caution when interpreting LAC results in patients receiving anticoagulants.<sup>3,4</sup> Given common use of low molecular weight heparin and unfractionated heparin for thromboprophylaxis in COVID-19 inpatients, false-positive results resulting from interference of these anticoagulants may be an important reason for the high positive rate of LAC mentioned in this letter. It has been recommended that the blood should be drawn for LAC testing after 12 hours since the last dose of low molecular weight heparin and 24 hours since that of rivaroxaban.<sup>3,5</sup>

#### CONFLICT OF INTEREST

None declared.

Ning Tang