In Response to "Coagulopathy of Coronavirus Disease 2019"

To the Editor:

We read with interest the comprehensive review by Iba et al (1) published in a recent issue of *Critical Care Medicine*. We wish to highlight a few further points of interest.

The authors listed sepsis-induced coagulopathy, a consumptive coagulopathy as a possible cause of raised activated partial thromboplastin time (aPTT). It is also important to note that coronavirus disease 2019 (COVID-19) infection predisposes to an immuno-thrombogenic state, and a raised aPTT could also be due to the presence of a lupus anticoagulant. This has several clinical implications.

First, it occurs not infrequently in severe COVID-19—in the series reported by Bowles et al (2), 20% had raised aPTT, and of these, 91% were found to have lupus anticoagulant. Second, clinicians may withhold pharmacological thromboprophylaxis due to a perceived hypocoagulable state, given their concerns that the clotting factors appear to be reduced since aPTT is prolonged. Quite the contrary, the presence of lupus anticoagulant may predispose to a prothrombotic state and is also associated with other prothrombotic antiphospholipid antibodies such as anticardiolipin and anti-B2-glycoprotein-1. Third, laboratory monitoring of heparin therapy with aPTT will not be appropriate due to prolongation of aPTT from the lupus anticoagulant, and anti-Xa activity levels should be monitored instead. This is particularly relevant in severe COVID-19 due to the potential need for therapeutic anticoagulation for arterial and venous thromboembolism, continuous renal replacement therapy, and extracorporeal membrane oxygenation. For the above reasons, a raised aPTT uncorrected with 50:50 mixing studies should prompt the clinician to consider further tests for lupus anticoagulant and antiphospholipid antibodies.

The authors quoted two studies in which viscoelastic test parameters are increased in subjects with severe COVID-19, suggestive of a hypercoagulable state. This is consistent with other small retrospective studies (3). However, it is important to note that these have not linked the observed viscoelastic parameters with the development of thromboembolism. Furthermore, while the use of viscoelastic tests to guide hemostatic therapy is well established, its role in the detection and management of hypercoagulable states is less clear. However, since then, some new data have emerged that associate hypercoagulable viscoelastic parameters with thrombotic events, including case reports of arterial (4) and venous thromboembolism. Mortus et al (5) also reported that hypercoagulable thromboelastogram parameters are associated with an increased rate of thrombotic events and have 100% sensitivity for occurrence of multiple thromboses. These reports lend weight to the concept of using viscoelastic tests to screen for thromboembolic risk, but it remains to be conclusively proven. It will also be interesting to study if a treatment or prophylaxis algorithm based on viscoelastic parameters does improve outcomes. Prospective studies are urgently needed to further define the role of viscoelastic tests in severe COVID-19.

The authors have disclosed that they do not have any potential conflicts of interest.

Jensen Ng, MMed (Anaesthesiology), FAMS, Department of Anaesthesiology, Intensive Care and Pain Medicine, Tan Tock Seng Hospital, Singapore, and Yong Loo Lin School of Medicine, Singapore, and Lee Kong Chian School of Medicine, Singapore; **Bingwen Eugene Fan, MMed (Int Med), MRCP (UK),** Department of Haematology, Tan Tock Seng Hospital, Singapore, Yong Loo Lin School of Medicine, Singapore, Lee Kong Chian School of Medicine, Singapore, and Department of Laboratory Medicine, Khoo Teck Puat Hospital, Singapore; **Yew Woon Chia, MMed (Int Med), MRCP (UK), FAMS, FRCP (Edinburgh),** Department of Cardiology, Tan Tock Seng Hospital, Singapore, Yong Loo Lin School of Medicine, Singapore, and Lee Kong Chian School of Medicine, Singapore

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