EDITORIAL

Thromboelastogram to Detect Hypercoagulability in Critically Ill COVID-19 Patients: Has Its Time Come?

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Coronavirus disease-2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is known to manifest a distinct coagulopathy, COVID-19-associated coagulopathy (CAC) which leads to thromboembolic complications, especially in critically ill patients.[1] The pathogenesis of hypercoagulability in COVID-19 is poorly understood. Mechanisms including direct invasion of endothelial cells by the SARS-CoV-2 virus, microvascular inflammation, endothelitis,[2] endothelial injury from the cytokine response and complement activation, significant elevations in the prothrombotic factors, such as, fibrinogen, factor VIII and von Willebrand factor, and circulation of various prothrombotic particles have all been invoked.[3]

D-dimer is a small protein made of crosslinked fibrin derived from fibrinolysis of a clot and serves as a surrogate for intravascular coagulation and thrombosis. Patients with COVID-19 are at a high risk of macrothrombosis akin to any other critically ill patient. In addition, microthrombosis related to endothelial injury, hypoxemia, and inflammation have been documented in this population. Elevated D-dimer levels have been documented consistently in patients with COVID-19, and have been linked to the presence of increased micro (and macro) vascular thrombosis. Several studies have also demonstrated the association of elevated D-dimer levels with worsened mortality in patients with COVID-19.[4] These findings have led to the practices of both frequent monitoring of D-dimer levels and the pre-emptive prescription of higher dose anticoagulation in moderate to severely ill COVID-19 patients, both of which are unfounded by robust evidence. There is a simultaneous emergence of data reporting increasing bleeding complications in patients afflicted with COVID-19 either due to the coagulopathy or due to the use of higher dose anticoagulation deployed in these patients.[5] Considering that the data on increased venous thromboembolism (VTE) in COVID-19 patients are discrepant, immune-mediated mechanisms not amenable to anticoagulation play a significant role and potential risks of bleeding, indiscriminate use of high-dose anticoagulation is riskier and not universally agreed upon. In this context, clinicians and investigators in the zeal to monitor hypercoagulability better have resorted to tools such as thromboelastography (TEG) that potentially provide a functional snapshot of the entire hemostatic system.

In the present issue of the Indian Journal of Critical Care Medicine, Talla et al. have presented the results of a simple retrospective study of 32 patients who had TEG done after admission to the intensive care unit (ICU) with COVID-19.[6] The authors report TEG evidence of hypercoagulability in about 62.5% of patients in this study. Several important points need to be considered before interpreting the study results. Considering TEG is not a routine test performed in critically ill patients with COVID-19, the authors have not clarified why this test was done in these patients in the first place. Serial TEGs at predefined time points during the ICU stay would have shed more light on the onset, degree, and course of any hemostatic derangements. However, this was a single-center retrospective study with a small number of patients and had one TEG performed at a random time-point. Therefore, this study is clearly underpowered and ill-equipped to discern a consistent pattern of hypercoagulability. Findings in TEG that generally point towards a hypercoagulable state include a very low R (reaction time) and K (kinetics), increased maximum amplitude (MA), and low or completely absent LY30 (clot lysis 30 minutes after maximum amplitude). Like most test results that report multiple parameters, TEG should be interpreted in toto after careful review of all parameters provided and not by looking only at specific individual values. Using this approach, only 25% (Table 3) of patients in this study had a high coagulability index with a low R with or without increased MA providing a reasonably convincing signal for a hypercoagulable state. In addition, a very low or complete absence of LY30, indicating attenuation or absence of fibrinolysis seen in previous studies[7] was not seen in this study. Lastly, no correlation of TEG findings with D-dimer values or more importantly clinical thrombotic events has been provided.

Despite all the above limitations, the study provides some useful insights. First, TEG traditionally has been utilized more as a tool to evaluate the pathophysiological reasons and as a guide for the use of blood products in bleeding. It is worth exploring the value of TEG in acute hypercoagulable states. For this, TEG results need to be correlated to clinically relevant VTE events and outcomes before its widespread advocacy to evaluate acute hypercoagulable states. Second, elevated D-dimer levels although extremely non-specific, automatically triggers an escalation of doses of anticoagulants and often a search for VTE with a venous Doppler and CT angiogram of the chest adding to the cost of care in patients admitted with COVID-19. A stepwise approach of incorporating TEG in patients with high D-dimer values to look for stronger evidence of hypercoagulability may help identify very high-risk patients who may benefit from further investigations or treatment. Such an approach needs to be

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evaluated in rigorous studies before TEG can be adapted as a useful tool in the diagnosis and management of the hypercoagulable state in COVID-19 patients.

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