Letter to the Editor: Venous Thromboembolism in COVID-19: Are Women Different?

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I read with interest the article[1] about therapeutic anticoagulation in patients with coronavirus disease 2019 (COVID-19) and considerations in women. I applaud the authors for performing rigorous review to address this important clinical concern in COVID-19. High prevalence of venous thromboembolism (VTE) was observed in 22.7% of patients in intensive care units.[2] Observational studies and initial autopsy series showed high rates of both venous and arterial thrombosis as well as prominent pulmonary microvascular thrombosis. Patients with COVID-19 were reported to have 6% more risk to develop VTE as compared to non-COVID-19 patients.[3] In addition, COVID-19-associated coagulopathy was recognized as a marker of disease severity and poor prognosis.

Contrasting results have been reported about the preferred anticoagulation therapy in patients with COVID-19 infection. As evident in the given article,[1] the recommendations by various societies and guidelines kept on changing as the evidence emerged. Elevated D-dimer levels were reported as predictive for breakthrough thrombosis[4] despite standard deep vein thrombosis prophylaxis. Some institutions started risk-stratifying patients for VTE based on the D-dimer cutoff points and started intermediate-dose prophylaxis in critically ill patients with COVID-19.[5] Follow-up studies have confirmed significant coagulopathy associated with severe COVID-19, characterized by marked elevation of fibrinogen, von Willebrand factor, and platelet and profound endothelia activation, but did not confirm predictive value for D-dimer as marker of thrombotic risk. Multicenter randomized trial refuted the benefit of intermediate-dose prophylaxis in changing outcomes in terms of incidence of VTE, treatment with extracorporeal membrane oxygenation, or 30-day mortality.[6]

Later retrospective studies suggested mortality benefit of therapeutic anticoagulation for critically ill patients, particularly those requiring mechanical ventilation.[7] In a randomized controlled trial, therapeutic anticoagulation resulted in improved gas exchange, decreased D-dimer, and higher prevalence of liberation from mechanical ventilation.[8] The two recent international, adaptive, multiplatform, randomized, controlled trials studied the effectiveness and safety of use of therapeutic-dose heparin or low-molecular-weight heparin in this patient population.[9,10] The main findings were that therapeutic-dose heparin or low-molecular-weight heparin reduced mortality among patients with moderate infection but not among those with severe infection. A possible explanation for this difference could be that when infection reaches its severe state, the damage surpasses the reversibility by anticoagulation.

The article methodically outlines the higher predilection of VTE in male population attributing to variant involvement of angiotensin converting enzyme-2. The current National Institutes of Health guidelines recommend prophylactic-dose anticoagulation for pregnant hospitalized patients. Because pregnant females were not included in most clinical trials, there is insufficient evidence either for or against therapeutic anticoagulation.

Trials to evaluate platelet inhibition, therapeutic interventions targeting the endothelium, and platelet activation as well as outpatient anticoagulation strategies are ongoing.

Conflict of Interest
None declared.

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