

## Coagulation Abnormalities, Hypercoagulability, and Empiric Anticoagulation for Thromboembolism in COVID-19 Infection

A number of recent studies have explored the connection between COVID-19 infection and coagulopathy, and over the last week it has become apparent that venous thromboembolic (VTE) disease is common in critically ill patients with severe COVID-19. This article describes how surgeons have developed a protocol to empirically anti-coagulate patients at highest risk/suspicion for VTE and to delay imaging until patient recovery.

Multiple studies have begun to detail the association between COVID-19 infection and coagulopathy. The most prominent changes noted have been in fibrinolysis parameters (D-dimer, fibrinogen [FIB], and fibrin degradation products [FDP]), although changes in coagulation and thrombosis parameters (prothrombin time [PT]) and antiphospholipid antibodies [APLAs anticardiolipin IgA, anti- $\beta_2$ -glycoprotein I IgA and IgG]) also have been reported.

To date, studies highlight a link between disordered coagulation, fibrinolysis, and COVID-19 disease severity and mortality. Greater elevations in D-dimer, PT, and FDP values have been associated with more severe or critical disease and serial increases in values have been correlated with disease progression.<sup>1</sup> However, several knowledge gaps remain. Are elevated D-dimer and coagulation abnormalities associated with macro- or microvascular thrombotic events?<sup>2</sup> What is the practical role of existing therapies, such as thromboprophylaxis or therapeutic anticoagulation, in preventing thrombosis or death?<sup>3</sup>

Over the last week, it has become apparent that venous thromboembolic (VTE) disease is common in critically ill patients with severe COVID-19 infection. Reported rates for VTE among the critically ill population, according to large meta-analyses, is ~ 5–6 percent. In the Netherlands, of 184 COVID-19-positive patients receiving standard doses of thromboprophylaxis, 31 percent developed thrombotic disorders: 25 pulmonary embolism, 3 deep vein thrombosis (DVT), and 3 ischemic strokes.<sup>4</sup> In 81 patients with severe COVID-19 in Wuhan, China, 25 percent developed VTE, of whom 40 percent died. In this small patient cohort, a D-dimer level of  $\geq 1.5$   $\mu\text{g/mL}$  predicted VTE with a sensitivity of 88 percent and specificity of 85 percent.<sup>5</sup> In our initial influx of patients (located just 40 miles west of Detroit, the epicenter in Michigan), we also observed a higher-than-normal rate of VTE compared with our historical rate of 6.2 percent in the surgical ICU. Of the first 12 patients referred to our diagnostic vascular lab with SARS-CoV-2 infection, 33 percent had DVT (two with extensive bilateral DVT, one with unilateral DVT, one with upper extremity DVT not associated with line placement). Two initial autopsies revealed evidence of peripheral lung and subpleural thrombosis. This finding is consistent with autopsy reports in preprint data from New Orleans, LA.

Official society recommendations suggest that, at minimum, severely ill patients should be treated with thromboprophylaxis. Nevertheless, in a pandemic setting, the logistics of obtaining diagnostic imaging for suspected VTE in patients can become extremely challenging because of the large number of patients, difficulty and time associated with cleaning equipment, risk to staff during transport of patients through the hospital or as multiple exams are performed, and patient instability or renal failure. Under these conditions, the most pragmatic strategy may be to assume the risk of short-term empiric anticoagulation (until the patient recovers and can be safely imaged without conferring undue risk to themselves or medical staff).

In the present situation, we have enacted a protocol to empirically anti-coagulate patients at highest risk/suspicion for VTE and to delay imaging until the patient recovers. A report focusing on our protocol will be published online in the *Journal of Vascular Surgery*.<sup>6</sup> Patients at high risk of both VTE and bleeding still obtain necessary diagnostic imaging, without overburdening the available resources. This early adoption of systemwide protocols can relieve the bedside physician of decision fatigue and moral distress, and real-time tracking of early outcomes can ensure the feasibility and safety of such protocols.

## References

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