Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

2. Seheult JN, Seshadri A, Neal MD. Fibrinolysis shutdown and thrombosis in severe COVID-19. J Am Coll Surg 2020;231:203–204.
3. Pretorius E, Vermeulen N, Bester J, et al. A novel method for assessing the role of iron and its functional chelation in fibrin fibril formation: the use of scanning electron microscopy. Toxicol Mech Methods 2013;23:352–259.
4. Hadadi A, Mortezazadeh M, Kolahdouzan K, Alavian G. Does recombinant human erythropoietin administration in critically ill COVID-19 patients have miraculous therapeutic effects? J Med Virol 2020;92:915–918.

Disclosure Information: Nothing to disclose.

Usefulness of Combining D-Dimers with Thromboelastography

Jecko Thachil, MD, FRCPath
Manchester, UK

Wright and colleagues[1] have elegantly shown that fibrinolytic shutdown is hugely contributory to the hypercoagulability in COVID-19. In addition, they demonstrate a very important clinical point that combining D-dimers with thromboelastography can predict the need for dialysis in patients with COVID-19. Several other important considerations can be derived from this study. First, it is well-known that D-dimers are an inflammatory marker and can elevate several inflammatory diseases, including COVID-19, even in the absence of thrombosis.[2] The report by Wright and colleagues would suggest the addition of thromboelastography to D-dimer would help in understanding how much of the D-dimers are from clot breakdown and how much are nonthrombotic D-dimers. Second, because D-dimers are markers of clot breakdown, their elevation in conjunction with fibrinolysis shutdown would mean some of these D-dimers are not created from plasmin action on crosslinked fibrin. It is possible that these D-dimers are created in the lungs from bronchoalveolar-specific clot breakdown, which might not be detected by thromboelastography on peripheral blood.[3] It is also possible that a proportion of D-dimers are not generated by clot breakdown at all, but by the action of plasmin on the extravascular fibrin. Lung exudates seen in acute lung injury could constitute large amounts of fibrinogen and thrombin leaked from the intravascular space along with other plasma proteins.[4] Plasmin breakdown of fibrin formed from these large amounts of fibrinogen could be another cause of these nonthrombotic D-dimers. In the case of extravascular D-dimers, these fibrinolytic markers would signify the intense intrapulmonary inflammatory reaction and could be considered a marker of ongoing or increasing inflammation. Recognizing the roles of this intense inflammation in combination with microvascular thrombi for renal impairment is crucial. Anticoagulation could only prevent the thrombotic component of this contribution and anti-inflammatory strategies might also be required to minimize the renal damage.[5] Of course, the dual anticoagulant and anti-inflammatory properties of heparin might be helpful in this scenario, but possibly only in the early stages before marked inflammation sets in. Future studies would complement this current article by examining the timing of marked D-dimer elevation and fibrinolysis shutdown by viscoelastic testing to better understand the thromboinflammatory concept.

REFERENCES

1. Wright FL, Vogler TO, Moore EE, et al. Fibrinolysis shutdown correlates to thromboembolic events in severe COVID-19 infection. J Am Coll Surg 2020;231:193–203.e1.
2. Favresse J, Lippi G, Roy PM, et al. D-dimer: preanalytical, analytical, postanalytical variables, and clinical applications. Crit Rev Clin Lab Sci 2018;55:548–577.
3. Levi M, Schultz MJ, Rijneveld AW, van der Poll T. Bronchoalveolar coagulation and fibrinolysis in endotoxemia and pneumonia. Crit Care Med 2003;31[Suppl]:S238–S242.
4. Wagers SS, Norton RJ, Rinaldi LM, et al. Extravascular fibrin, plasminogen activator, plasminogen activator inhibitors, and airway hyperresponsiveness. J Clin Invest 2004;114:104–111.
5. Fani F, Regolisti G, Delsante M, et al. Recent advances in the pathogenetic mechanisms of sepsis-associated acute kidney injury. J Nephrol 2018;31:351–359.

Disclosure Information: Nothing to disclose.

Untangling the Reasons Surgeons Choose to Leave Clinical Practice, including Retirement

Deborah Verran, MD
Sydney, Australia

Kim Templeton, MD
Kansas City, MO

Nicolas Sampron, MD
San Sebastián, Spain

Jonathan Braman, MD
Minneapolis, MN