Further Evidence Supporting the Use of Prophylactic Anticoagulation in Hospitalized Patients With COVID-19

Andrew B. Dicks, MD; Ido Weinberg, MD

Infection by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), the cause of COVID-19, has been associated with numerous other medical complications aside from the known respiratory effects. Specifically, it is recognized that COVID-19 predisposes patients to thrombotic events in both the arterial and venous circulations. As a result, guidelines from several medical organizations recommend the use of prophylactic anticoagulation in patients with COVID-19. Nonetheless, these guidelines rely on expert opinion–level recommendations, as firm data are lacking. Over time, our knowledge on the use of anticoagulation has been expanding, initially from case series, followed by systemwide reports and international registries. Numerous randomized trials are ongoing. Despite this, a systematic review published in October 2020 found insufficient evidence to determine risks and benefits of use of prophylactic anticoagulation in patients with COVID-19. It is in this landscape that the current study was performed.

Vaughn et al conducted a multicenter cohort study to evaluate the use of anticoagulation in hospitalized patients with COVID-19 infection across 30 hospitals in Michigan. The study included 1351 patients with COVID-19 and evaluated in-hospital mortality and 60-day mortality based on anticoagulation strategy, as well as anticoagulation nonadherence rates, during the first several months of the COVID-19 pandemic from March to June 2020. The study found that in-hospital use of both prophylactic- and treatment-dose anticoagulation for adults hospitalized with COVID-19 was associated with reduced in-hospital mortality; however, at 60 days, only prophylactic-dose anticoagulation remained associated with lower mortality. Additionally, the authors demonstrated that anticoagulation nonadherence, defined as missing 2 days or more of anticoagulation, was associated with a higher 60-day mortality but not an increase in in-hospital mortality. Anticoagulation adherence increased significantly over the course of time within the study.

We know from many studies that pharmacological thromboprophylaxis reduces the risk of hospital-associated VTE in acutely ill hospitalized patients. However, and perhaps surprisingly, there are limited data to support a mortality benefit from VTE prophylaxis in this population. Aside from 1 study published almost 40 years ago that suggested a mortality benefit, most studies do not demonstrate a mortality benefit. Despite this backdrop, the current study showed a mortality benefit in line with other recently published studies of patients infected with COVID-19. A nationwide cohort study involving over 4200 patients receiving care in the US Department of Veterans Affairs demonstrated a reduction in mortality at 30 days with initiation of prophylactic anticoagulation within 24 hours of hospital admission. Additionally, a retrospective, single-center study of over 4300 patients demonstrated a reduction in in-hospital mortality and intubation rates with both the use of therapeutic- and prophylactic-dose anticoagulation. If these results are replicated in the highly anticipated randomized trials currently being conducted, they will surely raise important questions about the nature of the COVID-19 disease and of the patients who are acutely ill with this disease.

While clinicians hoping to improve patient outcomes will surely find these results relevant, they will also probably find them limited. Numerous recent studies have focused on the question of optimal anticoagulation dosing for patients with COVID-19. Unfortunately, results thus far have been quite varied; both increases and reductions in mortality rate associated with treatment-dose anticoagulation have been observed. Similarly, the data in the current study are also insufficient to...
recommend one anticoagulation dose over another. Specifically, comparison of outcomes between the 2 doses observed (prophylactic and treatment doses) is limited by the study design (ie, nonrandomized), lack of sufficient granular clinical data (ie, bleeding rate was not reported for both groups), and potentially deficient matching. Regarding the latter, patients receiving treatment-dose anticoagulation were more likely to receive care in the ICU, require vasopressors, and need initiation of new dialysis. While the authors adjusted for numerous factors in their analysis, it does not appear that all of these factors were accounted for. As the treatment-dose group was “sicker” overall, can the loss of 60-day mortality benefit seen in this group be explained solely by the higher acuity of illness within the group or does the dose of anticoagulant have a role in this finding? Practically, we still lack the granular data we need to help guide us in patient-by-patient decision-making—such as anticoagulation agent choice, dosage, and duration of therapy—especially as dictated by acuity of patient illness.

Despite the limitations, this study (especially in the context of other published data) should make clinicians more confident that the use of prophylactic anticoagulation is warranted for hospitalized patients with COVID-19, as currently suggested by published societal guidelines. We eagerly await randomized trial data, while secretly hoping that by the time these are published we will have little need for their conclusions.

ARTICLE INFORMATION
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Corresponding Author: Ido Weinberg, MD, Massachusetts General Hospital, 55 Fruit St, Boston, MA 02114 (iweinberg@mgh.harvard.edu).

Author Affiliations: Fireman Vascular Center, Massachusetts General Hospital, Boston, Massachusetts.

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REFERENCES