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**Question or request:**

Guidance on COVID-19 associated coagulopathies

**Recommendation/s in bullet form:**

The guidelines for the treatment of COVID-19 associated coagulopathies are as follows:

- Administer standard-dose thromboprophylaxis for **all** hospitalized patients, unless contraindicated.
- Intermediate-dose thromboprophylaxis should be administered for **all** critically ill patients with sequential compression devices, unless contraindicated.
- Sequential compression devices should be used on all patients with a contraindication to coagulation.
- Standard therapeutic anticoagulation should be administered for strongly suspected VTE episodes that cannot be confirmed with imaging, unless contraindicated.

**Assessment:**

Multiple studies have identified that coagulopathy is a common complication with severe COVID-19.<sup>1-3</sup> Additionally, patients with severe COVID-19 illness are at risk for the development of acute respiratory distress syndrome<sup>4</sup> and disseminated intravascular coagulopathy,<sup>1</sup> both of which are associated with hypercoagulability.<sup>5,6</sup> Hospital-associated venous thromboembolism (VTE) is associated with significant morbidity and mortality and may be caused by immobility, illness, and other prothrombotic alterations.<sup>7</sup> Accordingly, patients with COVID-19 illness requiring hospitalization may be at an increased risk for VTE, particularly if immobilized.<sup>8</sup> Additionally, elevated D-dimer in COVID-19 illness has been shown to be associated with an increased risk of mortality,<sup>3</sup> and increased D-dimer is associated with an increased risk of VTE among hospitalized patients.<sup>9,10</sup> A recent study found that use of anticoagulation in patients with severe COVID-19 and coagulopathy was associated with decreased 28-day mortality.<sup>11</sup>

An increasing body of evidence, albeit lower in quality due to its retrospective nature, suggests that patients with severe COVID-19 illness may be at particularly high risk for thrombotic complications.<sup>8</sup> Recent studies have shown that nearly 1/3 of patients admitted to intensive-care units and receiving standard doses of VTE prophylaxis experienced thrombotic complications.<sup>12</sup> Standard VTE prophylaxis strategies may be insufficient in patients with severe COVID-19 illness. Optimal thromboprophylaxis strategies for patients with COVID-19 are still being determined; however, weight-based dosing strategies for enoxaparin<sup>13</sup> and increased doses of heparin prophylaxis (eg heparin 7,500 units q8h)<sup>14</sup> have been employed in other groups at high-risk for VTE and is reasonable in patients with severe COVID-19 illness.

The management of COVID-19-associated coagulopathy (CAC) is still evolving, and various institutions and organizations have recognized the need for increased vigilance of CAC.<sup>15-17</sup> Recent guidance from the International Society for Thrombosis and Hemostasis (ISTH) recommends monitoring of coagulation parameters in COVID-19 patients, including D-dimer, PT/INR, PTT, platelet count, and fibrinogen and pharmacologic VTE prophylaxis in all hospitalized patients with COVID-19 who do not have a contraindication.<sup>16</sup> The American Society of Hematology (ASH) also recommends pharmacologic prophylaxis in all hospitalized COVID-19 patients.<sup>18</sup> Bleeding is rare in COVID-19 patients: in those who initially present with less severe disease, the risk from failure to assess, reassess, and provide timely thromboprophylaxis (especially in a strained healthcare environment) is much higher than the risk of major bleeding from appropriately dosed thromboprophylaxis. However, given the rapidity of the current COVID-19 outbreak, management of CAC needs to continually incorporate information based new developments and the following guidance may be revised as deemed necessary.

**In the context of expert clinical guidelines and the current best available data, anticoagulation subject matter experts from Presbyterian Healthcare System and the University of New Mexico Health Sciences Center recommend the following for recognition and management of CAC:**

- Consider baseline and periodic CBC and coagulation studies at time of admit of all COVID-19+ patients or patients under investigation (CBC, D-dimer, PT/INR, PTT, fibrinogen) for monitoring of disease and prognostic status
  - Worsening of these parameters, specifically the D-dimer, indicates progressive severity of COVID-19 infection and predicts that more aggressive critical care may be needed
  - Worsening of these parameters is **not** an indication to escalate anticoagulation dosing
  - Abnormal coagulation parameters should **not** be corrected with blood products in non-bleeding patients
- Administer standard-dose thromboprophylaxis for **all** hospitalized patients, unless contraindicated
  - Due to the thrombophilic nature of COVID-19, dose-adjustment for obesity is *strongly* recommended
- Administer intermediate-dose thromboprophylaxis (e.g. enoxaparin 0.5 mg/kg BID, heparin 7500 units TID) for **all** critically ill patients and use sequential compression devices (SCDs), unless contraindicated
- SCDs should be used on all patients with a contraindication to anticoagulation (if no DVT)
- Administer standard therapeutic anticoagulation for strongly suspected VTE episodes that cannot be confirmed by imaging, unless contraindicated (*see Attached Guidance document with additional considerations*)
- Use of thrombolytics such as tPA outside of standard indications or clinical trials is not recommended due to unknown benefit and excess bleeding risk

**Red flags and concerns:**

There is a critical lack of high quality evidence regarding:

- optimal anticoagulation strategies for COVID-19 patients. The above recommendations are consistent with guidelines developed by national and international subject matter experts and deployed in those experts' own Centers of Excellence.
- the use of laboratory parameters such as D-dimer for prognostic surveillance purposes. Frequent monitoring of these parameters may lead to inappropriate decisions to intensify anticoagulation dosing or use blood products to correct non-bleeding coagulopathies.

**Contributors:**

This document was reviewed by the Clinical Care Drugs and Therapeutics Subgroup and the guidelines were supported with full consensus. These guidelines were developed by the following experts.

- Arand Pierce, MD (Presbyterian, TriCore, and UNM)
- Greg Hadlock, PharmD, PhD (Presbyterian)
- Allison Burnett, PharmD, PhC, CACP (UNM)

**Resources/Reference:**

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- <sup>10</sup> Darzi AJ, Karam SG, Charide R, et al. Prognostic factors for VTE and Bleeding in Hospitalized Medical Patients: a systematic review and meta-analysis. *Blood*. February 2020. doi:10.1182/blood.2019003603
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