



## Considerations in prophylaxis and treatment of VTE in COVID-19 Patients

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The following information should not be considered to be informed practice guidelines. In the rapidly evolving management of seriously ill patients affected with coronavirus disease 2019 (COVID-19) there is usually insufficient evidence available to make true practice guidelines. The question responses represent the opinion of a group of venous specialists who have reviewed the currently available evidence and have communicated with specialists in high volume sites in the US and internationally. These responses are, in their opinion, the best available responses based on current knowledge. Some areas are controversial and best patient management depends on individual patient situations. We have attempted to highlight these areas and provide the evidence available in the literature summary/references. We will attempt to update this document frequently as new information becomes available. Please send any questions or comments to [COVID-19@veinforum.com](mailto:COVID-19@veinforum.com).

**Note: Patients under investigation for COVID-19 due to suggestive signs/symptoms should generally be treated as COVID-19 positive until testing results are received**

**Is VTE risk assessment using one of the risk models (i.e. Caprini) necessary in admitted patients with COVID-19?**

- Patients with COVID-19 admitted to the hospital have a very high reported risk for venous thromboembolism (VTE) and microvascular thrombosis.<sup>1-3</sup> Therefore universally should be placed on chemical prophylaxis unless there is an absolute contraindication.
- Risk assessment at admission is important to identify the very high-risk patients with multiple risk factors present before the onset of the viral infection (Caprini score >8),<sup>4</sup> as their risk for VTE may require increased dose of anticoagulation. It is recommended that these individuals be given twice the normal dose of anticoagulation.<sup>5</sup>
- There are no randomized trials to substantiate this practice, however the tendency of these high-risk patients to develop fatal and nonfatal thrombotic events, plus the additional thrombotic risks associated with the virus appear to justify this approach.
- A final Caprini score should be completed before discharge and those with a score of >8, may benefit from extended chemical prophylaxis facilitated by use of one of the new oral anticoagulants.
- Risk assessment on admission and during hospitalization is suggested, but we realize may not always be practical in health care systems that are overwhelmed. In this situation, assessment at a minimum should be performed at discharge to determine need for extended prophylaxis.

**What hematologic laboratory tests should be obtained in patients with COVID-19?**

Following hematologic blood work during hospital course will help evaluate clinical progression and changes in hematologic status. Literature has shown that D-dimer levels tend to follow severity of disease and is a marker of worse clinical outcome, and therefore should be monitored during hospitalization.<sup>6-10</sup>



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Baseline hematologic laboratory work should include but not limited to:

- **CBC** – General hematologic abnormalities including an abnormally low platelet count should be noted when present.
- **PT/PTT** – Baseline levels and follow levels, as necessary.
- **Fibrin degradation products (FDP)** – Elevation suggests poorer prognosis and possible development of disseminated intravascular coagulopathy (DIC).
- **D-dimer** – COVID-19+ patients with significant elevation of D-dimer have been reported to have a poor prognosis and a higher incidence of thrombotic complications.<sup>6-10</sup>

### What should we use as prophylaxis in patients with COVID-19 at risk for VTE?

- Low molecular weight heparin (LMWH) – consider 30 mg BID or 40 mg QD with standard adjustments for renal insufficiency or obesity.
- Morbid obese patients (BMI >35) and very-high risk patients (Caprini score >8) – consider twice the normal dose of anticoagulation (LMWH 60 mg BID).
- If severe renal impairment (CrCl<30 mL/min) or acute kidney injury - Heparin 5000u SC TID.
- If prior history or concern for Heparin induced thrombocytopenia use fondaparinux.
- If platelets <30k, significant bleeding or other absolute contraindication to anticoagulation, use mechanical compression devices.
- Direct oral anticoagulants (DOAC) should not be used for prophylaxis in the acute inpatient setting.

### When should venous duplex be performed in patients with COVID-19?

Elevated D-dimers is a common laboratory finding in these patients, tend to follow severity of disease and is a marker of worse clinical outcome. Indications for venous duplex ultrasound in patients with COVID-19 should be similar to non COVID-19 patients (leg swelling/pain/erythema) and only if results will alter patient care.

Role of D-dimer levels as an indication for venous duplex ultrasound:

- If the D-dimer is normal, duplex ultrasound is not necessary.
- High levels of D-dimer should not be used as a sole indication for venous imaging.

Other important considerations:

- A normal venous ultrasound should not be used as a marker that anticoagulation is not required.
- Venous duplex ultrasound should be performed only if the results will alter patient management. Patients with severe disease markers who would be treated with full anticoagulation despite a normal venous ultrasound (see below) should not undergo the study unless there is another specific question that the information would be used to answer.



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### If venous duplex is required, what type of test is needed and how should it be performed?

- Point of care testing should be preferred in hospitalized patients with COVID-19.
- If available, wireless handheld ultrasound devices may be used as they allow maximal cleaning of the probe between patients and minimal risk of contamination.
- If venous duplex ultrasound is needed, full assessment is preferred over 2-point assessment.

### Which patients with COVID-19 should be considered for therapeutic anticoagulation?

- Limited literature has shown that patients with COVID-19 who die have a high incidence of VTE. Elevated D-dimer levels have been associated with increased overall mortality and administration of LMWH appears to decrease D-dimer levels.<sup>6-11</sup> Autopsy studies have shown that patients develop microvascular thrombosis in the end-organs (lungs, kidneys etc.) that may contribute to multi-system organ failure.<sup>2</sup>
- If a patient is on anticoagulation prior to admission, continuation of anticoagulation during admission is recommended (unless there are bleeding complications). If on Coumadin or DOAC, consider switching to Heparin drip or LMWH.
- There should be consideration for therapeutic anticoagulation in patients with significant D-dimer elevation. The D-dimer cut-off is arbitrary, with some centers using a cut-off of three times normal levels (age-adjusted) while others are using a numeric cut-off >3000ng/ml.<sup>11</sup>
- While there is no established numeric value of D-dimer to initiate anticoagulation, it is well-established that these patients are very pro-thrombotic. Decision when to start therapeutic anticoagulation is based on risks and benefits with each patient.
- Limited data has shown that patients treated with anticoagulation have a decrease in their D-dimers, clinically do better and have a lower mortality than those who are not anticoagulated.<sup>11</sup>
- In the limited literature available, use of therapeutic anticoagulation in patients with COVID-19 has not been associated with a high rate of severe bleeding complications. Bleeding complications are a concern if these patients progress to DIC so consistent monitoring and reconsideration of therapy is important. Given the rapid learning curve related to treatment of severely affected patients with COVID-19, these considerations may change as new information emerges.

### What anticoagulants and dosages are recommended for VTE treatment in COVID-19 patients?

During the acute phase of the illness, patients who have a VTE should be treated with Heparin to keep PTT therapeutic or LMWH (such as enoxaparin 1mg/kg BID).

- Unfractionated Heparin in acutely ill is generally preferred due to rapid reversibility.
- LMWH may also be considered and may be preferred due to the anti-inflammatory properties.
- Argatroban or Fondaparinux can be used in patients with evidence of Heparin induced thrombocytopenia.
- Coumadin should be avoided in the acutely ill patient.



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### What to do with patients after discharge?

During follow-up visit:

- If there is a documented thrombotic event (venous or arterial), continue therapeutic anticoagulation for three months and reassess.
- Patients that are very high-risk for VTE (morbid obesity, Caprini score >8) should be discharged on regular dose of chemical prophylaxis for six weeks.
- Patients who had 3x D-dimer levels during admission and started on therapeutic anticoagulation
  - Continue therapeutic anticoagulation and follow up in two to three weeks as an outpatient (or whenever the patient is no longer be considered to virally active).
  - If VTE was never confirmed with imaging, venous duplex ultrasound of upper and lower extremities to evaluate for evidence of recent DVT given the high incidence in this population.
  - If DVT present, continue anticoagulation for three months.
  - If no evidence of DVT, switch to regular dose of chemical prophylaxis for a total of six weeks post-discharge.
- If anticoagulation is continued and patient is on LMWH, consider switching to DOAC.

What anticoagulants to use as an outpatient:

- Anticoagulation can include LMWH or DOAC.
- DOAC may be preferred due to ease of use and compliance over LMWH.
- LMWH may be used in the short-term due to its anti-inflammatory effects particularly in more severely affected patients.
- Coumadin should be avoided due to the personal contact required for monitoring.

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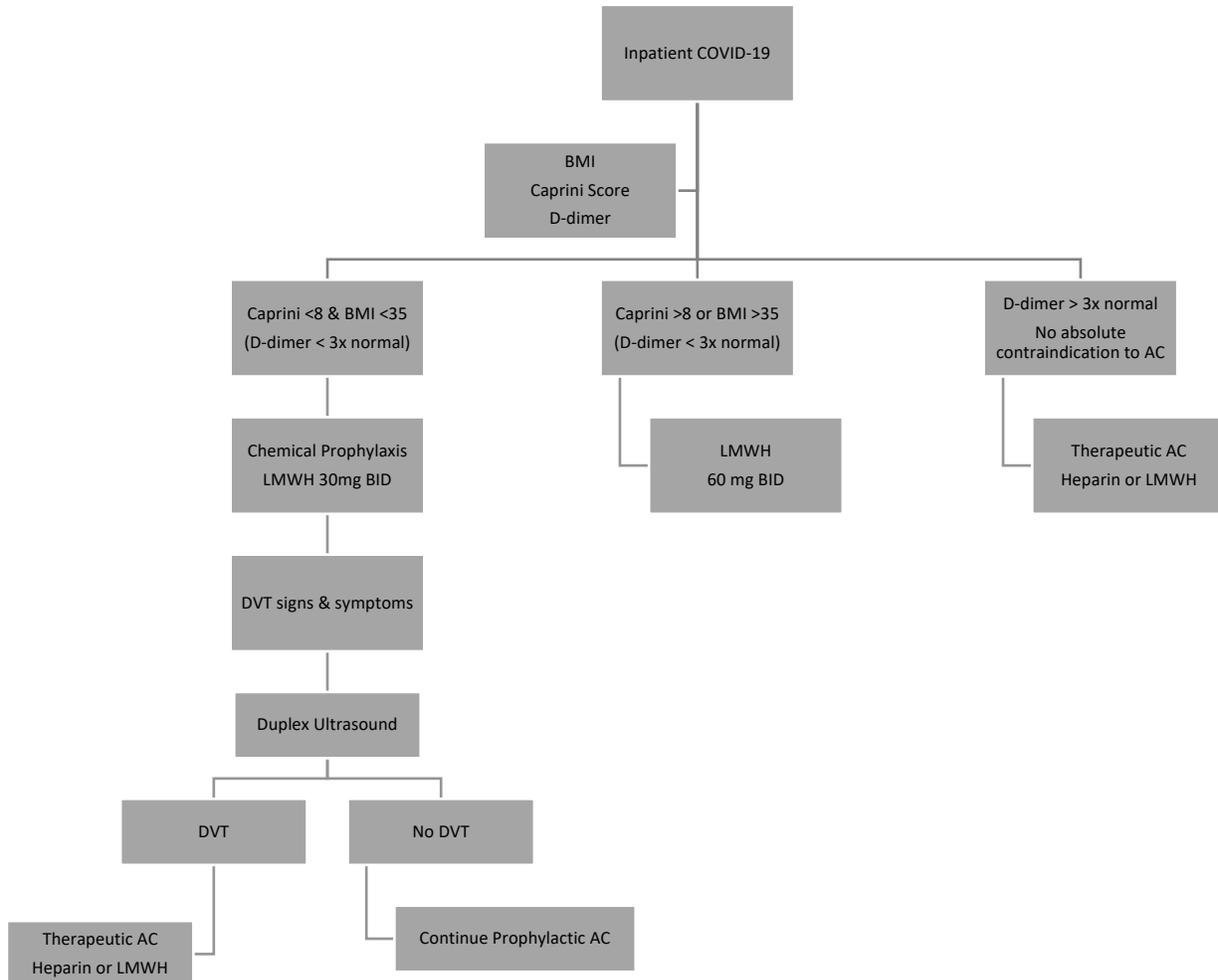
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## Considerations in prophylaxis and treatment of VTE in COVID-19 Patients

**Figure 1.** Anticoagulation (AC) algorithm in admitted COVID-19 patients



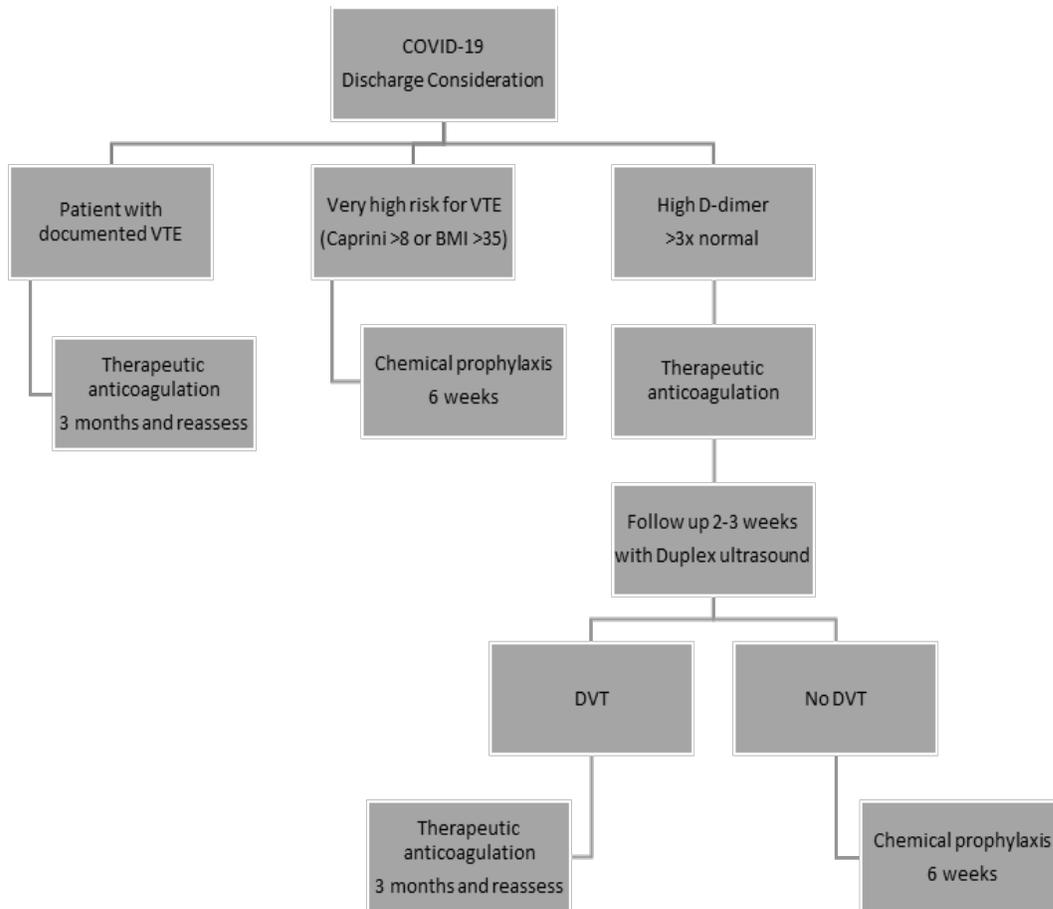
If patient has absolute contraindication to anticoagulation, IPC should be placed for VTE prophylaxis.

If a patient develops signs and symptoms of DVT while on anticoagulation (prophylactic or therapeutic), duplex ultrasound may be performed.



## Considerations in prophylaxis and treatment of VTE in COVID-19 Patients

**Figure 2.** Discharge algorithm of admitted COVID-19 patients



NOTE: The information presented in these flow diagrams represents the opinion of the authors based on limited evidence and anecdotal discussions with numerous clinicians working in high-volume centers treating patients affected with COVID-19. In some areas, the treatment choices are controversial and best treatment of individual patients should consider the risks and benefits of treatment to that individual patient. As new information emerges these considerations may change.