Guidelines for Anticoagulation in Hospitalized COVID-19 Patients ≥ 18 Years of Age

BACKGROUND

- Severe COVID-19 disease is associated with features of disseminated intravascular coagulation (DIC) and hypercoagulable states which can manifest as venous thromboembolism (VTE) and/or microthrombosis.[1,2]
- Centers for Disease Control and Prevention (CDC) estimates approximately 90% of hospitalized COVID-19 patients have underlying disease states such as obesity, hypertension, chronic lung disease, diabetes, and heart disease, which may increase the risk of thrombosis.[3]
- Critically ill patients with COVID-19 have been reported to have a VTE incidence rate around 30% which is significantly higher than non-COVID-19 critically ill populations[4,5]
- A study of 449 COVID-19 patients found that deep vein thrombosis (DVT) prophylaxis decreased 28-day mortality by 20% in patients with a D-dimer ≥ 3,000 ng/mL or a sepsis-induced coagulopathy (SIC) score ≥ 4 without increasing rates of major bleeding.[6]
- Elevated D-dimer is associated with worse outcomes;[7-9] Recent studies have found d-dimer above certain thresholds to have a high positive predictive value for VTE events and suggest these thresholds may be useful in determining when ultrasound screening and even empiric full dose anticoagulation is indicated.[4]
- Randomized controlled trials evaluating empiric full dose anticoagulation in patients with COVID-19 without a diagnosed indication (e.g. venous or arterial thrombosis, stroke prevention in atrial fibrillation, heart valve replacements) or clinical signs of clotting are currently underway. In the meantime, however many institutions are implementing empiric full dose anticoagulation based on the risk of VTE and overall low incidence of bleeding (3-5%).[10,11]
- Hospitalized patients with a diagnosis necessitating therapeutic anticoagulation should be treated with treatment dose unfractionated or low molecular weight heparin instead of direct oral anticoagulants (DOACs) and warfarin which are less desirable due to illness-related hepatic dysfunction, reduced appetite and poor oral intake which may affect absorption or affect response to warfarin, and the possibility of rapid deterioration.[12]
- Incidence of VTE and major bleeding in COVID19 patients post-discharge are unknown. The decision to prescribe extended thromboprophylaxis should be individualized and based on the patients VTE and bleed risk.[14]
- The algorithm below is intended to provide guidance for anticoagulation prophylaxis and treatment in COVID-19 patients and should not supersede clinical judgement. It may also be applied to "Persons Under Investigation" (PUIs) at the physician's discretion.

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All COVID-19 (+) patient ≥ 18 years of age admitted to the hospital ***should*** receive anticoagulant prophylaxis unless contraindicated

Critically Ill
DVT Prophylaxis

High suspicion/risk for thrombosis

- Any evidence of thrombosis (including superficial veins)
- Worsening hypoxemia despite improving X-ray and good lung compliance
- D-dimer ≥ 5,000 ng/mL or rapidly ↑ D-dimer

NO

High Dose Prophylaxis

Enoxaparin 0.5 mg/kg SC BID (TBW)**

CrCl < 30 mL/min:
Enoxaparin 0.5 mg/kg SC once daily**
< 50 kg: Heparin 5,000 units SC every 8 hrs
≥ 50 kg: Heparin 7,500 units SC every 8 hrs

All ICU patients should have four-extremity venous ultrasound every 7 days to evaluate the need for therapeutic anticoagulation

YES

Indication for therapeutic anticoagulation
(Including continuation of home therapy)

Enoxaparin 1 mg/kg SC BID (TBW) or
Heparin 18 units/kg/hr IV (TBW) with standard boluses and titrations per protocol (max initial rate 2,000 units/hr)

Patients escalated to therapeutic anticoagulation based on D-dimer ≥ 5,000 ng/mL may resume "**High Dose Prophylaxis**" (see under Critically Ill) once D-dimer decreases to ≤ 2,000 ng/mL

DOACs and Warfarin
DO NOT USE for critically ill patients
May consider use in patients anticipating discharge

Non-Critically Ill
DVT Prophylaxis

BMI < 40: Enoxaparin 40 mg SC once daily***
BMI ≥ 40: Enoxaparin 40 mg SC BID
BMI ≥ 50: Enoxaparin 60 mg SC BID

CrCl < 30 mL/min:
Enoxaparin 30 mg SC once daily**
Heparin 5,000 units SC every 8 hrs
≥ 100 kg: Heparin 7,500 units SC every 8 hrs

If D-dimer ≥ 2,000-3,000 ng/mL* consider Enoxaparin 40 mg SC BID or "**High Dose Prophylaxis**" (see under Critically Ill)

Avoid initiating DOACs for prophylaxis during hospitalization

Extended Thromboprophylaxis Up to 45 Days Post-Discharge
(Continued on next page)

*Clinicians should check D-dimer at baseline, then at least weekly and with changes in severity of illness.
**May consider checking LMW heparin assay 4 hrs after the 2nd dose to ensure target prophylaxis level (0.2-0.4) is achieved. High degree of inflammation may lead to a need for increased dosing.
***Patients presenting with trauma should continue to receive Enoxaparin 30 mg SC BID per standard practice.
DOACs = Direct oral anticoagulants (apixaban, rivaroxaban, dabigatran, edoxaban, betrixaban)

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Extended Thromboprophylaxis Up to 45 Days Post-Discharge

May be considered for patients at continued high risk of VTE and low risk of bleeding

Rivaroxaban 10 mg PO once daily (avoid in severe hepatic or renal dysfunction) **OR** Enoxaparin 40 mg SC once daily

CrCl < 30 mL/min:

Enoxaparin 30 mg SC once daily **OR** Heparin 5,000 units SC every 8 hrs

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