Guidelines for Anticoagulation in Adult Patients with COVID-19

BACKGROUND: COVID-19 patients with severe infection demonstrate a hypercoagulable profile. The recommendations below provide guidance, and are not intended to substitute clinical judgement. Optimal anticoagulant dosing for VTE prevention/treatment in COVID-19 patients is unknown. Patients on dual or single anti-platelet therapy should also be on chemical DVT prophylaxis.

STANDARD PROPHYLAXIS ALL PATIENTS: ALL hospitalized, floor patients with COVID-19 WITHOUT known thrombus and not in disseminated intravascular coagulation (DIC) [platelets < 50K, prolonged PT/aPTT, Fibrinogen level < 150 mg/dL AND elevated D-Dimer], should receive prophylactic doses of anticoagulation to prevent venous thromboembolism. If anticoagulation is contraindicated, we recommend therapy with sequential compression devices. There is insufficient data to consider elevated dose prophylaxis in this population.

<table>
<thead>
<tr>
<th>Standard DVT Prophylaxis</th>
<th>Obese patients (BMI greater than 40 kg/m² or &gt; 120 kg)</th>
<th>Low body weight patients (&lt; 50 kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 40 mg SubQ daily</td>
<td>CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 40 mg SubQ BID</td>
<td>CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 30 mg SubQ daily</td>
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<tr>
<td>CrCl 15 - 30 mL/min, Enoxaparin (Lovenox) 30 mg SubQ daily</td>
<td>CrCl &lt; 30 mL/min, Heparin 7,500 units SubQ every 8 hrs</td>
<td>CrCl &lt; 30 mL/min, Heparin 5,000 units SubQ every 8 or 12 hours</td>
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<tr>
<td>OR Heparin 5,000 units SubQ every 8 hours</td>
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<tr>
<td>OR Fondaparinux (Arixtra) 2.5 mg SubQ daily</td>
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ELEVATED DOSE PROPHYLAXIS: COVID-19 ICU patients or patients receiving ICU level of care WITHOUT known thrombus and not in DIC, but have elevated D-Dimer > 3 mcg/mL (6XUNL), elevated CRP and IL6 who are at risk for Cytokine Release Syndrome, with independent risk factors for VTE (i.e., malignancy, immobility, injury) should receive elevated prophylactic doses of anticoagulation to prevent venous thromboembolism. If anticoagulation is contraindicated, we recommend sequential compression devices, and baseline and routine lower extremity doppler. **Note: LMWH/UFH are preferred over oral anticoagulants due to shorter half-life and fewer drug interactions.**

<table>
<thead>
<tr>
<th>Elevated dose of DVT Prophylaxis</th>
<th>Obese patients (BMI greater than 40 kg/m² or &gt; 120 kg)</th>
<th>Low body weight patients (&lt; 50 kg)</th>
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<tr>
<td>CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 40 mg SubQ BID</td>
<td>CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 0.5 mg/kg SubQ BID, round per protocol (Max dose 100 mg SubQ BID)</td>
<td>CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 30 mg SubQ BID</td>
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<tr>
<td>CrCl &lt; 30 mL/min, Heparin 7,500 units SubQ every 8 hours</td>
<td>CrCl &lt; 30 mL/min, Heparin 10,000 units SubQ every 8 hrs</td>
<td>CrCl &lt; 30 mL/min, Heparin 7,500 units SubQ every 8 hours</td>
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</tbody>
</table>

THERAPEUTIC DOSING: For patients with confirmed VTE or suspected VTE (signs of organ failure, D-Dimer > 3 mcg/mL (6XUNL) AND persistent clotting of lines/devices/filters despite VTE prophylaxis and worsening clinical course, intensified anticoagulation may be considered via multidisciplinary discussion. Consider patient specific risks and benefits. Initiation of anticoagulation without confirmed or high suspicion of DVT/PE is controversial and is not recommended.

<table>
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<th>Anticoagulation: Therapeutic Dose</th>
<th>Notes</th>
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<tr>
<td>CrCl ≥ 30 mL/min, Enoxaparin 1 mg/kg SubQ every 12 hours</td>
<td>1. Routine monitoring is not recommended for enoxaparin, but if concern for bleeding or worsening coagulopathy, may monitor anti-Xa levels (if available) as needed (draw 4 hours post 3rd dose) with goal 0.6 - 1 units/mL.</td>
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<tr>
<td>CrCl &lt; 30 mL/min, Heparin drip, per entity approved protocol</td>
<td>2. If concern for heparin resistance after trial of heparin or enoxaparin OR if platelets drop by &gt; 50%, consider switching to an Argatroban drip – per entity approved protocol. Monitor and decrease dose in patients with moderate to severe hepatic dysfunction.</td>
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</table>

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Patients receiving chronic anticoagulation
For patients with moderate or severe COVID-19 on chronic therapeutic anticoagulation, continue full dose therapy. Monitor and screen for DIC and for patients who develop suspected or confirmed DIC without overt bleeding,

a. Review the indication for anticoagulation and weigh it against the risk of bleeding when making clinical decisions regarding dose adjustments or discontinuation.

b. Consider reducing the intensity of anticoagulation in this clinical circumstance, unless the risk of thrombosis is exceedingly high.

Patients receiving dual antiplatelet therapy
For patients with moderate or severe COVID-19 and an indication for dual antiplatelet therapy (e.g., percutaneous coronary intervention [PCI] within the past 3 months or recent myocardial infarction [MI]) and with suspected or confirmed DIC without overt bleeding, in the absence of evidence, decisions for antiplatelet therapy need to be individualized. In general, it is reasonable to:

a. Continue dual antiplatelet therapy if platelet count is ≥ 50,000,

b. Reduce to single antiplatelet therapy if platelet count is ≥ 25,000 and < 50,000

c. Discontinue if platelets are < 25,000.

NOTE: These guidelines may be revised upward or downward depending on the individualized relative risk of thrombotic complications versus bleeding.

Post Discharge Recommendations

- Consider extended out of hospital prophylaxis for 14 days to 30 days in patients not at risk for bleeding (gastro-duodenal ulcer, bleeding in the prior 3 months, admission platelets < 50,000, hepatic dysfunction, CV catheter, rheumatic diseases).

- Eligible patients include those 60 years of age or older, hospitalized for at least 5 days and have other risk factors for VTE such as current cancer and immobility.

- Other VTE risk factors were demonstrated by a total modified IMPROVE (International Medical Prevention Registry on Venous Thromboembolism) VTE risk score of ≥ 4 or VTE risk score of 2 or 3 with D-dimer > 2XULN.

- Choices include Enoxaparin 30 or 40 mg SubQ daily, Fondaparinux 2.5 mg SubQ daily, Rivaroxaban 10 mg PO daily. Avoid use in CrCl < 30 mL/min.

https://www.outcomes-umassmed.org/IMPROVE/risk_score/index.html
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