# COVID-19 ANTICOAGULATION and LABORATORY MONITORING GUIDE

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## LABORATORY DATA TESTING

for known or suspected COVID-19 cases

<table>
<thead>
<tr>
<th>Upon Admission</th>
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<tbody>
<tr>
<td>• CBC with differential, Retic count</td>
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<tr>
<td>• Ferritin</td>
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<tr>
<td>• D-dimer</td>
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<tr>
<td>• Prothrombin Time/INR</td>
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<td>• Fibrinogen</td>
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<table>
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<th>Consider Every 24-48 Hours</th>
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<th>Upon Admission to ICU (Once)</th>
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<tr>
<td>• LDH</td>
</tr>
<tr>
<td>• Haptoglobin</td>
</tr>
<tr>
<td>• C3/C4</td>
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<tr>
<td>• Ferritin</td>
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## Special Circumstances

### CVVRT Circuit Clotting

- Consider Cryoglobulin and Cryofibrinogen Panel, Serum and Plasma (MAYO Send-out):
  [https://www.mayocliniclabs.com/test-catalog/Overview/83659](https://www.mayocliniclabs.com/test-catalog/Overview/83659)

### Heparin Resistance (>35,000 units/d excluding bolus doses)

- Factor VIII, Fibrinogen, Antithrombin III Activity

### Arterial Thromboemboli (i.e., MI, CVA, etc)

- Lupus Anticoagulant
- Beta-2-Glycoprotein IgG and IgM
- Cardiolipin Antibody IgG and IgM
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Inpatient with COVID-19

Acute VTE, High Suspicion of Acute VTE, or on CRRT?

Therapeutic Anticoagulation

eGFR < 30 ml/min

Platelets < 25,000
- Hold anticoagulation
- Transfuse platelets to achieve adequate platelets
  - Enoxaparin 0.5 mg/kg SC q24h
  - Transfuse platelets to achieve adequate platelets
    - Unfractionated IV Heparin drip (Platelet goal > 50,000)

Platelets 25,000-50,000
- Enoxaparin 0.5 mg/kg SC q24h
- Transfuse platelets to achieve adequate platelets
  - Unfractionated IV Heparin drip (Platelet goal > 50,000)

Platelets > 50,000
- Unfractionated IV Heparin drip (preferred)
- Enoxaparin 1 mg/kg SC q24h

eGFR ≥ 30 ml/min

Platelets < 25,000
- Hold anticoagulation
- Transfuse platelets to achieve adequate platelets
  - Enoxaparin 0.5 mg/kg SC q12h (Platelet goal > 25,000)
  - Transfuse platelets to achieve adequate platelets
    - Unfractionated IV Heparin drip (Platelet goal > 50,000)

Platelets 25,000-50,000
- Enoxaparin 0.5 mg/kg SC q12h
- Transfuse platelets to achieve adequate platelets
  - Unfractionated IV Heparin drip (Platelet goal > 50,000)

Platelets > 50,000
- Enoxaparin 1 mg/kg SC q12h
- Unfractionated IV Heparin drip

In patients who develop clotting despite adequate coagulation, those with bleeding complications, or those with concerns for heparin refractoriness, consider hematology consult

COVID-19, High-Risk of VTE*

Defined: Admitted to the ICU AND
(Meets ≥ 1 of the below criteria)
- D-dimer > 6x normal
- Increased oxygen requirement
- Elevated Creatinine
- Pressor Support

*Recommend VTE diagnostic workup for patients with acute decompensation not otherwise explained and/or high clinical suspicion of VTE

Standard-dose Prophylactic Anticoagulation per institutional guidelines
Take into consideration weight and renal function for dosing

Intermediate Dose Anticoagulation

- eGFR ≥ 30ml/min and Platelets > 25,000
  - Enoxaparin 40mg SC q12h (or 60mg q24h)
  - Enoxaparin 0.5mg/kg SC q12h (or 1mg/kg q24h)
    - Consider for obese patients

- eGFR < 30ml/min and Platelets > 25,000
  - Unfractionated Heparin 7500 units SC q8h (obese)
  - Unfractionated Heparin 5000 units SC q8h

^Consider anti-Xa level (goal 0.1-0.3) as studies have shown only 55% of critically-ill normal weight patients are at goal

Monitoring

Heparin: Monitoring per institutional nomogram is recommended.
- Consider anti-Xa testing if difficulty obtaining therapeutic dosing with aPTT

Enoxaparin: Monitor using anti-Xa levels, if available
- Measure anti-Xa level 4 hours after 3rd or 4th dose
- Goal anti-Xa:
  - 12 hour dosing: 0.6 – 1
  - 24 hour dosing: 1 – 2
- Titrate dosing to achieved desired level
COVID-19, Discharge Thromboprophylaxis

Acutely ill medical patients have an increased risk of VTE following hospital discharge. Post-discharge prophylaxis could be considered in patients with high-risk features (see Table: Discharge Thromboprophylaxis High-Risk Criteria) who are anticipated to still have significant immobility upon returning home.

- Meta-Analysis has shown that extended thromboprophylaxis VERSUS standard thromboprophylaxis:
  - Reduces the rate of symptomatic VTE: Risk Ratio 0.52 (95% CI: 0.36-0.76)
  - Increases the rate of major bleeding: Risk Ratio 2.04 (95% CI: 1.42-2.91)

<table>
<thead>
<tr>
<th>Prophylactic Anticoagulation Options</th>
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<tr>
<td>eGFR &gt; 30 ml/min (alphabetical order)</td>
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<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>• Apixaban 2.5mg PO q12 hours <strong>30 days</strong></td>
</tr>
<tr>
<td>• Betrixaban 80mg PO q24 hours (with food) <strong>30 days</strong></td>
</tr>
<tr>
<td>• Enoxaparin 40mg SC q24 hours (Should not be used in patients with a history of HIT) <strong>10-14 days</strong></td>
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Discharge Thromboprophylaxis High-Risk Criteria

| Inclusion | Male or Female >= 40 years  
Acute Hospitalization for acute infection  
One of the following:  
- Age >= 75 OR  
- 60 – 74 with D-dimer >= 2ULN OR  
- 40 – 59 with D-dimer >= 2ULN and a history of either VTE or cancer  
Immobilization during hospital stay defined:  
- Severe Immobilization 24 hours - Confined to bed/chair and can only be mobile independently to the toilet.  
  - AND  
  - Moderate Immobilization ≥ 3 days – mobile independently to in-room toilet, off-ward with assist, mobilized by PT  
  - Hemoglobin > 10  
  - Total hospitalization >= 3 days | Male or Female >= 40 years  
Acute Hospitalization for acute infection  
One of the following (risk factors for VTE):  
- Severe Varicose veins  
- Chronic Venous Insufficiency  
- History of Cancer  
- History of DVT/PE  
- History of NYHA class III/IV HF  
- Known thrombophilia  
- Recent surgery/major trauma  
- Hormone Replacement Therapy  
- Age >= 75  
- BMI >= 35 kg/m2  
- Acute Infection  
Immobilization: (Both)  
- At least 24 hours’ bed bound (bathroom privileges allowed)  
- Anticipated >= 4 days of reduced mobilization in any setting | Male or Female >= 40 years  
Acute Hospitalization for acute infection  
Length of stay >= 3 days  
One of the following (risk factors for VTE):  
- History of Cancer  
- History of DVT/PE  
- History of Chronic Heart Failure  
- History of Chronic Pulmonary Disease  
- Hormone Replacement Therapy  
- Age >= 75  
- BMI >= 30 kg/m2  
Immobilization (one):  
- Moderately Restricted: Walking within the hospital room only  
- Severely Restricted: Confined to bed or chair during hospitalization |

| Exclusion | Body weight < 45 kg  
History of major bleed within 6 months  
History of significant GI, pulmonary or urogenital bleeding OR history of ongoing PUD or acute gastritis in the 2 years prior.  
Active lung cancer  
History of bronchiectasis  
End Stage Renal Disease  
History of ICH within 3 years  
Known intracranial lesions (i.e. metastatic cranial disease or primary brain tumor)  
PLT < 100,000  
INR > 1.4 OR aPTT > 1.4 x ULN  
Liver disease (e.g. AST and/or ALT > 2xULN)  
History of clinically significant bleeding within 30 days  
Major surgery within 6 weeks  
INR > 1.5  
History of hemorrhagic stroke, ever  
Known intracranial lesions (i.e. metastatic cranial disease or primary brain tumor)  
Severe renal insufficiency  
HIV Infection  
Liver disease  
Uncontrolled HTN = SBP >= 180 mmHg or diastolic >= 100 mmHg  
History of ongoing ETOH or drug use  
Actively Bleeding or High Risk for Bleeding  
Major surgery within 30 days  
Anemia with HGB < 9 g/dL  
Platelets < 100,000  
AST or ALT > 2xULN  
Total bilirubin > 1.5 x ULN  
Severe renal insufficiency (eGFR < 30 ml/min)  
Active Liver disease | Male or Female >= 40 years  
Acute Hospitalization for acute infection  
Length of stay >= 3 days  
One of the following (risk factors for VTE):  
- History of Cancer  
- History of DVT/PE  
- History of Chronic Heart Failure  
- History of Chronic Pulmonary Disease  
- Hormone Replacement Therapy  
- Age >= 75  
- BMI >= 30 kg/m2  
Immobilization (one):  
- Moderately Restricted: Walking within the hospital room only  
- Severely Restricted: Confined to bed or chair during hospitalization |
CLINICAL RESOURCES:

For patients with a history of HIT or suspicion of HIT, or heparin refractoriness the following substitutions are appropriate with dosing based on renal function:

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<td>- Direct Oral Anticoagulation</td>
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<td>- Bivalirudin - Titrate based on nomogram</td>
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<td>- Consider e-consult to hematology</td>
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*For patients with Antithrombin activity < 30%, the following substitutions are appropriate with dosing based on renal function:

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TOPICS:

COVID-19/SARS-CoV-2

Rate of thrombosis in COVID-19:
1. Incidence of thrombotic complications in critically ill ICU patients with COVID-19\(^{11}\)
2. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia.\(^{12}\)

Thromboprophylaxis and Mortality in COVID-19:
1. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy.\(^{13}\)

D-dimer is associated with increased mortality in COVID-19:
1. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.\(^{14}\)
2. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia.\(^{15}\)

SARS-CoV-1

Rate of thrombosis in SARS-CoV-1
1. Acute Respiratory Distress Syndrome in critically ill patients with SARS.\(^{16}\)
References:


