Subject: COVID-19 Anticoagulation Guidelines

Summary:

Published reports suggest that rising D-Dimers correlate with poor survival among COVID-infected patients. Autopsy reports suggest a microvascular thrombosis contributes to respiratory dysfunction in infected patients. These and anecdotal reports of overt VTE and significant dialysis-related thrombosis have led several centers to increase to higher or therapeutic dosing of heparins early in the course of moderate-severe COVID infection.

Attachments:

- Anticoagulation Leaflet (PDF)
- Appendix (PDF)

Keck Medical Center of USC
Keck Medicine of USC

COVID-19 Units
Anticoagulation Guidelines

v.3 Last Updated 4.15.20
Dr. Casey O'Connell

Monitoring Guidelines (at baseline and Q24-48 hrs)
Labs: CBC w/ Diff, CMP, D-Dimer, PT/INR, aPTT, CRP

Exclusion Criteria:
- Known bleeding diathesis
- Active bleeding
- Pre-existing coagulopathy (i.e. d/t cirrhosis and ascites (elevates baseline D-Dimer))
- Thrombocytopenia (< 50,000/mL)

Levels	Clinical Results			Recommended Interventions	
				If Cr Cl ≥ 30ml/min	**If Cr Cl ≤ 30 ml/min**
1	**No known VTE**	D-Dimer **<3,000** ng/mL	→	Enoxaparin 40 mg/day SC *If BMI > 30:* Enoxaparin 40mg Q12 hr SC	Enoxaparin 30 mg/day SC OR Unfractionated Heparin 5,000 units Q8hr SC
2		D-Dimer **>3,000** ng/mL **OR** D-Dimer **increases by ≥1000** ng/mL despite 48 hours of prophylactic LMWH or UFH	→	Enoxaparin 0.5 mg/kg Q12 hr SC *(Pharmacy to round to the nearest syringe size)*	Low Dose IV Unfractionated Heparin
3	**Suspected or Confirmed VTE OR Respiratory Decline on PPX** (increasing FiO2 requirement of > 50% for > 4 hrs)		→	Enoxaparin 1mg/kg Q12hr SC *(Pharmacy to round to the nearest syringe size)*	Treatment Dose IV Unfractionated Heparin
4	If **NEW** VTE, HIT, D-Dimer > 10k , or Clotting lines/filter **while on TREATMENT dose Heparin/LMWH**		→	**Check:** AT, APLS abs, HIT screen if indicated **CONSIDER** using anti-Xa to monitor LMWH **CONSIDER** TEG **CONSIDER** switching to Argatroban - aPTT target 1.5-3 x baseline **CONSIDER** tPA only for standard indications	

Anticoagulation Guidelines for COVID Patients at Keck & Norris Hospital

v. 4/14/2020*

EXCLUSION CRITERIA: Known bleeding diathesis, Active Bleeding, Pre-existing coagulopathy such as due to cirrhosis, Ascites (elevates baseline d-dimer), thrombocytopenia <50,000/mL**

CLINICAL CATEGORY	ACTION RECOMMENDED
LEVEL 1: **NO VTE** D-dimer < 3,000 ng/ml	IF CrCl≥30 ml/min: Enoxaparin prophylactic dose 40 mg/day subcutaneous IF BMI>30: Enoxaparin 40mg q 12 hrs subcutaneous IF CrCl<30ml/min: Enoxaparin 30 mg/day subcutaneous OR UFH 5,000 q8 hrs SC
LEVEL 2: **NO VTE** D-dimer ≥ 3,000 ng/mL OR D-Dimer increases by ≥1000 ng/mL despite 48 hours of prophylactic LMWH or UFH	IF CrCl≥30 ml/min: Enoxaparin 0.5 mg/kg q 12 hrs subcutaneous *(Pharmacy to round to the nearest syringe size)* IF CrCl<30ml/min: Low Dose IV UFHeparin Xa-driven protocol***
LEVEL 3: **KNOWN or SUSPECTED VTE** Also consider for increasing Fi O2 requirement >50% for > 4 hours while on Level 1 or 2 anticoagulation	IF CrCl≥30 ml/min: Enoxaparin 1 mg/kg q 12 hours subcutaneous *(Pharmacy to round to the nearest syringe size)* IF CrCl <30 ml/min Standard Treatment Dose IV UFHeparin Xa-driven protocol
LEVEL 4: While therapeutic on standard treatment dose of UFHeparin or enoxaparin, patient develops: VTE, Suspected HIT-T, D-Dimer remains >10,000 ng/mL or Unable to dialyze due to clotting in line, filter or machine	Check Antithrombin Activity, APLS antibodies, consider using anti-Xa for LMWH, consider TEG for monitoring anticoagulant effect Consider switch to Argatroban with aPTT target of 1.5-3 x baseline aPTT Consider tPA ONLY per standard indications

BASELINE STUDIES RECOMMENDED
D-Dimer PT/aPTT Fibrinogen CBC w/ diff CMP **REPEAT**: at min. D-dimer, CBC, CMP **q 24-48 hours**
LE Doppler for level 2 or 3 and with clinical indications

RATIONALE FOR CHOICE OF HEPARINS (unfractionated or low molecular weight): Heparins have anti-inflammatory and anti-complement activity and may bind viral proteins. Therefore,

For patients admitted for the treatment of COVID and on therapeutic doses of anticoagulation with a **DOAC**, we recommend switching to therapeutic dose enoxaparin or IV unfractionated heparin. DOACs may have drug-drug interactions with antiviral therapy, steroids, or other investigational treatments for COVID-19. Consult cardiology if DOAC is for coronary artery disease.

For patients admitted for the treatment of COVID and on therapeutic doses of warfarin for a **mechanical heart valve**, we recommend either continuing warfarin therapy or switching to treatment dose IV unfractionated heparin in consultation with Cardiology.

RATIONALE FOR INCREASING TO INTERMEDIATE DOSING OF HEPARINS: Published reports suggest that rising D-Dimers correlate with poor survival among COVID-infected patients. Autopsy reports suggest a microvascular thrombosis contributes to respiratory dysfunction in infected patients. These and anecdotal reports of overt VTE and significant dialysis-related thrombosis have led several centers to increase to higher or therapeutic dosing of heparins early in the course of moderate-severe COVID infection.

ANTIPLATELET THERAPY For patients on **antiplatelet therapy**, if platelets are >100,000/mL, we recommend continuing antiplatelet therapy and prophylactic doses of anticoagulation (Level 1 and 2). Should patient require full dose anticoagulation consider reducing dual antiplatelet therapy to single agent antiplatelet therapy or stopping antiplatelet therapy in consultation with Cardiology. For patients with platelets 50,000-100,000/mL consider holding antiplatelet

therapy. If COVID antiviral or other therapies planned, check for drug interactions such as via CYP3A4 effects.

***For patients with platelets <50,000/mL we recommend workup other etiologies and consulting hematology.**

****This Guideline may be updated as new data become available regarding optimal anticoagulation for COVID-infected patients.**

<table>
<tr><th colspan="2">***Low Dose Heparin Infusion (Target Anti-Xa 0.10 – 0.30 IU)</th></tr>
<tr><th colspan="2">Initial UFH infusion and bolus</th></tr>
<tr><td colspan="2">No initial bolus
Initial rate of infusion 7 units/kg/hr (not to exceed 1,000 units/hr).</td></tr>
<tr><th colspan="2">Laboratory monitoring</th></tr>
<tr><td colspan="2">Check anti- Xa 6 hours after initiating heparin infusion and 6 hours after any rate change.
If the infusion is interrupted and restarted according to protocol, the 6 hour period begins when the infusion is restarted.</td></tr>
<tr><th colspan="2">UFH infusion adjustment</th></tr>
<tr><th>Anti-Xa (IU)</th><th>Action</th></tr>
<tr><td>Less than 0.10</td><td>Increase rate of infusion by 2 units/kg/hr</td></tr>
<tr><td>0.10 – 0.30</td><td>Continue current infusion rate.
Recheck Anti-Xa in 6 hours.
If Anti-Xa is therapeutic on two consecutive measurements, recheck daily.</td></tr>
<tr><td>0.31 – 0.70</td><td>Decrease infusion by 1 unit/kg/hr</td></tr>
<tr><td>0.71 – 1.10</td><td>Hold infusion x 60 min, then restart at 2 units/kg/hr less than previous rate.</td></tr>
<tr><td>Greater than 1.10</td><td>Hold infusion x 60 min, then recheck Anti-Xa.
- If Anti-Xa is 0.70 or lower, restart infusion at 3 units/kg/hr less than previous rate.
- If Anti-Xa > 0.70, contact MD for instructions</td></tr>
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