Anticoagulation Dosing Guideline for Adult COVID-19 Patients

Enoxaparin is the preferred first line anticoagulant for patients diagnosed with COVID-19. The incidence of HIT with enoxaparin is less than 1%.

VTE Prophylaxis:

VTE prophylaxis will be considered for COVID-19 patients who are low risk.

Low risk COVID-19 patient

1. Not receiving mechanical ventilation
2. D-Dimer < 6 mg/L
3. ESRD on iHD without clotting

Kidney Function	**BMI** (kg/m^2)	**Dosing of Enoxaparin**	**Concern for HIT or LMWH Failure**
CrCL ≥ 30 mL/min	18.5-39.9	30mg SUBQ Q12H	Consult Hematology
	40-49.9	40mg SUBQ Q12H	
	≥ 50	60mg SUBQ Q12H	
CrCL < 30 mL/min OR ESRD/AKI on RRT	18.5-39.9	30mg SUBQ Q24H	Consult Hematology
	≥ 40	40mg SUBQ Q24H	
Special Population:	< 18.5 (or weight < 50kg)	**Heparin** 2500 SUBQ Q8H	Consult Hematology

*Contraindications: Platelets < 25 K/uL or Fibrinogen < 50 mg/dL or active bleeding

Therapeutic anticoagulation

Therapeutic anticoagulation will be considered for COVID-19 patients who are considered high risk or diagnosed with an acute VTE.

High risk COVID-19 patient (any one of the following criteria):

1. Receiving mechanical ventilation AND D-dimer ≥ 6 mg/L
2. Acute kidney injury (Scr increase 0.3 mg/dL above baseline) **+/-** CVVHD/AVVHD/SLED or IHD with clotting

Anti-Xa level goals for enoxaparin therapy (when indicated):

1. Therapeutic peak LMWH level (Drawn 4 hours after 3rd dose): 0.6-1 anti-Xa units/mL
2. Therapeutic trough LMWH level (Drawn 1 hour prior to 3rd dose): < 0.5 anti-Xa units/mL

Kidney Function	**BMI** (kg/m^2)	**Dosing of Enoxaparin**	**Concern for HIT or LMWH Failure**
CrCL ≥ 30 mL/min	12-49.9	1mg/kg SUBQ Q12H	Bivalirudin infusion (see Anticoagulation COVID-19 guidelines for dosing)
	≥ 50	0.8 mg/kg SUBQ Q12H **monitor peak anti-Xa level with 3rd dose • Consult pharmacist to assist with obtaining anti-Xa level and dose adjustment	
CrCL < 30mL/min	12-49.9	1mg/kg SUBQ 24H	Bivalirudin infusion (see Anticoagulation COVID-19 guidelines for dosing)
	≥ 50	0.8mg/kg SUBQ Q24H **monitor peak anti-Xa level with 3rd dose • Consult pharmacist to assist with obtaining anti-Xa level and dose adjustment	
ESRD or AKI on RRT		0.8 mg/kg SUBQ Q24H (MAX dose 1mg/kg Q24H) **monitor peak and trough anti-Xa level with 3rd dose • Consult pharmacist to assist with obtaining anti-Xa level and dose adjustment	Bivalirudin infusion (see Anticoagulation COVID-19 guidelines for dosing)
		If minor bleeding prior to obtaining steady state anti-Xa levels • Decrease dose to 0.5 mg/kg and monitor anti-Xa peak and trough with 1st dose of new regimen • Consult pharmacist to assist with obtaining anti-Xa levels and dose adjustment	

*Contraindications: Platelets < 50 K/uL or fibrinogen < 100 mg/dL or active bleeding

Intra-dialytic anticoagulation for renal replacement therapy

Nephrology service will determine the need for a booster dose of IV enoxaparin when ordering renal replacement therapy

- Renal replacement therapy (iHD/SLED/CRRT)
    - Enoxaparin 30 mg IV x 1 preferably prior to or within an hour of starting dialysis
    - If HIT positive or enoxaparin failure, recommend switching to bivalirudin

Bivalirudin: Therapeutic anticoagulation

Due to the liver injury that may be seen in patients with COVID-19, bivalirudin is the preferred direct thrombin inhibitor for the treatment of HIT, enoxaparin failure, or patients receiving extracorporeal membrane oxygenation (ECMO).

CrCl (ml/min)	Bivalirudin Initial dose (mg/kg/hour)
60	0.15 +/- 0.1
30-60	0.08 +/- 0.04
< 30	0.05 +/- 0.02
IHD (25% clearance by HD filters) or CRRT	0.07 +/- 0.03

IHD - intermittent hemodialysis, CRRT – continuous renal replacement therapy

Dose adjustments:

aPTT (seconds)	Dose adjustment	Monitoring recommendations
<50	Increase infusion rate by 20%	Re-check aPTT 4 hours after rate change
50-80	No change	Re-check aPTT at 4 hours; if 2 consecutive aPTTs are at goal, check aPTT q 24 hours
>80*	Decrease infusion rate by 20%	Re-check aPTT 4 hours after rate change

* If aPTT >3x baseline, consider holding infusion for 1 hour and re-starting at 50% lower rate

- Monitoring:
    - aPTT q 4 hours following initiation of infusion and following dosing adjustment – target aPTT 50-80
    - If 2 consecutive aPTT are at goal, check aPTT q 24 hours
    - CBC as appropriate based upon clinical status of patient

Bivalirudin: anticoagulation for renal replacement therapy

- CVVH: no loading dose, bivalirudin 2 mg/hour one hour prior to RRT until completion
    - If doses of 2 mg/hour are ineffective, increase bivalirudin dose by 20%

Discontinuation of Therapeutic Anticoagulation

- Patients who are transferred to a general medical floor should be transitioned from therapeutic enoxaparin to a prophylactic enoxaparin
    - Prior to discharge:
        - Patients with normal renal function should receive apixaban 2.5 mg bid x 4-6 weeks
        - Patients with AKI or ESRD should receive apixaban 2.5 mg bid x 2 weeks
            - In patients who do not have insurance coverage for a DOAC or in whom a DOAC may be contraindicated, prophylactic doses of enoxaparin may be used for the time frames listed above
            - Warfarin may be considered in patients who have confirmed HIT

References

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