MedStar Health

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COVID-19

MedStar Clinical Guide for Anticoagulation
Venous Thromboembolism (VTE) Management in Non-ICU, ADULT COVID-19 Positive Patients

Current literature is evolving, and no anticoagulant therapies have conclusively demonstrated improved outcomes in Covid-19 patients. For an up-to-date literature evaluation of therapies, click here. Clinical decisions should be made on a case by case basis.

A. **SUMMARY OF GUIDANCE** – the quick guides below offer a summary of major recommendations; detailed information can be found in the Tables 2 and 3 below.

Acute care COVID-19 patients (non-ICU, adult)

VTE	Clotting Risk*	Bleed Risk	Treatment / Prophylaxis Intensity
Suspected or Proven	High	Low	Therapeutic
		High	Therapeutic (UFH preferred)
Not Suspected or Proven	Average	Low	Standard Prophylaxis
		High	Consider standard prophylaxis
	Moderate	Low	Intermediate prophylaxis or standard prophylaxis
		High	Standard prophylaxis
	High	Low	Intermediate prophylaxis
		High	Intermediate prophylaxis or standard prophylaxis

***High risk =** known indication for anticoagulation, newly diagnosed VTE, high clinical suspicion for VTE; **Moderate risk** = hypercoagulable risk (clinical or lab -e.g. TEG, prior provoked clot or elevated VTE risk score), moderate clinical suspicion for VTE (unproven), presence of malignancy, clotting of central line, D-Dimer elevation and hypoxemia out of proportion to clinical pneumonia; **Average risk** = no known or suspected VTE.

Clinical Consideration	Standard	Intermediate	Therapeutic
CrCl ≥ 30	Enoxaparin 40 mg Q24h	Enoxaparin 1 mg/kg Q24h	Enoxaparin 1 mg/kg Q12h
CrCl 15-29	Enoxaparin 30 mg Q24h	UFH 7500 units Q8h	Enoxaparin 1 mg/kg Q24h
CrCl < 15 or HD or RRT	UFH 5000 units q12h or q8h	UFH 7500 units Q8h	UFH infusion [goal anti-Xa 0.3-0.7]
History or new diagnosis HIT	Fondaparinux 2.5 mg Q24h (for CrCl ≥ 30)	Consider Heme consult	Argatroban infusion [goal aPTT 50-80]

Discharging COVID-19 patients (adult)

Indication	Clotting Risk*	Bleed Risk+	Treatment / Prophylaxis Intensity
Proven VTE	High	Low	Therapeutic
		High	Therapeutic
Suspected VTE	High	Low	Therapeutic
		High	Therapeutic or extended VTE prophylaxis
Not Suspected or Proven VTE	Low	Low or High	None
	High	Low	Extended VTE prophylaxis
	High	High	None or extended VTE prophylaxis
Preexisting indication for therapeutic anticoagulation	High	Low or High	Follow usual anticoagulation guidelines per indication

* Assess clotting risk: elevated IMPROVE or IMPROVEDD risk score, moderate risk assigned in acute care setting (receiving intermediate-intensity VTE prophylaxis), reduced mobility, presence of active malignancy, history of remote or unprovoked VTE

+ Assess bleeding risk: low platelets or fibrinogen, HAS-BLED score, fall risk, liver dysfunction, concomitant medication use

Clinical Consideration	Therapeutic (preferred)	Therapeutic (alternate)	Extended VTE PPX (preferred)	Extended VTE PPX (alternate)
CrCl ≥ 30	Enoxaparin 1 mg/kg Q12h	Rivaroxaban or apixaban	Enoxaparin 40mgQ24h or 0.5 mg/kg (BMI>40) for 6-14 days	Betrixaban or rivaroxaban
CrCl 15-29	Enoxaparin 1 mg/kg Q24h	Apixaban or rivaroxaban or warfarin	Betrixaban	Apixaban or rivaroxaban or ASA
CrCl < 15 or HD	Warfarin	Apixaban (HD) or aspirin	Not defined, consider heme consult	Apixaban (HD) or ASA
History or new diagnosis HIT	Fondaparinux or DOAC (if covered by insurance)	Rivaroxaban or apixaban	Fondaparinux (if covered by insurance)	Betrixaban or rivaroxaban or apixaban

B. BACKGROUND and GUIDANCE STATEMENTS

COVID-19 inpatients demonstrate hypercoagulable profile: ↑ D-dimer, ↑ fibrinogen, relatively preserved PT/aPTT, and normal platelets.

Recent data suggest 31% rate of thromboembolic events (majority PEs) in ICU patients with COVID-19 despite use of prophylactic LMWH.

A retrospective study of pharmacologic prophylaxis suggested a mortality benefit in COVID-19 inpatients with elevated sepsis-induced coagulopathy score.

Therefore, ***we recommend pharmacologic prophylaxis or therapeutic anticoagulation (AC) for all non-bleeding inpatients with COVID-19.***

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Note: Avoid full therapeutic anticoagulation when platelets under 50K (except in treating HIT) and prophylactic anticoagulation regimens in setting of platelets < 25K or fibrinogen < 50

We advise choosing a therapeutic or high-risk regimen (if not contraindicated) if patient was previously on full dose AC for a standard indication.

For inpatients, choose Intermediate/moderate risk dose regimen (if not contraindicated) if patient was on low dose DOAC for secondary VTE as outpatient. Choose Therapeutic High dose regimen (if not contraindicated) if patient was on full dose DOAC for Primary or secondary VTE/CVA prophylaxis as outpatient.

Preference is for LMWH regimens if not otherwise contraindicated. Several randomized trials in the past compared subcutaneous LMWH and UFH for the initial treatment of VTE, the LMWH was at least as effective and safe as the UFH. Meta-analyses of data from these trials suggest that LMWHs are more effective than UFH in preventing recurrence (risk reduction, 34 to 61 percent) and cause less major bleeding (risk reduction, 35 to 68 percent). There is preference for using heparins in COVID based on the observation that COVID is a highly inflammatory state and the potential anti-inflammatory properties of LMWH and UFH.

There is no indication for using TPA in COVID patients outside of standard indications.

There is no evidence to use Thromboelastography (TEG) to guide AC decisions.

A D-Dimer <1 does rule out acute VTE but D-Dimer > 1 is NOT diagnostic of VTE.

USE SCDs for all high-risk patients and if all pharmacological VTE prophylaxis options are contraindicated.

If there is evidence of acquired ATIII deficiency while on heparin continuous infusion for ECMO, would advise using argatroban continuous infusion adjusting for liver function.

COVID patients should undergo evaluation for extended VTE prophylaxis at time of discharge, taking into consideration bleeding risks.

If a patient is started on high risk or therapeutic AC while inpatient for diagnosed or suspected VTE, duration of anticoagulation should extend at least 3 months total, and at least 1-month s/p discharge. Bleeding risk should also be considered.

C. Detailed Anticoagulant Guidance for Covid-19 Patients in the Acute Care Setting (non-ICU, adult)

Table 2.1: VTE Treatment Dosing Guidance for use in patients with confirmed or suspected VTE*

High Risk: Confirmed or Suspected VTE:
- Known indication for anticoagulation
- Newly Diagnosed VTE
- High Clinical Suspicion for VTE (Wells Criteria DVT, Wells Criteria PE)

Renal Function	Body Weight 40-150 kg	Body weight >150 kg	Suspected or Confirmed HIT
CrCl ≥ 30 mL/min	Enoxaparin 1 mg/kg SubQ Q12h Or Unfractionated heparin (UFH) infusion with anti-Xa goal 0.3 to 0.7 *[Preferred in high risk of bleeding]*	UFH continuous infusion goal anti-Xa 0.3-0.7	Argatroban continuous infusion** to PTT goal 50-80 Or Fondaparinux weight-based*** SubQ Q24h if low bleeding risk and clinically stable
CrCl 15-29 mL/ min but not on dialysis	Enoxaparin 1 mg/kg SubQ Q24h Or Unfractionated heparin (UFH) infusion with anti-Xa goal 0.3 to 0.7 *[Preferred in high risk of bleeding]*		
CrCl < 15 or on dialysis or high risk of bleeding	UFH continuous infusion goal anti-Xa 0.3-0.7		

*Avoid full therapeutic anticoagulation when platelets under 50K
**See local site argatroban protocol
*** Fondaparinux 5 mg SubQ Q24h if weight < 50 kg; 7.5 mg SubQ Q24h if weight 50-100 kg; 10 mg SubQ Q24h if weight over 100 kg

Table 2.2: Intermediate Intensity VTE Prophylaxis Dosing Guidance for use in patients at MODERATE risk for VTE*

Moderate Risk:

- Hypercoagulable risk (clinical or lab - e.g. TEG, prior provoked clot, elevated risk scores such as IMPROVE/IMPROVEDD/PADUA/CAPRINI scores)
- Moderate clinical suspicion for VTE (unproven)
- Presence of malignancy
- Clotting of central line
- D-Dimer elevation and hypoxemia out of proportion to clinical pneumonia

Renal Function	Body Weight (40-49 kg)	Body Weight ≥50 kg	Remote HIT
CrCl ≥ 30 mL/min	Enoxaparin 1 mg/kg SubQ Q24h (preferred) Or Enoxaparin 0.5 mg/kg SubQ Q12h Or UFH infusion with anti-Xa goal 0.1-0.3 [for high risk of bleeding]	Enoxaparin 1 mg/kg SubQ Q24h (preferred) Or Enoxaparin 0.5 mg/kg SubQ Q12h Or UFH infusion with anti-Xa goal 0.1-0.3 [for high risk of bleeding]	Fondaparinux 5 mg SubQ Q24h or consider hematology consult [for DOAC]
CrCl 15-29 mL/ min	UFH 5,000 units SubQ q8h Or UFH infusion with anti-Xa goal 0.1-0.3 [for high risk of bleeding]	UFH 7,500 units SubQ q8h Or UFH infusion with anti-Xa goal 0.1-0.3 [for high risk of bleeding]	SCDs and/or DOAC, consider hematology consult [for apixaban or rivaroxaban+ dosing]
CrCl < 15 mL/min or on dialysis			SCDs and ASA 81 mg po Q24h if not contraindicated [inferior option], consider hematology consult

*Avoid prophylactic anticoagulation regimens in setting of platelets < 25K or fibrinogen < 50

+ limited data available to support use of rivaroxaban in patients with an estimated CrCl 15-29 mL/min. Monitor closely for signs or symptoms of bleeding.

Table 2.3: Standard VTE Prophylaxis Dosing Guidance for use in patients at AVERAGE risk of VTE*				
Average Risk: • No known or suspected VTE				
Renal Function	**Body Weight (40-49 kg)**	**BMI <40 kg/m2 and Body Weight 50-149 kg**	**BMI >40 kg/m2 (for enoxaparin) or Body weight ≥150 kg (for UFH)**	**Remote HIT**
CrCl ≥ 30 mL/min	UFH 5,000 units SubQ Q12h	Enoxaparin 40 mg SubQ Q24h	Enoxaparin 40 mg SubQ Q12h (BMI> 40kg/m^2)	Fondaparinux 2.5 mg SubQ Q24h
CrCl 15-29 mL/min but not on dialysis	UFH 5,000 units SubQ Q12h	Enoxaparin 30 mg SubQ Q24h	UFH 7,500 units SubQ Q8h (Wt ≥ 150 kg)	SCDs and/or Apixaban 2.5 mg po Q12h, consider Hematology consult
CrCl < 15 or on Dialysis	UFH 5,000 units SubQ Q12h	UFH 5,000 units SubQ Q8h	UFH 7,500 units SubQ Q8h (Wt ≥ 150 kg)	SCDs and ASA 81 mg po Q24h if not contraindicated [inferior option], consider hematology consult

D. Detailed Anticoagulant Guidance for Covid-19 Patients at Discharge or Outpatient

1. Patient with new or recurrent confirmed VTE – see table 3.1 below
2. Patients with suspected VTE – see table 3.1 below, or if high risk of bleeding consider extended VTE prophylaxis dosing (table 3.2)
3. Patient with preexisting indication for therapeutic anticoagulation –follow usual anticoagulation guidelines per indication

Table 3.1: Post-Discharge Pharmacological Anticoagulation Treatment Regimens for Use in COVID-19 Patients with Confirmed or Suspected VTE		
Renal function	**Preferred VTE Treatment Regimen**	**Alternative VTE Treatment Regimen**
CrCl ≥ 30	Enoxaparin 1 mg/kg SubQ Q12h (rounded up to nearest syringe – max dose 150 mg)	Rivaroxaban initial 15 mg po Q12h X 21 days followed by maintenance 20 mg po Q24h *[subtract the number of days of full dose anticoagulation from 21 days]* Or Apixaban initial 10mg po Q12h X 7 days followed by maintenance 5 mg po Q12h *[start with 5 mg po Q12h if patient has received 7 days of full dose enoxaparin or UFH]* Or Warfarin [titrate to goal INR of 2-3] with minimum 5 days overlap with enoxaparin or UFH **Remote history of HIT:** Fondaparinux weight-based*** SubQ Q24h or DOAC (see above)
CrCl 15-29	Enoxaparin 1 mg/kg SubQ Q24h (rounded up to nearest syringe – max dose 150 mg)	Apixaban 10mg po Q12h X 7 days (if not previously loaded) then 5 mg po Q12h *[start with 5 mg po Q12h if patient has received 7 days of full dose enoxaparin or UFH]* Or Warfarin [titrate to goal INR of 2-3] with minimum 5 days overlap with enoxaparin or UFH Or Rivaroxaban initial 15 mg po Q12h X 21 days followed by maintenance 20 mg po Q24h *[subtract the number of days of full dose anticoagulation from 21 days]*

CrCl < 15 or on dialysis	Warfarin [INR goal of 2-3] should be at goal after minimum 5 days overlap with UFH PRIOR to DISCHARGE	**New VTE in ESRD patient on hemodialysis:** Apixaban initial 10mg po Q12h X 7 days followed by maintenance 5 mg po Q12h *[start with 5 mg po Q12h if patient has received 7 days of full dose UFH]* **New VTE in ESRD patient NOT on hemodialysis:** Advise hematology consult **Warfarin not feasible, consider:** Apixaban initial 10mg po Q12h X 7 days followed by maintenance 5 mg po Q12h *[after patient has received 7 days of full dose UFH as inpatient]* ***Inferior Option:*** ASA 81 mg po Q24h if not contraindicated

*** Fondaparinux 5 mg SubQ Q24h if weight < 50 kg; 7.5 mg Q24h if weight 50-100 kg; 10 mg SubQ Q24h if weight over 100 kg

4. In absence of confirmed VTE, decision to treat post-discharge is based on individual risk of bleeding versus clotting. Consider using the IMPROVE and IMPROVEDD risks scores as recommended by the ACC to help guide the evaluation of patients for post-discharge VTE prophylaxis. If it is determined that a COVID-19 patient needs extended VTE prophylaxis at the time of discharge, one of the following regimens in table 3.2 are recommended for 28-45 days. Assessment of risk of bleeding and clotting should include, but not be limited to, the following:
    a. Assess clotting risk: elevated IMPROVE or IMPROVEDD risk score, moderate risk assigned in acute care setting (receiving intermediate-intensity VTE prophylaxis), reduced mobility, presence of active malignancy, history of remote or unprovoked VTE (see moderate risk above – table 2.2)
    b. Assess bleeding risk: low platelets or fibrinogen, HAS-BLED score, fall risk, liver dysfunction, concomitant medication use

Table 3.2: Pharmacological Anticoagulation Regimens for Primary VTE Prophylaxis Post-Discharge or Outpatients at Low Risk for Bleeding for 28-45 days		
Renal function	**Preferred VTE Prophylactic Regimen^**	**Alternative VTE Prophylactic Regimen^**
CrCl ≥ 30	**Normal BMI ≤ 40:** Enoxaparin 40 mg SubQ Q24h for up to 28 days post-discharge Or **BMI > 40:** Enoxaparin 0.5 mg/kg SubQ Q24h (rounded up to nearest syringe – max weight 150kg) for up to 28 days post-discharge	Betrixaban 160 mg X1 day then 80 mg po Q24h for 35-42 days [including anticoagulant during hospital stay] Or Rivaroxaban 10 mg po Q24h for 31-39 days [including hospital stay] Or ***Off label:*** Apixaban 2.5 mg po Q12H for up to 45 days [including hospital stay] Or ***Inferior option:*** *ASA 81 mg po daily*
CrCl 15-29	Betrixaban 80 mg po x1 day then 40mg po Q24h for 35-42 days [including anticoagulant during hospital stay]	***Off label if low bleeding risk and intermediate/high VTE risk:*** Apixaban 2.5 mg po Q12h for up to 45 days [including hospital stay] Or Rivaroxaban 10 mg po Q24h for 31-39 days [including hospital stay]+ Or ***Inferior option:*** *ASA 81 mg po daily*
CrCl < 15 or on dialysis	**Not defined,** consider hematology consult	***Off label ONLY if deemed low risk bleeding and high risk for VTE, and:*** • ***On hemodialysis:*** Apixaban 2.5 mg po Q12H for up to 45 days [including hospital stay] • ***NOT on hemodialysis:*** consider hematology consult Or ***Inferior option:*** ASA 81 mg po daily

History of Remote HIT	**CrCL ≥ 30:** Fondaparinux 2.5 mg SubQ Q24h for up to 45 days [including hospital stay] O*r* *Consider a DOAC based on insurance coverage*	**CrCl ≥ 30:** Betrixaban 160 mg po x1 day then 80 mg po Q24h for 35-42 days [including anticoagulant during hospital stay] Rivaroxaban 10 mg po Q24h for 31-39 days [including hospital stay] (*off label:* Apixaban 2.5 mg po Q12h for up to 45 days [including hospital stay] **CrCl 15-29:** Betrixaban 80 mg po x1 on D1 then 40mg po Q24h for 35-42 days [including anticoagulant during hospital stay] Or Rivaroxaban 10 mg po Q24h for 31-39 days [including hospital stay] **CrCl < 15 or patient on dialysis:** ASA 81 mg po daily Or ***Off label CrCL < 30:*** Apixaban 2.5 mg po Q12h for up to 45 days [including hospital stay] for patients at low bleeding risk

+ limited data available to support use of rivaroxaban in patients with an estimated CrCl 15-29 mL/min. Monitor closely for signs or symptoms of bleeding.

^ duration of prophylaxis has not elucidated in COVID-19 disease

E. References

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