This document was also approved by CCOC.

I. Background and Aim:

This document will serve as an interim clinical practice guideline for the prophylaxis and treatment of venous thromboembolism (VTE) with anticoagulant medications in the adult intensive care unit (ICU), acute care areas (including the DCU field hospital) and subacute care areas (including Beaumont). During the COVID-19 pandemic, personal protective equipment (PPE) and medications commonly utilized for VTE prophylaxis or VTE treatment may not always be readily available. This document is subject to change with the ever-changing pandemic situation.

This document is intended to:

- provide a resource for VTE prophylaxis and anticoagulation treatment medications available
- provide practical recommendations for use of anticoagulants in COVID patients to decrease staff exposure and use of PPE through clustered care and decreasing frequency of drug administrations

II. Considerations for use of therapeutic anticoagulation in COVID:

In patients who are critically ill from suspected or confirmed COVID infection, therapeutic anticoagulation should be reserved ONLY for those patients with indications warranting anticoagulation treatment (e.g. DVT/PE, atrial fibrillation (AF), prosthetic heart valves, etc). While there is emerging evidence to suggest there may be additional thromboembolic risk that could warrant therapeutic anticoagulation in patients with confirmed COVID, this should still be assessed on a case by case basis. COVID positive patients have been observed to develop elevated D-Dimer levels and increased fibrinogen, but these lab values alone are not an indication to escalate to therapeutic anticoagulation therapy.

a. Patients on anticoagulation therapy at baseline:
   - Patients admitted to UMMMHC on anticoagulation therapy at baseline (e.g. AF, mechanical valves, VTE history, etc) with suspected or confirmed COVID should continue on their anticoagulation therapy unless new contraindication exists.
   - If patient on oral anticoagulation therapy and started on COVID therapy that interacts with DOAC (tociluzumab and sarilumab may decrease serum concentration of rivaroxaban and apixaban), the patient should be switched to alternative anticoagulation therapy with low molecular weight heparin (LMWH) preferentially over unfractionated heparin (UFH). If patient on warfarin at baseline and enrolled in convalescent plasma study please see study recommendations to determine if warfarin reversal is warranted.
   - If patient on oral anticoagulation therapy with DOAC and develops acute renal dysfunction, the patient should be switched to alternative anticoagulation therapy with UFH.

b. Patients on Continuous Renal Replacement Therapy (CRRT) during COVID: Most patients requiring CRRT do not require anticoagulation as standard therapy. Due to the premature and more frequent filter clotting observed in COVID positive patients and a shortage of the necessary disposables to run the Nxstage CVVH machines as a result of the COVID pandemic, empiric anticoagulation will be utilized in all

COVID patients unless contraindicated. Please see the interim guidance document for managing anticoagulation in CRRT during COVID for reference.

III. Therapeutic anticoagulation therapies for acute VTE:

1. Low molecular weight heparin (enoxaparin) therapy is first line therapy unless patient anuric, requiring CVVH/CRRT/HD (see alternative therapy UFH). LMWH preferred to minimize need for frequent labs and patient exposure in setting of COVID.
    a. CrCl ≥ 30 mL/min: 1 mg/kg SC q12h
    b. CrCl < 30 mL/min: 1 mg/kg SC daily

2. Unfractionated Heparin therapy reserved for patients with high risk of bleeding*, frequent procedures, or severe renal dysfunction (anuric/requiring CRRT: CVVH/AVVH/HD).
    a. See Unfractionated heparin orders for Atrial Fibrillation/Acute Coronary Syndrome and VTE within EMR.
    b. Some critically ill COVID patients have been observed to develop elevated aPTTs. If COVID patients have difficulty maintaining stable aPTT via heparin protocol, please contact Anticoagulation Consult Service (pg 4488) for assessment of patient and assistance with alternative Anti-Xa heparin protocol.

3. Alternative therapy requests for argatroban, fondaparinux, etc in suspected HIT(T) or in patients difficult to manage on UFH should be escalated to the Anticoagulation Consult Service (pg 4488).

4. Oral anticoagulation therapy with DOAC or warfarin with LMWH or UFH bridging is preferred once patient stable enough for oral therapy with appropriate renal and hepatic function and/or pending hospital discharge.
    a. See Oral Anticoagulation ordersets for Atrial Fibrillation and Venous Thromboembolism in EMR for dosing recommendations and algorithm.

Patients with Disseminated Intravascular Coagulation (DIC) in setting of COVID:

- Follow standard ICU protocol for blood product resuscitation. For complex presentations of DIC in the setting of COVID needing additional assistance for management, contact the hematology service for further treatment recommendations.

IV. Considerations for use of thrombolytic agents in setting of COVID:

Patients with COVID may present with elevated D-Dimer and fibrinogen levels and low anti-thrombin levels in the setting of ARDS leading us to suspect they be in a prothrombotic DIC state. Similarly as noted above in regards to anticoagulation in COVID patients, there is limited evidence to suggest the clear-cut indication for fibrinolytic/thrombolytic therapies in these patients with only a few case reports globally to support use. We currently do not recommend use of thrombolytic agents at baseline for these COVID patients who may present in DIC, but suggest further clinical discussion may be warranted for potential systemic thrombolytic use with alteplase if all other investigational therapies and supportive care have been exhausted.

V. **Considerations for use of VTE prophylaxis during COVID:**

All hospitalized patients with suspected or confirmed COVID-19 should receive VTE chemoprophylaxis unless they have a contraindication to treatment (active bleeding, thrombocytopenia: plts <25).

If chemoprophylaxis contraindicated, mechanical prophylaxis with SCD boots strongly recommended unless contraindicated.

VI. **VTE prophylaxis agent of choice and dosing:**

1. **Enoxaparin preferred as first line therapy for VTE prophylaxis in order to**:
   - decrease administration times in setting of COVID
   - reduce risk of heparin induced thrombocytopenia

   a. Calculate Creatinine Clearance with Cockcroft Gault Equation and actual body weight
   i. **Standard prophylaxis dosing with CrCl ≥ 30 mL/min**: enoxaparin 40 mg SC daily
   ii. **Standard prophylaxis dosing with obesity with CrCl ≥ 30 mL/min**:
      - BMI ≥40 kg/m^2: Enoxaparin 40 mg SC q12h

   iii. **Standard prophylaxis dosing in trauma patients and CrCl ≥ 30 mL/min**:
      - Enoxaparin 30 mg SC q12h
      - BMI ≥40 kg/m^2 or weight ≥ 100 kg: Enoxaparin 40 mg SC q12h

   iv. **Standard prophylaxis dosing with low body weight with CrCl ≥ 30 mL/min**:
      - Weight < 50 kg: Enoxaparin 0.5 mg/kg SC daily

   v. **Standard prophylaxis dosing with stable or improving renal dysfunction with CrCl 20-29 mL/min**:
      - Enoxaparin 30 mg SC daily

   b. If enoxaparin contraindicated due to renal failure with CrCl < 20 mL/min, new oliguria or anuria, or on CVVH/CRRT/AVVH/HD) unfractionated heparin (UFH) may be utilized as an alternative agent.

   c. **Standard prophylaxis dosing in critically ill COVID + and CrCl ≥ 30 mL/min:**
      - Weight ≥ 50 kg: increase chemoprophylactic dosing to enoxaparin 40 mg SC q12h
      - Weight < 50kg: increase chemoprophylactic dosing to enoxaparin 0.5 mg/kg SC q12h

2. **Unfractionated heparin preferred for patients with high bleeding risk*, significant renal dysfunction, or on CVVH/CRRT/AVVH/HD**.

   i. Standard prophylaxis dosing in patients with suspected or confirmed COVID with critical illness (requiring ICU care): heparin frequency of TID should be utilized
      1. Standard dosing: 7500 units SC

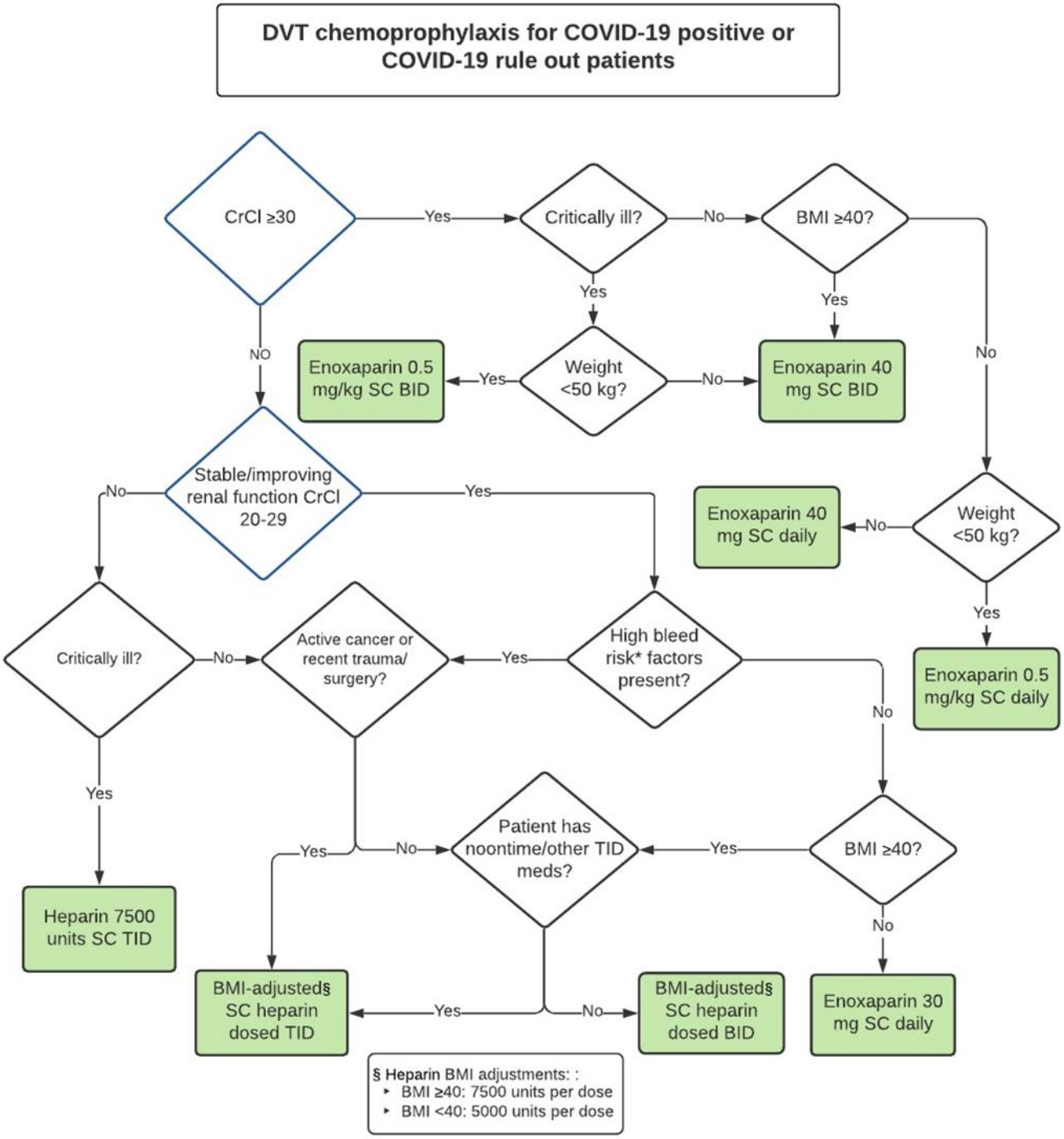
ii. **Standard prophylaxis dosing in COVID patients <u>without</u> critical illness with recent trauma, recent surgery, and/or active cancer, or on CVVH/CRRT/AVVH/HD: heparin frequency of TID should be utilized**
    1. Standard dosing: 5000 units SC
    2. Obesity dosing (BMI ≥40 kg/m^2): 7500 units SC

iii. **Standard prophylaxis dosing with suspected or confirmed COVID: heparin frequency of BID should be utilized for non-critically ill patients unless patient has other meds with ≥TID frequency (to minimize administration times in setting of COVID)**
    1. Standard dosing: 5000 units SC
    2. Obesity dosing (BMI ≥40 kg/m^2): 7500 units SC

VII. For all patients on anticoagulation or VTE prophylaxis with epidural anesthesia in place or to be placed, please reference Anesthesia Policy A3014: Guidelines for Regional Anesthesia in Anticoagulated Patients for medication restrictions and preferred best practice for administration.

VIII. VTE prophylaxis upon discharge: Typically VTE chemoprophylaxis is not recommended upon discharge, but in the setting of COVID, we recommend evaluation for need for post discharge prophylaxis on a case by case basis.

**high bleeding risk defined as thrombocytopenia (plts <25), severe anemia, prior GI bleed or life-threatening bleeding, arteriovenous malformation*



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