Anticoagulation in ADULT Patients with COVID-19 at MultiCare Health System

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Publications related to anticoagulant thromboprophylaxis and VTE treatment in the context of the COVID-19 continue to evolve. Given their observational nature and varying degrees of peer review, the evidence to date must be interpreted in relation to established VTE treatment and prophylaxis principles in hospitalized patients.

Background

Severe COVID-19 disease is associated with features of DIC and coagulopathy characterized by elevated D-dimer levels, increased fibrinogen levels, minimal prolongation of aPTT and/or PT, and minimal impact on platelet counts.[1,2] The hypercoagulable state can manifest as macrovascular and/or microvascular thrombosis, with VTE rates as high as 30% observed in critically ill patients with COVID-19, even in the presence of prophylaxis.[2,3,4] The rate of VTE in non-ICU patients appears to be increased to a lesser extent.[4,5]

Anticoagulation with confirmed VTE (or pre-existing indication for anticoagulation)

Treatment dose low molecular weight heparin (LMWH) is preferred to unfractionated heparin (UFH) to minimize staff exposure.[5,6] LMWH and UFH are preferred instead of direct oral anticoagulants (DOACs) and warfarin due to illness-related hepatic dysfunction, reduced appetite/poor oral intake which may affect absorption or affect response to warfarin, and the possibility of rapid deterioration.

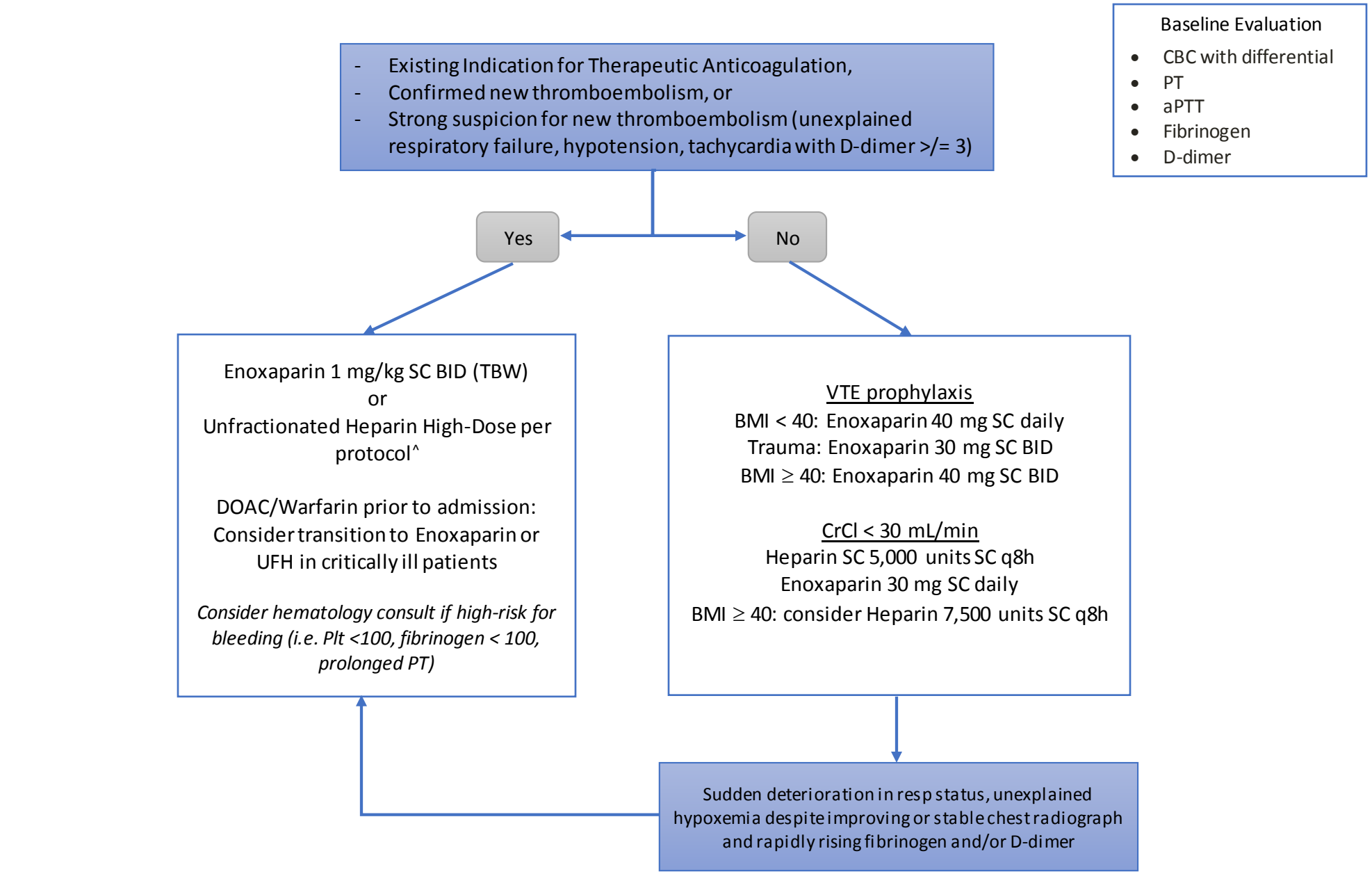
Anticoagulant use in the absence of confirmed VTE

Empiric therapeutic anticoagulation for patients who do not have confirmed VTE remains controversial. The current data are insufficient to clearly recommend for or against the use of therapeutic anticoagulation in COVID-19 patients in the absence of confirmed or suspected thrombosis.

All identified studies of VTE rates and non-conventional anticoagulant strategies in patients with COVID-19 are observational and conflicting.[7] For example, data derived from a US cohort of 786 hospitalized patients with COVID19 suggested a possible mortality benefit of therapeutic dose anticoagulation, whereas more recent observational data from 374 patients in CT revealed a significant increase in mortality associated with a preemptive therapeutic anticoagulation approach regardless of severity of illness.[8,9]

Several organizations have published interim guidance for the management of COVID-19-associated coagulopathy. The Anticoagulation Forum recommendations published May 21st suggest increased dose VTE prophylaxis for critically ill patients with COVID-19 based on expert opinion.[10] In contrast, several organizations including NIH, WHO, The International Society for Thrombosis and Haemostasis, and CHEST have recommended VTE prophylaxis according to the usual standard of care in all hospitalized adults with COVID-19 unless contraindicated.[11-16] They also do not recommend the using inflammatory markers or coagulation abnormalities alone to guide anticoagulation therapy decisions. Although a relationship between markedly elevated D-dimer levels and mortality has been shown, whether this can be applied to predicting or managing VTE risk is not currently known.[11-16,17]

VTE prophylaxis after hospital discharge (see page 3)



For confirmed or suspected Heparin Induced Thrombocytopenia, use fondaparinux (Arixtra) for VTE prophylaxis or argatroban for confirmed/suspected VTE
^the aPTT may be unreliable in those who have either a prolonged aPTT at baseline or evidence of heparin resistance and anti-factor Xa activity should be monitored to guide dosing

Post-Discharge VTE Prophylaxis in COVID-19 Patients

- In those with high risk for VTE following discharge, extended post-hospital VTE prophylaxis can be considered. Experience from the MAGELLAN, APEX and MARINER studies suggest that in select patients without COVID-19, post-discharge prophylaxis may be beneficial.
- Decision must be made on a case-by-case basis and should weigh the severity of illness during hospitalization and upon discharge, comorbidities, and bleeding risk. Consider evaluating the post-discharge VTE risk and bleeding risk using the IMPROVEDD-VTE and HAS-BLED scores below.
- Options include: apixaban 2.5 mg BID, rivaroxaban 10 mg daily, or enoxaparin 40 mg SQ daily
- Optimal duration is unclear, with current recommendations ranging from 14 up to 45 days based on risk of VTE
    - **VTE risk: Consider post-discharge anticoagulation in those with an IMPROVEDD VTE score ≥ 3**

IMPROVEDD Variable	Score
Previous VTE	3
Known Thrombophilia	2
Current lower limb paralysis or paresis	2
Current malignancy	2
D-dimer ≥ 2x Upper Limit of Normal (ULN)	2
Immobilization for at least 7 days	1
ICU or CCU admission	1
Age more than 60 years	1

Score	Predicted VTE risk	Score	Predicted VTE risk
0	0.4%	3	1.2%
1	0.6%	4	1.6%
2	0.8%	5-10	2.2%

    - **Bleeding risk: HAS-BLED score**
        - **Score = 2: give post-discharge anticoagulation only if risk of VTE risk is felt to outweigh bleeding risk**
        - **Score ≥ 3: post-discharge anticoagulation not recommended**

HAS-BLED Variable	Points
Hypertension	1
Renal disease (dialysis, transplant, SCr >2.26 mg/dL)	1
Liver disease (cirrhosis or bilirubin >2x ULN with AST/ALT/AP >3x ULN)	1
Stroke history	1
Prior major bleeding or predisposition to bleeding	1
Labile INR (unstable/high INRs, time in therapeutic range <60%)	1
Elderly (age >65)	1
Medication usage predisposing to bleeding (aspirin, clopidogrel, NSAIDs)	1
Alcohol usage (≥8 drinks/week)	1

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