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Anti-Coagulation Recommendations from the Department of Hematology & Oncology for Hospitalized Patients with COVID-19 at Ventura County Medical Center

Hematology guideline for COVID-19 has been prepared by VCMC hematology/oncology department. Due to the emerging and often conflicting data regarding COVID-19, this document is meant to guide clinicians. This guideline should be adapted to each specific patient based on the treating medical professional's independent professional judgment and consideration of the patient's needs, and any other unique circumstances.

During the early stages of the pandemic, VTE risk was in the range where experts suggested more aggressive thromboprophylaxis dosing of anticoagulants for VTE prevention. Since early pandemic, there has been newer data published with changes in recommendation as summarized below:

Inpatient VTE Prophylaxis:

- VTE Prophylaxis is appropriate in all hospitalized medical, surgical, and obstetric patients with COVID-19.
- INSPIRATION trial assigned 600 patients with COVID 19 in the ICU to receive enoxaparin at intermediate dose or standard prophylactic dose. Escalation to intermediate dosing did not improve a composite outcome of thrombosis or mortality. There was a trend towards increased bleeding in the intermediate-dose group that did not reach statistical significance.
- ACTION trial randomly assigned 615 patients hospitalized with COVID with elevated D-dimer to receive therapeutic anticoagulation or prophylactic dose anticoagulation. There was no major difference in efficacy (survival, duration of hospital stay). The risk of bleeding was higher in the therapeutic dosing group (RR 3.64)
- **Patients Admitted to ICU: Prophylactic dose anticoagulation recommended.**
- **Medical (Non-ICU): Prophylactic dose anticoagulation recommended.**
- Prophylactic dosing per pharmacy guidelines:
    - Enoxaparin 40mg daily (Crcl >30 mL/miin)
    - Enoxaparin 40mg BID for weight >120kg or BMI >35
    - Unfractionated heparin for Crcl <15 ml/min

Outpatient VTE Prophylaxis (COVID Positive):

- Post-discharge prophylactic anticoagulation not routinely recommended.
- It is reasonable to utilize the modified IMPROVE score (MARINER trial) and offer post discharge outpatient VTE prophylaxis when patients have a score of 4 or more, or score of 2 to 3 with D-dimer >2x ULN.
- VTE prophylaxis would consist of Rivaroxaban 10mg daily 31 to 39 days

The subject must be at increased risk for VTE by the total modified IMPROVE VTE Risk Score assessed at screening and verified at randomization.
a. If the total modified IMPROVE VTE Risk Score is ≥4, the subject meets this inclusion criterion.
b. If the total modified IMPROVE VTE Risk Score is 2 or 3, a D-dimer >2X ULN must have been obtained after the beginning of the index hospitalization and before randomization

Modified IMPROVE VTE Risk Score	
VTE Risk Factor	VTE Risk Score
Previous VTE	3
Known thrombophilia(a)	2
Current lower limb paralysis or paresis(b)	2
History of cancer(c)	2
ICU/CCU stay	1
Complete immobilization(d)≥1 day	1
Age ≥60 years	1

CCU= cardiac care unit; ICU= intensive care unit; VTE= venous thromboembolism.
a: A congenital or acquired condition leading to excess risk of thrombosis (eg, factor V Leiden, lupus anticoagulant, factor C or factor S deficiency).
b: Leg falls to bed by 5 seconds, but has some effort against gravity (taken from NIH stroke scale).
c: Cancer (excluding non-melanoma skin cancer) present at any time in the last 5 years (cancer must be in remission to meet eligibility criteria)
d: Immobilization is being confined to bed or chair with or without bathroom privileges.

Routine Inpatient Laboratory Testing (Daily):

- CBCD
- Coags (PT, aPTT, INR)
- Fibrinogen
- D-dimer

Distinguishing COVID Hypercoagulable State from DIC:

DIC Features:

- Bleeding in acute decompensated DIC
- Thrombosis in chronic compensated DIC
- Marked increase in D-dimer
- Mild thrombocytopenia
- Prolonged PT and aPTT

- Low fibrinogen
- Low factor VIII activity

Covid Hypercoagulable State:

- Thrombosis
- Marked increase in D-dimer
- Mild thrombocytopenia
- Normal or mildly prolonged PT and aPTT
- High fibrinogen
- High factor VIII activity (consumption of coagulation factor is not occurring)

DIC Management in COVID-19 Patients:

- Management of DIC similar to usual protocol.
- Supportive care if not bleeding
    - FFP or cryo if <150
- Platelet transfusion if below 30k
    - Consider holding anticoagulation at this point
- Give blood products if bleeding
    - FFP for bleeding with elevated PT/PTT
    - Avoid tranexemic acid due to concern for thrombosis
- Systemic Anticoagulation indicated in the following:
    - New VTE or organ failure due to clot

For Admitted Patients Already on Some Form of Anticoagulation:

- Therapeutic anticoagulation is continued as inpatient.
- For patients already on therapeutic anticoagulation and admitted for COVID infection, conversion from DOAC to LMWH/UFH is preferred due to flexibility of dosing as well as decrease in drug-drug interactions.
- For patients on “maintenance” DOAC in the form of indefinite anticoagulation for history of VTE (such as rivaroxaban 10mg daily), recommend conversion to THERAPEUTIC LMWH dosing. The rationale is that even at a lower intensity DOAC dose, the purpose of anticoagulation is still therapeutic anticoagulation. However, if a patient is on prophylactic DOAC (such as rivaroxaban 10mg in the post-surgical patient), would convert to PROPHYLACTIC LMWH dosing since the original intent is prophylaxis.
- If in doubt, consult hematology/cardiology/surgery for case specific discussion

References:

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