Hematologic Considerations for COVID-19 Patients

Disclaimer: There are no FDA-approved treatments for COVID-19, supportive care is standard of care. Limited treatment data are available & clinical judgment is warranted.

Purpose   To develop clinical guidelines for management of hematologic abnormalities for COVID-19 patients.

The Evidence
- There are case reports from the Wuhan experience suggesting there may be an increased incidence of VTE in COVID-19 patients (Xie et al, *Radiol Cardiothoracic Imaging,* 2020; Danzi et al. Eur Heart J 2020).
- One study suggests COVID-19 patients are at increased risk for thrombosis and bleeding (Xu et al, Pulmonology 2020 [preprint, under review]).
- Colleagues from Wuhan have reported finding microthrombi in pulmonary vasculature on autopsy, which theoretically could contribute to local V/Q mismatch or hydrostatic changes causing edema. (Luo et al, *Preprints*, 2020 preprint).
- Preliminary data from Wuhan suggest that prophylactic LMWH or UFH may be of benefit in those patients with severe COVID-19 and D-dimer levels > 6 times the upper limit of normal (Tang et al, JTH, Mar 27, 2020)
- In addition to prevention of thrombosis, heparin could reduce cytokine levels, thereby improving cytokine storm (Shi et al, BMJ Apr 7, 2020 **doi:** https://doi.org/10.1101/2020.03.28.20046144)
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Labs
- **D-dimer**: The diagnostic hallmark of COVID-DIC is a rapidly rising D-dimer (figure above). Patients with D-dimer >1,000 at admission are *twenty times* more likely to die than patients with lower D-dimer values (Zhou et al.).
- **Fibrinogen**: is generally *elevated*. However, in extremely severe and late-stage disease, consumption of fibrinogen may occur leading to hypofibrinogenemia (Han et al. 2020)
- **Thrombocytopenia** can occur, but this is *less* common than in other forms of DIC.
- **PTT and INR** may be somewhat elevated (but generally not dramatically so).
- **Thromboelastography (TEG)** – No published data, but anecdotally this may show a hyper coagulable pattern (usually with a *low* R-time, and often with an elevated maximal amplitude as well).

Treatment
1. Initiate prophylactic anticoagulation therapy for all COVID-19 patients unless otherwise contraindicated i.e. platelets <20,000 or bleeding and <50,000 for procedures
   - CrCl ≥ 30 ml/min
     1. BMI < 40: Enoxaparin 40 mg SQ daily
     2. BMI ≥ 40: Enoxaparin 40 mg SQ q 12 hrs
   - CrCl 15-29 ml/min
     1. BMI < 40: Enoxaparin 30 mg SQ daily
     2. BMI ≥ 40: Enoxaparin 40 mg SQ q daily
   - CrCl <15 ml/min:
     1. BMI < 40: Heparin 5000 units SQ every 8 hours
     2. BMI ≥ 40: Heparin 7500 units every 8 hours

2. If D dimer greater than 2 mcg/L FEU AND SIC* score (See Appendix 1) greater than equal to 4: use full dose anticoagulation
   - Heparin infusion for DVT/PE/AF protocol 18 units/kg/hr
   - May also use Enoxaparin 1 mg/kg SQ q 12 hrs – monitor anti-Xa levels

3. VTE Treatment – confirmed VTE or high clinical suspicion for VTE
   - Heparin infusion with DVT/PE/AF protocol 18 units/kg/hr

4. If sudden and unexplained change in O2 OR new asymmetrical upper or lower extremity edema, consider venous duplex of affected extremity

5. If patient on CRRT, use systemic anticoagulation with heparin infusion DVT/PE/AF protocol 18 units/kg/hr

   - If patient continues have clotting issues, consider using heparin plus citrate anticoagulation
   - If patient continues to have clotting issues, change heparin infusion to argatroban infusion

6. If the patient is on direct oral anticoagulants (DOACs) or Warfarin for Afib or VTE only, switch to full dose anticoagulation (LMWH or UFH, as indicated based on renal function or clinical scenario).

References:

1. Thachil J, Tang N, et al. Journal of Thrombosis and Haemostasis. ISTH interim guidance on recognition and management of coagulopathy in COVID-19, 25 March 2020.

2. Tang N, Bai H, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020 Mar 27. doi: 10.1111/jth.14817. [Epub ahead of print]

3. YNHHS initial treatment algorithm for hospitalized adults with COVID-19; https://medicine.yale.edu/intmed/COVID-19%20TREATMENT%20ADULT%20Algorithm%204.3.20_382832_5_v2.pdf

4. Brigham and Women's Hospital COVID019 Clinical Guidelines; https://covidprotocols.org/protocols/09-hematology

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Appendix 1

Sepsis-induced coagulopathy (SIC) score

Category	Parameter	0 point	1 point	2 points
Prothrombin time	PT/INR	≤ 1.2	>1.2	>1.4
Coagulation	Platelet count (x 109/L)	≥ 150	<150	<100
Total SOFA	SOFA four items	0	1	≥2

For calculation of SOFA score:
https://www.mdcalc.com/sequential-organ-failure-assessment-sofa-score

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