COVID-19, Clots and Critical Care

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Case

- 45 year old male, admitted with COVID-19 ARDS
- Intubated for hypoxic respiratory failure
- Started on remdesivir, steroids and therapeutic dose heparin
Three days into ICU stay

- Rapid hemodynamic deterioration
- Desaturation to 70% on 100% FiO2
- Unchanged ventilator pressures
Venous Thromboembolism in COVID-19

High incidence of thromboembolism:
- Venous Thromboembolism (VTE)
  - DVT
  - PE
- Arterial thrombosis

Preliminary data:
- VTE: 27-79% in various studies
- Arterial thrombosis: 3-5%

Virchow’s Triad

Endothelial Injury

Hypercoagulability

Venous Stasis
Virchow’s Triad

Endothelial Injury

Virchow’s Injury

Hypercoagulability

Venous Stasis
COVID-19 and Endothelial Injury


Virchow’s Triad

- Endothelial Injury
- Hypercoagulability
- Venous Stasis
Hypercoagulability in COVID-19

Multiple factors:

- Activation of the coagulation cascade by SARS-CoV-2
- Increased levels of von Willebrand factor
- Procoagulatory state by activation of tissue factor pathways
- Activation of the coagulation cascade by a cytokine storm
- Hypoxia induced thrombus formation
- Immune mediated damage
Hypercoagulable state

- Direct activation by SARS-CoV-2
- Increased levels of von Willebrand factor
- Tissue factor pathway activation
- Hyperviscosity
- Immune-mediated damage
- Antiphospholipid antibodies
- Thrombus formation
- Cytokine Storm
- Severe hypoxia
Virchow’s Triad

- Endothelial Injury
- Hypercoagulability
- Venous Stasis
### Table 3

**Venous thromboembolism risk factors**

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<th>ICU-acquired VTE risk factor</th>
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*VTE* venous thromboembolism
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*VTE* venous thromboembolism
Evidence- or lack of thereof

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Ning Tang¹ | Huan Bai¹ | Xing Chen¹ | Jiale Gong¹ | Dengju Li² | Ziyong Sun¹
Evidence- or lack of thereof

Letters

Association of Treatment Dose Anticoagulation With In-Hospital Survival Among Hospitalized Patients With COVID-19

Single center Retrospective
Evidence- or lack of thereof

Clinical Outcomes With the Use of Prophylactic Versus Therapeutic Anticoagulation in COVID-19


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3Department of Pulmonary and Critical Care, Danbury Hospital, Danbury, CT

Two center
Not peer-reviewed
One Possible Approach

**D-dimer <500**
Prophylactic Anticoagulation

- Enoxaparin subq preferred
  - Dose w/CrCl ≥ 30 mL/min
    - <150 kg: 40 mg daily or 30 mg q12h
    - BMI 40-50: 40 mg q12h
    - BMI > 50: 60 mg q12h
  - Dose w/CrCl <30 mL/min
    - <150 kg: 30 mg daily
    - BMI 40-50: 40 mg daily
    - BMI > 50: 60 mg daily
- Heparin subq if anuric/ESRD/AKI
  - 50-150kg: 5000 units q8h
  - <50kg: 5000 units q12h
  - BMI > 40: 7500 units q8h

**D-dimer 500-2000**
Equipose

- Consider RCT: PROTECT-COVID-19
  - Prophylaxis vs. therapeutic AC
  - Refer to Study Protocol
  - Prophylactic AC as reflected in D-dimer <500 box
- Therapeutic AC:
  - Enoxaparin 1 mg/kg q12h or
  - IV Heparin at 10 u/kg/hr titrate to antiXa 0.3-0.5 U/mL
- If not in trial, use Prophylactic Anticoagulation as reflected in D-dimer <500 box
  - Therapeutic AC may be considered if HIGH suspicion for DVT/PE

**D-dimer >2,000 & <10,000**
Consider Therapeutic AC

- Enoxaparin subq preferred
  - Dose w/CrCl ≥ 30 mL/min
    - <150 kg: 1 mg/kg q12h
    - BMI > 40: 0.75 mg/kg q12h – consider antiXa peak monitoring
  - Dose w/CrCl <30 mL/min
    - <150 kg: 1 mg/kg Qday
    - BMI > 40: 0.75 mg/kg Qd
- If enoxaparin contraindicated
  - IV Heparin at 10 units/kg/hr titrate to antiXa 0.3-0.5 U/mL – avoid bolus dose
  - Alternatively
    - Consider RCT: PROTECT-COVID-19
    - Prophylaxis vs. therapeutic AC

**D-dimer >10,000**
Therapeutic AC Preferred

- Enoxaparin subq preferred
  - Dose w/CrCl ≥ 30 mL/min
    - <150 kg: 1 mg/kg BID
    - BMI > 40: 0.75mg/kg BID – consider antiXa peak monitoring
  - Dose w/CrCl <30 mL/min
    - <150 kg: 1 mg/kg Qd
    - BMI > 40: 0.75 mg/kg Q4h
- If enoxaparin contraindicated:
  - IV Heparin at 10 units/kg/hr titrate to antiXa 0.3-0.5 U/mL – avoid bolus dose if PE not confirmed by CT
Future directions

- Evidence that assists with patient centered decisions:
  - Identify patients who should receive therapeutic anticoagulation
  - Outpatient trials
  - Duration of anticoagulation
  - Role for antiplatelet therapy
Thank you

- Questions