Hasbro Children's Hospital COVID-19 Thromboprophylaxis Guidelines

v.1/08/2021

**Background:** Patients with moderate to severe COVID-19 can develop coagulopathy and/or DIC and thus should be evaluated closely with platelet counts, PT/PTT, d-dimer and fibrinogen levels. Reports from Wuhan (JTH 2020) have demonstrated that adult COVID-19 patients with coagulopathy have worse survival outcomes compared to those without.(1,2) Patients may have evidence of DIC (low platelets and fibrinogen with elevated PT/PTT and d-dimer) or microangiopathy, with schistocytes on peripheral blood smear. Patients with COVID-19 associated coagulopathy however frequently have significant elevations in d-dimer and fibrinogen without significantly lowered platelet counts. (2)

Currently available data supports the use of prophylactic anticoagulation for all non-bleeding patients over the age of 12 with platelet counts >50 and fibrinogen >100 and **moderate to severe COVID-19 disease**. (3,4,5) Younger patients with additional comorbid risk factors may also be considered for prophylaxis.(5) Moderate to severe COVID-19 related illness will be defined as any patient requiring hospitalization **and** supplemental oxygen for management of COVID-19 related respiratory illness **or** meeting criteria for COVID-19 related MIS-C (see MIS-C clinical pathway). Management of patients with congenital bleeding disorders or other pre-existing comorbidities which will increase risk for bleeding should be discussed with Pediatric Hematology Oncology service separate from this guideline. Patients with mild or asymptomatic COVID-19 infections who require hospitalization for other reasons may also be considered for anticoagulation prophylaxis if numerous additional risk factors are present. (5) Of note, use of aspirin may also be considered in the setting of coronary ectasia, dilation or systolic dysfunction and the use of concurrent prophylactic anticoagulation is not contraindicated, however discussion regarding risks/benefits should be had with a multidisciplinary team including Pediatric Hematology Oncology and Pediatric Cardiology.

**Labs:** *Recommended prior to initiating prophylaxis and at least daily*

<table>
<thead>
<tr>
<th>CBC</th>
<th>PT/PTT</th>
<th>Fibrinogen</th>
<th>D-dimer</th>
<th>BUN/Cr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product replacement per PICU routine for DIC with/without active bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient status</th>
<th>Non-COVID risk factors*</th>
<th>D-dimer &gt; 5x ULN (HCH/RIH &gt;1500ng/mL)</th>
<th>Anticoagulant prophylaxis suggesteda</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized with moderate to severe COVID-19 related illness (incl MIS-C)</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>≥ 1</td>
<td>N/A</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Hospitalized with mild to asymptomatic COVID-19</td>
<td>0 – 2</td>
<td>N/A</td>
<td>No</td>
</tr>
<tr>
<td>≥ 3</td>
<td>N/A</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

*Adapted from Goldenberg, et al. 2020

*See below for list of risk factors

a If, Plts <50,000 and/or Fibrinogen <100, or other bleeding risk factors, consider in consultation with Pediatric Hematology Oncology
Risk factors which will increase risk of thrombosis include:
- Age $\geq 12$yo or pubertal/post-pubertal
- Active malignancy
- Sickle cell disease
- Inflammatory bowel disease
- Nephrotic syndrome
- Rheumatologic disorders
- Congenital heart disease
- Known thrombophilia or history of thrombosis
- Family history of VTE (at age <40 or unprovoked)
- Oral contraceptive use
- Obesity (BMI >95th%ile)
- Indwelling central venous catheter
- Mechanical ventilation

**Thromboprophylaxis:** Starting doses of LMWH (*lovenox, enoxaparin*), by age

<12y with comorbidities*

- <2 months  LMWH  0.75 mg/kg/dose every 12 hours (goal anti-Xa 0.2-0.4 u/ml)
- >2 mo – 12y  LMWH  0.5 mg/kg/dose every 12 hours (goal anti-Xa 0.2-0.4 u/ml)

12y – 18y  LMWH 0.5mg/kg/dose every 12 hours (goal anti-Xa 0.2-0.4 u/ml)

>18y  LMWH 40mg/dose once daily (no anti-Xa levels needed with normal renal function, otherwise goal anti-Xa 0.2-0.4 u/ml)

For patients with risk for bleeding, particularly those who are acutely ill with consumptive coagulopathy, prophylactic dosing of a heparin infusion may be considered. Low threshold should remain for evaluation of all COVID-19 positive patients for potential thrombotic events, particularly in those patients with significant elevations in d-dimer. Patients with documented thrombosis should transition to treatment dosing of anticoagulation (either LMWH or heparin infusion) where it is deemed safe to use full dose anticoagulation. Continued anticoagulation prophylaxis post-discharge be considered if d-dimer remains elevated and patient continues to have clinically significant risk factors. In all cases, the Pediatric Hematology Oncology Service should be consulted to discuss individual anticoagulation plans.

References:

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Approved By: S. Pels, R. Lulla, S. Welsh, M. Koster, M. Wynes  1/8/2021