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*

CBC
PT/PTT
Fibrinogen
D-dimer
BUN/Cr

→ Product replacement per PICU routine for DIC with/without active bleeding

Patient status	Non-COVID risk factors*	D-dimer > 5x ULN (HCH/RIH >1500ng/mL)	Anticoagulant prophylaxis suggested[&]
Hospitalized with moderate to severe COVID-19 related illness (incl MIS-C)	No	No	No
	≥ 1	N/A	Yes
	N/A	Yes	Yes
Hospitalized with mild to asymptomatic COVID-19	$0-2$	N/A	No
	≥ 3	N/A	Yes

Adapted from Goldenberg, et al. 2020

**See below for list of risk factors*

[&] 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 ≥ 12yo 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)

LMWH Prophylaxis Dosing Adjustments based on anti-Xa level (Pediatrics)

Anti-Xa Level (units/mL)	Hold Next Dose	Dosage Change	Next Anti-Xa Level
< 0.2	No	Increase 20%	4 hours after 3rd dose of next regimen
0.2-0.4	No	No	NA unless change in renal function
0.41-0.59	No	Decrease 20%	4 hours after 3rd dose of next regimen
0.6-0.8	No	Decrease 30%	4 hours after 3rd dose of next regimen
> 0.8	Until anti-Xa level < 0.2 units/mL	Decrease 40%	Every 12 hours until anti-Xa is < 0.2 Then 4 hours after 2nd dose of new regimen

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:

1. Tang et al, Anticoagulant Treatment Is Associated With Decreased Mortality in Severe Coronavirus Disease 2019 Patients With Coagulopathy, J Thromb Haemost, 2020

2. Tang et al, Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020 Apr;18(4):844-847. Epub 2020 Mar 13.
3. Thachil et al, ISTH interim guidance on recognition and management of coagulopathy in COVID-19, J Thromb Haemost, 2020.
4. American Society of Hematology COVID-19 coagulopathy guidelines: https://www.hematology .org/covid-19/covid-19-and-coagulopathy
5. Goldenberg NA, et.al.; Pediatric/Neonatal Hemostasis and Thrombosis Subcommittee of the ISTH SSC. Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalized for COVID-19-related illness. J Thromb Haemost. 2020 Nov;18(11):3099-3105.

Salley G. Pels, MD, Pediatric Hematology Oncology, Director of the Rhode Island Hemostasis and Thrombosis Center, Member of Hasbro CLABSI/VTE Committee

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