Aflac Clinical Practice Guideline for Work Up and Treatment of Venous Thromboembolism (VTE)

Final 03/2022

INCLUSION CRITERIA

Patient with venous thromboembolism on imaging or line-associated atrial clots in children with structurally normal hearts

EXCLUSIONS

Thrombi in intracardiac connections and devices or patients with significant renal disease or superficial thrombi

RISK FACTORS

- Central venous access device (CVAD) *
- Infection *
- Decreased mobility from baseline
- Surgery, trauma *
- Personal history of or first degree relative with DVT/VTE *
- Active cancer *
- Congenital heart disease
- Inflammatory/Rheumatologic diseases *
- Renal disorders (nephrotic syndrome)
- Sickle cell disease *
- Pregnancy
- Estrogen use
- Obesity
- Aberrant venous anatomy
- Post pubertal age or age <1

* Indicates risk factors for Cerebral Sinus (CSVT)

WORK UP

Suspected Acute VTE

Imaging

Extremity or Internal Jugular
- Doppler Ultrasound
- MRV if:
  - Left sided ileofemoral VTE (May-Thurner Syndrome)
  - Unprovoked upper extremity VTE (Thoracic Outlet Syndrome)
  - Proximal end of lower extremity clot is not seen on ultrasound
  - Replace MRV with CT with contrast if morbidly obese

Pulmonary Embolism (PE)
- CT Angiogram
- ECHO
- Bilateral upper and lower extremity Doppler Ultrasound

Renal or Portal
- Abdominal Doppler Ultrasound

Cerebral Sinus (CSVT)
- MRI/MRV

Consult Hematology

Does imaging suggest interventionalist consult[1]?

Yes → Consult interventionalist

No

Labs
- CBC
- DIC Panel
- CMP
- Antiphospholipid antibody testing (Lupus anticoagulant profile) in age ≥12 yo and/or post pubertal and/or personal or FHx of autoimmune conditions
- If PE, send troponin and BNP

Provoked clot? See risk factors

No → Send:
- Protein C activity
- Protein S activity
- Antithrombin activity
- Factor V Leiden Mutation
- Prothrombin G20210A Gene Mutation

Yes

Family history of thrombosis?

No → **Do NOT send thrombophilia testing**

Yes → Send:

Consider Treatment Options (see page 2)

1. Consult interventionalist for:

- Central venous system thrombosis
  - Axillary vein to heart
  - Iliac vein to heart
  - Massive PE with right heart strain or shock
  - May Thurner or Padget-Schrotter syndromes
  - Bilateral renal vein thrombi
  - SVC syndrome
  - See also catheter directed thrombolysis guideline

Interventional cardiology should be consulted for children with structurally abnormal hearts or history of cardiac surgery. Consult IR for all other children.

TREATMENT

1. Anticoagulation Contraindications

- Recent/active bleeding
- Invasive procedure in past 24 hrs
- History of heparin-induced thrombocytopenia
- Uncorrected coagulopathy/severe thrombocytopenia (<30K)
- Epidural catheter
- Religious objection to pork/pork allergy (heparin and enoxaparin only)

Are there contraindications for anticoagulation[1]?

Yes → Consider supportive care with close follow up imaging or IR interventions (IVC filter, suction thrombectomy)

No

Supportive care

- Order bleeding precautions:
  - Avoid use of aspirin or NSAIDs for fever/pain
  - No rectal temperatures
  - Use soft toothbrush or water irrigating device
  - Apply direct pressure to cuts for 10-15 minutes
  - Avoid arterial punctures if possible

2. Unfractionated Heparin Indications

- Significant renal impairment
- Increased bleeding risk
- Planned invasive procedure(s) OTHER than thrombolysis in next 24-48 hrs

Is unfractionated heparin indicated[2]?

Yes → Start unfractionated heparin. For dosing, see page 3

No

Going for thrombolysis?

Yes → Update ECMO team and ICU for support. See CDT Guideline

No

Is weight ≥ 35 kg?

No → Start enoxaparin. For dosing, see page 3

For patients who prefer oral therapy, consider enoxaparin bridge to warfarin. For dosing, see page 4

Yes

3. Direct Oral Anticoagulant (DOAC) Contraindications

ABSOLUTE	RELATIVE
• "Triple +" APLA	• Nephrotic syndrome
• Left ventricular thrombosis	• End stage renal disease
• CHILD PUGH grade ≥ B	• Risk of GI bleeding

Are there contraindications for DOAC[3]?

Yes → Start enoxaparin. For dosing, see page 3

No

DOAC as 1st line[4]

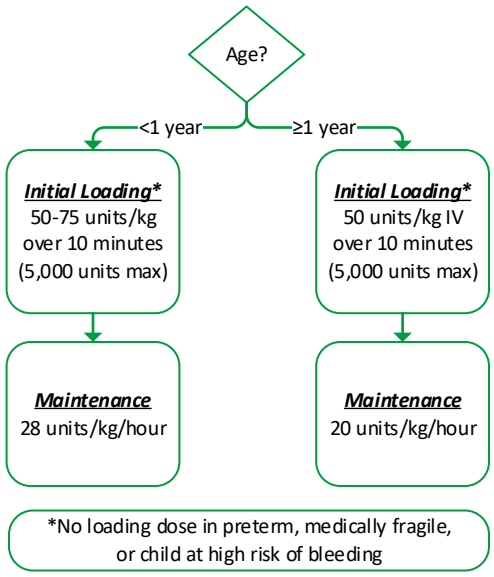
**Must be ordered by hematology or cardiology*

Drug	Weight	Absorption site
Apixaban	≥35 kg	Colon
Rivaroxaban	≥50 kg	Stomach

4. Length of MINIMUM initial treatment

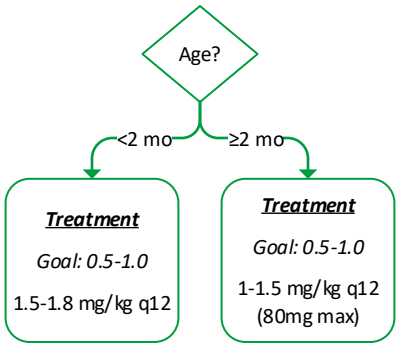
6 Weeks if:	<2 months old and VTE resolves **OR** central line associated clot and VTE resolves
3 Months if:	Provoked VTE (DVT or PE) **OR** Cerebral Sinus Venous Thrombosis
6 Months if:	Idiopathic/Unprovoked VTE (DVT or PE), May-Thurner Syndrome, **OR** Antiphospholipid antibody syndrome (may need indefinite treatment)

Therapeutic Unfractionated Heparin Dosing
GOAL: 0.35-0.70 units/mL



Therapeutic Unfractionated Heparin Dosage Titration *GOAL: 0.35-0.70 units/mL*		
Hep Assay (Units/mL)	**Dosage Adjustment**	**Time to Repeat Heparin Assay (Anti-Xa)**
<0.2	Give 50 units/kg bolus (5000 units max), and increase infusion rate by 15%	4 hours after rate change
0.21-0.34	Increase infusion rate by 10%	4 hours after rate change
0.35-0.7	Keep rate the same	Daily after 2 levels 4 hours apart are in goal range
0.71-0.79	Decrease infusion rate by 10%	4 hours after rate change
0.8-0.89	Hold infusion for 60 minutes, then decrease infusion rate by 10%	4 hours after infusion resumes
≥0.9	Hold infusion for 120 minutes, then decrease infusion rate by 15%	4 hours after infusion resumes

Therapeutic Enoxaparin Dosing
GOAL: 0.5-1.0 units/mL; all levels should be drawn 4 hours after administration



- Enoxaparin is **renally** cleared; refer to formulary for dosage modifications based on creatinine clearance; needs peak and trough levels
- With changes in creatine, more frequent heparin assay may be needed.
- Round to the nearest whole number if possible

Enoxaparin Dosage Titration while Inpatient		
Heparin Assay (Units/mL)	**Dose Titration**	**Time to Repeat Heparin Assay (AntiXa) Level**
<0.35	Increase dose by 25%	4 hours after 2nd dose
0.35-0.49	Increase dose by 10%	4 hours after 2nd dose
0.5-0.59	Keep same dosage	Next day, then weekly
0.6-0.89	Keep same dosage	Weekly
0.9-1	Keep same dosage	Next day, then weekly
1.1-1.5	Decrease dose by 20%	4 hours after 2nd dose
1.6-2	Hold next dose and decrease subsequent dose by 30%	12 hours (ensure level has dropped to <0.5 units/mL) then 4 hours after next dose given
>2	Hold all doses until HepAssay less than 0.5 units/mL then decrease dose by 40%	Every 12 hours until HepAssay is less than 0.5 units/mL then 4 hours after next dose given

Therapeutic DOAC Dosing

Must be ordered by hematology or cardiology

DOAC	Loading Dose	Maintenance Dose
Apixaban	10 mg PO BID for 7 days	5 mg PO BID
Rivaroxaban	15 mg PO BID for 21 days	20 mg PD QD

Continue enoxaparin or unfractionated heparin until INR >1.7

Warfarin Dosing			
Goal	**Day**	**Level**	**Dosing Adjustment**
INR of 2.0-3.0 for non-CICU patients	1-2		0.2 mg/kg (10 mg max dose)
	3-5		50% of loading dose
	Maintenance * Check INR on day 4 or 5	1.1-1.4	Increase by 20% of dose
		1.5-1.9	Increase by 10% of dose
		2.0-3.0	No Change
		3.1-3.5	Decrease by 10% of dose
		> 3.5	Reduce dose to 20% of current dose x2 days then repeat INR, If INR <3.5, restart at 20% less than previous dose
INR of 2.5-3.5 for CICU patients	1-2	1.0-1.3	0.2 mg/kg (10 mg max dose)
	3-5		50% of loading dose
	Maintenance * Check INR on day 4 or 5	1.1-1.9	Increase by 20% of dose
		2.0-2.4	Increase by 10% of dose
		2.5-3.5	No Change
		3.6-4.0	Decrease by 10% of dose
		> 4.0	Reduce dose to 20% of current dose x2 days then repeat INR. If INR <3.5, restart at 20% less than previous dose

REVERSAL

For reversal, see Anticoagulation policy:
PC 18.58

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REVISION HISTORY

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Approval: [Date/time]