Venous Thromboembolism (VTE) Treatment, Inpatient Clinical Practice Guideline

INCLUSION CRITERIA

Patient with suspected or confirmed 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

[2]RISK FACTORS

- Central venous access device (CVAD) *
- Infection *
- Decreased mobility from baseline
- Surgery, trauma *
- Personal history of or first degree relative with VTE *
- Active cancer *
- Congenital heart disease
- Inflammatory/Rheumatologic diseases *
- Renal disorders (nephrotic syndrome)
- Sickle cell disease *
- Pregnancy
- Estrogen use
- Obesity
- Aberrant venous anatomy
- ≥ 12yrs.&/or Post pubertal
- 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 thrombus not seen on ultrasound
- CT with contrast (replace MRV) if morbidly obese

For Pulmonary Embolism (PE)
- CT Angiogram

If PE Confirmed, Obtain:
- Echocardiogram
- Bilateral upper and lower extremity Doppler Ultrasound

Renal or Portal Vein
- Abdominal Doppler Ultrasound

Cerebral Sinus (CSVT)
- MRI/MRV

Diagnostic Imaging Confirms/Suggestive of VTE

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

Consult Hematology

Does Imaging Suggest Interventionalist consult[1]?

Yes → Consult Interventionalist[1]

No

Provoked clot? See Risk Factors[2]

No → **Obtain Thrombophilia Testing:**
- 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 if No Family History of Thrombosis**

Yes

Consider Treatment Options (see page 2)

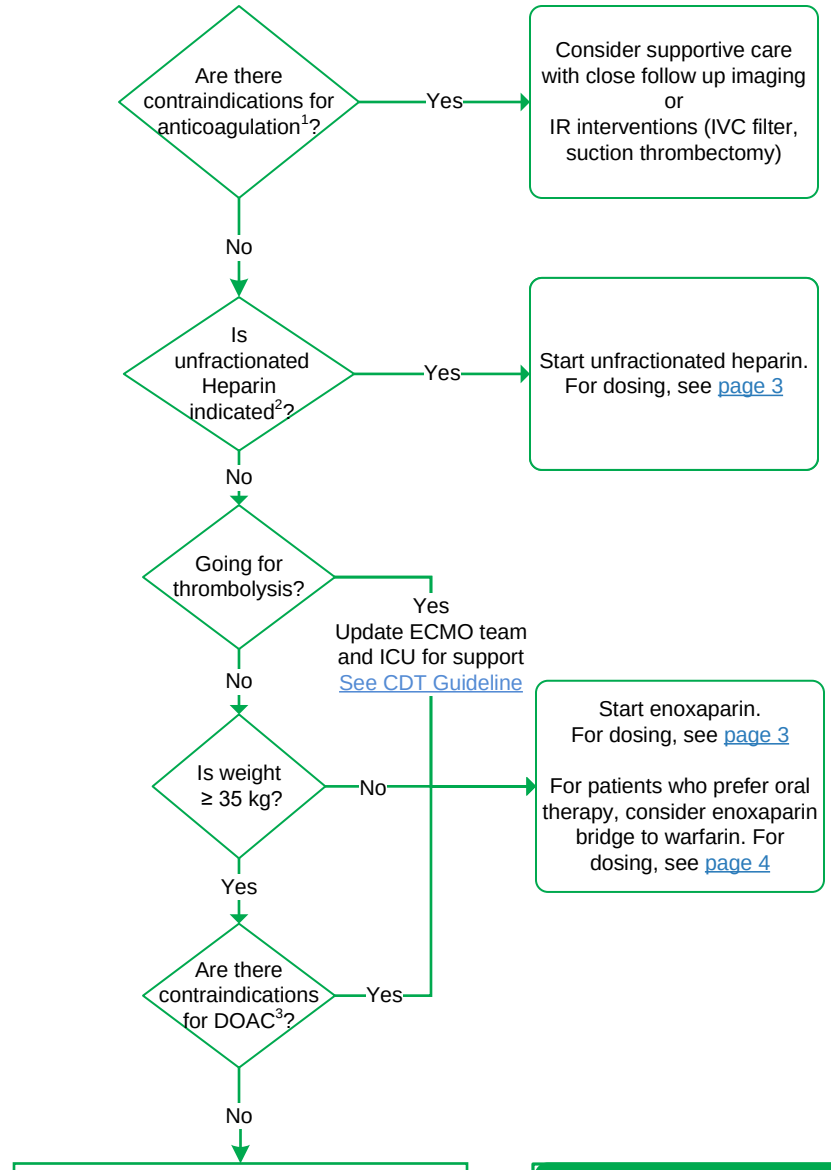
[1]Consult Interventionalist for:
- Central venous system thrombosis
  - Axillary vein to heart
  - Iliac vein to heart
- Consider Cardiology consult if right heart strain present
- May Thurner or Padget-Schrotter Syndromes
- Bilateral renal vein thrombi
- SVC Syndrome
- Consult Interventional cardiology for children with structurally abnormal hearts or history of cardiac surgery

See also catheter directed thrombolysis guideline

TREATMENT

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



[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)

[2]Unfractionated Heparin Indications

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

[3]Direct Oral Anticoagulant (DOAC) Contraindications

ABSOLUTE

- "Triple +" APLA
- Severe synthetic liver dysfunction
- Bilirubin >2x ULN
- AST/ALT >3x UNL
- Concurrent use of "-azole" (other than Fluconazole)
- Intolerance of enteral intake
- Presence of Mechanical heart valve
- Presence of venous stent

RELATIVE

- Nephrotic syndrome
- End stage renal disease
- Risk of GI bleeding
- Short Gut Syndrome
- Concurrent use of antiepileptics (phenobarbital, phenytoin, carbamazepine)

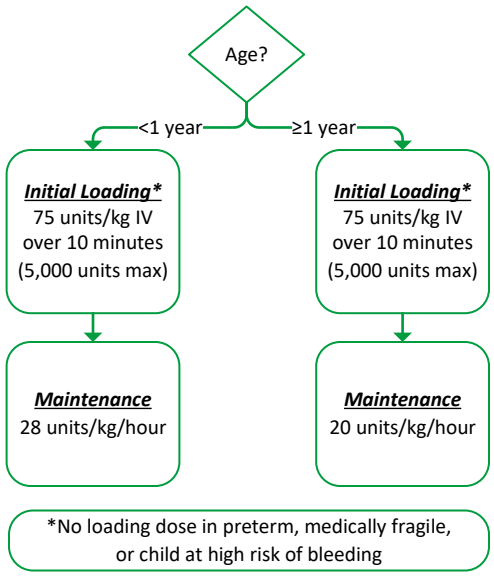
DOAC as 1st line[4]
**Must be ordered by hematology or cardiology*

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

[4]Length of MINIMUM Initial Treatment

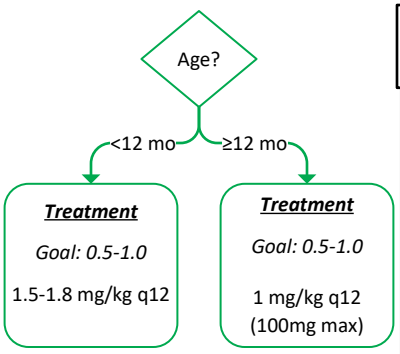
6 weeks if:	DVT, including CSVT, with obvious provoking risk factor
3 months if:	Provoked Pulmonary Embolism or persistently positive antiphospholipid antibodies at 6 weeks
6 months if:	Idiopathic/unprovoked VTE (DVT or PE) or stented May-Thurner Syndrome

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 PO QD

Warfarin

Pediatric Dosing and Monitoring Guidelines for Target

INR of 2-3 for non-cardiac Patients

I Day 1-2*	INR will need to be ordered	0.1-0.2 mg/kg (10 mg max dose)
II Day 3-5*	INR will need to be ordered	0.1 mg/kg (10 mg max dose)
III Maintenance Check INR on day 4 or 5	1.1-1.4 1.5-1.9 2.0-3.0 3.1-3.5 >3.5	Increase by 20% of dose Increase by 10% of dose No Change Decrease by 10% of dose Reduce dose

- *Consider maximum starting dose of 5mg for patients at high risk of bleeding
- When initiating warfarin follow the above chart section I and II to achieve Goal INR.
- Once the goal INR 2-3 has been reached follow section III in the above chart to maintain.
- Once Goal INR is maintained check weekly, then monthly INR levels should be ordered.
- Round doses to nearest 0.5 mg, avoid cutting pills if possible

Warfarin

Pediatric Dosing and Monitoring Guidelines for Target

INR of 2.5-3.5 for non-cardiac Patients

I Day 1-2*	1.0-1.3	0.1-0.2 mg/kg (10 mg max dose)
II Day 3-5*		0.1 mg/kg (10 mg max dose)
III Maintenance Check INR on day 4 or 5	1.1-1.9 2.0-2.4 2.5-3.5 3.6-4.0 >4.0	Increase by 20% of dose Increase by 10% of dose No Change Decrease by 10% of dose Reduce dose to 20% of current dose x2 days then repeat INR. If INR <3.5, restart at 20% less than previous dose

- *Consider maximum starting dose of 5mg for patients at high risk of bleeding
- When initiating warfarin follow the above chart section I and II to achieve Goal INR.
- Once the goal INR 2.5-3.5 has been reached follow section III in the above chart to maintain.
- Once Goal INR is maintained check weekly, then monthly INR levels should be ordered.
- Round doses to nearest 0.5 mg, avoid cutting pills if possible

For reversal, see Anticoagulation policy:
PC 18.58

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REVISION HISTORY

Revision #	Change Description	Date
0	Original Document	1/20/2021
1	Published for CE	3/11/2022
2	Evidence reviewed by Dr. Woods and Dr. Jain	11/30/2023
3	Evidence reviewed by Dr. Woods	1/26/2024