

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Vascular Thrombosis: Arterial Thrombosis
Evidence-Based Guideline

Definition: Arterial thrombosis is the formation of a blood clot (thrombus) inside an arterial blood vessel, obstructing the flow of blood through the circulatory system. Arterial thrombosis initially occurs under conditions of rapid blood flow and often is the result of a process that damages the vessel wall. ⁽¹⁾ The thrombus is composed of tightly coherent platelets that contain small amounts of fibrin and few erythrocytes and leukocytes (white thrombus). ⁽¹⁾ This guideline deals specifically with arterial thrombosis in the extremities.

Etiology: Arterial thrombosis occurring outside the central nervous system can be classified as catheter-related and non-catheter-related thrombus. ⁽²⁾ Placement of central lines, cardiac catheterizations, surgical procedures, low cardiac output states, and coagulopathies may all result in significant thrombus formation in vessels of children. ⁽³⁾ There are three factors that are associated with the development of thrombosis (Virchow's Triad): the blood vessel wall, the blood constituents, and blood flow. ⁽⁴⁾

Inclusion Criteria

- Patients at Texas Children's Hospital with arterial thrombosis in the extremities

Exclusion Criteria

- Pregnancy
- Active bleeding
- Arterial thrombosis in any location except extremities

Diagnostic Evaluation ⁽⁵⁾

History: Assess for

- Interventional catheterization – specifically balloon dilatation, valvotomy procedures
- Larger central line catheter size / sheath size for given weight of the patient
- Repeated central catheter manipulations
- Longer duration of cannulation

Physical Examination

- Evaluate limb for signs and symptoms of acute peripheral arterial occlusion:
 - Palpable pulses
 - Difference in blood pressure >10 mm Hg between right and left legs
 - Decreased skin temperature
 - Skin discoloration (pale or cyanosis)
 - Prolonged capillary refill time

Laboratory Tests

Initial Laboratory Studies:

- CBC
- DIC panel (includes PT, PTT, thrombin time, fibrinogen, D-dimer, heparinase PTT as needed, and platelet count)
- Antithrombin (AT) for patients <6 months of age
 - Inherited thrombophilia is rare in children with arterial thrombosis; hence, screening is not routinely recommended.

Diagnostic Imaging:

Doppler Ultrasound

- Diagnostic test of choice
- Observe for absent pulses
- Difference in blood pressure >10 mm Hg between limbs
- Include proximal access artery

MRA or CTA

Critical Points of Evidence*

Evidence-Based Recommendations

- Initiate anticoagulant therapy in symptomatic patients who have non-occlusive thrombus and repeat the ultrasound in 24 hours after initiation of therapy to reassess. ⁽⁶⁾ – Strong recommendation, very low quality evidence
- Monitor the affected limb with continuous pulse oximetry and with a handheld, portable Doppler. ⁽⁷⁻⁹⁾ – Strong recommendation, very low quality evidence
- Initiate anticoagulant therapy in patients with arterial thrombosis. ^(6,10) – Strong recommendation, very low quality evidence

Remarks: The agent to induce therapeutic anticoagulation is dependent on individual patient characteristics and the selection of the agent should be decided by the patient's care team. Considerations to selecting an agent would include the location of care, potential surgical interventions, line access, renal function, history of heparin-induced thrombocytopenia, bleeding risk, reversibility of the agent, or other patient-specific characteristics.

Consensus Recommendations

- Consider interventions in consultation with a multidisciplinary team to decide the appropriate sequence of interventions. – Consensus recommendation

Remarks: With a lack of evidence to guide decision-making, the team felt it was appropriate to recommend a multidisciplinary team approach to decide the sequence of interventions after a discussion of the individual patient's needs on a case-by-case basis.

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

General: Low dose continuous infusion of unfractionated heparin (UFH) through the catheter may prolong the patency of peripheral arterial catheters.

Treatment Recommendations

A multidisciplinary approach is recommended. The management of thrombosis is primarily based around anticoagulation. ⁽⁵⁾ Hematology consultation is recommended to identify appropriate anticoagulant therapy.

Anticoagulant Therapy: Unfractionated Heparin (UFH)

Anticoagulation with UFH should be initiated once arterial thrombosis is confirmed by imaging, but monitoring and maintaining UFH in a therapeutic range can require titration and careful monitoring. ⁽⁵⁾ If clinical findings worsen 4-6 h after initiation of UFH, consider thrombolytic therapy, surgical or mechanical thrombectomy after consulting plastic surgery to help assess and coordinate with vascular surgery, interventional cardiology, hematology, and/or other relevant consults.

Anticoagulant Therapy: Low Molecular Weight Heparin (LMWH)

In patients with clinical and/or radiologic improvement or stability of arterial thrombosis, consider switching UFH to LMWH. The minimum duration of anticoagulation therapy for arterial thrombosis is 7 days; consider additional therapy for 1 week for persistent clinical signs or partial/complete vessel obstruction on imaging.

Tissue Plasminogen Activator (tPA)

Thrombolytic agents act to dissolve established thrombus by converting endogenous plasminogen to plasmin, which can lyse existing thrombus. ⁽¹⁾ Refer to the [Texas Children's Cancer and Hematology Centers Guidelines for thrombolysis using tissue plasminogen activator \(tPA\) in pediatric patients](#) for guidance.

Mechanical or Surgical Thrombectomy

Mechanical or surgical thrombectomy may be considered for worsening clinical and/or imaging findings wherein tPA is contraindicated or for life/limb threatening arterial occlusion. This may include complete limb ischemia, pre-gangrenous changes, compartment syndrome, Doppler findings that demonstrate complete obstruction with no distal flow or impending organ damage.

- Local surgical complications

Complications of Arterial Thrombosis

Acute:

- Ulceration/Necrosis
- Gangrene

Long-term:

- Loss of digit(s)
- Loss of limb
- Loss of vascular access
- Limb length discrepancy

Consults/Referrals

Hematology

Plastic Surgery to help coordinate care

Vascular Surgery

Interventional Radiology

Interventional Cardiology

Pediatric Surgery

Transfusion Medicine

Follow-Up Care

- Follow-up is recommended for all patients with arterial thrombosis in the out-patient hematology clinic 1-3 months after diagnosis for assessing long term effects of arterial thrombosis.
- Continued follow-up recommended for patients with residual thrombosis on imaging and arterial thrombosis-related limb abnormalities

Measures

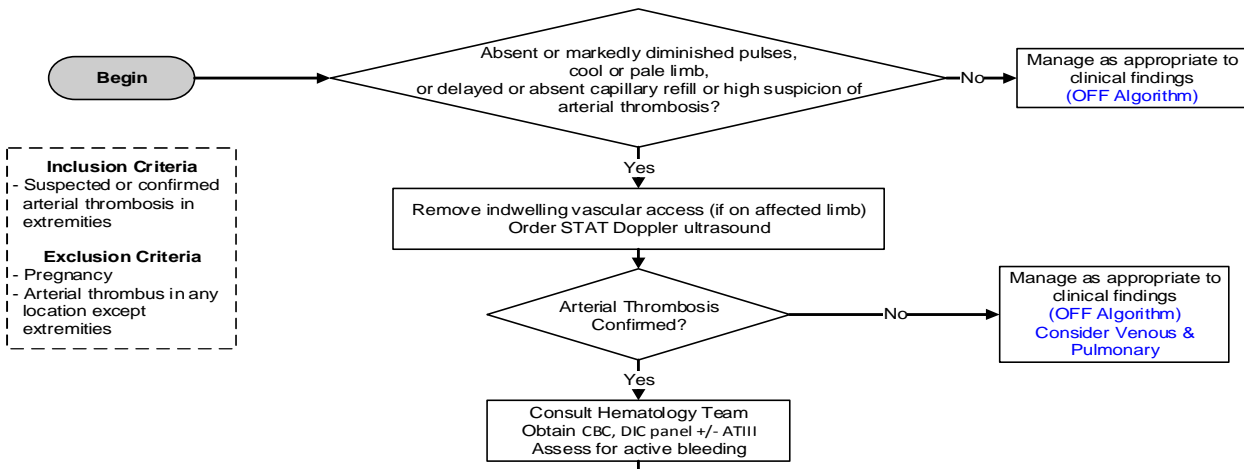
Process

- Frequency of tissue plasminogen activator use
- Frequency of mechanical/surgical thrombectomy

Outcome

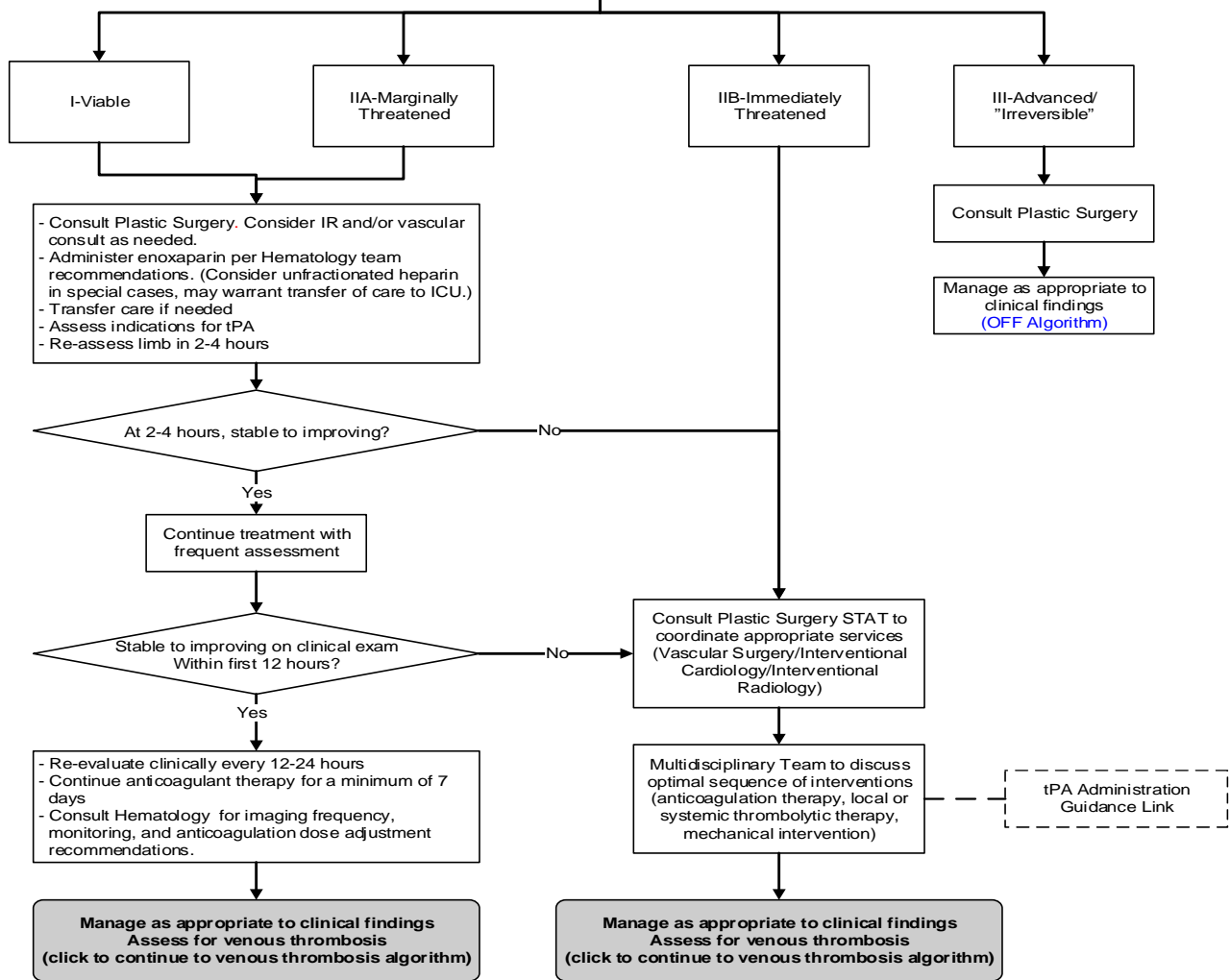
- Limb loss secondary to arterial thrombosis

**Texas Children's Hospital Evidence-Based Outcomes Center
Clinical Algorithm for Vascular Thrombosis
Diagnosis and Initiation of Treatment for Arterial Thrombosis**



- Inclusion Criteria**
- Suspected or confirmed arterial thrombosis in extremities
- Exclusion Criteria**
- Pregnancy
 - Arterial thrombus in any location except extremities

Category	Prognosis	Sensory Loss	Motor Deficit	Arterial Doppler	Venous Doppler
I-Viable	No immediate threat	None	None	Audible	Audible
IIA-Marginally Threatened	Salvageable if promptly treated	Minimal (toes) or none	None	Inaudible	Audible
IIB-Immediately Threatened	Salvageable if immediately revascularized	More than toes, rest, pain	Mild/Moderate	Inaudible	Audible
III-Advanced or "Irreversible"	Major tissue loss, permanent nerve damage inevitable	Profound, anesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible



Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.

References

1. Lanzkowsky, P, Lipton, J., & Fish, J. D. (Eds). (2016). *Manual of Pediatric Hematology and Oncology* (6th Ed.). Cambridge, MA: Academic Press.
2. Rizzi, M., & Albisetti, M. (2018). Treatment of arterial thrombosis in children: Methods and mechanisms. *Thrombosis Research*, 169, 113-119.
3. Qureshi, A. M., Petit, C. J., Crystal, M. A., Liou, A., Khan, A., Justino, H. (2016). Efficacy and safety of catheter-based rheolytic and aspiration thrombectomy in children. *Catheterization and Cardiovascular Interventions*, 87(7), 1273-1280.
4. Wolberg, A. S., Aleman, M. M., Leiderman, K., & Machlus, K. R. (2012). Procoagulant activity in hemostasis and thrombosis: Virchow's triad revisited. *Anesthesia & Analgesia*, 114(2), 275-285.
5. Campbell, S. & Monagle, P. (2017). Thrombosis in pediatric intensive care. In Fuhrman, B. P. & Zimmerman, J. J. (Eds.), *Pediatric Critical Care* (1282-1294).
6. Glatz, A. C., Keashen, R., Chang, J., Balsama, L. A., Dori, Y., Gillespie, M. J., ... Rome, J. J. (2015). Outcomes using a clinical practice pathway for the management of pulse loss following pediatric cardiac catheterization. *Catheterization and Cardiovascular Interventions*, 85(1), 111-117.
7. Alavi, A., Sibbald, R. G., Nabavizadeh, R., Valaei, F., Coutts, P., & Mayer, D. (2015). Audible handheld Doppler ultrasound determines reliable and inexpensive exclusion of significant peripheral arterial disease. *Vascular*, 23(6), 622-629.
8. Knirsch, W., Kellenberger, C., Dittrich, S., Ewert, P., Lewin, M., Motz, R., ... Kretschmar, O. (2013). Femoral arterial thrombosis after cardiac catheterization in infancy: Impact of Doppler ultrasound for diagnosis. *Pediatric Cardiology*, 34(3), 530-535.
9. Milan, A., Freato, F., Vanzo, V., Camporese, G., Baraldi, M., Chiandetti, L., & Zaramella, P. (2012). Near-infrared spectroscopy measure of limb peripheral perfusion in neonatal arterial thromboembolic disease. *Minerva Pediatrics*, 64(6), 633-639.
10. Romantsik, O., Bruschetini, M., Zappettini, S., Ramenghi, L. A., & Calevo, M. G. (2016). Heparin for the treatment of thrombosis in neonates. *Cochrane Database of Systematic Reviews*, 11, CD012185.

Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
 - PICO questions established
 - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
 - Children's Hospital of Philadelphia (2016) Post-Cath Pulse Loss Pathway
 - Society of Interventional Radiology (2013) Quality Improvement Guidelines for Percutaneous Management of Acute Lower-Extremity Ischemia
 - American College of Chest Physicians (2012) Antithrombotic Therapy in Neonates and Children Antithrombotic Therapy and

Prevention of Thrombosis Evidence-Based Clinical Practice Guidelines

3. Literature Review of Relevant Evidence
 - Searched: Cochrane Reviews, Cochrane CENTRAL, PubMed
4. Critically Analyze the Evidence
 - One systematic review and meta-analysis and five nonrandomized studies
5. Summarize the Evidence
 - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in an Arterial Thrombosis evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.

"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn from the evidence.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis and initial management of arterial thrombosis in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Comments
Oct 2010	Originally completed
Feb 2020	Updated