

**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. <sup>(1)</sup> The thrombus is composed of tightly coherent platelets that contain small amounts of fibrin and few erythrocytes and leukocytes (white thrombus). <sup>(1)</sup> 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. <sup>(2)</sup> 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. <sup>(3)</sup> 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. <sup>(4)</sup>

**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** <sup>(5)</sup>

**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. <sup>(6)</sup> – Strong recommendation, very low quality evidence
- Monitor the affected limb with continuous pulse oximetry and with a handheld, portable Doppler. <sup>(7-9)</sup> – Strong recommendation, very low quality evidence
- Initiate anticoagulant therapy in patients with arterial thrombosis. <sup>(6,10)</sup> – 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. <sup>(5)</sup> 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. <sup>(5)</sup> 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. <sup>(1)</sup> 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**

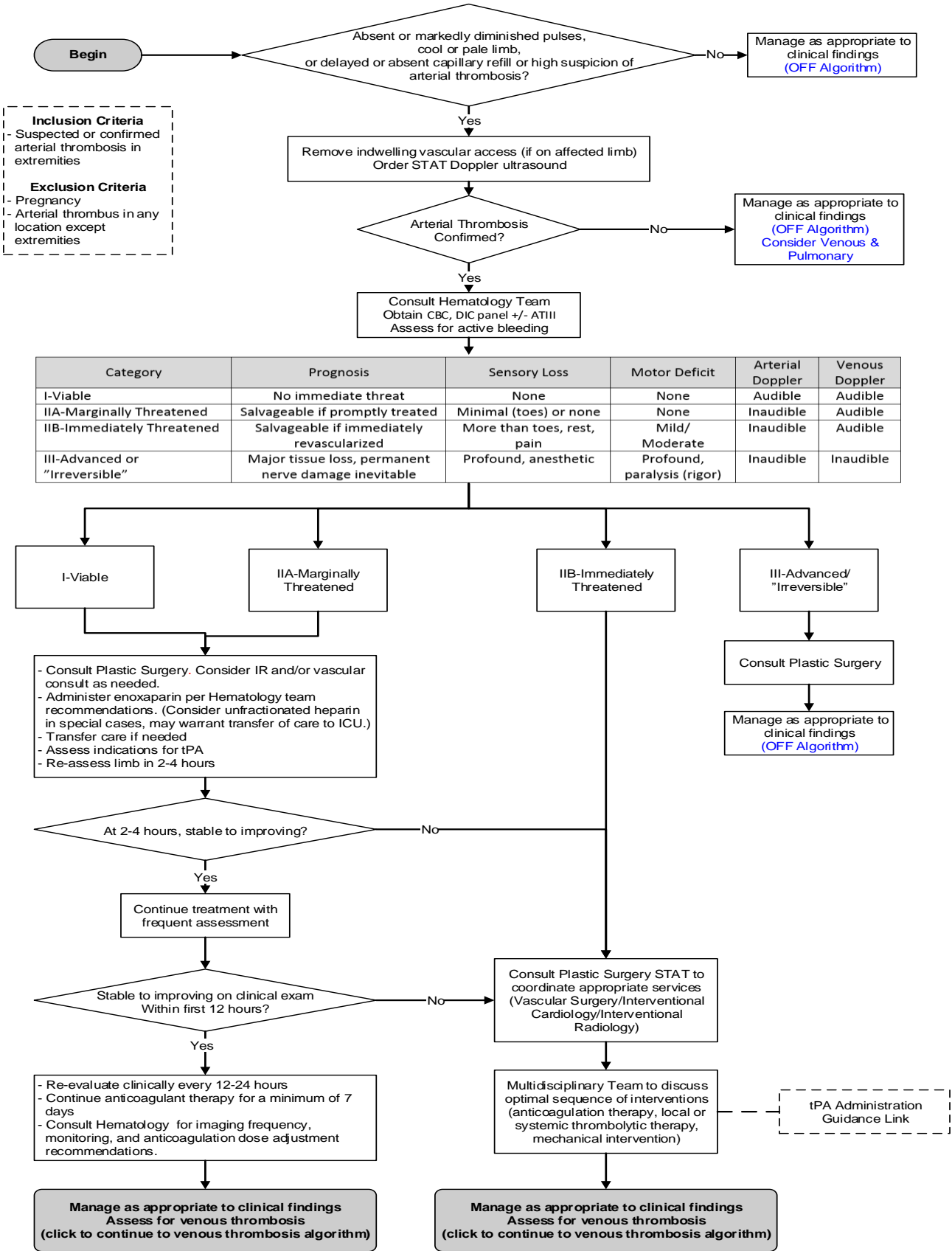
##### **Process**

- 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**



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

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### 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.

#### **Arterial Thrombosis Content Expert Team**

Karla Abela, MSN, RN—PICU Clinical Specialist  
 Godly Abraham, RN—Decentralized Quality Improvement Specialist, Cardiology  
 Iki Adachi, MD—Congenital Heart Surgery  
 Athis Arunahalam, MD, MBBS—Neonatology  
 Mubasheer Ahmed, MD—Critical Care  
 Jordana Goldman, MD—Critical Care  
 Lisa Hensch, MD—Transfusion Medicine  
 Henri Justino, MD—Cardiology  
 Lauren Kane, MD—Congenital Heart Surgery  
 Kamlesh Kukreja, MD—Radiology  
 Miguel Montero, MD—Vascular Surgery  
 Joseph Mills, MD—Vascular Surgery  
 Laura Monson, MD—Plastic Surgery  
 Eyal Muscal, MD—Pediatric Rheumatology  
 Binita Patel, MD—Emergency Medicine  
 William Christopher Pederson, MD—Plastic Surgery  
 Ricardo Quinonez, MD—Pediatric Hospital Medicine  
 Athar Qureshi, MD—Cardiology  
 Theresa Reed, RN—Vascular Access Team  
 Miranda Rodrigues, MSN, RN—CVICU Clinical Specialist  
 Karla Resendiz Trujano, PharmD—Clinical Pharmacist  
 Emily Rodman, PharmD—Clinical Pharmacist  
 Sarah Sartain, MD—Hematology  
 Lindsay Schmees, PharmD—Pharmacy  
 Jeffrey Shilt, MD—Orthopedics  
 Joan Shook, MD—Chief Safety Officer  
 Jun Teruya, MD—Transfusion Medicine  
 Sebastian Tume, MD—Critical Care  
 Adam Vogel, MD—Pediatric Surgery  
 Donald Yee, MD—Hematology

#### **EBOC Team**

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.

<b>Recommendation</b>	
<b>STRONG</b>	Desirable effects clearly outweigh undesirable effects or vice versa
<b>WEAK</b>	Desirable effects closely balanced with undesirable effects
<b>Quality</b>	<b>Type of Evidence</b>
<b>High</b>	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
<b>Moderate</b>	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
<b>Low</b>	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
<b>Very Low</b>	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 should 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.

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**Version History**

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