**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. The thrombus is composed of tightly coherent platelets that contain small amounts of fibrin and few erythrocytes and leukocytes (white thrombus). 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. 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. 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.

**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**

**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, hepzyme PTT as needed, and platelet count)
- Antithrombin (AT) for patients <6 months of age

**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

**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. – Strong recommendation, very low quality evidence
- Monitor the affected limb with continuous pulse oximetry and with a handheld, portable Doppler. – Strong recommendation, very low quality evidence
- Initiate anticoagulant therapy in patients with arterial thrombosis. – 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.

**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. [9] 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. [9] 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

Begin

Absence or markedly diminished pulses, cool or pale limb, or delayed or absent capillary refill or high suspicion of arterial thrombosis?

Yes

Remove indwelling vascular access (if on affected limb)
Order STAT Doppler ultrasound

Arterial Thrombosis Confirmed?

Yes

Consult Hematology Team
Obtain CBC, DIC panel +/- ATIII
Assess for active bleeding

No

Manage as appropriate to clinical findings (OFF Algorithm)

Arterial Thrombosis Confirmed?

Yes

Consult Hematology Team
Obtain CBC, DIC panel +/- ATIII
Assess for active bleeding

No

Manage as appropriate to clinical findings (OFF Algorithm)
Consider Venous & Pulmonary

Inclusion Criteria
- Suspected or confirmed arterial thrombosis in extremities

Exclusion Criteria
- Pregnancy
- Arterial thrombus in any location except extremities

<table>
<thead>
<tr>
<th>Category</th>
<th>Prognosis</th>
<th>Sensory Loss</th>
<th>Motor Deficit</th>
<th>Arterial Doppler</th>
<th>Venous Doppler</th>
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</thead>
<tbody>
<tr>
<td>I-Viable</td>
<td>No immediate threat</td>
<td>None</td>
<td>None</td>
<td>Audible</td>
<td>Audible</td>
</tr>
<tr>
<td>IIA-Marginally Threatened</td>
<td>Salvageable if promptly treated</td>
<td>Minimal (toes) or none</td>
<td>None</td>
<td>Inaudible</td>
<td>Audible</td>
</tr>
<tr>
<td>IIB-Immediately Threatened</td>
<td>Salvageable if immediately revascularized</td>
<td>More than toes, rest. pain</td>
<td>Mild/ Moderate</td>
<td>Inaudible</td>
<td>Audible</td>
</tr>
<tr>
<td>III-Advanced or “Irreversible”</td>
<td>Major tissue loss, permanent nerve damage “Irreversible”</td>
<td>Profound, anesthetic</td>
<td>Profound, paralyze (rigor)</td>
<td>Inaudible</td>
<td>Inaudible</td>
</tr>
</tbody>
</table>

I-Viable

- Consult Plastic Surgery. Consider IR and/or vascular consult as needed.
- Administer enoxaparin per Hematology team recommendations. (Consider unfractionated heparin in special cases, may warrant transfer of care to ICU.)
- Transfer care if needed
- Assess indications for tPA
- Re-assess limb in 2-4 hours

At 2-4 hours, stable to improving?

Yes

Consult Plastic Surgery STAT to coordinate appropriate services (Vascular Surgery/Interventional Cardiology/Interventional Radiology)

No

Manage as appropriate to clinical findings (OFF Algorithm)

IIA-Marginally Threatened

Multidisciplinary Team to discuss optimal sequence of interventions (anticoagulation therapy, local or systemic thrombolytic therapy, mechanical intervention)

Consult Plastic Surgery

IIB-Immediately Threatened

No

Manage as appropriate to clinical findings (OFF Algorithm)

III-Advanced or “Irreversible”

Manage as appropriate to clinical findings (OFF Algorithm)

Consult Plastic Surgery STAT to coordinate appropriate services (Vascular Surgery/Interventional Cardiology/Interventional Radiology)

At 2-4 hours, stable to improving?

Yes

Continue treatment with frequent assessment

Stable to improving on clinical exam Within first 12 hours?

Yes

Manage as appropriate to clinical findings (click to continue to venous thrombosis algorithm)

No

Consult Plastic Surgery

- Re-evaluate clinically every 12-24 hours
- Continue anticoagulant therapy for a minimum of 7 days
- Consult Hematology for imaging frequency, monitoring, and anticoagulation dose adjustment recommendations.

No

Manage as appropriate to clinical findings (OFF Algorithm)

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

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

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.

<table>
<thead>
<tr>
<th>Quality</th>
<th>Type of Evidence</th>
</tr>
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<tbody>
<tr>
<td>High</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Moderate</td>
<td>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</td>
</tr>
<tr>
<td>Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
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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.

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DATE: February 2020
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.

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