How to Diagnose and Manage Acute Limb Ischemia

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  – Arteriocyte, Inc.
  – State of Ohio, Department of Development
  – Third Frontier Commission
Objectives

• Pathology of in-situ thrombosis
• Emphasis on diagnosis and decision making
• General overview of treatment options
• Compartment syndrome
• Amputation
Acute Limb Ischemia

• Sudden and complete blockage of an axial artery in the affected extremity

• The distal tissue beds become ischemic, with energy metabolism shifting from an aerobic to an anaerobic phase

• Progressive ischemia leads to cell dysfunction and death, with nervous tissue, followed by muscle, being most susceptible
Acute Limb Ischemia

- 14 per 100,000
- 10 – 16% of vascular cases
- Men = women
- 10 day hospital stay
- 13% major amputation rate
- 20% mortality
Embolization

- Cardiogenic – 75% of all emboli
  - atrial fibrillation
  - mural thrombus
  - recent cardioversion
  - valvular disease
  - ventricular aneurysm
  - PFO

- Arterioarterial – 25% of all emboli
  - proximal plaque
  - aneurysm
In-situ Thrombosis

- Thrombosis of a chronically diseased vessel
- Hypercoagulable states
Pathology

- Intimal thickening
- Fatty streaks
- Fibrous plaques
- Plaque complication
Plaque Complications

- Necrotic core of lipid, macrophages, and smooth muscle cells
- Calcification
- Endothelial disruption
- Ulceration
- Hemorrhage
- Embolism
Plaque Complication

- Mural Thrombosis is a late event in the atherosclerotic process

- Foam cell rupture leads to exposure of EC to cytotoxic Ox-LDL and EC cell death

- This results in platelet deposition, fibrin formation, and thrombosis

- Atherosclerosis alone rarely causes total occlusion

- Usually plaque rupture occurs resulting in thrombosis and subsequent occlusion
Pathophysiology

- Thromboembolism
  - cardiogenic
  - arterioarterial
  - thrombosis of complicated plaque

- Inadequate tissue perfusion
Collateralization

• Collateralization refers to the formation of multiple arterial pathways that develop around a diseased axial vessel
• Resistance is always higher through collaterals than through axial vessels
• Axial vessel occlusions cause more severe symptoms if collaterals are undeveloped, which is why acute axial vessel occlusions may cause more profound ischemia
Collateralization

- A patient without underlying vascular disease and therefore minimal preexisting collateralization who develops an acute arterial blockage will develop irreversible functional damage within six hours.
History

- Heart disease
  - MI
  - Ventricular aneurysm
  - CHF
  - Arrhythmia
  - Valvular disease
  - Shunt
  - Look at recent cardiac evaluation
History

• Risk factors for pre-existing PAD
  – History of claudication or rest pain prior to ALI
  – DM
  – Smoking
  – Hypertension
  – Hypercholesterolemia
  – Family history of atherosclerotic disease
  – Prior revascularization!
History

• Trauma
• **Dissection!**
  – HTN
  – Connective tissue disorder
  – Chest pain
  – Back pain
Physical Exam

• Complete heart exam
Vascular Exam

• Complete bilateral pulse exam
  – Doppler
    • monophasic
    • multiphasic
  – 0, 1+, 2+, 3+, widened pulses
  – Bruits and thrills
Vascular Exam

- Dependent rubor
- Shiny skin
- Loss of hair
- Diminished nail growth
- Ulceration and gangrene
Neurologic Exam

• Sensation of light touch in toes, forefoot, hindfoot, and leg

• Motor function of toe and ankle plantar and dorsi flexion
  – 0/5
  – 1/5
  – 2/5
  – 3/5
  – 4/5
  – 5/5
Acute Limb Ischemia

• Pain
• Pallor
• Paresthesia
• Paralysis
• Pulselessness
• Poikilothermia
## LIMB ISCHEMIA CATEGORIZATION

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
<th>Neuromuscular Findings</th>
<th>Doppler</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Viable</td>
<td>No sensory or motor loss</td>
<td>Audible arterial and venous</td>
</tr>
<tr>
<td>IIa</td>
<td>Threatened (marginally)</td>
<td>Some sensory loss, no motor loss</td>
<td>Often inaudible arterial, audible venous</td>
</tr>
<tr>
<td>IIb</td>
<td>Threatened (immediately)</td>
<td>Sensory loss and some motor loss</td>
<td>Usually inaudible arterial, audible venous</td>
</tr>
<tr>
<td>III</td>
<td>Irreversible</td>
<td>Paralyzed and insensate</td>
<td>No signals</td>
</tr>
</tbody>
</table>
Acute Limb Ischemia

• **Embolization**
  – no history of claudication
  – profound ischemia
  – irregular rhythm, chest pain, SOB
  – normal contralateral pulses

• **In situ thrombosis**
  – may have a history of claudication
  – milder ischemia
  – absent contralateral pulses
  – trophic changes
  – thrombosis of previous bypass
<table>
<thead>
<tr>
<th></th>
<th>Embolism</th>
<th>In Situ Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
<td>Rapid onset</td>
<td>Vague onset</td>
</tr>
<tr>
<td></td>
<td>Prior cardiac event</td>
<td>No recent cardiac event</td>
</tr>
<tr>
<td></td>
<td>No prior PAD history</td>
<td>History of PAD</td>
</tr>
<tr>
<td><strong>Physical Exam</strong></td>
<td>Cold, mottled, paralyzed</td>
<td>Cool, bluish, paresthesias</td>
</tr>
<tr>
<td></td>
<td>Normal contralateral limb pulse exam</td>
<td>Abnormal contralateral limb pulse exam</td>
</tr>
<tr>
<td></td>
<td>Clear demarcation</td>
<td>No distinct demarcation</td>
</tr>
<tr>
<td><strong>Prior Vascular Surgery</strong></td>
<td>Usually no</td>
<td>Often yes</td>
</tr>
<tr>
<td><strong>Rapid Anticoagulation</strong></td>
<td>Yes—heparin</td>
<td>Yes—heparin</td>
</tr>
<tr>
<td><strong>Most Common Ischemic Class</strong></td>
<td>IIb</td>
<td>IIa</td>
</tr>
</tbody>
</table>
Testing?

• Arterial noninvasives
  – continuous wave doppler
  – duplex ultrasound
• CT angiography
• Catheter angiography is coincident with treatment
Pulse Volume Recording

Pressures

176  Brachial  186

- Ankle/Brachial - 0.83
Index
Treatment

• Heparin
  – Beware of HIT
• Hydration
• Alkalinization of urine
• Osmotic diuresis
• Revascularization
Class I Acute Ischemia

- Acute rest pain
- Often in situ thrombosis of chronic disease
- Elective angiogram
- Plan revascularization
Class Ila Acute Ischemia

- Often in situ thrombosis of chronic disease, but may be embolic
- Admit
- Heparinize
- Urgent angiogram
- Planned revascularization
  - embolectomy
  - thrombolysis
    - in situ thrombosis or thrombosed bypass
    - address causative lesion
  - revascularization with surgery or intervention
Class IIb Acute Ischemia

- Admit
- Heparinize
- Directly to OR
  - embolectomy
  - on table angiogram
    - embolectomy
    - urgent interventional or surgical revascularization
Results of a Prospective Randomized Trial Evaluating Surgery Versus Thrombolysis for Ischemia of the Lower Extremity

The STILE Trial

The STILE Investigators (Appendix A)

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Conclusions
Surgical revascularization of patients with < 6 months of ischemia is more effective and safer than catheter-directed thrombolysis. Although ongoing/recurrent ischemia is greater in the patients undergoing thrombolysis, 30-day clinical outcomes are similar, probably because of cross-over treatment to surgery. There is no difference in efficacy or safety between rt-PA and UK, although bleeding occurs in patients with greater fibrinogen depletion. A significant reduction in planned surgical procedure is observed after thrombolysis. Patients with acute ischemia (0–14 days) who were treated with thrombolysis had improved amputation-free survival and shorter hospital stays. However, for patients with chronic ischemia (> 14 days), surgical revascularization was more effective and safer than thrombolysis. Combining a treatment strategy of catheter-directed thrombolysis for acute limb ischemia with surgical revascularization for chronic limb ischemia offers the best overall results.
A COMPARISON OF RECOMBINANT UROKINASE WITH VASCULAR SURGERY AS INITIAL TREATMENT FOR ACUTE ARTERIAL OCCLUSION OF THE LEGS

Kenneth Ouriel, M.D., Frank J. Veith, M.D., and Arthur A. Sasahara, M.D., for the Thrombolysis or Peripheral Arterial Surgery (TOPAS) Investigators
<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>UROKINASE GROUP</th>
<th>SURGERY GROUP</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of occlusion —</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no./total no. of patients (%)</td>
<td></td>
<td></td>
<td>0.93†</td>
</tr>
<tr>
<td>Native artery</td>
<td>122/272 (45)</td>
<td>120/272 (44)</td>
<td></td>
</tr>
<tr>
<td>Bypass graft</td>
<td>150/272 (55)</td>
<td>152/272 (56)</td>
<td></td>
</tr>
<tr>
<td>Cause of occlusion —</td>
<td></td>
<td></td>
<td>0.71†</td>
</tr>
<tr>
<td>no./total no. of patients (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td>233/270 (86)</td>
<td>231/272 (85)</td>
<td></td>
</tr>
<tr>
<td>Embolism</td>
<td>37/270 (14)</td>
<td>41/272 (15)</td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms —</td>
<td></td>
<td></td>
<td>0.69‡</td>
</tr>
<tr>
<td>before randomization —</td>
<td>4.2±0.23 (272)</td>
<td>4.0±0.23 (272)</td>
<td></td>
</tr>
<tr>
<td>— days (no. of patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location of occlusion —</td>
<td></td>
<td></td>
<td>0.94†</td>
</tr>
<tr>
<td>no./total no. of patients (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axillofemoral</td>
<td>5/270 (2)</td>
<td>5/271 (2)</td>
<td></td>
</tr>
<tr>
<td>Infrainguinal</td>
<td>202/270 (75)</td>
<td>199/271 (73)</td>
<td></td>
</tr>
<tr>
<td>Suprainguinal</td>
<td>63/270 (23)</td>
<td>67/271 (25)</td>
<td></td>
</tr>
<tr>
<td>Length of occlusion —</td>
<td></td>
<td></td>
<td>0.73‡</td>
</tr>
<tr>
<td>cm (no. of patients)</td>
<td>32.4±1.42 (266)</td>
<td>31.7±1.44 (259)</td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 3. OPERATIVE INTERVENTIONS AND WORST OUTCOMES AT SIX MONTHS AND ONE YEAR.*

<table>
<thead>
<tr>
<th>INTERVENTION OR OUTCOME</th>
<th>UROKINASE GROUP (N=272)</th>
<th>SURGERY GROUP (N=272)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 MO 1 YR</td>
<td>6 MO 1 YR</td>
</tr>
<tr>
<td><strong>no. of interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amputation</td>
<td>48 58</td>
<td>41 51</td>
</tr>
<tr>
<td>Above the knee</td>
<td>22 25</td>
<td>19 26</td>
</tr>
<tr>
<td>Below the knee</td>
<td>26 33</td>
<td>22 25</td>
</tr>
<tr>
<td>Open surgical procedures</td>
<td>315 351</td>
<td>551 590</td>
</tr>
<tr>
<td>Major</td>
<td>102 116</td>
<td>177 193</td>
</tr>
<tr>
<td>Moderate</td>
<td>89 98</td>
<td>136 145</td>
</tr>
<tr>
<td>Minor</td>
<td>124 137</td>
<td>238 252</td>
</tr>
<tr>
<td>Percutaneous procedures</td>
<td>128 135</td>
<td>55 70</td>
</tr>
<tr>
<td><strong>% of patients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worst outcome‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>16.0 20.0</td>
<td>12.3 17.0</td>
</tr>
<tr>
<td>Amputation</td>
<td>12.2 15.0</td>
<td>12.9 13.1</td>
</tr>
<tr>
<td>Above the knee</td>
<td>5.6 6.5</td>
<td>6.1 7.5</td>
</tr>
<tr>
<td>Below the knee</td>
<td>6.6 8.5</td>
<td>6.8 5.6</td>
</tr>
<tr>
<td>Open surgical procedures</td>
<td>40.3 39.3</td>
<td>69.0 65.4</td>
</tr>
<tr>
<td>Major</td>
<td>23.6 24.3</td>
<td>39.3 39.3</td>
</tr>
<tr>
<td>Moderate</td>
<td>10.3 8.7</td>
<td>16.3 13.4</td>
</tr>
<tr>
<td>Minor</td>
<td>6.4 6.3</td>
<td>13.4 12.7</td>
</tr>
<tr>
<td>Endovascular procedures</td>
<td>16.9 15.4</td>
<td>2.1 1.7</td>
</tr>
<tr>
<td>Medical treatment alone</td>
<td>14.6 10.3</td>
<td>3.7 2.8</td>
</tr>
</tbody>
</table>

- Major bleeding 12.5% vs. 5.5%
Conclusions  Despite its association with a higher frequency of hemorrhagic complications, intraarterial infusion of urokinase reduced the need for open surgical procedures, with no significantly increased risk of amputation or death. (N Engl J Med 1998;338: 1105-11.)

Our data demonstrate that an initial strategy of thrombolysis, as compared with immediate surgery, reduces the number of open procedures required for acute ischemia of the lower leg and allows some patients to avoid surgical intervention altogether without a significant increase in mortality, the amputation rate, or the duration of hospitalization. The substitution of thrombolysis and closed procedures for open surgery should be attractive to both patients and health care providers. In many instances, thrombolysis can offer patients definitive treatment with less accompanying trauma than major surgery.
Compartment Syndrome

- Reperfusion injury
- Toxic metabolites
- Myoglobinemia and myoglobinuria
- Swelling
- Compromise of capillary perfusion
  - neurologic injury
  - muscle injury
  - skin and subcutaneous injury
Compartment Syndrome

• Anterior compartment – deep peroneal nerve
  – sensory in 1st web space
  – foot extension
• Lateral compartment – superficial peroneal nerve
  – sensory in web spaces 2 – 4
• Deep posterior compartment – posterior tibial nerve
  – sensory in plantar surface
  – toe flexion
• Superficial posterior compartment – sural nerve
  – sensory in lateral foot
  – ankle flexion
Compartment Syndrome

- Hydration
- Alkalination of urine
- Compartment pressures
- Fasciotomy
Class III ALI: Amputation

- Not always a failure!
- Nonambulatory patients with ALI
- Patients with comorbidities precluding revascularization attempts
- Systemic illness from tissue infarction
- Nonfunctional limb
Amputation

- The more distal the amputation, the better the functional outcome
- The more proximal the amputation, the better the likelihood of healing
- Feel for a pulse one level above the proposed amputation
- The skin should be warm and pink at the level of the proposed amputation
- A pressure of 50 mmHg at the level of the proposed amputation predicts healing
Amputation

• Overall mortality
  – BKA  30 day: 6%  3 year: 40%
  – AKA  30 day: 13%  3 year: 60%

• 50% of patients will need contralateral amputation in 3 years