CLI: Revascularization for Limb Salvage
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Disclosures
- Merit Medical Systems – paid consultant
- No off-label use

Outline
- Introduction to peripheral artery disease and critical limb ischemia
- Guidelines for medical treatment of peripheral artery disease
- Guidelines for multidisciplinary treatment of diabetic foot ulcer
- Appropriate indications for CLI revascularization
- Show and tell

Peripheral Artery Disease
- Atherosclerosis of the lower extremities
- Progressive restriction of peripheral blood flow without treatment
- Prevalence: 14.5% of US population over 70

Presentation and Treatment

<table>
<thead>
<tr>
<th>Rutherford Class</th>
<th>1</th>
<th>2,3</th>
<th>4,5,6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Presentation</td>
<td>Asymptomatic</td>
<td>Claudication</td>
<td>Critical Limb Ischemia</td>
</tr>
<tr>
<td>Treatment</td>
<td>Medical</td>
<td>Medical plus Interventional</td>
<td></td>
</tr>
</tbody>
</table>

Critical Limb Ischemia (CLI)
- CLI occurs when tissue perfusion decreases to a critical level
- Unable to support baseline tissue function
- Rutherford Class:
  - 4 = rest pain
  - 5 = minor tissue loss
  - 6 = major tissue loss
- >50% major amputation if no revascularization
Ankle-Brachial Index (ABI)

- The ratio of the higher of the two ankle arterial pressures (dorsalis pedis/posterior tibial) by the higher of the two brachial pressures

<table>
<thead>
<tr>
<th>ABI</th>
<th>Severity</th>
</tr>
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<tbody>
<tr>
<td>&gt; 1.30</td>
<td>Noncompressible</td>
</tr>
<tr>
<td>1.0-1.29</td>
<td>Normal</td>
</tr>
<tr>
<td>0.91-0.99</td>
<td>Borderline</td>
</tr>
<tr>
<td>0.4-0.9</td>
<td>Mild to moderate PAD</td>
</tr>
<tr>
<td>&lt;0.4</td>
<td>Severe PAD</td>
</tr>
</tbody>
</table>

ABI Interpretation

PAD in Diabetic Patients: Cardiovascular Morbidity

- 82% of amputations in the US related to diabetes
- DMA + foot ulcer + PAD = 50% mortality in 5 years
- Cardiovascular risk management
  - Smoking cessation
  - Treatment of hypertension
  - Statin
  - Aspirin or Plavix
  - Glucose control
- Aggressive risk management can reduce AMI and CVA by 50%*

PAD Screening and Diagnosis

- H & P:
  - Claudication or rest pain
  - Absent pulses with palpation
- ABI and TBI with distal Doppler:
  - ABI < 0.9
  - TBI < 0.7
  - Absent or monophasic pedal vessels on Doppler
- But... the utility of these parameters is limited in diabetics!

PAD in Diabetic Ulcer: 2011 Guidelines

- Comprehensive care
- Cardiovascular risk reduction
- Frequent debridement
- Biomechanical offloading
- Blood glucose control
- Treatment of co-morbidities
- Revascularization
- “Diabetic Foot Team”
  - Podiatrist
  - Wound Care
  - Infectious Disease
  - Vascular Specialist
  - Endocrinologist

PAD in Diabetic Ulcer: Treatment Recommendations

- Statin (2013 ACC/AHA Statin Guidelines)
- Antiplatelet agents
- Antihypertensive medications
- Lifestyle modifications
- Smoking cessation
- Exercise
- Diet
- Cilostazol (claudication)
- Revascularization for CLI and severe claudication, when appropriate

**Nicolaides A. Br J Cardiol 2010
Macro vs. Microvascular Theory of Pathogenesis in Diabetes

- Traditional theory: Gangrene due to a combination of microangiopathic PAD and peripheral neuropathy*
- Macrovascular Disease Theory: Large vessel disease more important in producing gangrene
- Multiple studies show improved prognosis when revascularization is added to wound care. Some reject “microvascular disease” completely**


Atherosclerotic PAD Versus Diabetic Macroangioopathy

- SPA stenosis with collateral
- After stents
- Distal occlusions

PAD in Diabetic and Nondiabetic Patients

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>DIABETIC MACROANGIOPATHY</th>
<th>PERIPHERAL ARTERIAL DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation</td>
<td>40-50</td>
<td>50-60</td>
</tr>
<tr>
<td>Sex</td>
<td>No sex prevalence</td>
<td>Male prevalence</td>
</tr>
<tr>
<td>Location</td>
<td>Infrapopliteal</td>
<td>Femoro-popliteal</td>
</tr>
<tr>
<td>Involvement</td>
<td>Multi-vessel, bilateral</td>
<td>Single-vessel, unilateral</td>
</tr>
<tr>
<td>Collateral circulation</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
<tr>
<td>Evolution</td>
<td>Critical limb ischemia</td>
<td>Chronic ischemia</td>
</tr>
<tr>
<td>Clinical symptoms</td>
<td>Reduced/absent Claudication/rest pain</td>
<td></td>
</tr>
<tr>
<td>Trophic lesions/necrosis</td>
<td>Frequent</td>
<td>Infrequent</td>
</tr>
</tbody>
</table>


PAD in Diabetic Ulcer: Risk Assessment with ABI

- If no symptoms, pulses are palpable, ABI > 0.6, toe pressure > 55 mmHg or TcPO2 > 50 mmHg...
- “If the wound healing response is poor, angiography should be strongly considered.”
- ABI <0.6, toe pressure <30 mmHg or TcPO2 <30 mmHg, then wound healing potential is poor
- Refer to vascular specialist

Non-invasive evaluation and probability of healing

CLI Revascularization in Diabetic Patients

- “If PAD of sufficient severity to impair wound healing is identified, revascularization must be considered in all patients.”
- Goal of revascularization: direct pulsatile flow in at least one pedal vessel, preferably to the appropriate angiosome
- “Time is tissue” = the infected ischemic diabetic ulcer is an URGENT problem

Rapid progression of tissue loss
Revascularization: Surgical Bypass

- Long history, refined technique
- 5-year fem-distal vein bypass patency 35-70%
- 5-year PTFE fem-distal bypass patency 15-20%
- Perioperative mortality 2-3%

In situ femoro-popliteal saphenous vein bypass

The First Angioplasty

- Dr. Charles Dotter, Chairman of Radiology, University of Oregon
- January 16, 1964

Elderly woman with digital gangrene

Revascularization: Balloon Angioplasty (PTA)

- Long history, but constantly evolving

Infrapopliteal Angioplasty

Angioplasty balloon

Before PTA

After PTA

Bypass vs. Balloon: The BASIL Trial*

- Randomized trial comparing open surgery vs balloon angioplasty in 452 patients with CLI
- Primary outcome = amputation-free survival
- No difference at 6 months, bypass better after 2 years
- Surgery more expensive
- “Endovascular First”

"Lancet, 2005"

Bypass vs Endovascular First

- Meta-analysis of infrapopliteal angioplasty for chronic limb ischemia


Patency vs Limb Salvage

- The “temporary bypass” concept
- Collateral flow is preserved or enhanced by subintimal angioplasty
- Long-term patency not necessary to maintain tissue integrity follow healing of index wound

Ingle et al. J Endovasc Ther 2002
Reekers et al. J Endovasc Ther 2002
Refining the Goals of Revascularization

- Medical and Endovascular Management of Critical Limb Ischemia

> Sustained (1-year) clinical success significantly better in non-diabetic patients with single intervention (43% vs 22%)
> Significantly improved success (identical to non-diabetics) with repeated intervention (61% vs 56%)
> Delayed revascularization associated with poor outcome
> Outcomes no different between surgical bypass and PTA at one year


Angiosome Model

- First described by Ian Taylor in 1987
- 3D volume of tissue fed by a source artery
- Importance of the angiosome concept for endovascular therapy in patients with critical limb ischemia


CLI in Diabetic Patients: Revascularization Outcomes

- Conventional wisdom: Single straight line flow to the foot is adequate for limb salvage

Paradigm Shift in CLI Revascularization

Direct versus Indirect Revascularization

- Long-term results of direct and indirect endovascular revascularization based on the angiosome concept in patients with CLI presenting with isolated below-the-knee lesions (73% DM)

Iida O, J Vasc Surg 2012
Current Evidence for Angiosomic Model

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Series</th>
<th>Clinical success without AM</th>
<th>Clinical success with AM</th>
<th>P</th>
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<tbody>
<tr>
<td>Neville</td>
<td>2009</td>
<td>Surg</td>
<td>62%</td>
<td>91%</td>
<td>P&lt;0.05</td>
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<tr>
<td>Varela</td>
<td>2010</td>
<td>Surg + Endovasc</td>
<td>73%</td>
<td>92%</td>
<td>P&lt;0.05</td>
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<tr>
<td>Iida</td>
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<td>Endovasc</td>
<td>69%</td>
<td>86%</td>
<td>P&lt;0.05</td>
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<tr>
<td>O’Brien-Irr</td>
<td>2010</td>
<td>Surg</td>
<td>61%</td>
<td>82%</td>
<td>P&lt;0.05</td>
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<tr>
<td>Alexandrescu</td>
<td>2011</td>
<td>Endovasc</td>
<td>67%</td>
<td>86%</td>
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<td>Blanes</td>
<td>2011</td>
<td>Endovasc</td>
<td>73%</td>
<td>79%</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Deguchi</td>
<td>2010</td>
<td>Surg</td>
<td>72%</td>
<td>73%</td>
<td>P&lt;0.05</td>
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Does Amputation Matter?

- 174 patients, 75% diabetic
- 5 year survival after successful bypass = 60%
- 5 year survival after amputation = 26%
- Very poor prognosis: ESRD and amputation

CLI: Improved Outcomes With Multi-vessel Revascularization?

- Results of infrapopliteal endovascular procedures performed in diabetic patients with critical limb ischemia and tissue loss from the perspective of an angiosome-oriented revascularization strategy


Prognosis After Amputation in DM

- 68% of diabetics with limb amputation die within 5 years
- 96% of amputations are because of a foot ulcer


Endovascular Intervention after Failed Lower Extremity Bypass

- 19 TASC Class D infra-inguinal chronic total occlusions
- 63% vein grafts, mean patency 27 months
- Successful endovascular recanalization 95%

Wrigley et al. JVIR 2014

OK, But Do Interventions Really Reduce Amputations?

- Decreased surgical bypasses, increased vascular interventions and significantly decreased number of amputations
CLI Revascularization: The New Dogma

- “No doubt that revascularization improves prognosis, even in the diabetic patient”*
- No pharmacologic therapy ensures limb salvage without revascularization**
- Arterial revascularization should be attempted in any patient with CLI if the 1-year probability of survival and limb salvage >25%^,^^
- Endovascular First

^^Kudo T, J Vasc Surg, 2005

Modern Endovascular Technology and Techniques

- Modern balloons, wires and high-resolution imaging
- Subintimal angioplasty
- Atherectomy
- Stents and stent grafts
- Directional re-entry
- Retrograde tibiopedal access
- Pedal-plantar loop technique

Example: Pedal Angioplasty

Example: Infra-popliteal Atherectomy

Example: Popliteal Atherectomy

Example: Total Endovascular Aorto-iliac Reconstruction
Total Endovascular Aorto-Iliac Reconstruction

Emerging Technologies
- Drug coated stents
- Drug coated balloons
- Gene therapy
- Cell therapy

What's next? The BEST-CLI Trial
- “Best Endovascular vs. Best Surgical Therapy in Patients with Critical Limb Ischemia”
- Prospective randomized multicenter trial
- Two year follow up
- Currently enrolling

www.clinicaltrials.gov

Emerging Technologies: The Balloon as a Drug Delivery Device
- DEFINITIVE AR Trial
  - Directional atherectomy followed by paclitaxel-coated balloon (DAART) vs. paclitaxel-coated balloon alone
  - Primary 1 year patency (lesions ≥ 10 cm)
    - DAART: 90.1%
    - DCB: 68.8%

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CLI Paradigm
- Challenging disease
- Challenging patients
- Follow published guidelines
- It takes a team

Varu V, et al., J Vasc Surg, 2010

Thank you
Hyperbaric Oxygen Therapy for Diabetic Foot Ulcers

  - Systematic review and meta-analysis
  - Improved healing rates of foot ulcers
  - Reduced major lower extremity amputations

  - Longitudinal observational cohort study
  - No improvement in healing rates
  - No reduction in lower extremity amputations
  - "It is entirely likely that HBOT enhances a specific aspect of wound repair and should not be used as a single agent to completely heal a wound."