Of Life and Limb
Best Practices for PAD Management

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Relevant Disclosure and Resolution

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I have no relevant financial relationships or affiliations with commercial interests to disclose.
Rationale for Talk

• Audience will often be first contact for patients with peripheral artery disease (PAD)
• Few diagnoses have a greater impact on patient morbidity and mortality
• PAD is extremely common
• PAD care is frequently suboptimal
  • Opportunity to help patients
Background- The Problem

- 64 yo female presents with right foot wound
- Comorbidities: diabetes, CAD, CKD
- Lifelong smoker
Background- The Problem
What treatment would you recommend?
A. Wound care only
B. Wound care plus surgical bypass
C. Wound care plus endovascular treatment
D. None of the above
Background- The Problem

- Patient received wound care and antibiotics with no “improvement”
- Patient told she has no options for revascularization
- Amputation performed 4 days later
Background and Definitions

- **Peripheral artery disease (PAD)** - atherosclerosis of the lower extremity arteries
- **Claudication** - ischemic muscle pain that occurs during exertion
- **Critical limb ischemia (CLI)** - end-stage form of PAD manifest by rest pain or tissue loss
  - Amputation precursor
In a primary care population defined by age and common risk factors, the prevalence of PAD was approximately one in three patients.

NHANES
Aged >40 years
4.3%

San Diego
Mean age 66 years
11.7%

NHANES
Aged 70 years
14.5%

Rotterdam
Aged >55 years
19.1%

Diehm
Aged 65 years
19.8%

PARTNERS
Aged >70 years, or 50–69 years with a history diabetes or smoking
29%

**Scope of the Problem**

- **Rotterdam Study (ABI <0.9)**
- **San Diego Study (PAD by noninvasive tests)**

![Bar chart showing the percentage of patients with PAD by age group from 55-89 years.](chart.png)

PAD - Who Is At Risk?

Relative Risk

- Smoking
- Diabetes
- Hypertension
- Hypercholesterolemia
- Hyperhomocysteinemia
- C-Reactive Protein

Hirsch et al. Circulation 2006;113;e463-654
PAD - Who Is At Risk?

- Age less than 50 years with diabetes, and one additional risk factor (e.g., smoking, dyslipidemia, hypertension, or hyperhomocysteinemia)
- Age 50 to 69 years and history of smoking or diabetes
- Age 70 years and older
- Leg symptoms with exertion (suggestive of claudication) or ischemic rest pain
- Abnormal lower extremity pulse examination
- Known atherosclerotic coronary, carotid, or renal artery disease

Hirsch et al. *Circulation* 2006;113;e463-654
29% of Patients in a Target Population Were Diagnosed With PAD Using An Office-Based ABI

Hirsch et al. *Circulation* 2006;113;e463-654
PAD Natural History

Limb morbidity

Stable claudication 70%-80%

Worsening claudication 10%-20%

CLI 1%-2%

Cardiovascular morbidity and mortality

Nonfatal cardiovascular events 15%-30%

Mortality 15%-30%

Cardiovascular 75%

Non-CV 25%

Hirsch et al. Circulation 2006;113;e463-654
PAD Natural History

![Graph showing patient survival and complications over time.](image)

Ouriel et al. *Lancet* 2001;358:1257-64
Symptoms at Presentation

- ~15% Typical Claudication
- ~33% Atypical Limb Symptoms
- 1-2% Critical Limb Ischemia
- 50% No Sx

Hirsch et al. *Circulation* 2006;113;e463-654
PAD Diagnosis

• High suspicion needed since typical symptoms at presentation are uncommon
• Combination of physical exam and diagnostic testing is needed
• Identification of PAD can lead to initiation of medical therapy which may improve long-term outcomes
PAD Diagnosis - Physical Exam

- Abnormal pulse exam
- Glabrous skin
- Nail changes
- Temperature changes
- Wounds/tissue loss
- Dependent rubor
# PAD Diagnosis- Physical Exam

<table>
<thead>
<tr>
<th>Variable</th>
<th>LR + (95% CI)</th>
<th>LR – (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claudication</td>
<td>3.30 (2.30-4.80)</td>
<td>-</td>
</tr>
<tr>
<td>Skin changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cool to touch</td>
<td>5.90 (4.10-8.60)</td>
<td>0.92 (0.89-0.95)</td>
</tr>
<tr>
<td>Wounds/sores</td>
<td>5.90 (2.6-13.40)</td>
<td>0.98 (0.97-1.00)</td>
</tr>
<tr>
<td>Discoloration</td>
<td>2.80 (2.40-3.30)</td>
<td>0.74 (0.69-0.79)</td>
</tr>
<tr>
<td>Hair/nail/atrophic changes</td>
<td>1.50 (1.20-1.70)</td>
<td>0.81 (0.72-0.92)</td>
</tr>
<tr>
<td>Bruit</td>
<td>5.60 (4.70-6.70)</td>
<td>0.39 (0.34-0.45)</td>
</tr>
<tr>
<td>Abnormal pulse</td>
<td>4.70 (2.20-9.90)</td>
<td>0.38 (0.23-0.64)</td>
</tr>
</tbody>
</table>

Khan et al. *JAMA* 2006;295:536-46
# PAD Diagnosis- Physical Exam

## Predictability of an Absent Pulse for Peripheral Arterial Disease

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Left leg (n=45)*</th>
<th>Right leg (n=37)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable pulse</td>
<td>37 (82.2%)</td>
<td>25 (67.6%)</td>
</tr>
<tr>
<td>Non-palpable pulse</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.18</td>
<td>0.32</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.99</td>
<td>0.98</td>
</tr>
<tr>
<td>Predictive value positive</td>
<td>0.67</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Collins et al. *Fam Med* 2006;38:38-42
PAD Diagnosis- Noninvasive Testing

- Hemodynamic tests
  - Ankle-brachial index (ABI)
  - Segmental limb pressures
  - Pulse volume recordings (PVRs)
  - Exercise ABIs
- Imaging
  - Duplex ultrasonography
  - CT
  - MRI
Limitations of the Ankle Brachial Index (ABI)

• Vessel calcification in diabetics and renal patients abnormally elevates recorded pressures

• Resting ABI is often normal with proximal PAD (eg iliac stenosis)
  • Exercise needed to elicit ankle pressure reduction

• Subjectivity in pressure measurement
Limitations of Imaging

- Poor definition of tibial vessels
- Overestimation of disease due to calcium
- Need for contrast and radiation
PAD Diagnosis- Take Home Points

• Don’t stop with normal pulses if suspicion is high
• Understand that a normal ABI does not exclude PAD (particularly if tissue loss)
• Consider additional diagnostic testing if diagnosis remains in doubt
  • Correct test is complicated and varies depending on locale
PAD Treatment Goals

- Reduce CV risk
  - Death
  - Myocardial infarction
  - Stroke

- Limb preservation
  - Improve function
    - QOL
    - Walking distance
  - Prevent amputation
Medical Therapy in PAD - The Problem

- Medical therapy is under-prescribed despite the excess cardiovascular risk associated with PAD
- Under-utilization is greater in the PAD population than other forms of cardiovascular disease

Subherwal et al. *Circulation* 2012;126:1345-54
Guideline-Directed Medical Therapy (GDMT)

- Antiplatelets
- Antithrombotics
- Statins
- Exercise Program
- Comorbidity Treatment
- Nicotine Cessation
Antiplatelets

• Aspirin reduces cardiovascular events in patients with coronary and cerebrovascular disease
• The benefits of antiplatelets in patients with PAD are less well established
• Monotherapy with aspirin or clopidogrel is a guideline recommendation
  • Symptomatic patients- Class I, LOE A
  • Asymptomatic patients- Class IIa, LOE C-EO

**Risk Reduction with Aspirin in PAD**

- Meta-analysis of 18 randomized trials involving 5,269 patients with PAD
- Non-significant decrease in events with aspirin compared to placebo (8.9 vs. 11.0%, P=NS)
- Aspirin significantly reduced stroke risk

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Event rate (CI), aspirin vs. placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite of mortality, MI, or stroke</td>
<td>8.2 vs. 9.6% (0.48-1.18)</td>
</tr>
<tr>
<td>Mortality</td>
<td>7.5 vs. 7.9% (0.75-1.22)</td>
</tr>
<tr>
<td>MI</td>
<td>3.3 vs. 4.5% (0.36-2.14)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.1 vs. 3.4% (0.42-0.99)</td>
</tr>
</tbody>
</table>

Berger et al. *JAMA* 2009;301:1909-19
Miscellaneous Therapies - Cilostazol

Rivaroxaban in PAD- COMPASS Results

- 7,470 patients with leg PAD or carotid disease
- Patients randomized to aspirin, rivaroxaban, or combo therapy
- Combo treatment reduced MACE compared to aspirin alone

Adverse limb events reduced with rivaroxaban


<table>
<thead>
<tr>
<th>Prespecified limb outcomes</th>
<th>Low-dose rivaroxaban plus aspirin (n=2492)</th>
<th>Rivaroxaban alone (n=2474)</th>
<th>Aspirin alone (n=2504)</th>
<th>Low-dose rivaroxaban plus aspirin versus aspirin alone</th>
<th>Rivaroxaban alone versus aspirin alone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p value</td>
<td>HR (95% CI)</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>Acute limb ischaemia‡</td>
<td>0.56 (0.32-0.99)</td>
<td>0.042</td>
<td>0.57 (0.32-1.00)</td>
<td>0.046</td>
<td></td>
</tr>
<tr>
<td>Chronic limb ischaemia‡</td>
<td>0.67 (0.35-1.26)</td>
<td>0.21</td>
<td>0.76 (0.41-1.40)</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>Major adverse limb event‡</td>
<td>0.54 (0.35-0.84)</td>
<td>0.0054</td>
<td>0.63 (0.41-0.96)</td>
<td>0.032</td>
<td></td>
</tr>
<tr>
<td>All vascular amputations</td>
<td>0.40 (0.20-0.79)</td>
<td>0.0069</td>
<td>0.61 (0.33-1.11)</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Major amputation‡</td>
<td>0.30 (0.11-0.80)</td>
<td>0.011</td>
<td>0.46 (0.20-1.08)</td>
<td>0.068</td>
<td></td>
</tr>
<tr>
<td>Major adverse limb event plus major amputation§</td>
<td>0.54 (0.35-0.82)</td>
<td>0.0037</td>
<td>0.67 (0.45-1.00)</td>
<td>0.046</td>
<td></td>
</tr>
</tbody>
</table>
Statins Reduce Amputation Risk

Arya et al. Circulation 2018;137:1435-46
Statins

• Statins should be prescribed to all patients with PAD- class I, LOE A
• Statins increase walking distance and physical activity in claudicants
• Statin use is associated with improved patency following lower extremity revascularization
• Statins improve limb salvage rates in patients who have undergone peripheral revascularization
• Statins reduce rates of stroke, myocardial infarction, and death in patients with PAD

Smoking Cessation Programs Work

- 124 smokers with PAD randomized to usual vs. intensive program
- Intensive program included counseling and education on pharmacologic methods

<table>
<thead>
<tr>
<th>Group</th>
<th>Abstinent (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 month follow up</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Minimal</td>
<td>6.8</td>
<td>-</td>
</tr>
<tr>
<td>Intensive</td>
<td>21.3</td>
<td>0.023</td>
</tr>
<tr>
<td>6 month follow up</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Minimal</td>
<td>10.2</td>
<td>-</td>
</tr>
<tr>
<td>Intensive</td>
<td>31.2</td>
<td>0.023</td>
</tr>
</tbody>
</table>

Hennrikus et al. *JACC* 2010;56:2105-12
Exercise Therapy Meta-Analysis

- Exercise prescriptions come in one of two forms
  - Supervised exercise
  - Home-based exercise program
- Randomized trials support both types of programs

![Graph showing change in treadmill walking distance (%)](image)

Onset of claudication pain
- Exercise training:
- Control:

Maximal claudication pain
- Exercise training:
- Control:

Gardner and Poehlman. JAMA 1995;274:975-80
CMS Coverage of Supervised Exercise Programs

- 30-60 min sessions in outpatient hospital or physician office setting
- Coverage of up to 36 sessions over 12 week period
- Sessions must be supervised by qualified personnel (physician, physician assistant, nurse practitioner)
- Exercise prescription must occur after face-to-face visit between patient and provider that includes counseling on cardiovascular disease prevention

Available at CMS.gov, Decision memo for supervised exercise therapy (SET) for symptomatic peripheral artery disease (PAD), accessed February 22, 2018
PAD- Medical Therapy Summary

• Your PAD patients should be on:
  • Antiplatelet (aspirin or alternative)
  • Statin

• Anticoagulant for select patients (eg rivaroxaban)

• Smoking cessation

• Exercise/walking program
PAD Treatment - Revascularization

- Adjunctive therapy in patients who are on medical therapy for PAD
- Indications
  - Claudication - lifestyle limiting symptoms that have persisted despite medical/exercise therapy
  - CLI (rest pain/tissue loss) - limb salvage
PAD Therapy - Revascularization

Clinical Research

Patients With Diabetic Foot Disease Fear Major Lower-Extremity Amputation More Than Death

Dane K. Wukich, MD, Katherine M. Raspovic, DPM, and Natalie C. Suder, MPH

Wukich et al. Foot Ankle Specialist 2018;11:17-21
CLI- Revascularization

• Amputation rates exceed 30% at one year without revascularization
• Revascularization should be employed if feasible
• Under-treatment the norm

Reinecke et al. *Eur Heart J* 2015;36:932-8
CLI - Geographic Variation

Amputation Rates

Revascularization Rates Prior to Amputation

Jones et al. *J Am Coll Cardiol* 2012;60:2230-6
CLI- Endo Example
CLI- Endo Example
CLI- Endo Example
Revascularization- Endo Examples
Impact of Revascularization

lida et al. *JACC Interventions* 2015;8:1493-1502
Revascularization Trends- The Good News

CLI Teams- The New Paradigm

Shishehbor et al. JACC 2016;68:2002-15
CLI Team Example: OU Limb Preservation Clinic

• Mission: amputation prevention, education, CV health promotion
• “Home” for patients with or at risk for PAD
• Expedited diagnostic testing
• Coordination with wound care/ancillary services
• Advanced revascularization techniques when needed
• Communication with referring providers
PAD- Best Practices

- Understand the epidemiology
  - Prevalent condition in diabetics and the elderly
- Diagnose using combination of exam and noninvasive testing
- Apply appropriate medical therapy and lifestyle modifications
- Recognize indications for revascularization
PAD- Best Practices

• Indications for referral to vascular specialists
  • Diagnosis in question
  • Severe symptoms
  • Progressive symptoms on medical treatment
  • Any CLI (rest pain or tissue loss)
  • Vasculopathies
Online Resources

• Save A Life Save a Limb Foundation (SALSAL)
• American Heart Association
• PAD Toolkit (Society for Cardiovascular Angiography and Interventions [SCAI])
Thank You

• OU Medicine Cardiovascular Institute
  Limb Preservation Clinic

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