Joslin Diabetes Center
Primary Care Congress for Cardiometabolic Health 2013
Minimally Invasive Treatments for Vascular Disease: The Era of the Stent

Minimally Invasive Therapies for PAD: Era of The Stent
Joslin Cardiometabolic Congress
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Agenda
- Epidemiology
- Risk Factors
- Prognosis
- Evaluation
  - History
  - Physical
  - Noninvasive
- Medical Therapy
- Endovascular Options
  - Claudication
  - Limb Salvage

Why Should We Be Interested in PAD?
- The major problems with peripheral arterial disease are cardiovascular
  - Those problems are not addressed effectively or on a continuing basis by "procedure types"
  - Atherosclerosis is a systemic disease and internists are facile with secondary prevention of this disorder

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PAD is a common disorder
- Occurs in approximately 1/3 of patients
  - Over age 70
  - Over age 50 who smoke or have DM
- Strong association with CAD
  - Obvious associated risk of stroke, MI, cardiovascular death
- Progressive disease in 25% with progressive intermittent claudication/limb threatening ischemia
- Outcomes
  - Impaired QoL
  - Limb Loss
  - Premature Mortality

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Risk Factors for PAD: Framingham Heart Study

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

Relative Risk

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<th>Risk Factor</th>
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<tr>
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</table>

Mean follow-up 38 years

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Natural History of Atherosclerotic Lower Extremity PAD

PAD Population (50 years and Older)

- Asymptomatic PAD 20%-50%
- Atypical leg pain 40%-50%
- Claudication 10%-35%
- Critical limb ischemia 1%-2%

Initial Assessment: Symptoms

- Intermittent claudication (derived from the Latin word for limp)
  - A reproducible discomfort of a defined group of muscles that is induced by exercise and relieved with rest.
  - Supply ≠ Demand

Natural History of Atherosclerotic Lower Extremity PAD

- Stable claudication 70%-80%
- Worsening claudication 10%-20%
- Critical limb ischemia 1%-2%
- Amputation (see CLI data)
- Nonfatal CV event 20%
- Mortality 15%-30%

CV causes 75%
Non-CV causes 25%


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Location, Location, Location!

- May Occur Singly or in Combination
- Buttock/hip
  - Aortoiliac occlusive disease (Leriche’s syndrome) manifests with, and, in some cases, thigh claudication.
  - Bilateral disease often associated with erectile dysfunction
- Thigh
  - Atherosclerotic occlusion of the common femoral artery may induce claudication in the thigh, calf, or both.
- Calf
  - Cramping in the upper 2/3 of the calf is usually due to SFA
  - Cramping in the lower 1/3 of the calf is due to popliteal disease.

The Presence of Symptoms with PAD Gives Prognostic Information

PAD Differential Diagnosis

- Deep venous thrombosis
- Musculoskeletal disorders
  - Osteoarthritis
  - Restless leg syndrome
- Peripheral neuropathy
- Spinal Stenosis (pseudoclaudication)
  - Pain with erect posture (lordosis) and relief by sitting or lying down.
  - May also find relief by leaning forward and straightening the spine (usually done with pushing a shopping cart or leaning against a wall).

Differential Diagnosis of Intermittent Claudication

The Distinct Syndromes of Severe Ischemia

**Critical Limb Ischemia:** Ischemic rest pain, non-healing wound, or gangrene

**Acute limb ischemia:** The five “P’s, defined by the clinical symptoms and signs that suggest potential limb jeopardy:
- Pain
- Pulselessness
- Pallor
- Paresthesias
- Paralysis (8 polar, as a sixth “p”).

Diagnosis is Limited with History Alone

- As mentioned, use of the history alone to detect peripheral arterial disease will result in missing up to 90 percent of cases.
- Asymptomatic patients with abnormal ABI have 50% increased risk of cardiovascular complications
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Physical Exam

- Record blood pressure in both arms
- Suggest examine carotid, radial, femoral, DP and PT
  - Grade pulse and symmetry
- Feel for abdominal aneurysm
- Exam may miss more than 50%
- Trophic Signs
  - Skin atrophy, thickened nails, hair loss, dependent rubor
  - Ulceration, gangrene

Physical Exam: Elevation and Dependency Test

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<tr>
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<th>Color Return(s)</th>
<th>Venous Filling(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>10</td>
<td>10-15</td>
</tr>
<tr>
<td>Adequate Collaterals</td>
<td>15-25</td>
<td>15-30</td>
</tr>
<tr>
<td>Severe Ischemia</td>
<td>&gt;35</td>
<td>&gt;40</td>
</tr>
</tbody>
</table>


Venous Insufficiency

- Venous ulcers develop slowly.
- Symptoms may include aching, heaviness, cramps, itching, burning, and swelling.
- These symptoms often worsen with prolonged standing and improve with leg elevation
- Venous ulcers represent up to 80% of all ulcers

Venous Ulcer

- Malleolar Area
- Superficial, Shaggy Borders
- Irregular
- Copious Fibrinous Drainage
- Lipodermatosisclerosis, venous stasis dermatitis, and atrophie blanche

Managing Venous Ulcers: 4 E’s

- Moisturizing Skin
- Elevate Feet at Night
- Compression is Mainstay (7 RCTs)
  - Elastic Component Helpful. Put on Immediately in Morning
- If no response with graduated compression hose, refer to specialist for high compression (Unna’s Boot, Multilayer Compression)-Need to exclude significant arterial disease

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Arterial Ulcers

- Located distally over bony prominences
- Dry Base
- Sharp Borders
- Surrounding skin is pale, shiny, without hair

Neuropathic Ulcers

- Site of Repetitive Trauma - sites of shoe pressure
- Abnormal monofilament exam
- Variable depth
- Surrounding callus
- Superimposed infection
- Pulse exam can be normal

Noninvasive Work-up

- The ankle-brachial index is 95% sensitive and 99% specific for PAD
- Establishes the PAD diagnosis
- Identifies a population at high risk of CV ischemic events
- “Population at risk” can be clinically & epidemiologically defined:

Performance of IM Residents in Measuring ABI is Poor

- 4% correctly measured ABI
- 10% correctly calculated ABI
- 45% correctly interpreted ABI

After Educational Intervention

- 50% correctly measured ABI
- 75% correctly calculated ABI
- 88% correctly interpreted ABI

How to Perform ABI

- Patient Supine for 5-10 min
- Continuous Wave Handheld Doppler
- Measure SBP in both arms
  - Higher # is Denominator of ABI
- Measure SBP in DP and PT
  - Higher # is Numerator of ABI

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Ankle Brachial Index

- Cornerstone of vascular evaluation of the lower extremities
- Blood pressure cuffs, Doppler
- Ankle (DP or PT) to brachial artery pressure

- Normal: 0.96
- Claudication: 0.50-0.95
- Rest Pain: 0.21-0.49
- Tissue loss: 0.20
- Significant change: 0.15 or more

Medicare will reimburse for this procedure (CPT 93922), if the ABI is obtained with a Doppler that includes a waveform printout for documentation purposes. Estimated time in office is 3-11 min/patient.

"Normal ABI" is not Necessarily Normal

Risk of All Cause Mortality

Exercise ABI

- Confirms the PAD diagnosis
- Assesses the functional severity of claudication
- May "unmask" PAD when resting the ABI is normal

Why Exercise them if the ABI is "Normal"?

The American Diabetes Association recommends screening for PAD in patients with diabetes

- A screening ABI should be performed in patients with diabetes
  - Those >50 years of age and have other risk factors associated with PAD
    - If normal an exercise test should be carried out
    - The ABI test should be repeated every 5 years

- Those <50 years of age
  - Smoking
  - Hypertension
  - Hyperlipidaemia
  - Duration of diabetes >10 years
  - Foot care is also important in diabetic patients as PAD is a major contributor to diabetic foot problems.
ACC/AHA/ADA Class I Recommendations for ABI

- Exertional leg symptoms
- Non-healing Wounds
- Asymptomatic Patients at high risk
  - ≥70 Years
  - ≥50 years with diabetes or tobacco

USPSTF

- “Screen only if symptoms”
- Rationale is that there is low yield
  - Low prevalence?
- Rx of asymptomatic patients may not improve outcomes
- May lead to unnecessary tests and procedures

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
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<tbody>
<tr>
<td>Ankle-brachial index</td>
<td>50-70</td>
<td>90-100</td>
</tr>
<tr>
<td>Femoral-brachial index</td>
<td>50-70</td>
<td>90-100</td>
</tr>
<tr>
<td>Femoral-femoral index</td>
<td>70-90</td>
<td>90-100</td>
</tr>
</tbody>
</table>

Is this enough?

- Noninvasive lab documents presence and severity of disease
- No comprehensive anatomic information
- No ability to plan interventions

Segmental Pressures

- Pneumatic cuffs at multiple levels
  - Doppler pressure at pedal artery
  - Drop >50 mm Hg between levels
  - Drop >20 mm Hg between limbs
- Reflects status of artery above drop in pressure
- Inaccurate with calcified vessels

Digital Subtraction Angiography (DSA)

- “Gold standard” of arterial imaging
- Compares a pre contrast image with a post contrast image using a computer, and “subtracts” elements common to both.
  - Prevents images of objects like bones etc from obscuring vascular details.

MRA vs. DSA

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MRA of the extremities is useful to diagnose anatomic location and degree of stenosis of PAD.

MRA of the extremities should be performed with a gadolinium enhancement.

MRA of the extremities is useful in selecting patients with lower extremity PAD as candidates for endovascular intervention.

MRA: Current Technique

- 3D gradient echo (fast acquisition)
- Gadolinium Enhanced
  - 20-40 cc
  - Automated Scan delay
- Renal arteries to toes
- Stepping table or bolus chase
- 45-min exam

CTA of the extremities may be considered to diagnose anatomic location and presence of significant stenosis in patients with lower extremity PAD.

CTA of the extremities may be considered as a substitute for MRA for those patients with contraindications to MRA.

Noninvasive Imaging Tests

Magnetic Resonance Angiography (MRA)

Computed Tomographic Angiography (CTA)

Who Doesn’t Need a CT or MRA?

- To make a diagnosis of PAD
  - There are better tests
- No Plan for Revascularization

PAD Summary

- Prevalence is high
  - Particularly in CAD patients
- Risk amputation/bypass is low
- Risk MI or death from other causes high
- History and Physical are important
- ABI is cornerstone
  - Exercise can unmask hidden disease
  - Non-invasive Imaging is well developed
- MRA and CTA can be used for noninvasive anatomic imaging to plan intervention
Medical Treatments for PAD

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking cessation</td>
<td>10-year mortality: 54% to 16% at 7 years, rest pain drops from 16% to 0%*</td>
</tr>
<tr>
<td>Antiplatelet agent</td>
<td>22%; in vascular events, possible increase in walking distance</td>
</tr>
<tr>
<td>Diabetes control</td>
<td>RR=0.94 (0.8 - 1.1) for mortality; RR=0.51 (0.21 - 0.94) for amputation</td>
</tr>
<tr>
<td>BP to &lt;140/85 mm Hg</td>
<td>RR=0.87 (0.81 - 0.94) for mortality, effect on PAD not known</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>RR=0.73 (0.61 - 0.86) for MI, stroke, or CV death</td>
</tr>
<tr>
<td>Exercise program</td>
<td>24% j in CV mortality; 150% further walking distance</td>
</tr>
<tr>
<td>Cholesterol decrease</td>
<td>RR=0.81 (0.72 - 0.87) for MI, stroke, or revascularization; no clinical benefit in PAD†</td>
</tr>
<tr>
<td>Cilostazol</td>
<td>significant ↑ in walking distance</td>
</tr>
</tbody>
</table>

Therapy of PAD

Treatment of IC with Exercise Program

- **Meta Analysis No. 1**
  - 49 publications
  - Statistically significant increase in:
    - Initial claudication distance: 139 meters
    - Absolute claudication distance: 176 meters
  - JAMA. 1995 Sep 27;274(12):975-80

- **Meta Analysis No. 2**
  - 33 publications
  - Statistically significant increase in:
    - Initial claudication distance: 179% (125.9 +/- 57.3 m to 351.2 +/- 188.7 m)
    - Absolute claudication distance: 122% (325.8 +/- 148.1 m to 723.3 +/- 591.5 m)
  - Arch of Intern Med 1999, 159: 337

Principles of a Walking Exercise

- **Structured Treadmill Exercise Program (Supervised)**
  - 3.5 times/week, 30 min sessions
  - Maintain at claudication intensity for 3.5 min, stop when pain is moderate
  - Resume walking until moderate discomfort recurs
  - Repeat cycle, increase by 5 min each session for goal 50-60 min/sessions
  - Continue program for at least 6 months
  - Maintenance program necessary or gains may be lost
  - Stewart K J et al. NEJM 2002; 347 no 24: 1941-51

- **Intermittent Walking Technique (Self-Administered )**
  - Walk until moderate to near maximal claudication pain
  - Rest briefly at severe claudication symptoms
  - May rest in a sitting or standing position
  - Resume walking when claudication symptoms tolerable
  - Repeat these cycles for at least 30-minute sessions, 3-5 times/week

Cilostazol

- Phosphodiesterase III inhibitor
- Inhibits platelet aggregation
- ? Vasodilator
- FDA approved for intermittent claudication
- Contraindicated in patients with CHF
- 516 patients 24 week program

Keys to Therapy of PAD

- Exercise programs are effective
  - Rutherford 1-3
- Progression to amputation is low
- Need for bypass is low
- Options now exist for alternative non-surgical revascularization

Stewart K J et al. NEJM 2002; 347 no 24: 1941-51

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Endovascular Therapy

When Does Someone Need Revascularization?
- Critical Limb Ischemia
- To reduce or avoid tissue loss
- To alleviate pain
- Lifestyle/Medically Limiting Claudication
- Improve Quality of Life
- Allow for increased activity to help manage cardiovascular risk factors

Who Are People with IC Who Do NOT Need a Procedure
- "My legs don’t bother me that much"
- "I get everything done that I want to do"
- "What? I have disease in my legs? I don’t want an amputation! Fix it!"
- "My back is killing me!"

Lower extremity claudication
- Iliac intervention long term patency
- Obviates central aortic procedure
- Infra-inguinal revascularization
- Stenting/angioplasty
- Plaque excision appears durable, reliable and reproducible
- Alternative therapies may be beneficial

Iliac and Renal Intervention
Infra-inguinal Intervention

Limb Salvage
Treatment Summary

- Risk factor modification
  - tobacco cessation
  - diabetic control/wound care
  - lipid/HTN control
- Exercise programs effective
- Endovascular therapy now the norm
  - Claudication: Quality of Life
  - Critical Limb Ischemia: Limb Salvage