Peripheral Arterial Occlusive Disease
Epidemiology

• Intermittant claudication
  – 2-3% of men over age 60
  – 1-2% of women over age 60

• PAD (ABI <0.9) over age 55
  – 17% of Men
  – 21% of Women
IC increases with age
Disease Progression in Claudicants

- 25% of Claudicants will ultimately require revascularization
  - Overall deterioration fastest in 1st year (6-9%) then 2-3% annually thereafter
- 5% will develop critical limb ischemia
- Overall major amputation rate 1-3% at 5 years
PAD is a marker of systemic atherosclerosis

- Cleveland Clinic study of routine heart catheterization prior to peripheral vascular surgery
  - 90% had CAD
  - 28% had severe, 3 vessel CAD
- Carotid ultrasound shows atherosclerosis in 25-50% of patients with PVD
- Over 10 years, overall 4.5x mortality risk for patients with PAD
Risk factors for PAD

• More common in elderly, men
• Smoking is most important modifiable risk factor
  – Smokers have 1.7-5.6x risk of PAD than nonsmokers
  – Smokers have 3x risk of intermittent claudication
  – Amputation more common in smokers (up to 11%)
• Diabetes
  – DM have 1.5-6x prevalence of PAD
  – DM have 2-4x more intermittent claudication
  – DM have 10x risk of amputation
  – However – there is some uncertainty that DM is a causative agent in PAD
Risk factors for PAD

• Hypertension
  – Men with HTN have 2.5x risk of PAD
  – Women with HTN have 4x risk of PAD

• Lipids
  – Total cholesterol/HDL ratio predictive
  – Hs-CRP predictive
<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Estimated Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette smoking</td>
<td>2.0-5.0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3.0-4.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.1-2.2</td>
</tr>
<tr>
<td>Hypercholesterolemia (per 40-50 mg/dl increase in total cholesterol)</td>
<td>1.2-1.4</td>
</tr>
<tr>
<td>Fibrinogen (per 0.7 g/liter increase in fibrinogen)</td>
<td>1.35</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>2.1</td>
</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>2.0-3.2</td>
</tr>
</tbody>
</table>
Framingham data

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Normal</th>
<th>High normal</th>
<th>Stage 1</th>
<th>Stage 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>170</td>
<td>220</td>
<td>240</td>
<td>280</td>
</tr>
<tr>
<td>Diabetes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>CHD</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Incidence of claudication (4-year risk per 100)
Diagnosis – H+P

• History of claudication
  – Pain in muscle groups with exertion
  – Relieved with rest (usually 5-10 minutes) but not positional
  – Claudication variants
    • Pseudoclaudication – neurogenic or muscular, requires positional change for relief
    • *Vasospastic – normal pulses at rest, LE ischemia at exercise with absent pulses; usually there is proximal subcritical disease
    • Venous – congestion with standing or walking, relief with leg elevation
    • Muscular distress – common with myopathies, muscular dystrophy, amyotrophic lateral sclerosis; associated muscular deficits

• Physical exam for pulses and bruits
### TABLE 54-4 Differential Diagnosis of Exertional Leg Pain

<table>
<thead>
<tr>
<th>Vascular causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>Thrombosis</td>
</tr>
<tr>
<td>Embolism</td>
</tr>
<tr>
<td>Vasculitis</td>
</tr>
<tr>
<td>Thromboangiitis obliterans</td>
</tr>
<tr>
<td>Takayasu arteritis</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
</tr>
<tr>
<td>Aortic coarctation</td>
</tr>
<tr>
<td>Fibromuscular dysplasia</td>
</tr>
<tr>
<td>Irradiation</td>
</tr>
<tr>
<td>Extravascular compression</td>
</tr>
<tr>
<td>Arterial entrapment (e.g., popliteal artery entrapment, thoracic outlet syndrome)</td>
</tr>
<tr>
<td>Adventitial cysts</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nonvascular causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbosacral radiculopathy</td>
</tr>
<tr>
<td>Degenerative arthritis</td>
</tr>
<tr>
<td>Spinal stenosis</td>
</tr>
<tr>
<td>Herniated disc</td>
</tr>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>Hips, knees</td>
</tr>
<tr>
<td>Venous insufficiency</td>
</tr>
<tr>
<td>Myositis</td>
</tr>
<tr>
<td>McArdle syndrome</td>
</tr>
</tbody>
</table>
Diagnosis - ABI

- Ankle-Brachial index
  - Most effective non-invasive test for detection of PAD
  - Resting ABI <90%; 95% sensitive, 99% specificity for >=mild PAD
  - Exercise – may bring out >20mm Hg ankle pressure drop if PAD present
  - When ABI >130%, consider vessel incompressibility, toe pressures should be examined
Interpretation of ABI

- In peripheral arteries, significant symptoms arise from 70-90% decrease in cross sectional area
- >20 mm Hg drop between segments is considered significant for lower extremity
  - (>10 mm Hg drop for upper extremity)
- Toe pressures should be >60% of brachial pressure
- Normal ABI – 0.9-1.0
- Claudication – 0.5-0.8
- Critical limb ischemia - <0.5
  - With ABI <0.4, <40% of patients can walk 6 minutes
- Ankle pressure <55 mm Hg predicts poor wound healing
**Interpretation of ABI**

- **> 1.30**: Noncompressible
- **0.91–1.30**: Normal
- **0.41–0.90**: Mild-to-moderate peripheral arterial disease
- **0.00–0.40**: Severe peripheral arterial disease

**Right ABI**
- Higher right-ankle pressure
- Higher arm pressure

**Left ABI**
- Higher left-ankle pressure
- Higher arm pressure

**Right-arm systolic pressure**

**Left-arm systolic pressure**

**Right-ankle systolic pressure**

**Left-ankle systolic pressure**
<table>
<thead>
<tr>
<th>Brachial Artery</th>
<th>Right leg</th>
<th>Left leg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper thigh</td>
<td>160</td>
<td>162</td>
</tr>
<tr>
<td>Lower thigh</td>
<td>110</td>
<td>140</td>
</tr>
<tr>
<td>Calf</td>
<td>108</td>
<td>100</td>
</tr>
<tr>
<td>Ankle</td>
<td>64</td>
<td>78</td>
</tr>
<tr>
<td>Ankle/brachial index</td>
<td>0.42</td>
<td>0.51</td>
</tr>
</tbody>
</table>
Exercise ABI

• Used to enhance detection of PAD
  – When rest ABI is normal with claudication symptoms
• Treadmill – 12% grade, 1.5-2.0 mph
• Dorsiflexion
Pulse Volume Recording

- Records blood volume changes in each segment of limb
  - Resembles arterial pulse
- Typically sharp systolic upstroke, short peak, dicrotic notch, concave down to baseline
- Distal to stenosis – blunted rise, rounded peak, loss of dicrotic notch, slow descent
- Compare segments upstream and contralateral
Diagnosis – Ultrasound and MRA

- **US**
  - May be useful to screen patients for PAD, or assess vasculature for revascularization
  - B-mode ultrasound + doppler
    - Look for rise in velocities to find stenosis
      - 2x increase in velocity = 50% stenosis
      - 3x rise in velocity = 75% stenosis
      - 4x rise in velocity = 90% stenosis

- **MRA**
  - 97% sensitive and 99% specific compared to angiography for detection of PAD
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Diagnosis - Screening

• Broad based screening not cost effective

• Target screening to patients
  – With exertional leg pain
  – >50 years old with risk factors (smoking, DM)
  – With DM >20 years
  – >70 years old
Noninvasive testing - followup

- For patients with stable intermittent claudication who have a deterioration in status, consider angiography.
- Noninvasive studies can be used for periodic followup of grafts or previously intervened segments.
Acute Limb Ischemia

- Worsening limb perfusion, causing a threat to limb viability
- Due to embolization or thrombosis
- Pain, Pulselessness, Pallor, Parasthesia, Paralysis
- 15% 30-day mortality rate
- 10-30% 30-day amputation rate
<table>
<thead>
<tr>
<th>Category</th>
<th>Description/Prognosis</th>
<th>Findings</th>
<th>Doppler Signals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sensory loss</td>
<td>Muscle weakness</td>
</tr>
<tr>
<td>I. Viable</td>
<td>Not immediately threatened</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>II. Threatened</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Marginally</td>
<td>Salvageable if promptly treated</td>
<td>Minimal (toes) or none</td>
<td>None</td>
</tr>
<tr>
<td>b. Immediately</td>
<td>Salvageable with immediate revascularization</td>
<td>More than toes, rest pain</td>
<td>Mild, moderate</td>
</tr>
<tr>
<td>III. Irreversible</td>
<td>Major tissue loss or permanent nerve damage inevitable</td>
<td>Profound, anesthetic</td>
<td>Profound, paralysis (rigor)</td>
</tr>
</tbody>
</table>

Acute limb ischemia

Arterial thromboembolism by initial clinical examination

Heparin unless contraindicated

Class I viable
- Treat as per chronic limb ischemia

Class IIA marginally threatened
- Close monitoring
- Urgent arteriography

Class IIB immediately threatened
- Urgent thromboembolectomy

Class III not viable
- Amputation after demarcation

Endovascular or surgical therapy based on:
- Location of occlusion
- Embolism vs. thrombus
- Duration of ischemia
- Native artery or graft
- Patient related risks
- Intervention related risks
- Contraindications to thrombolysis

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Chronic Critical Limb Ischemia

- Includes ischemic rest pain, ulcers, gangrene, or at risk for major amputation
- Absolute ankle pressure $\leq 50$ mm Hg
- Toe pressure $\leq 30$ mm Hg
Pathophysiology of Microvascular circulation in Critical Ischemia

- Disturbance of normal vasomotion
- Arteriolar constriction?
- Impaired autoregulation

Endothelial swelling
Platelet plugging

High blood viscosity
RBC plugging
Reduced and unevenly distributed flow

PMN plugging
Increased permeability and tissue edema

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<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical description</th>
<th>Grade</th>
<th>Category</th>
<th>Fontaine Clinical description</th>
<th>Rutherford Objective description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>0</td>
<td></td>
<td>Asymptomatic</td>
<td>Normal treadmill test</td>
</tr>
<tr>
<td>IIa</td>
<td>IC,* painfree walking distance &gt;200 m</td>
<td>1</td>
<td></td>
<td>Mild IC</td>
<td>Treadmill exercise limited to 5 min; ankle pressure after exercise &gt;50 mm Hg, but at least 20 mm Hg lower than at rest</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td>Moderate IC</td>
<td>Between Rutherford 2 and 3 disease</td>
</tr>
<tr>
<td>IIb</td>
<td>IC, painfree walking distance &lt;200 m</td>
<td>3</td>
<td></td>
<td>Severe IC</td>
<td>Treadmill exercise limited to &lt;5 min; ankle pressure after exercise &lt;50 mm Hg</td>
</tr>
<tr>
<td>II (complicated)</td>
<td>Lesions without CLI* (ankle pressure &gt;50 mm Hg and/or great toe pressure &gt;30 mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Rest pain</td>
<td>II</td>
<td>4</td>
<td>Rest pain</td>
<td>Ankle pressure &lt;40 mm Hg and/or great toe pressure &lt;30 mm Hg; pulse volume recording barely pulsatile or flat</td>
</tr>
<tr>
<td>IV</td>
<td>Ischemic lesion (ulcer, gangrene, necrosis)</td>
<td>III</td>
<td>5</td>
<td>Limited ischemic lesion</td>
<td>Ankle pressure &lt;60 mm Hg and/or great toe pressure &lt;30 mm Hg; pulse volume recording barely pulsatile or flat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td>Extended ischemic lesion (above metatarsal level)</td>
<td></td>
</tr>
</tbody>
</table>

*IC, intermittent claudication; CLI, critical leg ischemia.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>II</td>
<td>Intermittent claudication</td>
</tr>
<tr>
<td>IIa</td>
<td>Pain-free, claudication walking &gt;200 m</td>
</tr>
<tr>
<td>IIb</td>
<td>Pain-free, claudication walking &lt;200 m</td>
</tr>
<tr>
<td>III</td>
<td>Rest and nocturnal pain</td>
</tr>
<tr>
<td>IV</td>
<td>Necrosis, gangrene</td>
</tr>
</tbody>
</table>

Copyright © 2005 by Elsevier Inc.
<table>
<thead>
<tr>
<th>Grade</th>
<th>Category</th>
<th>Clinical Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>Asymptomatic, not hemodynamically correct</td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>Mild claudication</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate claudication</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe claudication</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Minor tissue loss: nonhealing ulcer, focal gangrene with diffuse pedal ulcer</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>Major tissue loss extending above transmetatarsal level, functional foot no longer salvageable</td>
</tr>
</tbody>
</table>

Treatment

• Address and treat risk factors
• PAD is a CAD equivalent
• Medical management prior to revascularization for claudication
• Revascularization for chronic limb ischemia
• Limb salvage preferable to amputation
Peripheral arterial disease
Management of leg symptoms

Claudication: assess severity
History, questionnaires
Treadmill testing

Claudication therapy:
Supervised exercise
Cilostazol

Symptoms improve
Continue medical management

Symptoms deteriorate

Localize the lesion:
Hemodynamic localization
Duplex ultrasound imaging
Magnetic resonance angiography
Conventional angiography

Revascularization:
Angioplasty
Bypass surgery

Critical leg ischemia
Lifestyle Modification

• Low fat diet
• DM, HTN, HLP control
• Regular exercise (30-40 min/day, 4-5 times/week)
• Smoking cessation
Antiplatelet Therapy

• ASA 75-150mg/d results in 23% relative risk reduction in MI, stroke, CV death
• CAPRIE trial supports use of Plavix over Aspirin for PAD (3.7% vs 4.9% annual risk of major vascular event)
• No data yet to support combination of ASA + Plavix
Adjunctive Agents

• Pentoxifylline not useful, average benefit of 44m of maximal walk distance
• Cilostazol (Pletal) approved for symptom relief, improves walk distance more than ASA or Pentoxifylline
• Prostaglandin I$_2$, E$_1$, and iloprost have shown improvement for severe PAD
  – Not commonly used as no oral form available
Catheter-based revascularization

• Reserved for lifestyle disabling claudication, wounds without adequate arterial supply, or chronic limb ischemia

• Contraindications include abnormal hemostasis, CHF class 4, occlusion of abdominal aorta or calcified occlusions of iliac or femoral arteries (occlusions >10 cm have less favorable outcomes)
Percutaneous treatment

• Acute or Subacute occlusion below inguinal ligament
  – Thrombus aspiration, thrombolytic infusion
  – Angioplasty

• Small trials support use of 2b-3a
Restenosis following catheter intervention

- Iliac arteries – 10-20% over 5 years
- Tibial vessels – 50% over 5 years
- Depends on length of intereved segment
- Most restenosis can be re-intereved
- Radiation therapy delays intimal hyperplasia
- Drug eluting stents being evaluated
Surgical Revascularization

• Rarely indicated for intermittent claudication
• Aortobifemoral bypass uses prosthetic graft
• Venous graft preferred for infrainguinal bypass
• Higher success with more proximal disease
• 25-75% failure rate of femoral-distal grafts
Antithrombotic Therapy

• Data supports use of antiplatelet therapy (ASA) following vein or prosthetic graft
• ASA should be started preoperatively
• Coumadin better at preserving patency of vein grafts; ASA better for prosthetic grafts
• However, coumadin reserved for patients at risk for graft failure
  – Femoral-distal bypass graft
  – Marginal quality vein
  – Poor arterial runoff
  – Previously failed bypass graft