Diagnosis and Management of Chronic Lower Extremity PAD

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Opening Statement

• Surgical bypass for limb-threatening ischemia and conservative management for less severe ischemia have been the accepted standard of care for 5 decades

• “Paradigm Shift” (mid-1990’s) - movement away from conservative therapy to one of active intervention for all levels of PAD, driven by cardiologists…

• Despite continued advances in techniques, innovative new technologies and improved collaboration between specialist, critical limb ischemia too often leads to limb loss…or does it?
Patients with one manifestation often have coexistent disease in other vascular beds

Coronary Artery Disease

Cerebrovascular Disease

Peripheral Arterial Disease

38% overlap ≥2 vascular beds

Atherosclerosis Epidemiology

- PAD affects >20 million Americans
- Prevalence 3-10% (increases with age)

NHANES study - ABI < 0.9
- Age 50-59, 1-2% PAD
- Age 60-69, 7% PAD
- Age 70-79, 14.5% PAD
- Age >80, 23.5% PAD

- 3 ax:1 sx PAD ratio
Natural History of PAD

5-year outcomes

Limb morbidity

Stable claudication 70%-80%
Worsening claudication 10%-20%
Critical limb ischemia 1%-2%
Amputation 25%

CV morbidity & mortality

Nonfatal cardiovascular Event (MI or stroke) 20%
Mortality 15%-30%
CV causes 75%
Non-CV causes 25%

Natural History of PAD

• Local Extremity Symptoms:
  ➢ (in pts with IC, 5-year outcomes)
    – 65% will experience no progression of local limb symptoms
    – 25% will demonstrate progression of claudication symptoms
    – 10% will require some form of operative or interventional revascularization or experience limb loss
### Table 2. Classification of Peripheral Arterial Disease: Fontaine’s Stages and Rutherford’s Categories

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical</th>
<th>Fontaine</th>
<th>Rutherford</th>
<th>Category</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>0</td>
<td>0</td>
<td></td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication</td>
<td>I</td>
<td>1</td>
<td>Moderate</td>
<td>Mild claudication</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate-severe claudication</td>
<td>I</td>
<td>2</td>
<td>Moderate</td>
<td>Moderate claudication</td>
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<tr>
<td></td>
<td></td>
<td>I</td>
<td>3</td>
<td>Severe</td>
<td>Severe claudication</td>
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<tr>
<td>III</td>
<td>Ischemic rest pain</td>
<td>II</td>
<td>4</td>
<td></td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or gangrene</td>
<td>III</td>
<td>5</td>
<td>Minor</td>
<td>Minor tissue loss</td>
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<tr>
<td></td>
<td></td>
<td>IV</td>
<td>6</td>
<td>Ulceration or gangrene</td>
<td></td>
</tr>
</tbody>
</table>
Quiz #1: Define the origin of these wounds
Guidelines-Critical Limb Ischemia

**CLI Definition-**

- Persistent ischemic rest pain
- Opiate analgesics for >14 days
- Ulceration or gangrene
- ABI <0.4
- Toe pressure <30 mmHg
- Systolic ankle pressure <50mmHg
- Flat PVRs
- Absent distal pulses
Lower Extremity Ischemia Pathology

1) Atherosclerosis
2) Embolic
3) Arteritis
4) Hypercoagulable State
5) Trauma
6) Popliteal Artery Entrapment Syndrome
7) Adventitial Cystic Disease
8) Aneurysm
9) Exercise induced comp syndrome
10) Buerger’s Disease
Risk Factors for PAD

- Age >55:
  - 1.5-2.0x inc. per 10 yrs.

- Diabetes:
  - 3x inc. (higher Hgb A1c>7)

- Smoking: 10-20x inc.,
  - risk to baseline 2-5 yrs.

- Hyperlipidemia:
  - 5-10x inc.

- HTN:
  - 2-5x inc.

- Homocysteine:
  - 2-4x inc.

- Obesity & Sedentary Life style:
  - ?
Outcome from childhood obesity?

What is most likely to happen by age 50?

a) amputation 
b) AMI/stroke 
c) rest pain 
d) death 
e) claudication
Natural History of PAD

5-year outcomes

Limb morbidity
- Stable claudication: 70%-80%
- Worsening claudication: 10%-20%
- Critical limb ischemia: 1%-2%
  - Amputation: 25%

CV morbidity & mortality
- Nonfatal cardiovascular event (MI or stroke): 20%
  - CV causes: 75%
  - Non-CV causes: 25%
- Mortality: 15%-30%
  - CV causes: 75%
  - Non-CV causes: 25%

• Systemic Symptoms (in pts with IC, 5-year outcome)
  – 30% all cause mortality (a 2.5 fold increase when compared to aged matched general population)
  – 20% will experience a non-fatal myocardial infarct or a cerebrovascular event

• Asymptomatic patients with PAD (defined by ABI<0.9) have nearly the same risk of death and cardiovascular events when compared to symptomatic patients

Annual mortality was higher among patients with PAD than patients with MI.
Quiz #2: The joys of wound care ????

UPMC Heart and Vascular Institute
Ankle-Brachial Index

- Objective quantitative data
- Quick, cost effective, accurate & highly reproducible
- 95% sensitive and 99% specific for PAD

Clinically useful:
1) Identifies patients with PAD
2) Major indicator of premature MI, CVA and mortality
3) Predicts limb survival and wound healing
Interpretation and Limitations of ABI

Main limitations:

- Medial calcification of tibial vessels results in falsely elevated ABI (DM, CRF)
- Normal ABI found in patients with aorto-iliac disease
- Doesn’t discriminate level of disease

ABI Interpretation:

- 0.90-1.20- normal
- 0.71-0.90- mild PAD
- 0.41-0.70- moderate PAD
- 0.00-0.40- severe PAD

* TBI- normal >0.7
Natural History of CLI - Level of Disease

Proximal lesions have a 2.5-3.5x increased risk of mortality
Quiz #3: Type of Ulceration?

- 4 layer compression wrap
- Topical steroids
- Elevation
- Antibiotics
**PAD Management Strategies**

- **Preventing Death**
  - Smoking cessation
  - Antiplatelet agents
  - Cholesterol lowering: “statins”
  - Diabetes: optimize glucose control
  - ACE inhibitors

- **Reducing Symptoms**
  - Exercise
  - Pharmacologic therapy: cilostazol/pentoxifylline
  - Surgical/endovascular intervention

- **Saving Limbs**
  - Percutaneous revascularization
  - Surgical revascularization
PAD Management Strategies: A Partnership with All Care Providers

- PCP, radiology, endocrine, podiatry, PT, ortho, general surgery, cardiology, etc.
- The risk of limb loss is much less than the risk of mortality this provides the rationale for global vascular care.
- Global care must be the best medical care for atherosclerotic disease involving all vascular beds in addition to local care.
- This care should encompass both aggressive risk factor modification and antiplatelet therapy.
## PAD Management Strategies

### Treatment of Symptoms

**Objective**
- Reduce symptoms in patients to increase mobility, exercise tolerance, and functional capacity

**Exercise**

**Pharmacologic therapy**
- Cilostazol
- Statins
- Ace Inhibitors

**New Horizons-Gene Therapy**

**Selective use of interventional therapy**

### Risk Reduction of Atherothrombotic Events

**Objective**
- Reduce the risk of atherothrombotic events

**Control of risk factors**
- Smoking
- Hyperlipidemia
- Hypertension
- Diabetes

**Antiplatelet therapy**
- ASA
- Clopidogrel bisulfate

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ACC/AHA PAD Guidelines Recommend CV Risk Reduction and Symptom Relief

<table>
<thead>
<tr>
<th>CV Risk Reduction</th>
<th>Treatment for Claudication*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendations</strong></td>
<td><strong>Evidence Basis</strong></td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>I A</td>
</tr>
<tr>
<td>Antihypertensive therapy</td>
<td>I A</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>I B</td>
</tr>
<tr>
<td>Statin therapy</td>
<td>I B</td>
</tr>
<tr>
<td>Glucose control therapy</td>
<td>Ila C</td>
</tr>
</tbody>
</table>

Smoking Cessation

- Results in improved ankle pressure and exercise tolerance in patients with IC as early as 10 months after cessation.¹
- Results in reduced cardiac death and cerebral vascular event rate

Treatment Options
- Behavioral modification with regular counseling
- Bupropion Hydrochloride
- Nicotine Supplements (gum, transdermal, nasal spray…all work the same and are safe)
- Combination therapy Bupropion+Nicotine Supplement
- Chantix
- Long-term success rates are poor!

¹Quick et al. Br J Surg 1982;69 (suppl.):S24-26
Treatment of Symptoms
Exercise Therapy

– Regular aerobic exercise reduces cardiovascular risk (lowers cholesterol and BP) and produces symptomatic improvement in patients with PAD.

– Mechanisms:
  • Improved endothelial vasodilator function
  • Improved skeletal muscle metabolism
  • Decreased blood viscosity
  • Improved oxygen extraction
Treatment of Symptoms
Exercise Therapy

  - Metaanalysis of randomized trials of exercise in patients with intermittent claudication:
    - 180% improvement in pain free walking time
    - 150% improvement in maximal walking time
- Supervised exercise therapy is the most effective symptomatic therapy for patient with IC
  - Limitations
    - Lack of patient motivation
    - Lack of long term compliance
    - Lack of reimbursement for supervision
Treatment of Symptoms
Diet & Exercise Therapy

• For LDL lowering and BP lowering
  – Diet emphasizing: vegetables, fruits, whole grains, Includes low-fat dairy, poultry, fish, legumes, non-tropical vegetable oils and nuts
  – Limit intake of sweets, sugar-sweetened beverages, red meats
    • 5-6% of calories from saturated fats
    • Limit sodium to < 2400Mg daily
• Engage in physical activity 3-4 sessions/wk lasting 40 min with moderate to vigorous intensity
Treatment of Symptoms and Risk Reduction
Pharmacotherapy

• Statins
  – Lipid modification has been associated with stabilization and even regression of femoral atherosclerosis\(^1\)
  – Simvastatin and atorvastatin have been shown to increase pain free walking distance\(^2\)
  – Lowering the total cholesterol and LDL by 25% reduces cardiovascular mortality and morbidity in patients with PAD by 25% irrespective of patient age, sex or baseline cholesterol concentration\(^3\)

• Treat with maximum tolerated statin intensity in groups shown to benefit:
• Therefore: the panel makes no recommendation for or against specific LDL-C or non-HDL-C targets for primary or secondary prevention
• Hypertension
  – No studies are available which evaluate whether antihypertensive therapy directly alters progression of symptomatic PAD or alters the incidence of PAD
  – Well established that BP control (<140/90mmHg) results in a reduction in cardiovascular events in patients with PAD.
  – ACE therapy has been associated with improvements in both pain free walking distance and maximal walking distance as well as modest improvement in the ABI\(^1\)
  – Recommended target blood pressure in patients with PAD is <140/90mmHg.

\(^1\)Roberts et al. Lancet 1987;ii:650-653
Figure. 2014 Hypertension Guideline Management Algorithm

1. Adult aged ≥18 years with hypertension
2. Implement lifestyle interventions (continue throughout management).
3. Set blood pressure goal and initiate blood pressure lowering-medication based on age, diabetes, and chronic kidney disease (CKD).

General population (no diabetes or CKD) vs. Diabetes or CKD present

- Age ≥60 years
  - Blood pressure goal
    - SBP < 150 mm Hg
    - DBP < 90 mm Hg
- Age <60 years
  - Blood pressure goal
    - SBP < 140 mm Hg
    - DBP < 90 mm Hg
- All ages
  - Diabetes present
    - Blood pressure goal
      - SBP < 140 mm Hg
      - DBP < 90 mm Hg
  - No CKD
  - Blood pressure goal
    - SBP < 140 mm Hg
    - DBP < 90 mm Hg

- All ages
  - CKD present with or without diabetes
  - Blood pressure goal
    - SBP < 140 mm Hg
    - DBP < 90 mm Hg

Nonblack vs. Black vs. All races

- Initiate thiazide-type diuretic or ACEI or ARB or CCB, alone or in combination.
- Initiate thiazide-type diuretic or CCB, alone or in combination.
- Initiate ACEI or ARB, alone or in combination with other drug class.

JNC VIII guidelines (JAMA 2014;311:507-520)
• Diabetes Control
  – No prospective data looking at diabetes control in patients with PAD exists.
  – Intensive blood sugar control prevents the micro-vascular effects of diabetes but it is unknown whether this benefits the macro circulation.
  – HbA1c <7% has been established to reduce the risk of cardiovascular events by > 40%.
    • For each 1% increase in HbA1c a 28% increase in the incidence of PAD is noted.
    • Tight glycemic control is recommended with a target HbA1c level < 7 in all patients with PAD.

Diabetes Control and Complications Trial (DCCT):

Cumulative Incidence of the First of Any of the Predefined Cardiovascular Disease Outcomes

HgA1c
9.1
7.4
• **Antiplatelet Agents**
  – An underlying prothrombotic state exists in patients with PAD.\(^1\)
  – Recommended to prevent associated cardiovascular morbidity and mortality, have no utility with regard to symptoms of IC.
  – Antithrombotic Trialists’ Collaboration
    • In over 9000 patients with PAD, those on antiplatelet agents (ASA, ticlodipine, dipyridamole), demonstrated a 23% reduction in cardiovascular events\(^2\)

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• Antiplatelet Agents

• Clopidogrel (Plavix)
  – CAPRIE Trial (19,000 patients)
    • Clopidogrel vs ASA randomized trial
    • Clopidogrel was associated with a significant reduction in the rate of MI, ischemic stroke and vascular death (8.7% benefit) compared to ASA.
    • The PAD subgroup (6,400 patients) within this trial experience a 25% relative risk reduction in cerebrovascular event.
  – Clopidogrel is the only antiplatelet agent approved by the FDA specifically for the reduction of cardiovascular events in patients with PAD.
Antithrombotic Trialists’ Collaboration:
MI, Stroke, CV Death in Patients With PAD

<table>
<thead>
<tr>
<th>Category</th>
<th>APT</th>
<th>CTRL</th>
<th>Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent claudication</td>
<td>6.4%</td>
<td>7.9%</td>
<td>23±9</td>
</tr>
<tr>
<td>Peripheral artery bypass graft</td>
<td>5.4%</td>
<td>6.5%</td>
<td>22±16</td>
</tr>
<tr>
<td>Peripheral angioplasty</td>
<td>2.5%</td>
<td>3.6%</td>
<td>29±35</td>
</tr>
<tr>
<td>All high-risk patients</td>
<td></td>
<td></td>
<td>22±2 (P&lt;.001)</td>
</tr>
</tbody>
</table>

From Antithrombotic Trialists' Collaboration. *BMJ. 2002;324:71-86*
Treatment of Symptoms
Pharmacotherapy

• Cilostazol
  – Phosphodiesterase Inhibitor
  – Mechanisms:
    • Antiplatelet agent
    • Promotes vasodilation
    • Increases HDL
    • True mechanism is unknown
    • Cilostazol increased pain free and maximal walking distance by 40-70% and 65-83%, respectively after 12-24 weeks (100mg po bid)
    • Prospective randomized trial comparing cilostazol with pentoxifylline and placebo, cilostazol treated patients had a significantly improved walking distance compared to the other 2 groups
Summary PAD Management Strategy

• Life Style Modifications
  ➢ ≥40 minutes moderate-to-vigorous intensity physical activity 3 x a week
  ➢ Weight maintenance/reduction
  ➢ Low cholesterol diet
• Smoking
  ➢ Complete cessation
• Diabetes mellitus
  ➢ HbA1c <7%, treat other risk factors
• Dyslipidemia
  ➢ High-intensity statin therapy
• Hypertension
  ➢ BP <140/90
• ACE Inhibitors
• Antiplatelet therapy (aspirin or clopidogrel)
Interventional Techniques
Peripheral Vascular Disease

Treatment - Minimally Invasive Techniques

- Guidewire placement
Peripheral Vascular Disease

Treatment - Minimally Invasive Techniques

- Guidewire advanced past lesion
Peripheral Vascular Disease

Treatment - Minimally Invasive Techniques

- Balloon dilatation
- Percutaneous Transluminal Angioplasty
Peripheral Vascular Disease

Treatment - Minimally Invasive Techniques

- Stent expansion by a balloon catheter over a guidewire
Peripheral Vascular Disease

Treatment - Minimally Invasive Techniques

- Thrombolysis
- Post-thrombolytic infusion revealing stenosis
Peripheral Vascular Disease

Aorto/Iliac Disease
Peripheral Vascular Disease

Aorto/Iliac Disease
Peripheral Vascular Disease

Aorto/Iliac Disease
Peripheral Vascular Disease

Aorto/Iliac Disease
Peripheral Vascular Disease

Aorto/Iliac Disease
Peripheral Vascular Disease

Aorto/Iliac Disease - Pre & Post PTA/Stent
Peripheral Vascular Disease

Subclavian Disease
Peripheral Vascular Disease

Subclavian Disease
Peripheral Vascular Disease

Subclavian Disease - Pre & Post PTA
Introduction

- Femoropopliteal occlusive disease may contribute to disabling symptoms
- Endovascular intervention is now considered first-line therapy for short segment superficial femoral artery (SFA) occlusive disease
- Reported primary patency rates following SFA angioplasty and stenting range from 56-87% at one year
Endovascular Treatment

• While endovascular treatment has benefits over surgical treatment, attempted recanalization fails in up to 10% of cases due to difficulty in reliably crossing and gaining re-entry using standard catheters and guidewires.
Adjunctive Tools

Laser

Frontrunner

Re entry devices

UPMC Heart and Vascular Institute
Technique

• Contralateral Approach is best for treatment of SFA disease
  – Allows for adequate assessment of inflow disease
  – Allows for easy access to the SFA origin
  – Less likelihood of access site related complications
Technique

- Position long sheath in “over the top” fashion with distal tip within the contra lateral CFA
- Anticoagulation should be initiated (ACT 200-250)
- Select SFA with glide wire and supportive catheter
  - Stenotic non-occlusive lesions best to stay within the flow lumen
  - Occlusions are best crossed in the subintimal plane with “looped wire” technique
Technique

- Looped wire usually re-enters true lumen in disease free segment (85%)
- Device position can always be confirmed with sheath injections
- Failure to re-enter true lumen is overcome with re-entry devices (Outback LTD or Pioneer)
- After re-entry established exchange for working wire for angioplasty
Technique

• Appropriately size balloons for PTA
  – aggressive oversizing can lead to flow limiting dissections and vessel rupture

• At least nominal inflation pressures for 1-2 minutes produces optimal results

• Stenting is indicated if post PTA:
  – > 30 % residual stenosis exists
  – Flow limiting dissection is identified
Technique

- Nitinol stents should be chosen
- Stents should be oversized approx. 1mm but dilated to the true lumen size of the vessel
- Stents should be placed to cover the entire length of the diseased segment
- Utilization of stent grafts should be limited to cases of recurrent in stent stenosis, recurrent vessel occlusion or vessel rupture
Simple SFA TASC II A

Flow Lumen

PTAS
Simple SFA

Flow Lumen

Post PTA

er in l...
Complicated SFA
Complicated SFA

Position image intensifier to show OUTBACK® LTD Re-Entry Catheter adjacent to true lumen.

Point "L" marker toward the true lumen by turning the proximal rotating hub (rotating hemostasis valve - RHV).
Simple Iliac

Stenosis

Po

Post PTAS
Complications

- Access site
- Vessel perforation
- Vessel rupture
- AV fistula
- Distal embolization
- Acute occlusion
- Stent fracture
- Restenosis
Complications

Type 3 Stent Fracture

Total Occlusion
Summary

- PAD effects between 8-12 million people in the United States
- PAD patients have a 2.5 fold risk of annual mortality when compared to age matched general population
- A dual treatment strategy should be employed addressing both the symptoms of PAD as well as risk factor modification to prevent cardiovascular mortality and morbidity
- BEST CLI- ongoing NIH funded study