Atherosclerosis and Peripheral Arterial Disease

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Disclosures

• No financial disclosures
• Sub-Investigator for BEST-CLI and ANGES trials
Objectives

• Review the pathophysiology of atherosclerosis
• Discuss specific risk factors and epidemiology for lower extremity peripheral arterial disease
• Discuss presentation of patients with peripheral arterial disease
• Compare different forms of evaluation and work up for peripheral arterial disease
• Discuss and compare potential interventions-open surgical and endovascular
Introduction

• Definition: thickening of the arterial wall as a result of accumulation of fatty materials

• Greek roots:
  • Athere=gruel
  • skleros=hard
**Initial lesion**
- histologically “normal”
- macrophage infiltration
- isolated foam cells

**Fatty streak**
- mainly intracellular lipid accumulation

**Intermediate lesion**
- intracellular lipid accumulation
- small extracellular lipid pools

**Atheroma**
- intracellular lipid accumulation
- core of extracellular lipid

**Fibroatheroma**
- single or multiple lipid cores
- fibrotic/calcific layers

**Complicated lesion**
- surface defect
- hematoma-hemorrhage
- thrombosis
Risk Factors

• Modifiable risk factors
  • Nicotine use (i.e., Tobacco smoking, chewing)
  • Diet (contributing to hyperlipidimia)
  • Hypertension
  • Diabetes
  • Sedentary life style
  • Elevated CRP
  • Hyperhomocysteinemia

• Non modifiable risk factors
  • Age
  • Gender
  • Family history
Relative Risk

- Smoking
- Diabetes
- Hypertension
- Hypercholesterolemia
- Hyperhomocysteinemia
- C-Reactive protein
Prevalence

![Bar chart showing PAD prevalence by age group and gender.](chart.png)
Symptoms

• Asymptomatic
• Intermittent claudication
  • Latin: claudicare “to limp” from clouds “lame”
  • Reproducible, exercise-induced lower extremity pain that is relieved at rest
• Ischemic rest pain
• Tissue loss
  • Minor and major
Symptoms Based on Location of Disease

- Aorto-iliac disease
  - Hip, thigh, buttock claudication
  - Erectile dysfunction
  - Can have calf claudication
- Femoropopliteal Disease
  - Calf and foot claudication
## Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical</th>
<th>FONTAINE</th>
<th></th>
<th>RUTHERFORD</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>0</td>
<td>0</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication</td>
<td>I</td>
<td>1</td>
<td>Mild claudication</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate–severe claudication</td>
<td>I</td>
<td>2</td>
<td>Moderate claudication</td>
</tr>
<tr>
<td></td>
<td></td>
<td>I</td>
<td>3</td>
<td>Severe claudication</td>
</tr>
<tr>
<td>III</td>
<td>Ischemic rest pain</td>
<td>II</td>
<td>4</td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or gangrene</td>
<td>III</td>
<td>5</td>
<td>Minor tissue loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV</td>
<td>6</td>
<td>Ulceration or gangrene</td>
</tr>
</tbody>
</table>

*Image Source: Carondelet Heart & Vascular Institute. Be well.*
Evaluation

- Non-invasive
  - ABI’s-Pre & Post exercise
  - Pulse Volume Recording (PVR)/Segmental pressures
  - Arterial duplex
  - MRA
  - CTA
- Invasive
  - Contrast angiography
ABI’s

• Ratio of ankle to brachial systolic blood pressure

• Can be limited by medial calcification, significant peripheral edema

• Post-exercise ABI’s in patients with suspicion for claudication to confirm diagnosis
ABI Interpretation

- >1.4: Falsely elevated
- 0.95-1.39: Normal
- 0.75-0.94: Mild arterial insufficiency
- 0.50-0.74: Moderate arterial insufficiency
- <0.50: Severe arterial insufficiency
PVR/Segmental Pressures

- Helps to identify levels of disease
- Compare to proximal segments and contralateral leg
- Technician dependent
- Some limitation with calcified arteries
Arterial Duplex

- Helps to specifically identify location of lesions
- Very technician dependent
- Can be limited by calcification
- Monitor post procedure (surgical or endovascular)
Arterial Duplex
# Arterial Duplex

<table>
<thead>
<tr>
<th>PSV*</th>
<th>Stenosis Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triphasic &lt;100 cm/s</td>
<td>Normal</td>
</tr>
<tr>
<td>&gt;30% increase in PSV</td>
<td>20% to 49%</td>
</tr>
<tr>
<td>Doubling of PSV( greater than 100% relative to the adjacent proximal segment and reduced systolic velocity distal to the stenosis)</td>
<td>50% to 99%</td>
</tr>
<tr>
<td>No Doppler flow in artery</td>
<td>Occluded</td>
</tr>
</tbody>
</table>
MRA

- Tool for patients with renal dysfunction
- Not as limited by heavily calcified lesions
- Time consuming
- Claustrophobia
CTA

- Good evaluation of disease from aorta to popliteal arteries
- Tibial evaluation can be limited especially in calcified tibial
- Less expensive, quicker
- Exposure to contrast and radiation
Contrast Angiography

- Best identifies extent and location of disease
- Can often treat at the same time of the diagnosis
- Invasive
- Iodine based contrast used—can use CO2
- Subjects patient, physician and personnel to radiation
## Recommendations: Diagnosis of Peripheral Arterial Disease

<table>
<thead>
<tr>
<th></th>
<th>Grade</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1. We recommend using the ABI as the first-line noninvasive test to establish a diagnosis of PAD in individuals with symptoms or signs suggestive of disease. When the ABI is borderline or normal (&gt;0.9) and symptoms of claudication are suggestive, we recommend an exercise ABI.</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>2.2. We suggest against routine screening for lower extremity PAD in the absence of risk factors, history, signs, or symptoms of PAD.</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>2.3. For asymptomatic individuals who are at elevated risk, such as those aged &gt;70, smokers, diabetic patients, those with an abnormal pulse examination, or other established cardiovascular disease, screening for lower extremity PAD is reasonable if used to improve risk stratification, preventive care, and medical management.</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>2.4. In symptomatic patients who are being considered for revascularization, we suggest using physiologic noninvasive studies, such as segmental pressures and pulse volume recordings, to aid in the quantification of arterial insufficiency and help localize the level of obstruction.</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>2.5. In symptomatic patients in whom revascularization treatment is being considered, we recommend anatomic imaging studies, such as arterial duplex ultrasound, CTA, MRA, and contrast arteriography.</td>
<td>1</td>
<td>B</td>
</tr>
</tbody>
</table>

ABI, Ankle-brachial index; CTA, computed tomography angiography; MRA, magnetic resonance angiography.
Indications for Treatment

- All patients, regardless of symptoms must be medically maximized
- Rutherford 0-3
- Rutherford 4-6
Medical Management of PAD

- Smoking cessation
- Antiplatelets
- Statins
- Diabetes
- Hypertension
- Hyperhomocysteinemia?

Society for Vascular Surgery Lower Extremity Guidelines Writing Group: Michael S. Conte, MD, (Co-Chair),a Frank B. Pomposelli, MD, (Co-Chair),b Daniel G. Clair, MD,c Patrick J. Geraghty, MD,d James F. McKinsey, MD,e Joseph L. Mills, MD,f Gregory L. Moneta, MD,g M. Hassan Murad, MD,h Richard J. Powell, MD,i Amy B. Reed, MD,j Andres Schanzer, MD,k and Anton N. Sidawy, MD, MPH,l San Francisco, Calif; Boston and Worcester, Mass; Cleveland, Ohio; St. Louis, Mo; New York, NY; Tucson, Ariz; Portland, Ore; Rochester, Minn; Lebanon, NH; Hershey, Pa; and Washington, D.C.

Peripheral arterial disease (PAD) continues to grow in global prevalence and consumes an increasing amount of resources in the United States health care system. Overall rates of intervention for PAD have been rising steadily in recent years. Changing demographics, evolution of technologies, and an expanding database of outcomes studies are primary forces influencing clinical decision making in PAD. The management of PAD is multidisciplinary, involving primary care physicians and vascular specialists with varying expertise in diagnostic and treatment modalities. PAD represents a broad spectrum of disease from asymptomatic through severe limb ischemia. The Society for Vascular Surgery Lower Extremity Practice Guidelines committee reviewed the evidence supporting clinical care in the treatment of asymptomatic PAD and intermittent claudication (IC). The committee made specific practice recommendations using the GRADE (Grades of Recommendation Assessment, Development and Evaluation) system. There are limited Level I data available for many of the critical questions in the field, demonstrating the urgent need for comparative effectiveness research in PAD. Emphasis is placed on risk factor modification, medical therapies, and broader use of exercise programs to improve cardiovascular health and functional performance. Screening for PAD appears of unproven benefit at present. Revascularization for IC is an appropriate therapy for selected patients with disabling symptoms, after a careful risk-benefit analysis. Treatment should be individualized based on comorbid conditions, degree of functional impairment, and anatomic factors. Invasive treatments for IC should provide predictable functional improvements with reasonable durability. A minimum threshold of a >50% likelihood of sustained efficacy for at least 2 years is suggested as a benchmark. Anatomic patency (freedom from restenosis) is considered a prerequisite for sustained efficacy of revascularization in IC. Endovascular approaches are favored for most candidates with aortoiliac disease and for selected patients with femoropopliteal disease in whom anatomic durability is expected to meet this minimum threshold. Conversely, caution is warranted in the use of interventions for IC in anatomic settings where durability is limited (extensive calcification, small-caliber arteries, diffuse infrainguinal disease, poor runoff). Surgical bypass may be a preferred strategy in good-risk patients with these disease patterns or in those with prior endovascular failures. Common femoral artery disease should be treated surgically, and saphenous vein is the preferred conduit for infrainguinal bypass grafting. Patients who undergo invasive treatments for IC should be
<table>
<thead>
<tr>
<th>Medical treatment for intermittent claudication</th>
<th>Grade</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1. We recommend multidisciplinary comprehensive smoking cessation interventions for patients with IC (repeatedly until tobacco use has stopped).</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>4.2. We recommend statin therapy in patients with symptomatic PAD.</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>4.3. We recommend optimizing diabetes control (hemoglobin A1c goal of &lt;7.0%) in patients with IC if this goal can be achieved without hypoglycemia.</td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>4.4. We recommend the use of indicated β-blockers (eg, for hypertension, cardiac indications) in patients with IC. There is no evidence supporting concerns about worsening claudication symptoms.</td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>4.5. In patients with IC due to atherosclerosis, we recommend antiplatelet therapy with aspirin (75-325 mg daily).</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>4.6. We recommend clopidogrel in doses of 75 mg daily as an effective alternative to aspirin for antiplatelet therapy in patients with IC.</td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>4.7. In patients with IC due to atherosclerosis, we suggest against using warfarin for the sole indication of reducing the risk of adverse cardiovascular events or vascular occlusions.</td>
<td>1</td>
<td>C</td>
</tr>
<tr>
<td>4.8. We suggest against using folic acid and vitamin B12 supplements as a treatment of IC.</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>4.9. In patients with IC who do not have congestive heart failure, we suggest a 3-month trial of cilostazol (100 mg twice daily) to improve pain-free walking.</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>4.10. In patients with IC who cannot tolerate or have contraindications for cilostazol, we suggest a trial of pentoxifylline (400 mg thrice daily) to improve pain-free walking.</td>
<td>2</td>
<td>B</td>
</tr>
<tr>
<td>4.11. We suggest the ACEI ramipril (10 mg/d) to improve pain-free and maximal walking times in patients with IC. (ACEIs are contraindicated in individuals with known renal artery stenosis).</td>
<td>2</td>
<td>B</td>
</tr>
</tbody>
</table>
Walking Program

- Walk, walk, walk
- >30 minutes at a time
- >3 times per week
- >6 months in duration
- Supervised vs unsupervised
Surgical Treatment

- Open vs endovascular
- First line therapy for patients with life limiting/disabling claudication
- Failure of medical treatment for claudication
- Treat critical limb ischemia due to risk for limb loss
Principles of Revascularization

- **Inflow**
  - Optimize hemodynamics to improve patency
- **Outflow**
  - Number of outflow vessels improve patency
- **Conduit**
  - Vein
  - Prosthetic
Endovascular Techniques

- Percutaneous Transluminal Angioplasty (PTA)
  - Drug coated balloons
- Stents
  - Drug eluting stents
  - Covered stents/stent grafts
- Atherectomy
Outcomes of Revascularization for AIOD

<table>
<thead>
<tr>
<th>References (first author)</th>
<th>Modality</th>
<th>FU duration, years</th>
<th>Patency (PAP), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yilmaz, Soga, Ichihashi, Indes</td>
<td>PTA + stent</td>
<td>5</td>
<td>63-79</td>
</tr>
<tr>
<td>deVries, Rutherford, Reed, Brewster, Chiu</td>
<td>AFB</td>
<td>5</td>
<td>81-93</td>
</tr>
<tr>
<td>Cham, Meliere, Van der Vliet, Chiu, Ricco</td>
<td>IFB</td>
<td>5</td>
<td>73-88</td>
</tr>
<tr>
<td>Criado, Ricco, Mii</td>
<td>FFB</td>
<td>5</td>
<td>60-83</td>
</tr>
</tbody>
</table>

AFB, Aortofemoral bypass; FFB, femorofemoral bypass; FU, follow-up; IFB, iliofemoral bypass; PAP, primary assistant patency; PTA, percutaneous transluminal angioplasty.
TASC Classification

Type A
Endovascular treatment of choice

Type B
Currently, endovascular treatment is more often used but insufficient evidence for recommendation

Type C
Currently, surgery treatment is more often used but insufficient evidence for recommendation

Type D
Surgical treatment of choice
Surgical Revascularization
Surgical Revascularization
Surgical Revascularization
Endovascular Revascularization
Endovascular Revascularization
Endovascular Revascularization
Endovascular Revascularization
# Outcomes of Revascularization for Infrainguinal Disease

<table>
<thead>
<tr>
<th>References (first author)</th>
<th>Modality</th>
<th>FU duration, years</th>
<th>Patency (PAP), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunink, Muradin, Schillinger</td>
<td>PTA</td>
<td>2</td>
<td>26-68</td>
</tr>
<tr>
<td>Schillinger, Laird, Matsumura</td>
<td>PTA + stent</td>
<td>2</td>
<td>51-68</td>
</tr>
<tr>
<td>Kedora, Shackles, Geraghty</td>
<td>Covered stent</td>
<td>1</td>
<td>53-77</td>
</tr>
<tr>
<td>Pereira, Klinkert</td>
<td>FP vein</td>
<td>5</td>
<td>70-75</td>
</tr>
<tr>
<td>Robinson, Klinkert, Pereira</td>
<td>FP prosthetic</td>
<td>5</td>
<td>40-60</td>
</tr>
</tbody>
</table>

*FP, Femoropopliteal; FU, follow-up; PAP, primary patency; PTA, percutaneous transluminal angioplasty.*
Type A lesions
- Single stenosis ≤10 cm in length
- Single occlusion ≤5 cm in length

Type B lesions:
- Multiple lesions (stenoses or occlusions), each ≤5 cm
- Single stenosis or occlusion ≤15 cm not involving the infrageniculate popliteal artery
- Single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass
- Heavily calcified occlusion ≤5 cm in length
- Single popliteal stenosis

Type C lesions
- Multiple stenoses or occlusions totaling >15 cm with or without heavy calcification
- Recurrent stenoses or occlusions that need treatment after two endovascular interventions

Type D lesions
- Chronic total occlusions of CFA or SFA (>20 cm, involving the popliteal artery)
- Chronic total occlusion of popliteal artery and proximal trifurcation vessels
Surgical Revascularization
Endovascular Revascularization
Endovascular Revascularization
Patency of Endovascular Revascularization

Primary patency

52.2 ± 7.5% at 12 months
27.5 ± 9.4% at 24 months

Assisted-primary patency

88.4 ± 4.2% at 12 months
74.2 ± 10.9% at 24 months

% of patients with patent femoropopliteal segments

Follow-up in months

Patients at risk: 73

Follow-up in months

Patients at risk: 73

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Just because we can, should we?

- The Benefit of Revascularization in Nonagenarians with Lower Limb Ischemia is Limited by High Mortality: (Saarinen, E. EJVES. 2015; 49:420–425.)
- And of course there is the New York Times Article: “Medicare Payments Surge for Stents to Unblock Blood Vessels in Limbs”
What does the future hold?

- BEST-CLI
- Stem cell therapy
Questions??
Carondelet Heart & Vascular Institute. Be well.