Peripheral Arterial Disease

CLAUDICATION TO LIMB THREATENING ISCHEMIA
THE HOW AND WHEN TO EVALUATE AND TREAT

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Nothing to Disclose
PAD: Peripheral Arterial Disease

- Obstruction of any “peripheral artery”
- Causes
  - Atherosclerosis
  - Emboli
  - Extrinsic compression
  - Vasculitis
PAD

- Effects more than 15 million Americans
- Majority of patients are asymptomatic
- African Americans and Hispanics are at ↑ risk
- Diabetics with PAD are at significant ↑ risk for amputations (Neuropathy + PAD)
PAD Risk Factors

- Male gender (cf female)
- Age (per 10 years)
- Diabetes
- Smoking
- Hypertension
- Dyslipidemia
- Hyperhomocysteinemia
- Race (Asian/hispanic/black vs. white)
- C-reactive protein
- Renal insufficiency

Odds ratio

1 2 3 4
PAD: PREVALENCE vs AGE

The bar chart shows the prevalence of PAD (Peripheral Arterial Disease) in men and women across different age groups. The x-axis represents age groups, ranging from <60 to ≥75 years, while the y-axis represents the PAD prevalence (%) ranging from 0 to 25. The chart indicates a higher prevalence in women compared to men across most age groups.
Growth of U.S. Older Adult Population

- 65-74
- 75-84
- 85+

Number in Millions

1900 1920 1940 1960 1980 2000 2020 2040
PAD: More Prevalent and More Deadly Than Many Leading Diseases

Disease Prevalence (Millions)

Five-Year Mortality Rate

Source: American Cancer Society, American Heart Association, Alzheimer's Disease Education/Referral Center, American Diabetes Association, SAGE Group
PAD: LONG-TERM MORTALITY

The graph illustrates the survival rates over years for different groups:

- **Normal Subjects**
- **Asymptomatic LV-PAD**
- **Symptomatic LV-PAD**
- **Severe Symptomatic LV-PAD**

Survival rates decrease over time, with the least survival rate observed in the **Severe Symptomatic LV-PAD** group.
Atherosclerosis is a Systemic Disease

Lesion Location
- Carotid, cerebral
- Aorta, arch
- Coronary artery
- Renal artery
- Mesenteric
- Iliac artery
- Femoral artery
- Tibial artery

Consequence
- Stroke
- Aneurysm
- MI
- HTN, CRF
- Bowel infarct
- Impotence
- Claudication
- Limb loss
Atherosclerosis

Thrombosis

Stable angina
Intermittent claudication

Unstable angina
MI
Ischemic stroke/TIA
Critical leg ischemia
Cardiovascular death

There is a 5 fold increase in the relative risk of a Cardiovascular ischemic event.

Total Mortality is increased 2-3 X.
Visual Cues to PAD and Arterial Insufficiency

- Cool, dry, atrophic skin on legs
- Thickened or deformed nails-dystrophic
- Hair loss or uneven distribution on legs
- Muscle weakness or atrophy
- Bruits on auscultation
- Ulcers or wounds on lower extremities
Peripheral Arterial Occlusive Disease

- Asymptomatic
- Claudication
- Ischemia
- Rest pain
- Gangrene
Claudication

- *Claudico* = To Limp
- Pain, Weakness, or Cramping in muscles
- Worse on walking up incline
- Relief of symptoms by standing ≤ 5 min
- Reproducible at same distance
- Nonpositional
Claudication

- Obstruction is found one level above location of symptoms

- Calf claudication more commonly due to disease in femoral arteries and less commonly due to disease in popliteal or proximal tibial or peroneal arteries

- Hip/Thigh/Buttock claudication due to aortoiliac disease
Claudication: Pathophysiology

During exercise, oxygen demand increases

Muscles operate anaerobically

Produce lactic acid and other metabolites

Leg pain
Differential Diagnosis for Claudication

- **Spinal stenosis**
  - To obtain relief must sit down or lean over
  - Takes up to 10-30 min to get relief

- **Neuropathy**
  - Unrelenting occurring at rest or walking
  - Associated with Diabetes

- **Arthritis**
  - Pain centered around joints or feet
  - Groin/Thigh Pain = ?Hip
Critical Limb Ischemia

- Rest Pain
  - Multi-level occlusive disease
  - Pain in extremity with leg elevation relieved by placing in dependent position
  - Dependent rubor

- Non healing or slow healing wounds
Blue Toe Syndrome

- Atheroemboli from proximal vascular lesion
- If bilateral - indicates aortic origin
- If unilateral - iliac/femoral/poplitial
- Must rule out proximal aneurysm
Buerger’s Disease
Thromboangiitis Obliterans

- Nonatherosclerotic vasculopathy
- Involves medium to small arteries
- Can also affect veins/nerves
- T-cell mediated
- Treatment = Stop Smoking
Differential Diagnosis of Atherosclerotic PAD

- Calciphylaxis
  - Associated with hyperparathyroid
  - CRF

- DM Foot ulcers
  - Neuropathy
  - Pressure points

- Venous Disease
  - Leg Edema
  - Stasis changes
  - Hx of DVT
Differential Diagnosis of Atherosclerotic PAD

- Vasculitis

- Reflex Sympathetic dystrophy
  - Post injury

- Livido Reticularis
  - Marbled Appearance
Non-Atherosclerotic Causes

- Popliteal artery entrapment
- Mucinous cystic degeneration
- Buerger's disease
- Abdominal aortic coarctation
- Emboli
- Bechet’s Syndrome

- Fibrodysplasia
- Pseudoxanthoma elasticum
- Persistent sciatic artery
- Iliac artery syndrome of cyclist
- Primary arterial tumors
- Remote trauma/irradiation
Diagnosis of PAD

- Arterial Doppler Studies
- Duplex Imaging
- CTA
- MRA
- Arteriogram
Ankle/Brachial Index

\[ \text{ABI} = \frac{\text{DP or PT systolic pressure (Higher)}}{\text{Brachial artery systolic pressure}} \]
Ankle/Brachial Index

- May be normal yet have PAD

- Index $\geq 1.3$ suggests calcified arteries making test inaccurate (Diabetes??)

- Treatment based on symptoms not absolute number

- Use as a marker for Atherosclerotic disease

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.91-1.2</td>
</tr>
<tr>
<td>Mild PAD</td>
<td>0.90-0.71</td>
</tr>
<tr>
<td>Moderate PAD</td>
<td>0.70-0.41</td>
</tr>
<tr>
<td>Severe PAD/CLI</td>
<td>&lt;0.40</td>
</tr>
</tbody>
</table>
ABI Interpretation

- **Index > 1.3** Non-compressible
  - Toe-Brachial Index (TBI)

- **Index 0.91-1.29**
  - Low suspicion for PAD
    - No further testing
  - High suspicion for PAD
    - Check ABI after treadmill testing, if drop > 20mmHg from resting, then PAD.

- **Index < 0.90**
  - PAD diagnosis
  - Consider further evaluation and testing *if warranted*
ABI related to survival

- ABI > 1.0
- ABI: 0.9-1.0
- ABI: 0.8-0.9
- ABI < 0.8

Years: 0 1 2 3 4 5 6

Patient survival: 1.0 0.9 0.8 0.7 0.6
Limb Threatening PAD: Critical Limb Ischemia

ABI < 0.4 or ankle systolic pressure of 50mmHg or less, or a Toe pressure of 30mmHg

- Only half of the patients will be alive without a major amputation one year after the onset of critical limb ischemia.

- Treatment of CLI is dependent on increasing blood flow to the affected extremity to relieve pain, heal ischemic ulcerations, and avoid limb loss
PAD: NONINVASIVE LAB EVALUATION (PVR)

Right high thigh:
- Pressures: 191, 184

Right low thigh:

Right calf:
- Pressures: 255, 225, 171 PT, 161 DP
- ABI: 0.75, 1.01, 0.75, 0.90

Right ankle:
- Pressures: 208, 128, 112 PT, 103 DP
- ABI: 1.09, 0.67, 0.64, 0.43

Right digit:

Left high thigh:

Left low thigh:

Left calf:

Left ankle:

Left digit:

Typical waveform:
Age 50-69 y, if patient smokes or has diabetes
Age ≥70 y
Leg pain with exertion
Abnormal results on vascular examination of leg
Coronary, carotid, or renal arterial disease

Measure ankle-brachial index (ABI)

ABI >1.30
Pulse-volume recording
Toe-pressure measurement
Duplex ultrasonography

Normal results: no PAD
Abnormal results

ABI 0.91-1.30
Measure ABI after treadmill test

Normal postexercise ABI: no PAD
Evaluate other causes of leg symptoms
Decreased postexercise ABI

PAD
**Arterial Duplex Scan**

- Combination of B-mode U/S and Doppler velocity measurement
- Gives anatomic not physiologic info
- Calcium prevents imaging of vessel
- ???Endovascular Tx???
CTA

- Relative non-invasive
- Still requires “dye” so watch for kidney disease
- Calcium can make it difficult to discern the amount of blockage present
MRA

- Reader Dependent

- ? Claustrophobic patient

- Most accurate when used with contrast

- Must avoid Gadolinium contrast in those patients with kidney disease
Arteriogram

“Gold Standard”

Invasive

Use of Iodinated contrast

Watch for kidney disease (can use CO$_2$)
PAD Evaluation

- Treat the patient not the results

- If limb threatening ischemia proceed with further testing

- For Non-limb threatening ischemia (claudication) determine whether patient desires treatment
  - What activities do your leg symptoms keep you from doing?
  - Is this a mild, moderate or severe disability to you?
Who Will Deteriorate?

Best Predictors

- ABI <0.5
- Low ankle pressures (40-60 mmHg)
  - 8.5%/y risk of severe ischemia or limb loss
Risk of developing CLI

- Lipids
- CRI
- ABI
- Diabetes
- Smoker
- Age
PAD: Who Do We Treat?
PAD: Who Do We Treat?

EVERYONE!!
Treatment of PAD

Medical management

- Risk factor modification

- STOP SMOKING

- Statins (Goal to get LDL <100 mg/dl)

- Clopidogrel vs ASA

- Rivoxiban and ASA- Voyager Trial
VOYAGER PAD: Study Design

Patients with symptomatic PAD undergoing recent (≤ 10 days) peripheral revascularization, randomized 1:1

- Rivaroxaban 2.5 mg twice daily + aspirin 100 mg daily
- Placebo + aspirin 100 mg daily

Stratification by procedure and clopidogrel use

- Surgical
  - Rivaroxaban + aspirin
  - Placebo + aspirin
- Endovascular with clopidogrel
  - Rivaroxaban + aspirin
  - Placebo + aspirin
- Endovascular without clopidogrel
  - Rivaroxaban + aspirin
  - Placebo + aspirin

Event-driven: MI, ischemic stroke, CV death, acute limb ischemia, major amputation
Primary Endpoint
Acute limb ischemia, major amputation for vascular cause, myocardial infarction, ischemic stroke, CV death

- Placebo
- Rivaroxaban

- 6 Months ARR 1.5%
- 1 Year ARR 2.0%
- 3 Year ARR 2.6%
- HR 0.85
- 95% CI 0.76 – 0.96
- P=0.0085
Objective: To evaluate outcomes of treatment with rivaroxaban/aspirin vs. placebo/ aspirin for peripheral artery disease (PAD) patients undergoing revascularization.

6,564 patients

Inclusion criteria: Patients aged ≥50 years with lower extremity PAD evidenced by abnormal ABIs, imaging, and ischemic symptoms that underwent successful lower extremity revascularization

Rivaroxaban 2.5 mg twice daily/aspirin (n = 3,286) vs. Placebo/ aspirin (n = 3,278)

**PRIMARY OUTCOME**

- CV death, acute limb ischemia, major amputation, MI, or stroke %
  - HR 0.85; 95% CI, 0.76 to 0.96; P=0.009

- Thrombolysis in Myocardial Infarction (TIMI), major bleeding %
  - HR 1.43; 95% CI, 0.97 to 2.10; P=0.07

**SECONDARY OUTCOME**

- ISTH major bleeding %
  - HR 1.42; 95% CI, 1.10 to 1.84; P=0.007
Natural history of PAD: claudication

- 70% will remain stable on medical management
- 25% will develop worsening symptoms with 70% of these patients desiring treatment
- 5% will develop limb threatening ischemia
Treatment of PAD/Claudication

- Cilostazol - 3 month follow-up
- Exercise Program
- Weight loss to treat metabolic syndrome
- 30-50% improvement in walking distance
- Orthotic Footwear/Podiatry Care
Medical Treatment of PAD

- Prevent disability and restore mobility
- Stop disease progression
- Lower the risk of other systemic ATH disease processes
Treatment of PAD

SURGERY

VS

ENDOVASCULAR
Treatment of PAD

In the past we thought surgery was the only option

Endovascular Procedures provide patients with PAD, who often have multiple co-morbid conditions, a less invasive means for treatment

THINK ENDO 1st !!!!!!!

Since many of these patients may have a shortened life expectancy don’t try to hit the home run when a base hit will do
PAOD REVASCULARIZATION

*Surgery vs Endovascular: 2002 - 2009*

2002

- Surgery: 42%
- Endo: 70%

2009

- Surgery: 70%
- Endo: 30%
Endovascular options

- Angioplasty
- Atherectomy
- Stents
- Lasers
Endovascular treatment

LONG TERM RESULTS???
Surgical options

- Bypass

- Endartectomy

- Durable but not without risks
BYPASS SURGERY FOR PAD
Advantages of Endovascular Therapy

- Less Risk
- Less Morbidity
- Shorter LOS
- Acceptable Clinical Outcomes
- Cost Efficacy
Advantages of Open Bypass

Can be more durable outcomes

Sometimes only option

Less need for re-intervention
Limb Salvage

Goal is to preserve limb and amputation
### Survival Analysis

**Graph Description:**
- The graph shows the survival rates over time for two groups: Primary Byp and Salvage Byp.
- The survival rates are compared using Kaplan-Meier curves.

**Key Statistics:**
- **HR = 1.58 (95% CI: 1.03 to 2.44), p = 0.04**

**At Risk Table:**

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<thead>
<tr>
<th>Years from randomisation</th>
<th>Primary Byp</th>
<th>Salvage Byp</th>
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<tbody>
<tr>
<td></td>
<td>190</td>
<td>49</td>
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<tr>
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<td>6</td>
<td>10</td>
<td>0</td>
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</tbody>
</table>

**Notes:**
- The graph illustrates the percentage survival over time, with the blue line representing Primary Byp and the red line representing Salvage Byp.
- The survival rates are shown at various time points, with 60% survival for Primary Byp and 40% for Salvage Byp.
- The hazard ratio indicates a significant difference in survival rates between the two groups, with a p-value of 0.04.
Limb Salvage

Avoid at all cost

Below-Knee Amputation

Above-Knee Amputation
In Summary

- PAD is usually asymptomatic

- If need diagnostic testing, ABI is first test to order. Can order further studies if warranted

- Always treat with medical management to decrease overall morbidity and mortality

- Always treat the patient and not the numbers

- Save the limb
Suggested Reading

- Society for Vascular Surgery website [www.vascular.org](http://www.vascular.org)
- Download SVS guideline app in app store “SVS iPG”
- Overview of lower extremity peripheral artery disease. [UpToDate](https://www.uptodate.com)
- Management of claudication due to peripheral artery disease. [UpToDate](https://www.uptodate.com)
- Management of chronic limb-threatening ischemia. [UpToDate](https://www.uptodate.com)