Objectives

1. Appreciate the long term implications of PAD
2. Appreciate the under-appreciation of PAD
3. Briefly review key diagnostic modalities in PAD
4. Provide an update on the pillars of medical management in PAD
Potential Conflicts of Interest

- Speaker’s Bureau: BMS/Pfizer
- Will not affect the content of this talk
PAD Defined

- Obstruction in any artery from any cause
  - Separate from CAD and CVD
- Traditionally, a blocked leg artery although many other possible vascular beds involved
  - Mesentery
  - Renal artery disease
  - Carotid artery disease
PAD incidence in a population > 70 OR > 50 with either DM and/or smoking history

- A. 5-10%
- B. 10-15%
- C. 15-20%
- D. 20-25%
- E. 25-30%
PAD ➔ Not trending on Twitter!!
PAD Awareness, Risk and Treatment: New Resources for Survival study*

- “What is the prevalence of PAD in American primary care practice?”
- PAD → 29% of the study population
- PAD Dx new in 55% of PAD only group and 35% of those with multi-vascular bed disease!
- Similar numbers replicated in many other studies

*Hirsch AT et al. JAMA 2001;286 (11): 1317-
PAD, not as well studied

- More common than you might think\(^1,2\)
  - 202 M people worldwide alive with PAD…
- Overall Prevalence increasing: Lower > higher income countries
- US prevalence: 5.9% (8-12 million)
  - High risk subgroups \(\rightarrow\) **at least** 30% prevalence!!
- Bottom-line:
  - “Safe bet” some of your patients **have** PAD unbeknownst to either you or them!!

But what’s the big deal anyways?

- Over 10 years → 10-15 x risk of CV death**
- 3-4 x risk CV events **even if** asymptomatic
- 1 in 5 with PAD → nonfatal CV event
- Another 1 in 5 will die (CV death)
- CLI (rest pain or tissue loss), outcomes are dire*:
  - 25% amputation
  - 25% DIE!!

CV morbidity & mortality

Nonfatal cardiovascular event (MI or stroke) 20%

Mortality 15%-30%

CV causes 75%

Non-CV causes 25%
Critical limb ischemia 1%-2%

1-year outcomes

- Alive with two limbs 50%
- Amputation 25%
- CV Mortality 25%
PAD is a pain in the @%$# but this is your life and this is who you are!!
PAD Diagnostics
How Should I diagnose PAD?

A. Simple, just take a history!
B. Even easier, just do a pulse exam!
C. The Rose Questionnaire is, by far, the most accurate way to diagnose PAD
D. Ankle to Brachial Index
Dx pearls:

- Pt reported symptoms **underestimate** PAD prevalence
  - Remember, almost 50% are asymptomatic!
  - Atypical is the typical → nonspecific symptoms
    - Leg fatigue, multiple areas of pain, buttock pain
- Physical Exam NOT reliable
  - Pulse exam **overestimates** disease by 2-fold
- Rose/WHO Questionnaire; 1962, several modifications through the years
  - Many “upgraded” renditions, all inferior vs ABI
ABI is the diagnostic test for PAD

Sensitivity: 90-95%
Specificity 95%
**ABI**

- Normal ABI → 1-1.4
- ≤ 0.9 *diagnostic* of PAD
- 0.9-1.00 “No-man’s land” now considered “low nl”
  - CV event rate increased by 10-20%
- > 1.4 = calcified vessels, non-compressible
  - Very elderly, long standing DM, advanced CKD
  - TBI useful (digital arteries typically spared of calcification) < 0.7
ABI and CV disease

- Strong/consistent relationship b/t abnl ABI and presence of coronary/cerebrovascular disease
- Abnormal ABI (even if asymptomatic) + known CAD = higher cardiovascular event rates
  - 5 year survival rate based on ABI:
    - ABI < 0.5 → 63%
    - ABI 0.5-0.69 → 71%
    - ABI 0.7-0.89 → 91%
Several consensus documents/practice guidelines recommend screening for PAD in:
- All > 65 years of age OR…
- Age > 50 + h/o DM OR smoking

WHY screen? → identify pts with increased CV risk

Unfortunately, No symptoms = No Reimbursement
- Despite ½ being ASYMPTOMATIC
- This is your tax dollars at work people!! (i.e. CMMS)
PAD Medical Management
“I can hardly walk to my mailbox anymore”

- 65 y/o male previous smoker, no known vascular disease
- Gradual onset over past 2 months
- No tissue loss/rest pain
- Has DM, HTN and FH of CAD
- MROS negative
- Rest ABI normal; precipitous drop post exercise ABI
- Angio shows…
In terms of gains in Peak Walking time, Supervised Exercise training is...

- inferior to stenting.
- as effective as stenting.
- a bit better than stenting.
- superior to stenting.
Claudication: Exercise Versus Endoluminal Revascularization*

- Aortiliac stenting vs supervised exercise
  - All with optimal medical management
- primary endpoint: peak walking time
- Secondary endpoint: Quality of Life

*Murphy TP et al. Circulation 2011; 123:87
Clever findings...

- Peak Walking Time (after 6 months)
  - significantly improved in SE and stenting OVER optimal medical management
  - significantly higher in SE than stent group!!
- Quality of Life: trend toward favoring stenting group
- Stenting: assists in the durability of PWT
  - 18 month f/u: Stenting group catching up to SE only group
- No arm for SE + Stenting—> poor recruitment
Endovascular Revascularization and Supervised Exercise*

- BOTH endovascular + SE vs SE alone
- 1 yr: combo group → greater improvements in Max Walking Distance (MWD) and health-related QOL scores
- Both groups → dramatic improvement in MWD, pain-free walking distance, QOL
  - SE → 285 m to 1240 m (net gain of 955 m)
  - SE + endo → 264 m to 1501 m (net gain of 1237 m)
- Take-away:
  1. combo Rx = most effective strategy for many with claudication
  2. reconfirms that SE alone markedly improves MWD, pain-free walking distance

*Fakhry F et al. JAMA 2015; 314:1936
Exercise works

- Improved skeletal mm metabolism
- Changes endothelial function
- Improves gait biomechanics
- Best if supervised
  - Unsupervised with tracking device catching up
- Cheap!
  - Although sneakers are getting more $$$
The real benefit...
The rub with exercise

- Motivation
- Not covered by insurance!?
Prescribing Exercise

- "You should get some exercise" → not effective
- Typical program: 12 weeks, best if supervised
- Many published programs, general principles
  - 3-5 d/w
  - 45 min/session
  - Pushing to moderate claudication symptoms → rest → go
  - Able to make 8 minutes?
    - speed up OR raise incline
**TABLE 1** A Practical Home Exercise Program for Patients With PAD

<table>
<thead>
<tr>
<th>Frequency</th>
<th>3-5 days per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modality</td>
<td>Treadmill (this program can be adapted for walking outside)</td>
</tr>
<tr>
<td>Method</td>
<td></td>
</tr>
<tr>
<td>1. Begin at 2 mph and a grade of 0 (flat)</td>
<td></td>
</tr>
<tr>
<td>2. Try not to hold onto the treadmill. Use the side panels for balance only.</td>
<td></td>
</tr>
<tr>
<td>3. Stop the treadmill completely when pain is 3-4 on claudication discomfort scale*</td>
<td></td>
</tr>
<tr>
<td>4. When the discomfort has ceased, resume exercise at the same intensity</td>
<td></td>
</tr>
<tr>
<td>5. Repeat rest/exercise cycles</td>
<td></td>
</tr>
<tr>
<td>6. Progress to a higher workload when you can walk for 8 min without having to stop for leg symptoms</td>
<td></td>
</tr>
<tr>
<td>a) Increase speed by 0.2 mph each time you can walk for 8 min</td>
<td></td>
</tr>
<tr>
<td>b) Once you are able to walk at 3.4 mph, or reach a speed at which you can no longer keep up, begin increasing the grade by 1%</td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>The total exercise period, including rest periods, should equal 45 min per day</td>
</tr>
<tr>
<td>Tips for success</td>
<td></td>
</tr>
<tr>
<td>1. Do not continue walking past 3-4 on claudication pain/discomfort scale. This way the pain/discomfort should go away in 2-5 min. If you walk until you are in severe pain, you will build up lactic acid in your muscles, and it will take much longer for the pain to go away.</td>
<td></td>
</tr>
<tr>
<td>2. When at 3-4 on pain/discomfort scale, stop walking completely. Do not slow down, but stop and stand on the treadmill until the discomfort is gone.</td>
<td></td>
</tr>
</tbody>
</table>

This works if you do it! Not only will this improve your walking performance, decrease your discomfort, and improve your quality of life, this type of program is also beneficial for your heart, blood pressure, and lipid (cholesterol and triglyceride) levels.

*Claudication pain scale: 1 = no pain or discomfort; 2 = onset of claudication; 3 = mild pain or discomfort; 4 = moderate pain or discomfort; 5 = severe pain or discomfort. Adapted from Weinberg et al. (40).

PAD = peripheral artery disease.
Optimal Medical Therapy
### The PAD “Prescription”

#### Decrease the Risk of MI, Stroke, and CV Death
- Discontinue Tobacco Use
- Walking Program
- Control Blood Pressure to Goal (ACE Inhibitor)
- High-Dose Statin Therapy
- Antiplatelet Therapy

#### Improve Symptoms, Quality of Life, and Prevent Amputation
- Discontinue Tobacco Use
- Walking Program
- Cilostazol
- Good Foot Care: -Moisturizing cream, nail care, treat and prevent tinea, orthotics to prevent abnormal pressure points
- Revascularization
Doc, What’s in it for me?

4 Therapies:
- Statin
- Ace
- Antiplt
- No smoking

Hazard ratio, 0.64; 95% CI, 0.45-0.89; P=0.009

Major Adverse Cardiovascular Events, %

Follow-Up (Months)

Number at risk
<4 Guideline 502 450 391 355 322 288 256
4 Guideline 237 222 207 180 156 143 123
Hazard ratio, 0.55; 95% CI, 0.37-0.83; P=0.005

Number at risk
4 Guideline
<4 Guideline Therapies
4 Guideline Therapies
Smoking Cessation

- #1 lifestyle modification in preventing CLI, amputation, and MACE in PAD
- 5 year outcomes in quitters vs non-quitters (after LE PCI)
  - Lower mortality → 14% vs 31%
  - Improved amputation free survival → 81% vs 60%
- Guidelines
  - Tobacco use status addressed at every visit
  - Offer counseling/assistance in developing quit plan
    - Pharmacotherapy and/or referral to formal smoking cessation program
  - UND smoking cessation program → all my smokers
Smoking cessation strategies

- Success rates at one year
  - On own: 0.1%
  - Physician advice + frequent f/u: 5%
  - Nicotine replacement therapy: 16%
  - Bupropion/Varenicline: ~30%
- Varenicline superior?
- Ultimately, cost effective.
Pharmacotherapy for Claudication

- Cilostazol (Pletal), Type III phosphodiesterase inhibitor
  - Lackluster efficacy
    - Clearly inferior to walking program
- Side effect profile = poor compliance
  - HA, palpitations, diarrhea
- Contraindicated in CHF
- May take up to 4 months to derive max benefit
Ace Inhibitors

- a/w significant reduction in MACE
- MACE incidence in HOPE PAD cohort:
  - 16.4% Ramipril vs 22% placebo
  - Lower incidence regardless of symptoms
- Shown to increase walking time in those with intermittent claudication
Statins and PAD

- No surprise, lower MACE
- Surprise, reduced adverse limb outcomes
  - REACH registry (all with symptomatic PAD)
    - Those on statins a/w sig reduction in combined endpoint of worsening claudication, new CLI, new revascularization, or amputation
    - Absolute 4 year event rates: 22% vs 26.2%
    - Ischemic amputation rates: 3.8% vs 5.6%
  - Post-LE revascularization: lower amputation rates
  - Among CLI, improved 1 yr rate of primary and secondary patency, and improved limb salvage after endovascular intervention
- Bottom-line: convincing evidence of efficacy both MACE and limb related outcomes
  - Despite this, most studies show that statin prescription rates are <75%
ASA Therapy and PAD

- ASA is a mainstay despite relatively little evidence of efficacy
- Meta-analysis: ASA for PAD; 18 trials; 5269 pts
  - If on ASA monotherapy, nonsignificant reduction in CV events RR 0.75 (95% CI 0.48-1.18)
  - Significant reduction in nonfatal stroke → HR 0.64 (95% CI 0.42-0.99)
- 2 recent trails assessing fatal and nonfatal CV events or revascularization
  - Neither trial able to show efficacy over placebo
  - Both trials used somewhat borderline ABIs
    - ABI < 0.99 PAPADAD trial
    - ABI < 0.95 AAA trial
      - Used the lower of the two pedal pressures (not considered standard of care)
Endovascular Therapy and PAD

No CLI
- Exercise + Cilostazol
- No better at 6 months:
  - Consider revascularization
  - Less invasive trumps invasive

CLI
- Urgent revascularization
- Extremely high risk of amputation and CV events
Peripheral Artery Disease

Evolving Role of Exercise, Medical Therapy, and Endovascular Options

Jeffrey W. Olin, DO, Christopher J. White, MD, Ehrin J. Armstrong, MD, MSc, Daniella Kadian-Dodov, MD, William R. Hiatt, MD
In Summary

- PAD is a marker of systemic vascular disease with bleak prognosis.
- Despite increasing prevalence, PAD remains under recognized and under treated.
- Lack of recognition translates into many needlessly suffering MACE.
- PAD is easily and noninvasively diagnosed: ABI.
- Combining exercise + intervention best for optimally managed lifestyle-limiting claudication.
- Smoking cessation is the largest single intervention in the Rx of PAD.
- Statins, Ace inhibitors, antiplatelet agent, save lives and limbs.
Thank You

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