INNOVATIONS IN CARDIOVASCULAR INTERVENTIONS.
WHAT SHOULD YOU KNOW?
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DISCLOSURES
• None related to this presentation

OUTLINE
• Peripheral Arterial Disease
• Intervventional management of resistant hypertension
• Intervventional management of valvular heart disease
  • Aortic stenosis
  • Mitral regurgitation
DEFINITIONS
• Peripheral artery disease (PAD)
  • Atherosclerotic of lower extremity arteries
  • Exclusive of renal, mesenteric, carotids
• Spectrum
  • Asymptomatic
  • Intermittent claudication
  • Critical limb ischemia

DEFINITIONS
• Intermittent claudication
  • Recurring pain or fatigue that occurs at a reproducible distance
  • Relieved with rest (Usually quickly)
• Critical limb ischemia
  • Advanced, limb-threatening form of PAD manifest by ischemic rest pain or tissue loss

RUTHERFORD CLASSIFICATION

<table>
<thead>
<tr>
<th>Grade</th>
<th>Category</th>
<th>Patient presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>Mild claudication</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Moderate claudication</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Severe claudication</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>Minor tissue loss</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>Major tissue loss</td>
</tr>
</tbody>
</table>

5 = CLI
### PAD - CLINICAL PRESENTATION

- **Typical Claudication:** ~15%
- **Atypical Limb Symptoms (functionally limited):** ~33%
- **Critical Limb Ischemia:** 1-2%
- **No Symptoms:** 50%

### PAD - PREVALENCE

<table>
<thead>
<tr>
<th>Study</th>
<th>PAD Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHANES aged &gt;70</td>
<td>4.3%</td>
</tr>
<tr>
<td>NHANES aged 50–69</td>
<td>5%</td>
</tr>
<tr>
<td>Rotterdam</td>
<td>14.3%</td>
</tr>
<tr>
<td>Aged &gt;55 years</td>
<td>19.1%</td>
</tr>
<tr>
<td>NHANES aged &gt;65</td>
<td>19.8%</td>
</tr>
<tr>
<td>PARTNERS</td>
<td>29%</td>
</tr>
</tbody>
</table>

When common risk factors were included, the prevalence of PAD was approximately one in three patients.

### PAD - PREVALENCE IN COMMUNITY

- **n = 6979**
- **29% of Patients Were Diagnosed With PAD Using ABI**

- 29% Patients diagnosed with PAD
- 44% PAD only
- 56% PAD and CAD

ANKLE-BRACHIAL INDEX (ABI)

\[
\text{ABI} = \frac{\text{Ankle SBP}}{\text{Brachial SBP}}
\]

- \(>1.3\): Noncompressible
- 0.91-1.3: Normal
- 0.41-0.90: Mild-Moderate PAD
- 0.00-0.40: Severe PAD

The ABI is 90% sensitive, 98% specific for detecting PAD (stenosis >50%)

NONINVASIVE TESTING

- Hemodynamic tests
  - Ankle-brachial index (ABI)
  - Segmental limb pressures
  - Pulse volume recordings (PVRs)
  - Exercise ABIs
- Imaging
  - Duplex ultrasonography
  - CT
  - MRI
HEMODYNAMIC TESTING
- ABI
  - Diagnoses PAD (ABI <0.90)
  - Quantifies severity
- Limb pressures/pulse volume recordings
  - Provides location
    - Medical Rx versus revascularization
    - Procedural planning
    - PVRs particularly useful with noncompressible vessels
- Exercise ABIs
  - Valuable when symptoms are compelling and resting hemodynamics are relatively normal

HEMODYNAMIC TESTS

IMAGING: DUPLEX, CT, MRI
TREATMENT GOALS

- Reduce CV risk
- Death
- Myocardial infarction
- Stroke
- Limb preservation
- Improve function
- QOL
- Walking distance
- Prevent progression to CLI and/or amputation

PAD-ANTIPLATELETS

<table>
<thead>
<tr>
<th>Category</th>
<th>APT</th>
<th>CTRL</th>
<th>Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>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±15</td>
</tr>
<tr>
<td>All high-risk patients</td>
<td></td>
<td></td>
<td>22±2</td>
</tr>
</tbody>
</table>

Antithrombotic Trialists’ Collaboration. BMJ. 2002;324:71-86

PAD-ANTIPLATELETS

- Antiplatelet is indicated to reduce death, stroke, MI in symptomatic PAD (1A)
- Clopidogrel may be substituted for ASA allergy/intolerance
- Antipletelets can be beneficial in asymptomatic PAD (2A)

ADDITIONAL RECOMMENDATIONS

- Nicotine cessation
- Dietary modifications
- Weight reduction
- Diabetes - A1C <7.0%
- HTN - standard goals

Hirsch et al. Circulation 2006;113:e463-65

PAD - EXERCISE

Meta-analysis of 21 Studies

Change in treadmill walking distance (%)

Gardner and Poehlman. JAMA 1995;274:975-980
**PAD - CILOSTAZOL**

Cilostazol (100 mg BID) is recommended for all claudicants to improve walking capacity.

Cilostazol is contraindicated in heart failure.

Pentoxifylline (400 mg TID) may be used as an alternative to cilostazol but efficacy is less established (IIB).


**OBJECTIVE #3 MEDICAL THERAPY**

- Medical Rx serves to reduce CV risk and preserve limb function
  - Aspirin, statins for all
  - Cilostazol
  - Nicotine cessation
  - Exercise counseling


**INDICATIONS FOR REVASCULARIZATION**

- Lifestyle-limiting symptoms that persist despite appropriate medical therapy
  - Anatomy amenable
  - Appropriate patient
  - Limb salvage
    - Adjunctive wound care/hygiene
    - Poor prognosis (mortality 15-25% at 1 year)
"MODERN" REVASCULARIZATION
• Endovascular (PTA/stent) increasingly utilized in place of surgical bypass
  • Less peri-procedural risk
  • Technical success rates >90%
• Endovascular failure/restenosis usually doesn’t eliminate possibility of future bypass
• CLI- no longer a “surgical” disease in most institutions

INTERVENTIONAL MANAGEMENT OF RESISTANT HYPERTENSION

HYPERTENSION EPIDEMIOLOGY

HYPERTENSION

- 50% of patients on medical treatment achieve target BP
- Drs inertia
- Patients compliance
- Patients with resistant HTN
  - At least 3 drugs
  - Including diuretic
  - Max tolerated dose

PATHWAYS OF SYMPATHETIC ACTIVITY LEADING TO HYPERTENSION
SURGICAL SYMPATHETIC NERVE MODULATION FOR THE TREATMENT OF HTN

- Before medical treatment
- Radical surgical methods successful to lower BP
- High peri-operative mortality and morbidity
  - Bowel
  - Bladder
  - Erectile dysfunction
  - Severe orthostatic hypotension
- Abandoned in the early 1970s
• Nerves arise from T10-L2
• Primarily lie within the adventitia
• Exclusively noradrenergic
• Endovascular radio frequency renal sympathetic denervation (RSD)
• Targets and ablates the connections between the brain and renal sympathetic nerves.
• Systems specifically designed for RSD are most likely to maximize patient comfort, procedural safety, and efficacy.
• Several variations of RFA technology designed for RSD are under clinical study or are in development.
- 4-6 two-minute treatments per artery
- Proprietary RF generator
  - Automated
  - Low power
  - Built-in safety algorithms


Initial Cohort – Reported in the Lancet, 2009:
- First-in-man, non-randomized
- Cohort of 45 patients with resistant HTN (SBP ≥ 160 mmHg on ≥ 3 anti-HTN drugs, including a diuretic; eGFR ≥ 45 mL/min). 12-month data

Expanded Cohort – This Report (Symplicity HTN-1):
- Expanded cohort of patients (n=153), 36-month follow-up

*Expanded results presented at the American College of Cardiology Annual Meeting 2012 (Krum, H.)

BASELINE PATIENT CHARACTERISTICS (N=153)

Demographics

- Age (years): 57 ± 11
- Gender (% female): 39%
- Race (% non-Caucasian): 5%

Co-morbidities

- Diabetes Mellitus II (%): 31%
- CAD (%): 22%
- Hyperlipidemia (%): 68%
- eGFR (mL/min/1.73m^2): 83 ± 20

Blood Pressure

- Baseline BP (mmHg): 176/98 ± 17/15
- Number of anti-HTN meds (mean): 5.1 ± 1.4
- Diuretic (%): 95%
- ACE/ARB (%): 91%
- Beta-blocker (%): 82%
- Calcium channel blocker (%): 75%
- Alpha-1 blocker (%): 19%

BP REDUCTIONS THROUGH 3 YEARS

- *Expanded results presented at the American College of Cardiology Annual Meeting 2012 (Krum, H.)*

PERCENTAGE RESPONDERS OVER TIME

Responder was defined as an office SBP reduction ≥ 10 mmHg
CHRONIC SAFETY OUT TO 3 YEARS

- One progression to RF treatment (stented without further sequelae)
- One new moderate stenosis which was not hemodynamically relevant and no treatment
- 3 deaths within the follow-up period; all unrelated to the device or therapy
- No hypotensive events that required hospitalization
- There were no observed changes in mean electrolytes or eGFR

SYMPLECTIC HTN-2

**THE LANCET**

- **Purpose:** To demonstrate the effectiveness of catheter-based renal denervation for reducing blood pressure in patients with uncontrolled hypertension in a prospective, randomized, controlled, clinical trial
- **Patients:** 106 patients randomized 1:1 to treatment with renal denervation vs. control

MEDICATION CHANGES AT 6 AND 12 MONTHS POST-RENAL DENERVATION

<table>
<thead>
<tr>
<th></th>
<th>RDN (n=47)</th>
<th>6 month</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decrease (# Meds or Dose)</strong></td>
<td>20.9% (9/43)</td>
<td>27.9% (12/43)</td>
<td></td>
</tr>
<tr>
<td><strong>Increase (# Meds or Dose)</strong></td>
<td>11.6% (5/43)</td>
<td>18.6% (8/43)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Crossover (n=35)</th>
<th>6 months post-RDN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decrease (# Meds or Dose)</strong></td>
<td>18.2% (6/33)</td>
<td></td>
</tr>
<tr>
<td><strong>Increase (# Meds or Dose)</strong></td>
<td>15.2% (5/33)</td>
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</table>

Physicians were allowed to make changes to medications once the 6 month primary endpoint was reached.

RENASL FUNCTION RESULTS

<table>
<thead>
<tr>
<th></th>
<th>RDN N=47</th>
<th>Treated at Randomisation</th>
<th>6 month</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>eGFR</strong> (ml/min/1.73m²)</td>
<td>88.8 ± 20.7 (n = 35)</td>
<td>86.3 ± 18.5 (n = 35)</td>
<td>85.2 ± 18.3 (n = 35)</td>
<td></td>
</tr>
<tr>
<td><strong>Cystatin C (mg/L)</strong></td>
<td>0.80 ± 0.17 (n = 27)</td>
<td>0.82 ± 0.16 (n = 26)</td>
<td>0.89 ± 0.20 (n = 26)</td>
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<table>
<thead>
<tr>
<th></th>
<th>Crossover N=35</th>
<th>Treated after 6-month follow-up</th>
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INTERVENTIONAL MANAGEMENT OF VALVULAR HEART DISEASE

AORTIC VALVE STENOSIS (AS)
- 2-9% of patients > 65 y.o. have some form of AS
- 2010 census 40 million > 65 (2 million with AS, 20% with critical AS)
- 60,000 AVR in USA / year
- < 20% of patients with severe AS that would benefit
- 65% of pts over 65 y.o. not offered surgery as option
- Life expectancy of pts with severe AS s/p AVR is similar to matched controls without AS
TRANS CATHETER AORTIC VALVE IMPLANTATION/REPLACEMENT (TAVI/R)

- Percutaneous Aortic Balloon Valvuloplasty
- 1st report of Percutaneous Aortic Valve Replacement by Cribier in 2002 in a 57 y.o male deemed inoperable
- ? Viable alternative to surgical AVR when deemed to be a prohibitive surgical risk
TRANSAPICAL TAVR

THE PARTNER (PLACEMENT OF AORTIC TRANSCATHETER) TRIAL

• Prior data from tens of thousands of patients in Europe with the Edwards SAPIEN and Medtronic CoreValve showed that this modality might be an effective way to treat critical aortic stenosis

• The PARTNER trial was the first randomized trial to evaluate the stent valve in humans across the United States

THE PARTNER TRIAL CONSISTS OF TWO INDIVIDUALLY POWERED PATIENT COHORTS.

• In Cohort A, the safety and effectiveness of the balloon-expandable Edwards SAPIEN Transcatheter Heart Valve (THV) was compared to AVR in high-risk patients with severe symptomatic aortic stenosis.

• In Cohort B, the safety and effectiveness of the balloon-expandable Edwards SAPIEN THV was compared to standard therapy (best medical management) in inoperable patients with severe symptomatic aortic stenosis.

SUMMARY

• Interventional cardiovascular procedures continue to evolve and expand
• Able to treat patient with more resistant diseases
• Able to treat patient with no other treatment options historically

THANK YOU!