Overview

An Internal Medicine perspective of:
- Carotid artery disease
- Diseases of the aorta
- Peripheral artery disease

Internal Carotid Artery Disease: Symptom Status Sets Revascularization Priority

<table>
<thead>
<tr>
<th>Symptomatic disease</th>
<th>Asymptomatic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency!</td>
<td>Low stroke risk</td>
</tr>
<tr>
<td>Immediate revascularization</td>
<td>Revascularization requires thoughtful risk:benefit analysis</td>
</tr>
</tbody>
</table>


Typical Symptoms of Internal Carotid Artery Atherosclerotic Disease

- Contralateral to lesion
  - Weakness
  - Paresthesia or sensory loss
  - Neglect

- Ipsilateral to lesion
  - Monocular blindness (Amaurosis Fugax)
  - Homonymous hemianopsia [loss of (right or left) visual field]

- Aphasia handedness dependent

Symptoms Not Often Attributable to ICA Disease

- Non-focal neurological events
  - Syncope
  - Acute confusion
  - Bilateral weakness
  - Transient global amnesia
Consensus U/S Criteria for Diagnosis of ICA Stenosis

<table>
<thead>
<tr>
<th>Degree of Stenosis (%)</th>
<th>ICA PSV (cm/sec)</th>
<th>Predictive accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 125</td>
<td>&gt; 95%</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>&lt; 125</td>
<td>~ 90%</td>
</tr>
<tr>
<td>50-69</td>
<td>125-230</td>
<td>~ 50%</td>
</tr>
<tr>
<td>≥ 70</td>
<td>&gt; 230</td>
<td>~ 85%</td>
</tr>
<tr>
<td>Near occlusion</td>
<td>High, low, or undetectable</td>
<td>&gt; 90%</td>
</tr>
</tbody>
</table>

CCA: common carotid artery. PSV: Peak systolic velocity.

Symptomatic ICA Disease: Acute Recurrence Risk Mandates Immediate Intervention

- TIA predicts a 13% risk of stroke in the first 90 days
- Revascularization benefit greatest within 2 weeks
- Revascularization benefit may be lost after:
  - 4 weeks in women
  - 12 weeks in men

Benefit of CEA Compared to Medical Therapy for Symptomatic Carotid Disease

Pooled individual patient and standardized definitions (angiograms and outcomes) analysis of trials of symptomatic carotid disease.

<table>
<thead>
<tr>
<th>Degree of Stenosis*</th>
<th>Any stroke or operative death</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-99%</td>
<td>0.53 (0.42, 0.67)</td>
</tr>
<tr>
<td>50-69%</td>
<td>0.77 (0.63, 0.94)</td>
</tr>
</tbody>
</table>

*No benefit observed if near occlusion or < 50% stenosis.

The Annual Risk of Stroke Associated With High-Grade Asymptomatic Carotid Stenosis is Less Than 1%

<table>
<thead>
<tr>
<th>Year</th>
<th>Annual event rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1985</td>
<td>20</td>
</tr>
<tr>
<td>1990</td>
<td>10</td>
</tr>
<tr>
<td>1995</td>
<td>5</td>
</tr>
<tr>
<td>2000</td>
<td>3</td>
</tr>
<tr>
<td>2005</td>
<td>2</td>
</tr>
<tr>
<td>2010</td>
<td>1</td>
</tr>
</tbody>
</table>


What is the current risk of CEA performed for asymptomatic ICA disease?

<table>
<thead>
<tr>
<th>Symptom status</th>
<th>Stroke Events/Patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>12/749</td>
<td>1.6%</td>
</tr>
<tr>
<td>Total</td>
<td>126/3526</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

The current risk of stroke is < 1% per year.

What are the competing risks in patients with asymptomatic carotid disease?

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>Stroke*</th>
<th>Cardiac event</th>
<th>Death†</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50%</td>
<td>1.3</td>
<td>2.7</td>
<td>1.8</td>
</tr>
<tr>
<td>50-75%</td>
<td>1.3</td>
<td>6.6</td>
<td>3.3</td>
</tr>
<tr>
<td>&gt; 75%</td>
<td>3.3</td>
<td>8.3</td>
<td>6.5</td>
</tr>
</tbody>
</table>

*25% of observed strokes were contralateral
†Most deaths were vascular

Carotid artery stenting versus carotid endarterectomy: a meta-analysis of trial data

- 13 randomized trials, 7,477 participants.
- Standardized outcomes.

<table>
<thead>
<tr>
<th>Short-term Event</th>
<th>CAS Rate</th>
<th>CAS versus CEA OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periprocedural death, MI, or stroke</td>
<td>6.7%</td>
<td>1.31 (1.08-1.59)</td>
</tr>
<tr>
<td>Periprocedural death or stroke</td>
<td>6.4%</td>
<td>1.65 (1.34-2.02)</td>
</tr>
<tr>
<td>Periprocedural stroke</td>
<td>5.8%</td>
<td>1.67 (1.34-2.08)</td>
</tr>
<tr>
<td>Periprocedural MI</td>
<td>0.01%</td>
<td>0.45 (0.28-0.71)</td>
</tr>
</tbody>
</table>


The Cornerstone of Carotid Disease Treatment is Medical Therapy

- Platelet inhibitors
  - Aspirin
  - Plavix
  - Aggrenox
    - Plavix and Aggrenox both better than aspirin
    - Plavix and Aggrenox equivalent, but Plavix better tolerated, and associated with less bleeding
- High-intensity statin therapy
- Excellent blood pressure control (< 130/80 mm Hg)

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<td>Revascularization requires thoughtful risk:benefit analysis</td>
</tr>
<tr>
<td>Benefit greatest within 2 weeks</td>
<td>Cumulative risk of stroke with medical therapy less than revascularization</td>
</tr>
<tr>
<td>After 12 weeks patient may now be in asymptomatic category</td>
<td>Stroke may be least cardiovascular concern</td>
</tr>
</tbody>
</table>


Diseases of the Aorta

- Dissection
- Intramural hematoma
- Penetrating atherosclerotic ulcer
- Acute aneurysm expansion
- Trauma


Acute Aortic Syndromes
Aortic Dissection Types

Type A Aortic Dissection Natural History

1% / hr MORTALITY x 24 hrs
75% MORTALITY at 2 weeks
90% MORTALITY at 3 months

Estimation of Pretest Risk of Thoracic Aortic Dissection

High Risk Pain Features
Chest, back, or abdominal pain features described as pain that:
• is abrupt or instantaneous in onset.
• is severe in intensity.
• has a ripping, tearing, stabbing, or sharp quality.

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease.

High Risk Exam Features
• Pulse deficit
• Systolic BP limb differential > 20mm Hg
• Focal neurologic deficit
• Murmur of aortic regurgitation (new or not known to be old and in conjunction with pain)

2010 ACCF/AHA Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease.

Thoracic Aortic Dissection: Predisposing Conditions

• Marfan Syndrome or other connective tissue disease*
• Family history of aortic disease
• Known aortic valve disease
• Recent aortic manipulation (surgical or catheter-based)
• Known thoracic aortic aneurysm
• Genetic conditions that predispose to AoD†
• Pregnancy
• Cocaine

* Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, Turner syndrome, or other connective tissue disease.
† Patients with mutations in genes known to predispose to thoracic aortic aneurysms and dissection, such as FBN1, TGFBR1, TGFBR2, ACTA2, and MYH11.

Aortic Dissection: Management

• EARLY STABILIZATION
• DIAGNOSTIC VERIFICATION
• DEFINITIVE THERAPY
  • MEDICAL
  • SURGICAL
  • PERCUTANEOUS
• LONG-TERM SURVEILLANCE

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease.
Aortic Dissection: Stabilization

- First: Control of $\Delta P/\Delta T$
  - Beta Adrenergic Blockade
    - Esmolol
    - Metoprolol
- Then: Control of Blood Pressure
  - Nitroprusside
  - ACE inhibitors
  - Calcium Channel Blockers
- Control of Pain
  - Narcotic analgesia

Aortic Dissection Diagnostic Imaging: Time is of the Essence

- Echocardiography
  - Transthoracic
  - Transesophageal
- Computerized tomography
- Magnetic resonance imaging
- Angiography

Aortic Dissection: Indications for Surgery

- Acute
  - Acute Type A Dissection
  - Acute Type B Dissection with
    - Rupture
    - Malperfusion
    - Rapid Expansion
    - Marfan syndrome
- Chronic
  - Type A > 5.5 cm
  - Type A with severe aortic regurgitation
  - Type B > 5.5 cm (6 cm if comorbidities)

Indications For Elective Thoracoabdominal Aortic Aneurysm Repair

- Ascending
  - 5.5 cm
  - 6 cm if co-morbidities
- Descending
  - 4.5 – 5 cm if Marfan syndrome or bicuspid aortic valve
  - 5.5 to 6.0 cm* (6 if comorbidities)

Malperfusion

- A syndrome of regional ischemia with systemic complications
- CNS, coronary, renal, mesenteric, limb
- Occurs in approximately 1/3 of patients with acute aortic dissection
- Portends higher risk for death or major disability for both Type A and Type B dissection
- Diagnosis can be challenging

Intramural Hematoma

- The most common aortic dissection variant
- 5-10% of acute aortic syndrome patients
- Mortality follows the pattern of classic aortic dissection
- Management follows aortic dissection
  - Type A IMH should have urgent surgical repair
  - Type B IMH should be managed medically

*syllabus states 6 cm

*syllabus states 6.5 to 7.0 cm

*Courtesy of Dr. Patrick O’Gara, 2011.
Penetrating Atherosclerotic Ulcer

- Ulceration of an atherosclerotic plaque that penetrates into media
- Can extend through wall to cause rupture
  - More often causes pseudoaneurysm
- Most common in descending aorta
- If acute presentation or complication, surgery
- If incidental or stable, medical therapy
- May be amenable to endovascular therapy

Abdominal Aortic Aneurysm: Size > 3 cm

- Normal aorta
- Aorta with large abdominal aneurysm

Abdominal Aortic Aneurysm: Symptoms

- Majority are asymptomatic and discovered incidentally
- Chronic abdominal pain, weight loss, elevated ESR: inflammatory aneurysm
- Acute abdominal and/or back pain, hypotension, pulsatile mass: acute rupture

Abdominal Aortic Aneurysm: Screening by Ultrasonography

- Men age 60+ with first degree relative with AAA
- Men age 65 to 75 who have ever smoked
  - Medicare Guideline 2010
  - Eligible beneficiaries must receive a referral as a result of their Welcome to Medicare exam in the first 6 months of Medicare eligibility

AAA Surveillance & Repair

- AAAs < 4.0 cm: image every 2-3 years
- AAAs 4.0 to 5.4 cm: image every 6 months
- Repair if patients have symptoms
- Repair infrarenal aneurysm ≥ 5.5 cm

Endovascular Aneurysm Repair (EVAR): EVAR-1 & EVAR-2

<table>
<thead>
<tr>
<th>EVAR-1</th>
<th>EVAR-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-year events</td>
<td>Open Repair</td>
</tr>
<tr>
<td>All death</td>
<td>46%</td>
</tr>
<tr>
<td>Aneurysm-related death</td>
<td>7%</td>
</tr>
</tbody>
</table>

EVAR-1 & EVAR-2: Endovascular Repair Complication Rates

<table>
<thead>
<tr>
<th></th>
<th>All complications</th>
<th>Reintervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR</td>
<td>46%</td>
<td>24%</td>
</tr>
<tr>
<td>EVAR-2</td>
<td>48%</td>
<td>27%</td>
</tr>
</tbody>
</table>

*Complications and need for reintervention accumulated at a steady rate over the trial period


Abdominal Aortic Aneurysm Stent-Grafts: Types of Leaks (Endoleaks)

- Type I: End(s) of graft leak
- Type II: Leakage into aneurysm sack from aortic branch vessels (e.g. lumbar artery, inferior mesenteric)
- Type III: Leak between graft components (i.e. left iliac branch and aorta components)
- Type IV: Leakage directly through graft material

Post-EVAR Surveillance

- CT scan at 1 & 6 months, then every CT scan every 6-12 months
  - Expensive, cumulative radiation and contrast dose
  - Absence of endoleak early predicts better long-term outcomes
- Ultrasound and/or less frequent scanning may be appropriate in some patients

Relatives of Patients with Aortic Disease Need Consideration

- A family history of ‘MI’ or sudden death might have been an acute aortic syndrome
- Aortic imaging recommended for first degree relatives of patients with thoracic aortic aneurysm or dissection
- First degree relatives of patient with bicuspid aortic valve should be screened for both aortic valve and aortic disease
- If a first degree relative is found to have aortic disease, second-degree relatives should be screened

Aortic Disease: Key Points

- Acute aortic syndromes are a medical emergency
- Abrupt onset severe pain that travels
  - 5.5 cm / 6.5 cm / 5.5 cm
- Lower threshold if Marfan’s, bicuspid AoV, etc.,
- EVAR: up front safety, long-term equivalence, but at price of reinterventions
- Relatives require consideration
Peripheral Artery Disease

- The presence of a stenosis or occlusion in the aorta or arteries of the limbs
- Usually caused by atherosclerosis
- 5% of adults > 40 years, 20% of adults > 70 years
- Associated with an increased risk of death, myocardial infarction, and stroke
- May impair walking or cause critical limb ischemia

Risk Factors for PAD

- Smoking
- Diabetes
- Hypertension
- Hypercholesterolemia
- Hyperhomocysteinemia
- Chronic renal insufficiency
- C-Reactive Protein

Clinical Presentations of PAD

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Percentage of Patients with PAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic (no claudication or ischemia)</td>
<td>50%</td>
</tr>
<tr>
<td>Intermittent Claudication</td>
<td>18 - 30%</td>
</tr>
<tr>
<td>Critical Limb Ischemia</td>
<td>2%</td>
</tr>
</tbody>
</table>

The Rose Questionnaire / San Diego Claudication Questionnaire to assess symptomatic PAD

- Leg pain [calf, thigh, or buttock] occurring with walking and relieved within 10 minutes of rest, that does not resolve if walking continues and does not occur at rest*.

  10% sensitivity, 95% specificity.

*PAD causing rest pain = critical limb ischemia!

Comprehensive Vascular Examination

- Pulse Examination
  - Carotid
  - Radial/ulnar
  - Femoral
  - Popliteal
  - Dorsalis pedis
  - Posterior tibial
  
  Scale
  0 = absent
  1 = diminished
  2 = normal

- Bilateral arm blood pressure
- Cardiac exam
- Palpation of abdomen for aneurysm
- Auscultation for bruits
- Examination of legs and feet
Differential Diagnosis of Exercise-induced Pain

- Peripheral artery disease
- Osteoarthritis of the hip or knee
- Peripheral nerve pain
  - Herniated disc
  - Sciatic nerve
  - Neuropathy (endocrinologic)
- Chronic exertional compartment syndrome
- Venous obstruction
- Muscle spasms/cramps/restless leg syndrome

Critical Limb Ischemia

<table>
<thead>
<tr>
<th>Rutherford</th>
<th>Grade</th>
<th>Category</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>I</td>
<td>Mild claudication</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>I</td>
<td>Moderate claudication</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>I</td>
<td>Severe claudication</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>II</td>
<td>Ischemic rest pain</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>III</td>
<td>Minor tissue loss</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>IV</td>
<td>Ulceration or gangrene</td>
<td></td>
</tr>
</tbody>
</table>

Hemodynamic Noninvasive Tests

- Resting Ankle-Brachial Index (ABI)
- Exercise ABI
- Segmental pressure examination
- Pulse volume recordings

These traditional tests continue to provide a simple, risk-free, and cost-effective approach to establishing the PAD diagnosis as well as to follow PAD status after procedures.

The Ankle-brachial Index (ABI)

\[ \text{ABI} = \frac{\text{highest of each ankle SBP}}{\text{higher brachial SBP}} \]

- < 0.9 = PAD
- > 90% accuracy

An automated BP cuff can be placed on each arm and calf to give a reasonable estimate of the ABI.

Anatomic Imaging Tests*

- Duplex ultrasonography
  - Labor intensive, preferred for follow-up of intervention
- Magnetic resonance angiography
  - Excellent detail, nephrogenic systemic fibrosis
- Computed tomographic angiography
  - Excellent detail, ionizing radiation and iodinated contrast
- Conventional contrast angiography
  - The gold standard

*Generally, anatomy only needed if planning revascularization.

Natural History of PAD is Dominated By Non-Limb Events: 5-year Outcomes

- Limb morbidity
- Cardiovascular morbidity and mortality
  - Nonfatal cardiovascular events 15%-30%
  - Mortality 15%-30%
- Cardiac events 75%
- Non-cardiac events 25%

PAD is Associated With a High Cardiovascular Event Rate Regardless of Symptom Status

<table>
<thead>
<tr>
<th>PAD/Symptom Status</th>
<th>Death</th>
<th>Death or CV event</th>
<th>Limb event</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PAD</td>
<td>20 (18-21)</td>
<td>27 (25-29)</td>
<td>1.5 (1-2)</td>
</tr>
<tr>
<td>Asymptomatic PAD</td>
<td>42 (35-48)</td>
<td>60 (52-69)</td>
<td>11 (8-15)</td>
</tr>
<tr>
<td>Symptomatic PAD</td>
<td>53 (44-62)</td>
<td>105 (91-119)</td>
<td>32 (25-39)</td>
</tr>
</tbody>
</table>

Asymptomatic PAD: 5-year major adverse cardiovascular event rate 20-25%


One Year Outcomes in Critical Limb Ischemia

- Critical Limb Ischemia
- Alive with two limbs: 50%
- Amputation: 25%
- Deceased: 25%

In the United States estimated 75,000 leg amputations annually due to critical limb ischemia


Two Goals in Treating Patients With PAD

<table>
<thead>
<tr>
<th>Limb</th>
<th>Cardiovascular morbidity and mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Improved ability to walk</td>
<td></td>
</tr>
<tr>
<td>• Prevention of progression to CLI and amputation</td>
<td></td>
</tr>
<tr>
<td>• Decrease in mortality from MI, stroke, and cardiovascular death</td>
<td></td>
</tr>
<tr>
<td>• Decrease in nonfatal MI and stroke</td>
<td></td>
</tr>
</tbody>
</table>

PAD Cardiovascular Risk-reduction Therapies

- Lifestyle modifications
  - Weight maintenance/reduction/exercise
- Smoking
  - Complete cessation
- Diabetes mellitus
  - HbA1c <7.0%, treat other risk factors
- Dyslipidemia
  - LDL <100 mg/dL, modify HDL and TG
- Hypertension
  - BP <140/90 mm Hg
- Antiplatelet therapy

Potential risk reduction of intensive medical therapy of PAD

<table>
<thead>
<tr>
<th>Preventive therapy</th>
<th>Individual therapy relative risk reduction (%)</th>
<th>Cumulative relative risk reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Intensive statin</td>
<td>20</td>
<td>36</td>
</tr>
<tr>
<td>Antiplatelet agent</td>
<td>12</td>
<td>44</td>
</tr>
<tr>
<td>Intensive antihypertensives</td>
<td>20</td>
<td>55</td>
</tr>
</tbody>
</table>

- 5,000,000 adults with PAD and no known CAD
- Anticipated 15% 5-year major CVD event rate
- Event rate reduced to 9%
- Potential 300,000 major CVD events prevented per 5 years


Treatment of the Symptomatic Leg

- Supervised exercise rehabilitation
- Pharmacotherapy
- Revascularization
Intermittent Claudication:
Exercise Therapy

- Frequency: 3–5 supervised sessions/week
- Duration: 35–50 minutes of exercise/session
- Type of exercise: treadmill or track walking to near-maximal claudication pain
- Length: ≥6 months
- Results: 100%–150% improvement in maximal walking distance


Pharmacotherapy For Claudication:
Cilostazol Works, Pentoxifylline Does Not

- Cilostazol 100 mg bid
- Pentoxifylline 400 mg tid
- Placebo

P<0.05 at all time points


Indications for Revascularization

- Persistent, lifestyle-limiting claudication despite maximal medical therapy
- Rest pain
- Nonhealing ulcer
- Gangrene

Options in Revascularization

- Iliac arteries highly amenable to PCI
- Femoral arteries largely amenable to PCI
- Infrapopliteal arteries less amenable to PCI
  - Infrapopliteal bypass also with relatively poor patency rates
- Surgery versus PCI decision often determined by local expertise/practice
- Surveillance of stent/venous bypass graft by U/S at 1 month, 6 months, and annually

PCI: Percutaneous intervention

PAD: Take-home messages

- PAD is common and often asymptomatic
- PAD confers a high risk of CV events regardless of symptom status
- ABI and PVR for physiology
- Ultrasound and CTA/MRA for anatomy
- Exercise training best treatment for claudication, then cilostazol
- Revascularization for disabling claudication or rest ischemia

QUESTION

Repair of an abdominal aortic aneurysm should be considered at a diameter of
a. 2.5 cm
b. 3.0 cm
c. 5.5 cm
d. 4.0 cm
QUESTION

An abnormal ankle brachial index identifies:

- a. Peripheral arterial disease
- b. Hypertension
- c. Increased cardiovascular risk
- d. All of the above
- e. a and c

Selected References