Advances in the Treatment of Peripheral Arterial Disease

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Asian Heart and Vascular Symposium
November 17, 2007

What is Peripheral Arterial Disease?

Peripheral Arterial Disease: PAD

- Common manifestation of atherosclerosis
- Affects blood flow to critical arteries that supply brain, viscera, and limbs
- "Peripheral" - frequently affects legs and feet
- Associated with smoking, high blood pressure, diabetes, age, and hypercholesterolemia

Disclosures

- Grant support, honoraria, consultant:
  - W.L. Gore
  - Cook, Inc.
  - Bard
  - Cordis
Prevalence of PAD

- 12-14% of general population
- > 20% over age 75

Claudication
Muscle pain, ache, cramps, fatigue
30%-35%
2-4 million

Critical Limb Ischemia
Pain at rest, ulceration, gangrene
<10%
400,000-1 million

Ethnic Specific Prevalence of PAD

Men
Women


Growth of U.S. Older Adult Population
Atherosclerosis Is a Systemic Disease

<table>
<thead>
<tr>
<th>Artery</th>
<th>Consequence</th>
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<tbody>
<tr>
<td>Carotid</td>
<td>Stroke</td>
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<tr>
<td>Aorta</td>
<td>Aneurysm</td>
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<tr>
<td>Coronary</td>
<td>MI</td>
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<tr>
<td>Renal</td>
<td>HTN, renal failure</td>
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<tr>
<td>Mesenteric</td>
<td>Bowel infarction</td>
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<tr>
<td>Iliac</td>
<td>Claudication, impotence</td>
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<tr>
<td>Femoral</td>
<td>Claudication</td>
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<tr>
<td>Tibial</td>
<td>Limb loss</td>
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</table>

Atherosclerosis “The Killer”

- Major cause of death in U.S.
  - Cardiovascular disease - #1
  - Stroke - #3
  - Aortic aneurysm - #13

Atherosclerotic Diseases Overlap

35% overlap ≥2 vascular beds

33% of patients with one manifestation often have coexisting disease in other vascular beds.

Atherosclerosis: One-Year CV Event Rate

Steg JAMA 2007
Ankle-Brachial Index (ABI)

- Independent predictor of cardiovascular and all-cause mortality
- ABI < 0.9
  - 3.8 increased risk of all cause mortality

Feringa, Arch Int Med, 2006

Peripheral Arterial Disease

- Intermittent claudication
  - “claudico” – to limp
  - Pain with walking
  - Relieved by rest

- Critical Limb Ischemia
  - Pain at rest, ulcers, or gangrene

Peripheral Arterial Disease

Natural History of Claudication
5 Year Outcomes

- Risk factor modification
- Exercise
- Pharmacologic
- Revascularization for refractory or disabling symptoms

- Non-fatal CV events 20%
- Mortality 15%-30%
  - CV causes 75%

Weitz JI, Circulation 1996
Natural History of CLI
1 Year Outcomes

- Rest Pain
- Ulceration
- Gangrene

Critical Limb Ischemia 1%-2%

Alive with both limbs 50%
Amputation 25%
Dead 25%

Waltz JJ, Circulation 1996

CLI: Scope of the Problem in the US

- 67% of patients with CLI receive major amputation as primary therapy
  - Approximately 200,000 major amputations performed annually
  - < 50% have any vascular evaluation prior to amputation (ABI or angiography)
  - < 50% of all amputees will achieve mobility
  - Within 1 year > 50% of amputees are dead

Allie D, 2005

We Can Do Better Than That!

Patients with CLI should undergo expedited evaluation for possible revascularization with the goal of limb salvage

Operative Treatment of LE PAD

- Aortoiliac:
  - Aortofemoral bypass (AFBG)
  - Aortoiliac endarterectomy
  - Extraanatomic bypass

- Infrainguinal:
  - Femoropopliteal bypass
  - Femoropopliteal endarterectomy
  - Distal bypass

W.L. Gore
Above-knee Fem-pop: The "Gold Standard" for Infrainguinal Intervention

Patency is good, however ...

Morbidity of open surgery often compromises functional outcomes
< 50% patients report a return to "normal" by 6 months postoperatively

Endovascular Therapy?

Benefits of Endovascular Approaches

- Avoid general anesthetic
- Percutaneous - no wounds
- Short hospital stay
- Lower morbidity and mortality
- Excellent technical success
- Durability remains issue
- Technology driven and rapidly evolving

> 80% Endovascular
Advances in the Treatment of PAD

Lower Extremity Ischemia

Past
- Amputation
- Vein Bypass
- Synthetic Bypass
- Endarterectomy

Present
- Angioplasty
- Stents
- Atherectomy
- Surgery

Aortic and Iliac

Advances in the Treatment of PAD

Foxhollow Atherectomy

Cryoplasty Balloon

Nitinol Stent

Viabahn Stent Graft

Ultrasound Reentry Catheter
BASIL: Bypass Vs. Angioplasty

- Decreased morbidity in PTA group
- Shorter hospital stay
- PTA less expensive
- More reinterventions in PTA group
- PTA preferred, especially for “high risk” patients

Amputation-free Survival

Overall Survival

PTA for SFA Occlusions *

* Meta-Analysis 923 pts
Nitinol Stents

- Longer stents
- Increased flexibility
- More resilient
- Low profile

<table>
<thead>
<tr>
<th>Device</th>
<th>Author</th>
<th>Year</th>
<th># limbs</th>
<th>Length (cm)</th>
<th>Primary Patency (years)</th>
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<td>Weighted Average</td>
<td></td>
<td></td>
<td>11.6</td>
<td>90%</td>
<td>84%</td>
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</table>

SFA PTA vs. Stent

Restenosis Rates

Walking Distance

Schillinger M, NEJM, 2006
Problems with SFA Stents

- Restenosis – Intimal hyperplasia
- Stent fractures

Challenges of SFA Intervention

- Long vessel
- Diffuse disease common – multifocal stenoses and occlusions
- Calcification
- Unique mechanical forces
- High incidence of restenosis
Advances in the Treatment of PAD

**Stent Grafts**
**Surgical Bypass vs. Viabahn**
- Prospective randomized, single-center study comparing the GORE VIABAHN® Endoprosthesis to surgical fem-pop bypass
- 100 patients enrolled
- Long SFA lesions
  - 80% > TASC C or D
  - average length 25 cm
- Equivalent primary and secondary patency at one year
- Hospital stay and procedural time significantly shorter for VIABAHN patients

**Long-term VIABAHN Data**
- Prospective, non-randomized study of 65 patients
- Long (average ~15 cm) total occlusions
- 56% primary patency @ 9 years
- 84% secondary patency @ 9 years

**GORE VIABAHN® Endoprosthesis with Heparin Bioactive Surface**

**PAD**
- **Past**
  - Amputation
  - Vein Bypass
  - Synthetic Bypass
  - Endarterectomy
- **Present**
  - Angioplasty
  - Stents
  - Atherectomy
  - Surgery
- **Future**
  - Drug Eluting Stents
  - Resorbable Stents
  - Percutaneous Bypass
Carotid Artery Disease

Stroke
- Affects > 700,000 in US annually
- 3rd leading cause of death
- Leading cause of adult disability
- Estimated annual cost of $62 billion

Most Strokes are Ischemic
- 87% of all strokes are ischemic
- Different than MI
  - Embolic, not plaque rupture
- Extracranial source in 85%
  - Carotid (arterial-arterial)
  - Cardiac
- 1/3 of all strokes are from carotid disease

Carotid Endarterectomy
The Gold Standard
- 98,000 performed in US in 2004
- Most common vascular operation
- Level I evidence
  - Symptomatic
  - Asymptomatic
Endarterectomy or Stent?

1. Filter
2. Balloon
3. Stent
4. Retrieval

Embolic Protection Devices

- Filter
- Balloon
- Stent
- Retrieval
Advances in the Treatment of PAD

Carotid Artery Stenting

• Advantages
  – Treatment option for patients contraindicated for CEA
  – Avoids the risk of cranial nerve damage
  – Does not require general anesthesia

• Disadvantages
  – Limited safety and efficacy data
  – Potential for embolization resulting in stroke
  – Not all patients are suitable for carotid stenting
    • Severe aortic arch and supra-aortic vessel tortuosity
    • Thrombus
    • Very long severe lesions
    • String sign
    • Heavy circumferential calcification

FDA Approves Carotid Stenting

August 31, 2004

FDA granted the first approval for carotid stenting in the U.S for high risk patients who have had symptoms of a stroke or asymptomatic patients who have ≥ 80% stenosis and are not good candidates for endarterectomy.
**CREST Lead-In**

30-day Outcomes by Age

- N=1303
- % MACE 30 days
- Age groups: < 60, 60-69, 70-79, > 80

**EVA-3S**

- Multi-center, randomized, non-inferiority
- Symptomatic > 60% (NASCET)
- CAS (n=261) vs. CEA (n=255)
- Any stroke at 30d

**SPACE**

- 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial

- Multi-center, randomized, non-inferiority
- Symptomatic > 50% (NASCET)
- CAS vs. CEA (n=1183)
- Any stroke at 30d
The Endovascular Explosion

- Many recent technological advances in the treatment of PAD – lowered morbidity and increased safety
- Screen for PAD as a marker of systemic atherosclerosis
- Patients with PAD remain at increased risk for CV events and death
- Patients with CVD risk factors or PAD should be treated aggressively with risk-factor modification and appropriate medications

Endarterectomy or Stent?

- **Endarterectomy**
  - Difficult anatomy
  - Arch disease
  - Tortuosity
  - Heavy calcification
  - Thrombus
  - String sign
  - Age > 80

- **Carotid Artery Stent**
  - “Hostile neck”
    - Prior neck surgery
    - Radiation
    - Tracheotomy
  - High bifurcation
  - “High Risk” for surgery

So, What Do We Know About CAS?

“… as we know, there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns - the ones we don't know we don't know.”

Donald Rumsfeld, 2003