Future Perspectives in Peripheral Intervention

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Conflicts of Interest

- **Consultant**
  - Cordis Endovascular (Modest)
  - Boston Scientific (Modest)
  - Pathway Medical (Modest)
  - Paragon IP (Modest)
  - Proteon Therapeutics (Modest)
  - X-Tent, Inc (Modest)
  - Harvard Clinical Research Institute (Modest)
  - Bacchus Vascular, Inc (Modest)

- **Equity**
  - Access Closure, Inc (Modest)
  - Square One, Inc (Modest)
  - Vascular Therapies, Inc (Modest)
  - Icon Interventional, Inc (Modest)
  - Setagon (Modest)

- **Speaker’s Bureau**
  - Bristol-Myers/Sanofi-Aventis Pharmaceuticals Partnership (Modest)

- **Research Support**
  - Pfizer, Inc.
  - Abbott Vascular
  - Genzyme
  - ActivBiotics

April, 2007
Rate of Deaths Due to Atherosclerosis is Increasing in U.S.

The Evolution of America
The Health of America
Persons Diagnosed with DM in US

So, There’s Plenty of Work for All…

Let each man pass his days in that wherein his skill is greatest…

Sextus Propertius (50-16 BCE), Elegies
But Here is the Reality!

Peripheral Stent Procedures in Medicare by Specialty
(CPT Code 37205)
Is There Differential Specialty Procedural Growth?

Distribution of Medicare Peripheral Stent Procedures in 2005
(CPT 37205)

- Cardiology: 39%
- Internal Med: 2%
- Diag. Radiology: 24%
- Clinic: 0%
- Vascular Surgery: 16%
- Interventional Radiology: 7%
- Other: 4%
- Gen. Surgery: 8%
The Specialties Involved...

**Vascular Surgery**
- Knowledge
- Surgical Skills
- No endo skills
- Low interest in med Rx

**Interventional Radiology**
- Knowledge
- Endo Skills
- No surg skills
- Low interest in med Rx

**Cardiology/Vascular Medicine**
- No Knowledge
- Endo Skills
- No surgical skills
- Some interest in med Rx
The Public Perception of Physicians

A Trial of Disclosing Physicians’ Financial Incentives to Patients

Steven D. Pearson, MSc, MD; Ken Kleinman, ScD; Donna Rabinah; Wendy Levinson, MD

Arch Intern Med 2006;166:623-628

Medical Researcher Moves to Sever Ties to Companies

By ANDREW POLLACK
Published: January 25, 2005

Doctors Take Stock, Supply Data Concerns Over Conflict of Interest: Some Physicians Evaluating Device Own Options

By Gregory Zuckerman, The Wall Street Journal, 1643 words
Aug 15, 2005

OPERATING PROFITS: Mining Medicare; How One Hospital Benefited From Questionable Surgery

By HURT EICHENWALD
Published: August 12, 2003

When Perks Influence the Doctor

Published: October 6, 2002

Clinic executive out
Doctor failed to fully disclose financial ties to device maker
Friday, August 18, 2006
Joel Rutchick
Plain Dealer Reporter
Maybe We Should Have a Randomized Trial of Skills/Management by Each Specialty?

Do You Need a Randomized Trial to Determine What This Person Should do RIGHT NOW???
So, What Should Be Done About All of These Turf Battles?

We KNOW That a Parachute is the Only Reasonable Option…
Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

Abstract

Objectives To determine whether parachutes are effective in preventing major trauma related to gravitational challenge.

Conclusions As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials. Advocates of evidence based medicine have criticised the adoption of interventions evaluated by using only observational data. We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, crossover trial of the parachute.
We Need Data!
Stent revascularization for the prevention of cardiovascular and renal events among patients with renal artery stenosis and systolic hypertension: Rationale and design of the CORAL trial

Christopher J. Cooper, MD, a Timothy P. Murphy, MD, b Alan Matsumoto, MD, c Michael Steffes, MD, d David J. Cohen, MD, e Michael Jaff, DO, f Richard Kuntz, MD, g Kenneth Jamerson, MD, h Diane Reid, MD, i Kenneth Rosenfield, MD, f John Rundback, MD, j Ralph D’Agostino, MD, k William Henrich, MD, l and Lance Dworkin, MD b Toledo, OH; Providence, RI; Charlottesville, VA; Minneapolis, MN; Boston, MA; Ann Arbor, MI; Bethesda and Baltimore MD; and Teaneck, NJ
CORAL Trial Design

Suspected Renal Artery Stenosis

- Informed Consent

- Selective Angiography + Pressure Determination

  - ≥60% with 20mmHg gradient or ≥80%

  - Stent + Embolic Protection
  - No Stent

Optimal Medical Therapy

Follow-up for CV-Renal Events
Public Policy is in Jeopardy
Effectiveness of Management Strategies for Renal Artery Stenosis: A Systematic Review

Ethan Balk, MD, MPH; Couri Raman, MD; Mei Chung, MPH; Stanley I. Albin, MD; Batia Talpaz, MD; Attila Alnso, MD; Patricia Chew, MPH;
Scott J. Gilbert, MD

Background: Renal artery stenosis occurs commonly in patients with cardiovascular disease. There is no standard approach to medical and radiological treatment of this condition.

Purpose: To conduct a systematic review of the literature on the effects of angioplasty and stent placement in patients with atherosclerotic renal artery stenosis.

Data Sources: All relevant databases were searched for English-language articles.

Study Selection: The authors selected prospective studies of renal artery revascularization or medical treatment of patients with atherosclerotic renal artery stenosis that reported mortality rates, kidney function, blood pressure, cardiovascular events, or adverse events at 6 months or later after study entry.

Data Extraction: A standardized protocol with predefined criteria was used to extract details on study design, interventions, outcomes, study quality, and applicability. The overall body of evidence was then graded as robust, acceptable, or weak.

Data Synthesis: No study directly compared aggressive medical therapy with angioplasty and stent placement. Two randomized

Conclusions: Available evidence does not clearly support one treatment approach over another for atherosclerotic renal artery stenosis.

For author affiliations, see end of text.
We’ve Got Plenty of Data on Carotid Stenting….Don’t We?
SAPPHIRE: Study Design

Evaluated by panel of physicians (interventionalist, surgeon, neurologist) who concur on qualification of patient n = 747

- Surgeon: unacceptable risk for CEA
  - Non-Randomized Stent Arm n=406
  - Stent Treatment n=167

- Surgeon & Interventionalist will treat patient
  - RCT 334 Randomized (310 Treated)
  - Treatment:
    - Stent Treatment n=167
    - CEA Treatment n=167

- Interventionalist: unacceptable risk for stenting
  - Non-Randomized CEA Arm n=7

©Cordis Corporation 2007 155-5223
Primary Endpoint: 360-day MAE

Non-Inferiority Statistics

**Stent Non-inferior to CEA**

\[ p=0.0035 \]

\[ \Theta = 0.50764 [-0.03620, 1.05149] \]

<table>
<thead>
<tr>
<th>Stent</th>
<th>CEA</th>
<th>% Difference [95% C.I.]</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.0% (20/167)</td>
<td>19.2% (32/167)</td>
<td>(-7.2%[-14.9%, 0.6%])</td>
</tr>
</tbody>
</table>
Cumulative Percentage of Death at 1080 days

All Randomized Patients

LR p = 0.280

CEA 24.2%
Stent 20.0%

<table>
<thead>
<tr>
<th>Days</th>
<th>Stent</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>167</td>
<td>167</td>
</tr>
<tr>
<td>90</td>
<td>167</td>
<td>164</td>
</tr>
<tr>
<td>360</td>
<td>153</td>
<td>136</td>
</tr>
<tr>
<td>720</td>
<td>136</td>
<td>108</td>
</tr>
<tr>
<td>1080</td>
<td>115</td>
<td>86</td>
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</table>
Cumulative Percentage of Stroke to 30 Days & Ipsilateral Stroke from 31-1080 Days

All Randomized Patients

<table>
<thead>
<tr>
<th>Days</th>
<th>0</th>
<th>30</th>
<th>360</th>
<th>720</th>
<th>1080</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent</td>
<td>167</td>
<td>167</td>
<td>147</td>
<td>130</td>
<td>107</td>
</tr>
<tr>
<td>CEA</td>
<td>167</td>
<td>154</td>
<td>131</td>
<td>104</td>
<td>82</td>
</tr>
</tbody>
</table>

LR p = 0.799

Stent 8.0%  
CEA 6.7%  
Stent 4.9%  
CEA 5.8%  
Stent 3.6%  
CEA 3.1%
Cumulative Percentage of Stroke to 30 Days & Ipsilateral Stroke from 31-1080 Days

All Randomized Patients

<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Randomized</td>
<td>6.7</td>
<td>8.0</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>5.4</td>
<td>7.8</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>7.3</td>
<td>8.0</td>
</tr>
</tbody>
</table>

LR p = 0.799

LR p = 0.831

LR p = 0.848

3-year results based on Kaplan-Meier analysis
1 Year Composite MAE Endpoint
Carotid Stenting Trials

Patients (%)

- BEACH: 9.1%
- CABERNET TCT 2004: 3.3%
- MAVeRIC TCT 2004: 4.5%
- SAPPHIRE Randomized: 5.6%
- SAPPHIRE Registry: 6.0%
- SECuRITY TCT 2003: 6.9%
- ARCHeR 2 IFU 2004: 8.6%
- SHELTER: 6.3%

OPC + delta = 16.6%
CAPTURE 3500:
30 Day Outcomes by Symptomatic Status

§ §
Denotes statistically significant difference at the 0.05 level

** Hierarchical Events
Includes only the most serious event for each patient and includes only each patient first occurrence of each event.

- All pts (N=3500)
- Symp (N=482)
- Asymp (N=3018)

% of all patients

- All stroke & Death*
- Major stroke & Death*

5.7 2.9 10.6 6.2 4.9 2.4

§§

§ Denotes statistically significant difference at the 0.05 level

* Hierarchical Events – Includes only the most serious event for each patient and includes only each patient first occurrence of each event.
Study Design

Prospective, multicenter (73 sites), single arm, open-label study
August 2003 – October 2005

Primary Endpoint:
30-day composite of major adverse events (MAE)
including all death, stroke, and/or myocardial infarction

Patients Enrolled
n = 1,493

30-Day Clinical Follow-up:
91.5% (1348/1473)
30-Day Events Compared with SAPPHIRE

- **CASES-PMS (n=1493)**
- **SAPPHIRE Randomized CAS (n=167)**
- **SAPPHIRE Randomized CEA (n=167)**
30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial

The SPACE Collaborative Group*
Randomized CEA vs. CAS symptomatic patients

**Primary Endpoint**

30 day death and stroke (%)

- **CEA**
  - 6.34
  - 595

- **CAS**
  - 6.84
  - 605

**Abs diff: 0.51, 90%CI 1.89-2.91, P=0.09 (non-inferiority)**

SPACE collaborators. Lancet 2006;368:1239-47
Endarterectomy versus Stenting in Patients with Symptomatic Severe Carotid Stenosis
EVA-3S

All Stroke/Death

CEA: 3.9% (P = 0.01)
CAS: 9.6%

Major Stroke/Death

CEA: 1.5%
CAS: 3.4% (P = 0.26)

N = 520

Mas J-L, et al. NEJM 2006;355:1660-71
Asymptomatic carotid stenosis: what to do
Jessica N. Redgrave and Peter M. Rothwell

Curr Opin Neurol 2007;20:58-64

Recent findings
Optimal medical treatment is the most important aspect of management of patients with asymptomatic carotid stenosis. On the basis of previous trials, endarterectomy is only of overall benefit in men, and this benefit may now be obviated by improved medical treatment. There is insufficient evidence to advocate the routine use of carotid angioplasty or stenting in patients with asymptomatic stenosis. Inaccuracy in the measurement of carotid stenosis may contribute to conflicting estimates of stroke risk in relation to the degree of asymptomatic stenosis. Advances in noninvasive imaging of plaque morphology and inflammation and the detection of microembolic signals may help to risk stratify patients but data on clinical usefulness are lacking.
And What About Peripheral Arterial Disease…Plenty of Data Here…Right?
The Prevalence of P.A.D. Increases with Age


Peripheral Arterial Disease: Why Care about P.A.D.?

A “Call to Action” to Recognize, Diagnose, and Treat P.A.D.

- Major cause of acute and chronic disability
- Limits functional capacity
- Impairs quality of life
- Major cause of limb amputation
- Marked increased risk of nonfatal cardiovascular ischemic events (MI and stroke) and death
- Early detection and treatment decreases risk of MI, stroke and death

Peripheral Arterial Disease: Consequences of undiagnosed and untreated P.A.D. extend well beyond leg stenosis

The prognosis of patients with lower extremity P.A.D. is characterized by an increased short-term risk for cardiovascular ischemic events due to concomitant coronary artery disease and cerebrovascular disease.
Contemporary P.A.D.
Myocardial Infarction and Death

3649 subjects (average age, 64 yrs) followed up for 7.2 years.

Screening for Peripheral Arterial Disease: Recommendation Statement

U.S. Preventive Services Task Force

Summary of Recommendation

The USPSTF recommends against routine screening for peripheral arterial disease. D recommendation.

We Cannot Even Agree on Screening for PAD!
The United States Preventive Services Task Force Recommendation Statement on Screening for Peripheral Arterial Disease
More Harm Than Benefit?

Joshua A. Beckman, MD, MS; Michael R. Jaff, DO; Mark A. Creager, MD
Estimated Mortality Reduction with Targeted Screening

N | PAD | 7 Yr Mortality | Deaths | Lives Saved
---|-----|---------------|--------|-------------
100 | 29 | 8 | 2 | 25%
27% | 8 | 4 | 50%
29% | 8 | 2 | 25%
29% | 8 | 4 | 50%
39% | 11 | 3 | 25%
39% | 11 | 6 | 50%
57% | 17 | 4 | 25%
57% | 17 | 9 | 50%

Circulation 2006;114:861-6
Future Perspectives?

- We need data!
- **Carotid Stenting**
  - CREST
  - ACT 1
  - COAST
- **Renal Artery Stenting**
  - CORAL
  - ASTRAL
- **Peripheral Arterial Stenting**
  - We need a head to head trial of different technologies for the SFA, Popliteal, Tibial arteries
  - We need proof that screening for PAD results in effective COLY saved