Carotid Artery Disease and Stroke

Michael R. Jaff, DO, FACP, FACC
Director, Vascular Medicine
Massachusetts General Hospital
Boston, Massachusetts
Michael R. Jaff, DO
Conflicts of Interest

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

- **Equity**
  - Access Closure, Inc (Modest)
  - Square One, Inc (Modest)
  - Vascular Therapies, Inc (Modest)
  - Icon Interventional, Inc (Modest)
  - Setagon (Modest)
  - I.C. Sciences, Incorporated (Modest)

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

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

June, 2007
Burden of Stroke in the U.S.

- 1 stroke every 45 seconds (700,000 per year)
- 2.4 million non-institutionalized stroke survivors
- Stroke causes 1 in 15 deaths
- Approximately 30% aged 70-80 have silent brain infarction
- Stroke cost = 58.8 billion/year
What is a Stroke?

- Reduction in arterial blood flow to the brain, resulting in ischemia to the brain itself.
- The brain has geographic territories responsible for our higher functions.
Transient Ischemic Attack (TIA)

- 15% of all strokes are heralded by a TIA.
- 1/3 of TIAs would be infarction based on diffusion weighted MRI findings.
- Males and blacks have higher rates of TIA.
- Half fail to report TIA to their healthcare providers.
- 90-day risk of stroke is 3-17% after TIA, highest within the first 30 days.
- Carotid-associated TIA: 20% 90-day stroke risk
TIA Characteristics

- Duration <24 h, usually <15 min
- Symptoms:
  - motor and sensory dysfunction of contralateral limbs
  - pure sensory dysfunction
  - isolated aphasia/dysphasia
  - transient monocular blindness
TIAs Cause Early Stroke and Cardiovascular Events

Follow up of 1707 subjects diagnosed with TIA in ED

Risk Factors for Events:

- Age > 60 y: 1.8
- Diabetes: 2.0
- >10 Min TIA: 2.3
- Weakness: 1.9
- Speech: 1.5

JAMA. 2000;284:2901-2906
What Are The Common Causes of Ischemic Stroke?

**TABLE 1. APPROXIMATE DISTRIBUTION OF MAJOR SUBTYPES OF ISCHEMIC STROKE.**

<table>
<thead>
<tr>
<th>Type of Stroke</th>
<th>Proportion of Strokes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large-vessel atherothrombotic</td>
<td>15</td>
</tr>
<tr>
<td>Due to internal-carotid-artery stenosis</td>
<td>9</td>
</tr>
<tr>
<td>Small-vessel (lacunar)</td>
<td>25</td>
</tr>
<tr>
<td>Embolic</td>
<td>60</td>
</tr>
<tr>
<td>Due to atrial fibrillation</td>
<td>15</td>
</tr>
<tr>
<td>Other (due to dissection or other causes)</td>
<td>3</td>
</tr>
</tbody>
</table>

*The data are from the Stroke Data Bank of the National Institute of Neurological and Communicative Disorders and Stroke and the Framingham Study. The percentages do not total 100 because of a modification of the categories of stroke used.

Furie KL, Kistler JP, NEJM 2000
Artery to Artery Embolism
Does Risk of Stroke Increase with Greater Degrees of ICA Stenosis?

- 696 Patients evaluated with Carotid Duplex Ultrasonography
- 369 Male/327 Female
  - Mean Age 64 years
- Mean Follow-Up 41 months
- Duplex Ultrasonography Categories
  - Mild  <50% Stenosis
  - Moderate  50-75% Stenosis
  - Severe  >75% Stenosis

Stroke 1991;22:1485
## Vascular Risk of Asymptomatic Carotid Stenosis

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>TIA</th>
<th>CVA</th>
<th>Cardiac Event</th>
<th>Vascular Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50%</td>
<td>303</td>
<td>1</td>
<td>1.3</td>
<td>2.7</td>
<td>1.8</td>
</tr>
<tr>
<td>50-75%</td>
<td>216</td>
<td>3</td>
<td>1.3</td>
<td>6.6</td>
<td>3.3</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>177</td>
<td>7.2</td>
<td>3.3</td>
<td>8.3</td>
<td>6.5</td>
</tr>
</tbody>
</table>

75% of Events were Ipsilateral to the Stenosis

Stroke 1991;22:1485
What Can the Physical Exam Tell You About the Etiology of Stroke?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diagnosis/Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fib/Flutter, Bradycardia</td>
<td>Likely Cardiogenic Embolus</td>
</tr>
<tr>
<td>No pulse below knee</td>
<td>Recurrent systemic embolus</td>
</tr>
<tr>
<td>Carotid Bruit</td>
<td>Severe Extracranial Carotid Stenosis</td>
</tr>
<tr>
<td>Head/Orbital Bruit</td>
<td>AV Malformation</td>
</tr>
<tr>
<td>Fever and Acute CVA</td>
<td>Endocarditis and Cardiogenic Embolus</td>
</tr>
<tr>
<td>Stroke and Altered MS</td>
<td>Check Glucose, EtOH, Narcotics, O/D, other Toxins</td>
</tr>
</tbody>
</table>
Cervical Bruit

- Marker of systemic atherosclerosis
- Not indicative of severity of internal carotid artery stenosis
  - NASCET: Sensitivity 63%/Specificity 61%
- Frequency of Cervical Bruits
  - ~1-3% in adults aged 45-54 years
  - ~8% in adults ≥75 years
Causes of Cervical Bruit (Systolic, Diastolic, or Both)

- Carotid atherosclerosis
- Thyrotoxicosis
- Transmitted cardiac murmur
  - Aortic Stenosis (systolic)
  - Aortic Insufficiency (diastolic)
- Arteriovenous Fistula (systolic/diastolic)
- Venous Hum (systolic or systolic/diastolic)
The Diagnosis of Carotid Artery Disease

- Complete neurologic history and physical examination
- Complete medical history and physical examination
- Carotid Duplex Ultrasonography
- (?) Magnetic Resonance Arteriography
- (?) CT Angiography
- (?) Arteriography
Indications for Carotid Duplex Ultrasonography

- Cervical bruit in an asymptomatic individual
- Amaurosis Fugax
- Transient Ischemic Attack
- Stroke in a potential candidate for CE or stent
- Follow-up of known stenosis (>20%) in asymptomatic individuals
- Follow-up after carotid endarterectomy or stent
- Intraoperative assessment of carotid endarterectomy
- Drop attacks (rare)
What is the Relationship Between PSV and Carotid Arteriographic Stenosis

Radiology 2000;214:247-252
80-99% Internal Carotid Artery Stenosis
Carotid MRA
Preoperative Evaluation of Carotid Artery Stenosis: Comparison of Contrast-MR Angiography and Duplex Ultrasonography with Digital Subtraction Angiography


71 vessels-39 symptomatic patients

MRA

- Sensitivity: 94.9%
- Specificity: 79.1%

Duplex

- Sensitivity: 92.9%
- Specificity: 81.9%

Combined Concordant

- 80% of vessels

Concordant 80% of vessels

for identification of stenoses ≥ 70%
CT Angiography

- New and emerging technology
- Requires intravenous iodinated contrast
- Requires significant radiation exposure
- Allows for three dimensional wide field of view
- Able to detect and characterize calcification
CTA for Assessment of Carotid Disease

meta-analysis of 28 studies

Stroke. 2004;35:2306
Carotid Duplex Ultrasonography Ipsilateral to Bruit
Modern Diagnostic Algorithm for Extracranial Carotid Disease

Suspicion of Extracranial Carotid Disease

Carotid Duplex Ultrasonography

- <50% Stenosis
  - Appropriate F/U DUS

- 50-99% Stenosis in Appropriate Clinical Scenario
  - MRA/CTA
    - DUS/MRA/CTA Agree?
      - YES
        - CAS
      - NO
        - Angio

- Occlusion
  - Appropriate F/U DUS

Surgery

Med Rx
Once in an ED, You Must Get an Imaging Test IMMEDIATELY!

Classic Wedge-Shaped Acute Right MCA Stroke
Important Characteristics of the CT Scan

- Within 3 hours of onset of ischemia, the CT *without contrast* is virtually normal
- After 6-12 hours, there is evidence of hypodensity with brain edema
- Hemorrhage
  - Appearance will describe type
    - Subdural Hematoma: Crescent shape below dura
    - Subarachnoid Hemorrhage: Diffuse blood pattern along surface of brain in subarachnoid space
      - 5% of SAH have NORMAL CT!!! MUST perform Lumbar Puncture
      - Discern between SAH and traumatic LP
      - RBC Count in 4 tubes all similar
      - Xanthochromic Supernatant---old RBCs consistent with SAH
MRI Demonstrating Acute Right MCA CVA
Stroke Prevention Strategies

- Reduction in Blood Pressure
- Cessation of Tobacco Use
- Reduction in Serum Cholesterol
- Aggressive Glycemic Control
- Antiplatelet Therapy
- Revascularization of Carotid Stenosis
Control of Hypertension

- The most potent risk factor for stroke
- A factor in nearly 70% of all strokes
- 10-12 fold increase in risk when comparing highest diastolic BP compared to the lowest

Effect of Diuretic Therapy on Risk of Stroke in Patients with Hypertension

<table>
<thead>
<tr>
<th>Trial</th>
<th>Events, n Treatment:Control</th>
<th>Odds ratios and confidence limits Treatment:Control</th>
<th>Reduction, %, and SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDFP</td>
<td>102:158</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRC</td>
<td>60:109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 others</td>
<td>127:217</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All trials (heterogeneity $\chi^2 = 0.85; NS$)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Differences associated with long-term differences of 5 to 6 mm Hg DBP

Stroke 35%–40%?

Collins et al., Lancet, 1990
ACE Inhibition Prevents Recurrent Stroke: 
*The Progress Trial*

6105 subjects with previous stroke randomly assigned to perindopril (n=3051) or placebo (n=3054).

PROGRESS Collaborative Group. Lancet 2001:358; 1033
Stroke Prevention Strategies

- Reduction in Blood Pressure
- **Cessation of Tobacco Use**
- Reduction in Serum Cholesterol
- Aggressive Glycemic Control
- Antiplatelet Therapy
- Revascularization of Carotid Stenosis
Risk of CVA Among Women Who Smoke and Have Partners Who Smoke

5379 Women Who Smoke Followed for 8.5 Years

<table>
<thead>
<tr>
<th>Participants</th>
<th>Sample Size</th>
<th>No. of Events</th>
<th>Event Rate/100</th>
<th>Age-Adjusted RR (95% CI)</th>
<th>Multivariate-Adjusted RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarette-smoking women with nonsmoking spouse</td>
<td>443</td>
<td>28</td>
<td>6.3</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Cigarette-smoking women with cigarette-smoking spouse</td>
<td>1904</td>
<td>174</td>
<td>9.1</td>
<td>1.4 (0.95–2.1)</td>
<td>1.4 (0.9–2.0)</td>
<td>0.1</td>
</tr>
<tr>
<td>All strokes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarette-smoking women with nonsmoking spouse</td>
<td>443</td>
<td>2</td>
<td>0.5</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Cigarette-smoking women with cigarette-smoking spouse</td>
<td>1904</td>
<td>49</td>
<td>2.6</td>
<td>5.7 (1.4–24)</td>
<td>5.7 (1.4–24)</td>
<td>0.02</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarette-smoking women with nonsmoking spouse</td>
<td>443</td>
<td>2</td>
<td>0.5</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Cigarette-smoking women with cigarette-smoking spouse</td>
<td>1904</td>
<td>43</td>
<td>2.3</td>
<td>5.1 (1.2–21)</td>
<td>4.8 (1.2–20)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Stroke 2005;36:e74-e76
Stroke Prevention Strategies

- Reduction in Blood Pressure
- Cessation of Tobacco Use
- **Reduction in Serum Cholesterol**
- Aggressive Glycemic Control
- Antiplatelet Therapy
- Revascularization of Carotid Stenosis
Statins Decrease the Risk of Stroke in High Risk Patients: *Heart Protection Study*

**SIMVASTATIN: MAJOR VASCULAR EVENTS**

<table>
<thead>
<tr>
<th>Vascular event</th>
<th>STATIN (10269)</th>
<th>PLACEBO (10267)</th>
<th>Risk ratio and 95% CI</th>
<th>24% SE 2.6 reduction (2P&lt;0.00001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CHD</td>
<td>914</td>
<td>1234</td>
<td>STATIN better</td>
<td></td>
</tr>
<tr>
<td>Total stroke</td>
<td>456</td>
<td>613</td>
<td>STATIN worse</td>
<td></td>
</tr>
<tr>
<td>Revascularisation</td>
<td>926</td>
<td>1185</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANY OF ABOVE</td>
<td>2042 (19.9%)</td>
<td>2606 (25.4%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*50% reduction in CEA or angioplasty*
(simvastatin 42 [0.4%] vs placebo 82 [0.8%]; P=0.0003)

MRC/BHF HPS Investigators Lancet 2002; 360 (9326): 7
SPARCL

- 4731 patients with recent CVA/TIA (1-6 months before randomization)
- NO KNOWN CAD
- LDL-C 100-190 mg/dL
- Randomized to Placebo vs Atorvastatin 80 mg/d
- Primary Endpoint: First non-fatal or fatal stroke

SPARCL

Primary Endpoint


Fatal Stroke
Stroke Prevention Strategies

- Reduction in Blood Pressure
- Cessation of Tobacco Use
- Reduction in Serum Cholesterol
- Aggressive Glycemic Control
- Antiplatelet Therapy
- Revascularization of Carotid Stenosis
Diabetes Control and CV Events

- The DCCT (Diabetes Control and Complications Trial)
  - 1441 patients with Type 1 DM (1983-1993)
  - Randomized to conventional vs intensive glycemic control
  - Treated for mean of 6.5 years
  - 93% followed until February 2005

- CV Disease defined as: Non-Fatal MI, CVA, Death due to CV Disease, Angina, Need for CABG/PCI)

Cumulative Incidence of Non-Fatal MI, CVA, CV Death

Intensive Treatment:
- Reduced Risk of ANY CV Event by 42%
- Reduced Risk of Non-Fatal MI, CVA, CV Death by 57%
- Reduction in HbA1C explained vast majority of benefit

Stroke Prevention Strategies

- Reduction in Blood Pressure
- Cessation of Tobacco Use
- Reduction in Serum Cholesterol
- Aggressive Glycemic Control
- *Antiplatelet Therapy*
- Revascularization of Carotid Stenosis
Antiplatelet Trialists’ Collaboration

Efficacy in Prevention of Ischemic Events

**Clopidogrel vs Aspirin to Prevent Recurrent Ischemic Events**

Primary Analysis of MI, Ischemic Stroke, or Vascular Death

*ITT analysis.*

CAPRIE Study

Outcome by Subgroup

Mean & 95% CI

Aspirin better
Clopidogrel better

Stroke
MI
PAD
All patients

CAPRIE Steering Committee. Lancet. 1996;348:1329-1339
Aspirin & Dipyridamole Decreases Stroke after TIA

European Stroke Prevention Study

6602 pts with recent TIA or CVA followed for 2 years

Stroke (%)

ASA  DYP  ASA-DYP  Placebo

J Neurol Sci 1996; 143(1-2):1
So, What Works in Preventing Stroke?

- Reduction in Blood Pressure
- Cessation of Tobacco Use
- Reduction in Serum Cholesterol
- Aggressive Glycemic Control
- Antiplatelet Therapy
- Revascularization of Carotid Stenosis
Surgery for Carotid Stenosis

- **NASCET**
  - ASA: 26.0%
  - Surgery: 9.0%

- **ACAS**
  - ASA: 10.6%
  - Surgery: 4.8%
Early vs Deferred Carotid Endarterectomy in Asymptomatic Patients with >70% ICA Stenosis

- Prospective randomized multicenter trial in Europe
  - 126 hospitals in 30 Countries
  - Surgeons with documented perioperative CVA/Death rate <6% in prior 50 CEAs
- 3120 asymptomatic patients with asymptomatic ICA stenosis >60%
- Randomized to
  - Immediate CEA
  - Indefinite deferral of CEA
- Followed for up to 5 years (mean 3.4 y)

Early vs Deferred Carotid Endarterectomy in Asymptomatic Patients with >70% ICA Stenosis

- Risk of CVA/Death within 30 days of CEA
  - 3.1%

- 5-year CVA risk
  - 3.8% immediate CEA
  - 11% deferred CEA (p<0.0001)
    - Half of all CVAs were disabling

- Combining peri-op and non-peri-op CVA
  - 5-year CVA risk
    - 6.4% vs 11.8% (p<0.0001)

Early vs Deferred Carotid Endarterectomy in Asymptomatic Patients with >70% ICA Stenosis

Any Stroke or Perioperative Death

MRC Asymptomatic Carotid Surgery Trial (ACST): Medical RX

Problems:
- No pill counts/compliance reports
- No report of treatment goals attained

ACST Collaborative Group. Lancet 2004; 363: 1491
Carotid Endarterectomy

- **Complications**
  - Wound Complications
    - Hematoma 0.7-1.5%
    - Infection/Pseudoaneurysm 0.15%
    - Cranial Nerve Dysfunction
      - Hypoglossal Nerve 5-8%
      - All other Cranial Nerves <2%
  - Perioperative Stroke
    - Cleveland Clinic
      - 1.5% Asymptomatic
      - 2.7% Prior TIA
      - 3.8% Prior CVA
Carotid Artery Stenting
Why Carotid Stenting?

- Potential Advantages
  - Less Invasive Technique
    - More Widely Accepted by Patients
    - Less Discomfort
    - Faster Recovery Time
  - Less Expensive
  - Treat Difficult Lesions
    - Post Radiation ICA Stenosis
    - Restenosis after Endarterectomy
    - High Bifurcation Stenosis
    - Serious Co-Morbid Medical Conditions
Who Will Be Covered?

• Patients at **high risk for CEA** with a **SYMPTOMATOMIC** carotid artery stenosis ≥70%
• Patients at **high risk for CEA** with a **SYMPTOMATOMIC** carotid artery stenosis between 50% and 70% AND are enrolled in a Category B IDE Clinical Trial
• Patients at **high risk for CEA** with an **ASYMPTOMATOMIC** carotid artery stenosis ≥80% AND are enrolled in a Category B IDE Clinical Trial
Decision Memo for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R3)

Decision Memo

TO: Administrative File: CAG 00085R3
    Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting

FROM: Steve Phurrough, MD, MPA
       Director, Coverage and Analysis Group

       Marcel Salive, MD, MPH
       Director, Division of Medical and Surgical Services

       Sarah McClain, NHS
       Lead Analyst

       Joseph Chin, MD, MS
       Lead Medical Officer

       Rosemarie Hakim, PhD, MS
       Epidemiologist

SUBJECT: Coverage Decision Memorandum for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting

DATE: April 30, 2007
What is “High Risk”?

- **Serious Co-Morbid Medical Condition**
  - Congestive heart failure (class III/IV) and/or known severe left ventricular dysfunction
  - LVEF <30%
  - Open heart surgery needed within six weeks
  - Recent MI (>24 hrs. and <4 weeks)
  - Unstable angina (CCS class III/IV)
  - Severe pulmonary disease

- **Anatomic Challenges**
  - Contralateral carotid occlusion
  - Contralateral laryngeal nerve palsy
  - Radiation therapy to neck
  - Previous CEA with recurrent stenosis
  - High cervical ICA lesions or CCA lesions below the clavicle
  - Severe tandem lesions
  - Age > 80 years
Protected Carotid-Artery Stenting versus Endarterectomy in High-Risk Patients

Jay S. Yadav, M.D., Mark H. Wholey, M.D., Richard E. Kuntz, M.D., M.Sc., Pierre Fayad, M.D., Barry T. Katzen, M.D.,
Gregory J. Mishkel, M.D., Tanvir K. Bajwa, M.D., Patrick Whitlow, M.D., Neil E. Strickman, M.D.,
Michael R. Jaff, D.O., Jeffrey J. Popma, M.D., David B. Snead, Ph.D., Donald E. Cutlip, M.D.,
Brian G. Firth, M.D., Ph.D., and Kenneth Ouriel, M.D., for the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators*
SAPPHIRE STUDY
Trial Design and Patient Flow

Surgeon &/or Interventionalists Declare Willingness to Treat High Surgical-Risk Patient
n = 747

- Surgeon: too high risk for CEA
- Interventionalists: too high risk for stenting

Non-randomized
Stent Arm
n=406

RCT
334 Randomized (310 Treated)

- Surgeon & Interventionalist will treat patient

Non-randomized
CEA Arm
n=7

Stent Treatment
n=167

CEA Treatment
n=167
The SAPPHIRE Trial

Primary Endpoint: Stroke, MI, Death at 30 Days

Yadav S.  American Heart Association, Chicago, Illinois November 19, 2002
### SAPPHIRE Data

<table>
<thead>
<tr>
<th>Event</th>
<th>Intention-to-Treat Analysis</th>
<th>Actual-Treatment Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stenting (N=167) no. (%)</td>
<td>Stenting (N=159) no. (%)</td>
</tr>
<tr>
<td>Death</td>
<td>12 (7.4)</td>
<td>11 (7.0)</td>
</tr>
<tr>
<td></td>
<td>21 (13.5)</td>
<td>19 (12.9)</td>
</tr>
<tr>
<td>Stroke</td>
<td>10 (6.2)</td>
<td>9 (5.8)</td>
</tr>
<tr>
<td></td>
<td>12 (7.9)</td>
<td>11 (7.7)</td>
</tr>
<tr>
<td>Major ipsilateral</td>
<td>1 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>5 (3.3)</td>
<td>5 (3.5)</td>
</tr>
<tr>
<td>Major nonipsilateral</td>
<td>1 (0.6)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td></td>
<td>2 (1.4)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Minor ipsilateral</td>
<td>6 (3.7)</td>
<td>6 (3.8)</td>
</tr>
<tr>
<td></td>
<td>3 (2.0)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Minor nonipsilateral</td>
<td>3 (1.9)</td>
<td>3 (2.0)</td>
</tr>
<tr>
<td></td>
<td>4 (2.7)</td>
<td>3 (2.1)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5 (3.0)</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td></td>
<td>12 (7.5)</td>
<td>12 (8.1)</td>
</tr>
<tr>
<td>Q-wave</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2 (1.2)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Non–Q-wave</td>
<td>5 (3.0)</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td></td>
<td>10 (6.2)</td>
<td>10 (6.7)</td>
</tr>
<tr>
<td>Cranial-nerve palsy</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8 (4.9)</td>
<td>8 (5.3)</td>
</tr>
<tr>
<td>Target-vessel revascularization</td>
<td>1 (0.6)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td></td>
<td>6 (4.3)</td>
<td>6 (4.6)</td>
</tr>
<tr>
<td>Conventional end point (stroke or death at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr)</td>
<td>9 (5.5)</td>
<td>8 (5.1)</td>
</tr>
<tr>
<td></td>
<td>13 (8.4)</td>
<td>11 (7.5)</td>
</tr>
<tr>
<td>Primary end point (death, stroke, or myocardial infarction at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr)</td>
<td>20 (12.2)</td>
<td>19 (12.0)</td>
</tr>
<tr>
<td></td>
<td>32 (20.1)</td>
<td>30 (20.1)</td>
</tr>
</tbody>
</table>

*P Value*
Protected Carotid Stenting in High-Risk Patients With Severe Carotid Artery Stenosis

Robert D. Safian, MD,* John F. Bresnahan, MD,† Michael R. Jaff, DO,‡ Malcolm Foster, MD,§ J. Michael Bacharach, MD,∥ Brijeshwar Maini, MD,¶ Mark Turco, MD,# Subbarao Myla, MD,** Gustav Eles, MD,†† Gary M. Ansel, MD,‡‡ on behalf of the CREATE Pivotal Trial Investigators
CREATE

- Prospective non-randomized registry of 419 high-risk patients for CEA
- Technical success 97.4%
- Primary Endpoint
  - Death 8 (1.9%)
  - Nonfatal CVA 14 (3.3%)
  - Nonfatal MI 4 (1%)
- Independent Predictors of CVA/Death at 30 Days
  - Symptomatic Status
  - Duration of Filter Dwell Time
  - Baseline Renal Function

J Am Coll Cardiol 2006;47:2384-9
1 Year Composite MAE Endpoint
Carotid Stenting Trials

Patients (%)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BEACH</td>
<td>9.1%</td>
</tr>
<tr>
<td>CABERNET TCT 2004</td>
<td>3.3%</td>
</tr>
<tr>
<td>MAVeRIC TCT 2004</td>
<td>4.5%</td>
</tr>
<tr>
<td>Saphire Randomized</td>
<td>5.6%</td>
</tr>
<tr>
<td>Saphire Registry (TCT 2003)</td>
<td>12.0%</td>
</tr>
<tr>
<td>Security (TCT 2003)</td>
<td>7.2%</td>
</tr>
<tr>
<td>ARCHer 2 (IFU 2004)</td>
<td>8.7%</td>
</tr>
<tr>
<td>Shelter</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

OPC + delta = 16.6%
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*
Endarterectomy versus Stenting in Patients with Symptomatic Severe Carotid Stenosis
What Are The Benefits of rtPA in Acute Ischemic Stroke?

- 30% more likely to have no/minimal residual deficit compared to patients who received placebo
- Risk: 10-fold risk of intracerebral or any hemorrhagic complication
<table>
<thead>
<tr>
<th>Duration</th>
<th>&lt;3 h from onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT brain</td>
<td>No hemorrhage or clear infarction</td>
</tr>
<tr>
<td>Laboratory studies</td>
<td>Hematocrit, platelets, PT/PTT</td>
</tr>
</tbody>
</table>

If above are negative or normal, treat with intravenous tPA

Administer tPA, 0.9 mg/kg: 10% in 1 min; remainder in 60 min

Perform hourly neurologic examinations × 6, then every 2 h for first 24 h

Repeat CT and blood studies at day 2
Who Benefits from Carotid Therapy Today?

- Symptomatic patients with >70% ipsilateral carotid artery stenosis deserve revascularization
  - High Risk for CEA: Candidate for CAS
- The jury (CMS) remains out on ANYONE else
- Symptomatic patients with 50-69% ipsilateral carotid artery stenosis
  - Candidates for CEA (CAS if high risk and in trial)
- Asymptomatic patients with >60% carotid stenosis
  - ??? CEA
  - Trial to evaluate CAS
  - Optimize medical therapy?
  - Enroll in TACIT?
- EVERYONE gets optimal
  - Antiplatelet Therapy
  - Antihypertensive Therapy
  - Lipid Lowering Therapy
  - Strategies to Stop Smoking
  - Tight Glycemic Control