Asymptomatic Carotid Stenosis

“To Do or Not To Do”

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Neurosciences: Updates and Controversies

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Can You Do Too Much to Prevent a Stroke?

By JANE E. BRODY  OCTOBER 15, 2012 12:01 AM  61 Comments

Stroke is the fourth leading cause of death among Americans, and a much larger contributor to chronic disability and health care costs than any other cause of death. Preventive steps taken to avoid it can themselves become a risk, if they’re taken to extremes.

Yvetta Fedorova

What would you like to know?

RECENTLY ASKED

FITNESS

After rigorous exercise, the risk of a more acute a day or two later. Why is that?

Answered by GRETCHEN REYNOLDS

Are naps healthy?

Asked by Apollo
Principle Sources

Seemant Chaturvedi M.D. University of Miami
J. David Spence M.D., Western University, Ontario Canada
Topics of Discussion

• Epidemiology
• Clinical Correlates
• Landmark CEA studies
• Modern Medical Management of Carotid Stenosis recommendations
• Future of ACS (Asymptomatic Carotid Stenosis), Evaluation and Management
Prevalence

- Asymptomatic severe stenosis (>70%) in unselected patients 0 - 3.1% *
- In men > 70 years, 2-3% *
- In women > 70 years, roughly 1% *
- Higher rates in patients with DM *

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- In USPSTF – prevalence of high grade carotid stenosis fell from 1% (1992) to 0.5% (1998) likely secondary to improved medical management
- Ethnic Differences in Carotid Stenosis
  - Native Americans > Caucasians > Hispanics > African Americans > Asians

*De Weerd et al STROKE 2010, 41: 1294-97
Methods for diagnosis

U/S – 70-80% accurate
MRA
CTA
Conventional angiography

Prior to intervention, 2 studies recommended and angiography used for discordant cases
How are patients identified

- Carotid bruits
- Contralateral symptomatic lesion
- Screening for surgical procedures (CABG, AAA surgery)
- Screening due to atherosclerotic disease elsewhere

- General screening not recommended by USPSTF (2014)
Clinical Manifestation

- Purely asymptomatic
- Cognitive dysfunction? – Renewed interest
- Imaging evidence of silent brain infarction beyond ACS
- TIA or Stroke > 6 months earlier
- VB Symptoms
Risk for ACS

• Similar for CAD
  • Age
  • Male
  • Smoking
  • DM
  • Hypertension
  • High LDL
  • Low HDL

• Likely Risks:
  • Diet high in fat and cholesterol
  • Sedentary Life Style
  • Family History
  • Mental/Social Stress
Risk stratification in ACS

- Clinical variables – Age, gender and ethnicity
- Transcranial Doppler with embolus detection
- Plaque echolucency or ulceration
- Progression of stenosis
- MRI of the plaque (lipid core, intra-plaque hemorrhage)
TCD microembolus detection

• 319 ACS patients studied between 2000-2004
• 10% had high intensity signals indicative of microemboli
• Stroke risk at 1 year
  – No emboli – 1%
  – Emboli 15.6%

Spence Stroke 2005,36 2373-2378
Decline of microemboli with intensive medical therapy

• Prior to 2003 – 12.6%
• After 2003 – (intensive medical therapy) 3.7%
• Conclusion, reduction of microemboli equals reduction of stroke

Spence, Arch Neurol, 2010, 67: 180-6
Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study

Hugh S Markus, Alix King, Martin Shipton, Raji Tapalika, Marisa Cullimore, Sheila Thwaites, Nathan M Borrenes, Arjun Schnoor

Summary

Background Whether surgery is beneficial for patients with asymptomatic carotid stenosis is controversial. Better methods of identifying patients who are likely to develop stroke would improve the risk–benefit ratio for carotid endarterectomy. We aimed to investigate whether detection of asymptomatic embolic signals by use of transcranial doppler (TCD) could predict stroke risk in patients with asymptomatic carotid stenosis.

Methods The Asymptomatic Carotid Emboli Study (ACES) was a prospective observational study in patients with asymptomatic carotid stenosis of at least 70% from 26 centres worldwide. To detect the presence of embolic signals, patients had two 1 h TCD recordings from the ipsilateral middle cerebral artery at baseline and one 1 h recording at 6, 12, and 18 months. Patients were followed up for 2 years. The primary endpoint was ipsilateral stroke and transient ischaemic attack. All recordings were analysed centrally by investigators masked to patient identity.

Findings 482 patients were recruited, of whom 407 had evaluable recordings. Embolic signals were present in 77 of 407 patients at baseline. The hazard ratio for the risk of ipsilateral stroke and transient ischaemic attack from baseline to 2 years in patients with embolic signals compared with those without was 2.54 (95% CI 1.20–5.36; p=0.035). For ipsilateral stroke alone, the hazard ratio was 5.52 (1.63–19.32; p=0.007). The absolute annual risk of ipsilateral stroke or transient ischaemic attack between baseline and 2 years was 7.12% in patients with embolic signals and 1.04% in those without, and for ipsilateral stroke was 1.41% in patients with embolic signals and 0.78% in those without. The hazard ratio for the risk of ipsilateral stroke and transient ischaemic attack for patients who had embolic signals on the recording preceding the next 6-month follow-up compared with those who did not was 2.63 (95% CI 1.04–6.68; p=0.049), and for ipsilateral stroke alone the hazard ratio was 6.37 (1.19–32.57; p=0.009). Controlling for antplatelet therapy, degree of stenosis, and other risk factors did not alter the results.

Interpretation Detection of asymptomatic embolisation on TCD can be used to identify patients with asymptomatic carotid stenosis who are at a higher risk of stroke and transient ischaemic attack, and also those with a low absolute stroke risk. Assessment of the presence of embolic signals on TCD might be useful in the selection of patients with asymptomatic carotid stenosis who are likely to benefit from endarterectomy.

Funding British Heart Foundation.

Background About 15% of strokes are caused by carotid artery stenosis. In patients with symptomatic carotid stenosis greater than 90–99%, carotid endarterectomy reduces ipsilateral stroke risk by about 75% and is generally accepted as being cost effective. However, the situation in patients with asymptomatic carotid stenosis is less clear. Asymptomatic carotid stenosis is more benign than symptomatic carotid stenosis and has an ipsilateral stroke risk of 2% or less per year.1 Two large randomised trials, the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST),2 reported that about 32 patients needed to have carotid endarterectomy to prevent disabling stroke or death in one patient over a 5-year period. The cost-effectiveness of surgery for asymptomatic carotid stenosis has been questioned,3 and recently the benefit of surgery has been suggested to be even less because of the availability of more effective medical therapies.4 Nevertheless, asymptomatic carotid stenosis accounts for a large burden of stroke. Only 15% of strokes are preceded by transient ischaemic attack (TIA) and therefore waiting for strokes to become symptomatic may fail to prevent most strokes caused by carotid stenosis. Risk–benefit and cost–benefit ratios of carotid endarterectomy in asymptomatic carotid stenosis would be improved if surgery was only done in patients with asymptomatic carotid stenosis who are at particularly high risk of stroke.5 In patients with symptomatic carotid stenosis, the stroke risk increases markedly over the few months after symptom onset, and the mechanism of stroke is believed to be primarily embolic.6 If clinical embolism is a good predictor of the subsequent stroke risk, asymptomatic cerebral emboli might also predict clinical stroke risk. Transcranial doppler ultrasound (TCD) is a non-invasive technique that can be used to detect circulating emboli. These emboli appear as short-duration, high-intensity embolic signals and are...
ACES Study (Asymptomatic Carotid Emboli Study)

- 467 patients with ACS studied with TCD looking for microembolus signal
- 16% had embolic signals (84% no embolic signal)
- 3.6% annual stroke rate if + for embolic signal
- 0.7% annual stroke rate if – for embolic signal

Conclusion - Embolic signal = Stroke
No embolic signal = No stroke
ACES Study (cont.)

- Embolic signal plus plaque echolucency
- 37% had + plaque echolucency
- Echolucency predicts increase stroke rate
- Plaque echolucency plus microemboli additive risk

- Conclusion – Combined studies can identify high risk group (8% per year) and low risk group (<1% per year) based on echolucency and microemboli on TCD

- Neurology 2011, 77: 751-58
Progression of Stenosis

- Categories
- 0-49%, 50-69%, 70-89%, 90-99%, 100%
- Progression of stenosis by 2 or 3 categories associated with ipsilateral stroke of TIA
- 1469 patients studied
- 50 patients showed (2.9%) progressed by 2 categories
- However, regression was as likely as progression
- Likely secondary to medical therapy
Newer imaging techniques

- Will improve risk stratifications
- 3D U/S – revealing plaque ulceration and plaque echolucency (increased fat content in plaque)
- Plaque MRI – reveals intra-plaque hemorrhage
- PET Scan – reveals plaque inflammation
- TCD with embolus detection grossly under utilized

Stroke, 2014, 45:3720-3724
Best medical management 2015 for ACS

- Antiplatelet agents (? Dual)
- Aggressive use of high potency statins; Rosuvastatin (Crestor), Ezetimibe (Zetia)
- Targeted blood pressure lowering (< 140 systolic, <130 in DM)
- ACE/ARB utilizations (? Additional protective effect beyond blood pressure control)
- Smoking cessation
- Risk factor control (DM, A1C control)
- Life style interventions (regular exercise and Mediterranean type diet)
History of CEA – Where have we been?

- NASCET and ECST launched in 1980’s for **symptomatic** stenosis
- ACAS for **asymptomatic** stenosis
- ACST in 1990’s
- These studies resulted in sharp increase in CEA ~ 135,000 per year
- All studies done prior to aggressive medical therapy including statin use
250,000 Carotid Interventions worldwide

<table>
<thead>
<tr>
<th>Region</th>
<th>Asymptomatic (%)</th>
<th>Proportion Stented (%)</th>
<th>Proportion CEA</th>
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<tbody>
<tr>
<td>US</td>
<td>90</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>Europe</td>
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<tr>
<td>UK</td>
<td>20</td>
<td>10</td>
<td>90</td>
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Uncertainty about whether to intervene in asymptomatic patients as well as about choosing CEA vs. CAS
Absolute Benefits of CEA

• Symptomatic 70-99% - 8.5% absolute risk reduction
• Symptomatic 50-69% - 1.3% absolute risk reduction
• Asymptomatic  - 1.2% absolute risk reduction
• Conclusion – CEA in asymptomatic patients minimal value
Questions Remaining...

- Value in Women
- Value in Elderly > 75 years of age
- Not well established in either group
Annual Stroke Rates with Carotid Stenosis

• Pre-Statins use:
  • Symptomatic 70-90% (13%/yr)
  • Asymptomatic 60-90% (2–2.5%/yr)

• Statin use: Percentage of patients on statins
  • NASCET 14.5% (1980’s)
  • ACE 28% (1990’s)
  • ASCT 38% (2000’s)

• Statin use continuing to increase
Patients with ACS should be prescribed daily ASA and a statin. Patients should be screened for other treatable risk factors for stroke” Class I

It is reasonable to consider performing CEA in asymptomatic patients who have > 70% stenosis of ICA if the risks of perioperative stroke, MI and death is low (<3%).

However it’s effectiveness compared to contemporary best medical management alone is not well established.
ASA primary prevention

• “Prophylactic CAS might be considered in highly selective patients with asymptomatic carotid stenosis (minimum, 60% by angiography, 70% by validated Doppler U/S) but it’s effectiveness compared with medical therapy alone is not well established” (Class IIb; level of evidence B.)
ASA primary prevention

• “Selection of asymptomatic patients… should be guided by co-morbid conditions and life expectancy”
• “Prophylactic CEA with M&M less than 3% can be useful in highly selected patients”
• “3% threshold for complication rate may be high because of advances in medical therapy”
AAN
“Choosing wisely recommendations”

• Don’t perform imaging of the carotid arteries for simple syncope
• Don’t recommend CEA for asymptomatic stenosis unless the complication rate is <3%
## CREST Trial (Carotid Revascularization Endarterectomy vs. Stent Trial)

<table>
<thead>
<tr>
<th>Event Description</th>
<th>CEA</th>
<th>CAS</th>
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<tbody>
<tr>
<td>Stroke, Death, MI + ipsilateral stroke after 30 days</td>
<td>6.8 %</td>
<td>7.2%</td>
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<tr>
<td>Stroke w/in 30 days</td>
<td>2.3%</td>
<td>4.1%</td>
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<tr>
<td>MI w/in 30 days</td>
<td>2.3%</td>
<td>1.1%</td>
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<tr>
<th>Peri-Procedural Stroke or Death in Asymptomatic CREST patients</th>
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<tbody>
<tr>
<td>CAS</td>
<td>15</td>
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<tr>
<td>CEA</td>
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What about intensive medical therapy?

- There has never been a large multi-center study done to compare carotid revascularization + IMT vs. IMT alone

- Goals for IMT
  - LDL < 70mb/dl
  - SBP < 140 for Non-diabetics < 130 for DM
  - Statins
  - Dual anti-platelet therapy
  - Life style management
Potential Risk Reductions Estimated with IMT

• High Potency Statins – 33% RRR
• Dual Antiplatelet therapy – 10-32% RRR
• B/P control - 20-30% RRR
• Life Style Management -10-39% RRR
• Recent studies using modern medical therapy and risk stratification report stroke rates of .34% (Oxford Vascular Study); 0.3% (SMART); 0.7% (ACES)
• If confirmed by larger studies CAS/CEA will unlikely achieve these results

• SPARCL Trial, CHANCE Trial
Next generation of studies

- CREST 2
- ECST 2
- SPACE 2
- ACST 2

- All above studies will include best aggressive medical care arms
What might the future bring?

- Genetic Markers (Chromosome 9p21.3)
- Advanced imaging
- Bio-markers
- Risk stratification
Conclusions & Recommendations

• Asymptomatic carotid stenosis is uncommon in unselected patients

• Variety of diagnostic test available with variable reliability – Risk stratification may be extremely useful

• Early studies suggest value of endarterectomy and possibly carotid stenting

• With intensive medical therapy the risk of stroke or death in patients with ACS appears below the risk of endarterectomy or stenting (SPENCE)
Conclusions & Recommendations

• Most ACS patients (approx. 90%) will be better off with medical therapy than either intervention (SPENCE)

• The few patients that may benefit from intervention can be identified with TCD w/ embolus detection and/or advanced imaging of the plaque (SPENCE)

• The vast majority of patients should be treated with IMT including high potency statins and ezetimibe (Zetia), life style changes, dual anti-platelet and effective B/P control (SPENCE)