I want Medical Therapy for my ASYMPTOMATIC patients with Carotid Disease

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Really?
Disclosures

**Speaker’s Bureau:**
- W.L. Gore Company
- Covidien

**Medical/Scientific Boards:**
- Sparrow Clinical Research Institute

**Consultant:**
- RTI Surgical
Carotid Artery Disease

Stroke

• 3rd cause of death in US
• 150,000 deaths/year
• 600,000 cases/year
• 2 million/year handicapped people

HIGH SOCIAL / ECONOMIC COST

Mellière et al. J Mal Vasc, 1993
Stroke

- From 1995–2005, the stroke death rate fell ~30 percent and the actual number of stroke deaths declined ~14 percent.

- Nearly three-quarters of all strokes occur in people over the age of 65.
Stroke

- 8-10% of ischemic strokes are related to extracranial carotid artery disease
- Increased incidence with age (33% < 45 yrs and 80% >50 yrs)

Carotid Artery Disease

Ischemic stroke causes

- Hemorrhagic: 13%
- Extracranial Carotid: 8%
- Intracranial Carotid: 8%
- Unknown: 44%
- Lacunar: 20%
- Cardio-embolic: 20%

Stroke Etiology

Carotid Artery Disease

2000-2006 U.S. Stroke Deaths by County
Multiple medical specialties are involved in treating patients with carotid artery disease.

Reimbursement incentives are malaligned.

Best Medical Therapy, Stenting Techniques, and Surgical approach to CEA are rapidly evolving.

Risk Factors and Health Care Delivery are constantly changing.
Carotid Artery Disease

The Problem

Where is the evidence?
Endarterectomy Trials

The efficacy of Carotid Endarterectomy (CEA) for patients with asymptomatic high-grade carotid stenosis was evaluated in three high-quality randomized controlled trials. These were the Veterans Affairs Cooperative Study Group (VA trial), the Asymptomatic Carotid Atherosclerosis Study (ACAS), and the Asymptomatic Carotid Surgery Trial (ACST).
A meta-analysis of these trials found that CEA for asymptomatic carotid stenosis is associated with a small absolute risk reduction (ARR) for the outcome of any stroke.

- In the VA trial, the ARR was 1.0 percent over a mean follow-up of 4 years
- In ACAS, the ARR was 3.0 percent over 2.7 years
- In ACST, the ARR was 3.1 percent over 3.4 years
## Carotid Artery Disease

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<th>Study</th>
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Carotid Artery Disease

- 1984: Stroke - Roederer and colleagues examined 167 patients with <80% stenosis

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<td>Stable &lt;80% stenosis</td>
<td>1.5%</td>
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<tr>
<td>Progressive stenosis &gt;80%</td>
<td>46%</td>
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Sources:
From April 1994 to December 2000, asymptomatic high-grade (80% to 99%) carotid stenosis was identified in 196 carotid arteries in 180 male veterans.

The NOM group and the OP group had no significant difference in their ipsilateral neurologic event-free rate out to 3 years (96% +/- 6.8% versus 95% +/- 2.7%).
Outcome of nonoperative management of asymptomatic high-grade carotid stenosis.

**CONCLUSION:**

- Although CE is the preferred treatment for asymptomatic high-grade carotid stenosis, NOM is an acceptable alternative in selected patients at high risk with diminished life expectancy.
OF NOTE

These trials enrolled from the late 1980s through the early 2000s, a time when medical therapy was suboptimal compared with contemporary standards.

Therefore, the efficacy of CEA for asymptomatic carotid disease compared with best medical therapy in modern practice is controversial, and must be questioned.
The Problem

Despite numerous Randomized Controlled Studies comparing treatment options, and monumental resources allocated to studying Carotid Artery Disease, a unified approach to treatment still eludes us in 2015.
Carotid Artery Disease

The Problem

Stroke Risk has decreased!

We cannot accept historical medical controls or diagnostic imaging modalities for comparators to guide today's therapy.
Can we use Imaging to Guide Therapy?

Four common methods of carotid imaging

- Duplex Ultrasonography
- CT Angiography
- MRA – High resolution
- Digital Subtraction Angiography
• Duplex Ultrasonography
  • <50%
  • 50-70%
  • 70-80%
  • 80-99%

Detection of echolucent plaques using duplex ultrasonography, embolic signals using TCD have proved helpful
• CTA
  • % Stenosis
  • Ulceration
  • Dissection
  • Calcium
MR Carotid Plaque Imaging and Contrast-Enhanced MR Angiography Identifies Lesions Associated with Recent Ipsilateral Thromboembolic Symptoms: An In Vivo Study at 3T


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Carotid Artery Disease

Plaque Imaging at 3T

What were the identifiable characteristics:
- Lipid rich necrotic core
- Juxtaluminal calcification
- Hemorrhage
- Fibrous cap status
- Histologically correlated
Plaque Imaging at 3T

- Histopathologic confirmation
Plaque Imaging at 3T

Necrotic Core
Simple small lipid rich/necrotic core (LR/NC)
Non-enhancing region on post-gad T1WI
Plaque Imaging at 3T

**Juxtataluminal calcifications**

- Dark on all imaging sequences,
- esp 3D TOF MRA
Plaque Imaging at 3T

Intraplaque hemorrhage

Bright on T1WI, 3D TOF MRA, 3D MP RAGE
Plaque Imaging at 3T

Fibrous cap status
Can determine if cap is thick, thin, or ruptured. Identify inflammation (loose matrix) as bright on T2WI.

Later inflamed cap will enhance possibly due to neovascularity.
High Resolution Carotid MR Angiography

500-600 micron resolution CE MRA

Excellent agreement between CE MRA and DSA
Carotid Artery Disease

HD-MRA Consistent and Reliable

Soft plaque w/ hemorrhage
Carotid Artery Disease

HD-MRA Potential to prevent Strokes and guide Rx
Carotid Artery Disease

HD-MRA Can Guide Definitive Therapy

Asymptomatic patient with 74% stenosis and moderate size partially hemorrhagic necrotic core. The size of the necrotic core has increased despite continued statin therapy. The carotid stenosis is now severe, measuring 85%. Patient underwent CEA.
Carotid Artery Disease

HD-MRA Can Monitor Medical Therapy

After 5 years of treatment with single dose of a statin there is a large necrotic core.

After 8 months of treatment with a different statin, there is considerable decrease in the necrotic core with developing loose matrix and deep calcifications.

After 14 months of treatment with different statin, almost all the necrotic core has resolved and replaced with loose matrix. The deep calcification has increased in size.
Carotid Artery Disease

HD-MRA Can Demonstrate Regression of Disease

Despite Lipitor 40 mg and LDL=91 for 3 years, there is a large intraplaque hemorrhage.

After 3 years of Lipitor 80 mg and LDL=64, almost all the intraplaque hemorrhage has resolved and the distal CCA stenosis is less severe.
How Do We Treat?

- **Symptomatic Patients**
  - < 70% stenosis
    - HR-MRA
      - At risk – Eversion Endarterectomy
      - Low risk – Medical Therapy
  - > 70% Stenosis
    - Eversion Endarterectomy
    - If High Risk or anatomically unfavorable Stenting
How Do We Treat?

• Asymptomatic Patients
  • < 50% stenosis
    • Risk Factor Modification
    • Lipid therapy
    • Head to Toe Risk Assessment

• 50 - 70% Stenosis
  • HD-MRA
    • High Risk – Eversion Endarterectomy
    • Low Risk – Medical Therapy yearly followup
Carotid Artery Disease

How Do We Treat?

• Asymptomatic Patients
  • 70 - 80% Stenosis
    • HD-MRA
      • High Risk – Eversion Endarterectomy
      • Low Risk – Aggressive Medical Therapy 6 month followup
  • 80 - 99% Stenosis
    • HD-MRA
      • Eversion Endarterectomy
      • Unless Calcified stable plaque
The importance of the best medical treatment cannot be overstated, as more advanced pharmacological agents, and more stringent management of atherosclerotic risk factors, have dramatically changed the management and outcomes of atherosclerotic disease.
Carotid Artery Disease

What constitutes “Best” Medical Therapy in 2015

• Smoking Cessation
• Blood Pressure Control
• Lipid Management
• Physical Activity
• Weight Management
• Diabetes Management
• Antiplatelet Therapy
• Renin-angiotensin system blockers
• B-Blockers
• We Treat?
Carotid Artery Disease

What constitutes “Best” Medical Therapy in 2015

• **Smoking Cessation**
  • Goal: Complete cessation

• **Blood Pressure Control**
  • Goal: < 140/90 mm Hg

• **Lipid Management**
  Goal: Treatment with statin therapy; use statin therapy to achieve an LDL-C of 100mg/dL; for very high risk* patients an LDL-C 70 mg/dL is reasonable; if triglycerides are 200 mg/dL, non–HDL-C† should be 130 mg/dL, whereas non–HDL-C 100mg/dL for very high risk patients is reasonable
What constitutes “Best” Medical Therapy in 2015

• **Physical Activity**
  
  Goal: At least 30 minutes, 7 days per week (minimum 5 days per week)

• **Weight Management**
  
  • Goals:
    
    Body mass index: 18.5 to 24.9 kg/m²
    
    Waist circumference: women 35 inches (89 cm), men 40 inches (102 cm)

• **Diabetes Management**
  
  • Initiation of pharmacotherapy interventions to achieve target HbA1c may be reasonable. *(Level of Evidence: A)*
    
    A target HbA1c of 7% may be considered. *(Level of Evidence: C)*
What constitutes “Best” Medical Therapy in 2015

- **Antiplatelet Therapy**
  - Aspirin 75–162 mg daily is recommended in all patients with carotid artery disease unless contraindicated. *(Level of Evidence: A)*
  - Clopidogrel 75 mg daily is recommended as an alternative for patients who are intolerant of or allergic to aspirin. *(Level of Evidence: B)*

- **Renin-angiotensin system blockers**
  - Consider adding ACE and ARB’s in patients with concomitant EF 40%

- **B-Blockers**
  - Add in patients with Heart Failure or previous MI
Carotid Artery Disease

What constitutes “Best” Surgical Therapy in 2015

- Eversion Endarterectomy
  - 438 consecutive cases
  - Stroke rate 0.46%
  - STEMI 1.3%
  - NSTEMI 1.8%
  - 35 to 55 minute procedure
  - 24 hour hospital stay
  - Low recurrence rate 2.5% vs. 5.2%
What constitutes “Best” Interventional Therapy in 2015

- Cerebral Protection Carotid Stenting
  - 200 consecutive cases
  - *Stroke rate* 3.5%
  - *STEMI* 1.5%
  - *NSTEMI* 2.5%
  - *Post balloon or not*
    - Lower stroke vs. higher recurrence
  - *24 hour hospital stay*
  - *Less invasive approach*
Treatment

CEA vs. CAS

The CREST ("carotid revascularization endarterectomy vs. stenting trial") and SAPPHIRE ("stenting and angioplasty with protection in patients at high risk for endarterectomy") are 2 randomized trials comparing CEA and CAS. Neither SAPPHIRE nor CREST address the question now posed by improvements in BMT, namely whether patients with ACS should undergo any revascularization procedure.
Carotid Artery Disease

Treatment

**CEA vs. CAS vs. BMT**

Whether CEA and CAS are comparable treatment options in ACS or whether a revascularization is better than BMT is currently investigated in the ongoing SPACE-II trial, including patients with >70% carotid stenosis that are randomized into 3 arms (CEA, CAS, BMT) as well as in the ACST-2 trial that plans to recruit 5000 patients and follow them up for at least 5 years.
Asymptomatic Carotid Artery Disease has been shown to be independently associated with traditional risk factors assessed individually and through the Framingham Risk Score.

In every category of Framingham risk, prevalence of Carotid Artery Disease was strongly related to the degree of cervicocephalic stenosis.

Therefore, detection of an Asymptomatic Carotid Stenosis should lead to a cardiac workup and to an optimal treatment of vascular risk factors.
CONCLUSIONS

In order to answer the Question at hand we will have to await the ongoing SPACE-II trial, as well as in the ACST-2 trial.
CONCLUSIONS

Patients with ACS have a high overall vascular risk. A cardiac workup and an optimal treatment of vascular risk factors should be done.

CEA is an evidenced-based therapeutic option. However, most data come from the last century. Actually, the available data for CAS are not sufficient to judge the role of CAS as compared to CEA and BMT.

BMT has led to a significant reduction of stroke risk (<1% per year) in patients with ACS. Therefore, the indication or a CEA should be done with restraint and based on life expectancy, sex, and comorbidity.
CONCLUSIONS

Medical Management
When and Why is this Preferred Treatment for CAD

Asymptomatic non-operative disease
Post intervention Therapy
Post operative therapy
Symptomatic non-operative disease

IN FACT:

Medical Therapy is the preferred Treatment for ALL patients with Carotid Artery Disease
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Thank You
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