Carotid Artery Stenosis
Etiology, Diagnosis, Management

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Disclosures

- Prior consultant for Phillips Imaged Guided Therapy Corporation
- I was trained to be a vascular surgeon with bias towards surgery

Goals

- Describe the etiology and diagnosis of carotid artery disease and ischemic stroke
- Compare outcomes of carotid artery revascularization
Background, Etiology, Epidemiology

History

- Chiari – autopsy study (1905)
- Fischer – carotid plaque
- DeBakey – CEA (1951)
- Eastcott – CCA-ICA bypass (1953)
- Transfemoral stent (1989)
- TCAR (2009)

Operative Record (Dictated and corrected by Dr. M. E. DeBakey)

Surgery by: M. E. DeBakey, M. D.
Date: August 7, 1953

Preoperative Diagnosis - Atherosclerotic stenosis of left common and internal carotid arteries

Postoperative Diagnosis - Same as preoperative diagnosis

Procedure - Thromboendarterectomy of left common and internal carotid arteries.

Findings - Partially organized and fresh thrombus of internal carotid artery arising at origin of internal carotid artery and attached to well-localized atherosclerotic lesion producing acute occlusion of common carotid artery with patent external carotid artery which could be felt pulsating by intraglandular flow.

Procedure - Under general anesthesia, using Pentothal supplemented by ether and cyclopropane, the patient was prepared and draped to expose the left side of the neck. A longitudinal incision was made along the anterior border of the sternocleidomastoid muscle, and the anterior jugular vein was divided and ligated. The common carotid artery was exposed by retracting the internal jugular vein and the strap muscles, and the carotid sheath was opened. The internal and external carotid arteries were then dissected free of surrounding tissues for about 5 cm above the bifurcation. Unilateral tapes were then placed around the common carotid, internal carotid, and common carotid arteries. Halothane revealed a weak pulse in the external carotid artery but none in the internal carotid artery or the common carotid artery. The internal carotid artery was clamped, and the common carotid artery was freed from the arch by sharp dissection. The incision was carried down to the skin and closed with interrupted sutures.

Dr. DeBakey, M. E.: The preparations for this procedure were made by Dr. Eastcott, and I assisted.

Dr. Eastcott, M. E.: The operation was performed under hypothermia and after adequate intravenous fluid administration. The patient tolerated the procedure well, and the postoperative course was uneventful.

Dr. DeBakey, M. E.: The postoperative course was uneventful, and the patient was discharged on the 12th postoperative day.

Dr. Eastcott, M. E.: The postoperative course was uneventful, and the patient was discharged on the 12th postoperative day.
Background

- 795,000 strokes/year
- $45 billion annually
- 87% of strokes are ischemic
- Leading cause of long-term disability
- 1 of every 20 death

Risk Factors for Ischemic Stroke

- Sex
- Race
- Hypertension
- Family History
- Atrial fibrillation
- Cigarette smoking
- Hypercholesterolemia
- Diabetes
- Sedentary lifestyle
Pathophysiology of CAS and Ischemic Stroke

- 20% of ischemic strokes
- Embolization and hypoperfusion
- Hollenhorst reported on embolization to retinal vessels

Screening and Diagnosis
Screening

- No randomized trials evaluating utility of screening
- Rationale for not screening?
  - Prevalence of severe disease
  - Annual risk of ipsilateral stroke is low
  - Other characteristics?
  - Physical Exam?

Carotid duplex is not recommended for routine screening of asymptomatic patients who have no clinical manifestations of or risk factors of atherosclerosis.

Ultrasound screening of the carotid arteries may be considered for patients who have other symptomatic atherosclerotic disease (PAD, CAD, aortic aneurysm) or have two or more risk factors for atherosclerotic disease.
Screening – Guidelines

2014 guidelines indicate screening *low-risk* populations for asymptomatic carotid artery stenosis is not recommended.

USPSTF in 2021 reaffirmed their 2014 position recommending against screening for asymptomatic disease in the *general* adult population.

Screening – Guidelines

- Considered in asymptomatic patients who are at an increased risk of carotid stenosis especially those willing to consider carotid intervention
- Clinically significant PAD
- 65 years or older with history of CAD, smoking, hypercholesteremia
- Prior to CABG
Diagnostic Evaluation

- Once carotid artery stenosis has been identified it is important to determine the severity
- Cerebral angiogram is the classic gold standard
- Asymptomatic: carotid ultrasound
- Symptomatic: CTA

Carotid Duplex Ultrasound

- Advantages: Non-invasive, safe, inexpensive
- Disadvantages: “Operator dependent”, less sensitive for occlusion
- Provides ranges for stenosis

<table>
<thead>
<tr>
<th>Classification</th>
<th>Stenosis</th>
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<tbody>
<tr>
<td>Mild</td>
<td>&lt; 50%</td>
</tr>
<tr>
<td>Moderate</td>
<td>50-69%</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt; 70%</td>
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</table>

- Careful interpretation needed in the setting of contralateral occlusion
MRA

- Advantages: No radiation, no contrast with TOF imaging
- Disadvantages: Expensive, time-consuming

CTA

- Advantages: anatomic detail, rapid
- Disadvantages: contrast, radiation
Catheter Based Cerebral Angiography

- Advantages: entire carotid evaluation compared to ultrasound, lesion morphology, collateral circulation
- Disadvantages: invasive, cost, risks

Management

Asymptomatic Disease

Carotid Stenosis

Asymptomatic

Symptomatic
Risk Factor Modification

- Risk equivalent for cardiovascular disease
- Smoking cessation
- Glycemic control in patients with diabetes
- Healthy diet and exercise
  - RRR 25%
- Obesity
  - RRI of 1.64

Medical Therapy

- Antiplatelet
  - No RCT data to support DAPT over aspirin
  - Clopidogrel can be used as monotherapy if intolerant of aspirin
- Lipid lowering agents
  - ACST: 10-year risk of stroke on statin vs no statin (13% vs 24%)
- Antihypertensives
  - Reduces stenosis progression (14% vs 31%)
  - Every 20 mmHg SBP or 10 mmHg DBP associated with 2-fold increase in stroke/death
### Surveillance of Asymptomatic Disease

<table>
<thead>
<tr>
<th>Indication</th>
<th>At 3-5 months</th>
<th>At 6-8 months</th>
<th>At 9-12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal prior exam</td>
<td></td>
<td></td>
<td>Inappropriate</td>
</tr>
<tr>
<td><strong>Surveillance Frequency During First Year</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plaque without significant stenosis</td>
<td>Inappropriate</td>
<td>Inappropriate</td>
<td>Inappropriate</td>
</tr>
<tr>
<td>Mild stenosis (&lt;50%)</td>
<td>Inappropriate</td>
<td>Inappropriate</td>
<td>Inappropriate</td>
</tr>
<tr>
<td>Moderate stenosis (50-69%)</td>
<td>Inappropriate</td>
<td>Uncertain</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Severe stenosis (70-99%)</td>
<td>Uncertain</td>
<td><strong>Appropriate</strong></td>
<td>Uncertain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Surveillance Frequency After First Year</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque without significant stenosis</td>
</tr>
<tr>
<td>Mild stenosis</td>
</tr>
<tr>
<td>Moderate stenosis</td>
</tr>
<tr>
<td>Severe stenosis</td>
</tr>
</tbody>
</table>

### Who to revascularize?

- VA Trial (50-99%)
  - NEJM 1993
- Asymptomatic Carotid Atherosclerosis Study (ACAS) (60-99%)
  - JAMA 1995
- Asymptomatic Carotid Surgery Trial (ACST)
  - Lancet 2004
- **Meta-analysis:** CEA associated with absolute risk reduction of 1% per year over 3 years (NNT 33). Perioperative risk of stroke or death was 2.9%

<table>
<thead>
<tr>
<th></th>
<th>BMT</th>
<th>BMT+CEA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsi-stroke or any peri-op stroke or death</td>
<td>11.0%</td>
<td>5.1%</td>
<td>p=0.004</td>
</tr>
<tr>
<td>Ipsi-TIA/stroke or any perio-op TIA/stroke/death</td>
<td>19.2%</td>
<td>8.2%</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>
Life expectancy?

- ACST Trial – stratified by age
  - Age < 65: 5-year risk of any stroke 1.8% vs 9.6%
  - Age 65-75: 5-year risk of any stroke 2.2% vs 9.7%
  - Age >75: 5-year risk of any stroke 5% vs 8.8%

SVS recommends patients should have a 3 to 5-year life expectancy and perioperative stroke/death rates ≤3% to benefit from CEA.

Recent Data

Incidence of Ischemic Stroke in Patients With Asymptomatic Severe Carotid Stenosis Without Surgical Intervention

- JAMA 2022 by Robert W. Chang, et al
- 3737 patients (57% male)
- Mean follow-up of 4.1 years
- 133 ipsilateral strokes with mean annual stroke rate of 0.9%
- Kaplan-Meier estimate of ipsilateral stroke by 5 years was 4.7%
Should we wait for 80%?

- Oxford Vascular Study with systematic review and meta-analysis
- Published in The Lancet Neurology in 2021

5-year risk of ipsilateral ischemic stroke

- 70-99% 14.6% (6 of 53)
- 50-69% none (0 of 154)
- p<0.0001

- 80-99% 18.3% (5 of 34)
- 50-79% 1% (1 of 173)
- p<0.0001

Management

Symptomatic Disease

Carotid Stenosis

Asymptomatic

Symptomatic
Medical Management

- Acute treatment of stroke is outside the scope of this talk but in general patients that present within 6 hours of onset should be considered for intervention including systemic thrombolysis or percutaneous thrombectomy.
- Basic management includes permissive hypertension, checking/modifying risk factors, antiplatelet/anticoagulant.
- Imaging is obtained with a stroke and often includes CT head, MRI/MRA, CTA Head/Neck.

Who benefits?
Patient selection

Likely to Benefit

• Moderate and Severe Stenosis

Unlikely to Benefit

• Mild stenosis
• Severe comorbidity due to other surgical or medical illness
• Persistent, severe deficit and disability
• No benefit with total occlusion

North American Symptomatic Carotid Endarterectomy Trial (NASCET)

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>CEA</th>
<th>BMT</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50%</td>
<td>15%</td>
<td>19%</td>
<td>0.16</td>
</tr>
<tr>
<td>50-69%</td>
<td>16%</td>
<td>22%</td>
<td>0.045</td>
</tr>
<tr>
<td>70-99%</td>
<td>9%</td>
<td>26%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
European Carotid Surgery Trial (ECST)

- Primary outcome at 3 years with 80-100% stenosis
  - 14.9% vs 26.5% (p=0.001)

Timing Carotid Revascularization
Timing of Revascularization – Wait 2 days

- We want to balance the risk of hemorrhagic conversion and recurrence of stroke
- Recommended to wait at least 2 days for a non-disabling stroke

- 500 consecutive patients underwent CEA in Italy. Grouped by time to CEA from stroke. 0-2 days, 3-7 days, 8-14 days, >15
  ▪ CEA performed < 2 days from stroke increased risk of stroke (OR 9.7)

Timing of Revascularization – Before 14 days

- 549 patient series found patients who experience their stroke after TIA, 43% of strokes occurred within 7 days of index TIA

5-Year ARR in Ipsilateral Carotid Territory Ischemic Stroke (Including the Perioperative Risk) Conferred by CEA in Patients with a NASCET 50%-69% and 70%-99% Stenosis, Stratified for Delay from Index Event to Randomization and Patient Sex

<table>
<thead>
<tr>
<th></th>
<th>50%-69% Stenosis</th>
<th>70%-99% Stenosis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ARR</td>
<td>NNT</td>
</tr>
<tr>
<td>ALL PATIENTS</td>
<td>14.8%</td>
<td>7</td>
</tr>
<tr>
<td>&lt;2 weeks</td>
<td>3.3%</td>
<td>30</td>
</tr>
<tr>
<td>2-4 weeks</td>
<td>4.0%</td>
<td>25</td>
</tr>
<tr>
<td>&gt;12 weeks</td>
<td>-2.9%</td>
<td>nb</td>
</tr>
</tbody>
</table>

Early carotid endarterectomy is associated with improved outcomes
Timing of Revascularization

- Stroke in evolution
- Crescendo TIA

Stroke and Death with CEA
20.2% Stroke in Evolution
11.4% Crescendo TIA

≤30% MCA territory volume
2-8% Stroke in Evolution
0-2% Crescendo TIA
Carotid Endarterectomy

Perioperative Stroke and MI

- Stroke rates from larger trials 2-3%
- Etiology must be rapidly determined
  - Plaque emboli, improper flushing, poor cerebral protection, relative hypotension

- MI rates ~2%
Cerebral Hyperperfusion Syndrome

- Ipsilateral headaches, often improved by upright posture
- Intracerebral hemorrhage
- Seizures
- Higher risk with high-grade stenosis
- Prevention: SBP < 150 mmHg
- Severe headache should prompt head CT and potential admission and BP control

Hematoma

- Can be a catastrophic complication with abrupt loss of airway
- Overall incidence 3.4%
- Uncontrolled hypertension during emergence from anesthesia
- Increased risk when concomitant CABG is performed
Cranial Nerve Injury

- Occurs in ~5%
- Hypoglossal nerve most common
- Facial nerve 1.9%, Vagus, glossopharyngeal 0.7%

Infection
Restenosis

- Reported in 2-10% at 5 years
- Early (within 2-3 years) and Late
  - Early tends to be highly cellular and minimally ulcerated intimal hyperplasia (LOW risk of symptoms)
  - Late tends to be recurrence of disease
- Most are asymptomatic and found by follow-up carotid imaging
- Risk factors age <65, smokers, females, elevated Cr, hyperlipidemia

Restenosis

- Indications same as primary stenosis
- Re-operative CEA
  - Wide range of complication reporting
- Carotid stenting increasingly being used
- Similar rates of death/perioperative stroke with TF-CAS and CEA
- VQI review of 4425 patients from 2016-2020 who underwent redo CEA, TF-CAS, and TCAR
  - TCAR vs redoCEA: Stroke/TIA 1.3% vs 3.5%
  - TCAR vs TF-CAS: Stroke/TIA: 1.3% vs 3.1%
Transfemoral carotid artery stenting (TF-CAS)

- Inaccessible carotid lesions
- Radiation-induced stenosis
- Restenosis after CEA
- Clinically significant cardiopulmonary disease increasing anesthetic risk
- Unfavorable neck anatomy: contralateral vocal cord paralysis, open tracheostomy, or prior radical surgery

Carotid Revascularization Endarterectomy vs Stenting Trial (CREST)

- NEJM 2010, Brott TG, et al
- Multicenter, unblinded, parallel group, randomized, superiority trial across 117 centers in US/Canada
- 2502 patients, split between stent and CEA
- Primary endpoint was composite of any stroke, MI, or death during the periprocedural period or ipsilateral stroke within 4 years after randomization
- 47% were asymptomatic

- 4 years composite
  - 7.2% vs 6.8%
- 10 years composite
  - 11.8% vs 9.9%

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
<th>95% CI / p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periprocedural</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite</td>
<td>5.2%</td>
<td>4.5%</td>
<td>0.82-1.68</td>
</tr>
<tr>
<td>Death</td>
<td>0.7%</td>
<td>0.3%</td>
<td>p=0.18</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.1%</td>
<td>2.3%</td>
<td>p=0.01</td>
</tr>
<tr>
<td>MI</td>
<td>1.1%</td>
<td>2.3%</td>
<td>p=0.03</td>
</tr>
</tbody>
</table>
ACST-2

- Published in Lancet in 2021

<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disabling stroke or death procedurally</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Non-disabling procedural stroke</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Transcarotid artery revascularization (TCAR)

- Hybrid surgical approach accessing the common carotid
- Avoids risk of crossing the aortic arch
- Distal embolic protection by reversal of flow
- Has anatomic constraints
  - Diameter CCA needs to be 6 mm
  - Need 5 cm of CCA
TCAR vs TF-CAS

- JAMA 2019, Schermerhorn ML, et al
- 3286 paired patients

<table>
<thead>
<tr>
<th></th>
<th>TCAR</th>
<th>TF-CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital Stroke or Death</td>
<td>1.6%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.3%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Death</td>
<td>0.4%</td>
<td>1.0%</td>
</tr>
<tr>
<td>MI</td>
<td>0.2%</td>
<td>0.3%</td>
</tr>
<tr>
<td>1-year ipsilateral stroke or death</td>
<td>5.1%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Access site complication</td>
<td>1.3%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

ROADSTER 2

- Stroke 2020, Kashyap VS, et al
- Single-arm, post-approval registry study evaluating patients at high risk for complication with CEA
- 632 adherent to protocol
- Symptomatic patients ≥50% (26% of patients) or Asymptomatic ≥80%
- Primary endpoint: procedural success encompassing technical success plus absence of stroke, MI, or death within the 30-day postoperative period

- 0.6% stroke, 0.2% death, 0.9% MI
- Composite 1.7%
Looking Ahead

- CREST-2
- ECST-2
- ROADSTER-3

Summary

- Carotid artery stenosis a significant cause of ischemic stroke
- Screening is beneficial in the correct population
- Cardiovascular risk factor modification is critical to reducing not only stroke risk, but risk from coronary artery disease and death
- Benefit from carotid revascularization in asymptomatic disease is evolving but likely not warranted below 80% stenosis
- Carotid revascularization is indicated with at least 50% stenosis in symptomatic patients
- Carotid endarterectomy is a safe procedure in a properly selected patient
- TCAR has equal stroke risk to CEA, and less than TF-CAS
References

References

- Kashyap VS, Schneider PA, Foteh M, et al. Early Outcomes in the ROADSTER 2 Study of Transcarotid Artery Revascularization in Patients With Significant Carotid Artery Disease. Stroke. 2020;51(9):2620-2629. doi:10.1161/STROKEAHA.120.030550