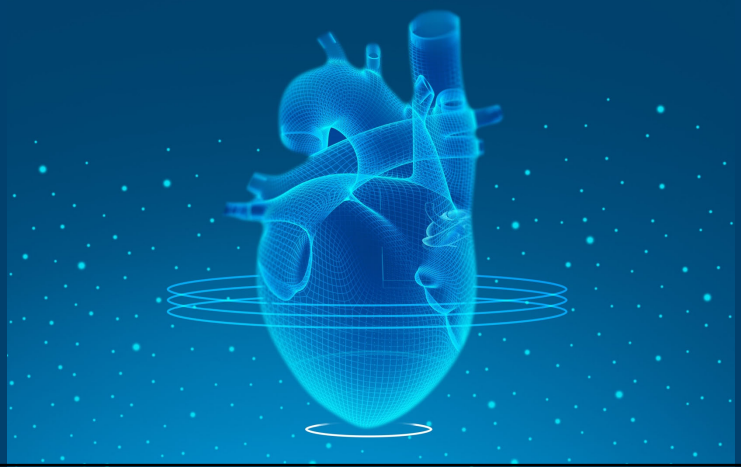
Minneapolis Heart Institute Foundation

GRAND ROUNDS



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Carotid Artery Stenosis

Etiology, Diagnosis, Management

Christopher Pedersen, MD

2/26/2024

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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

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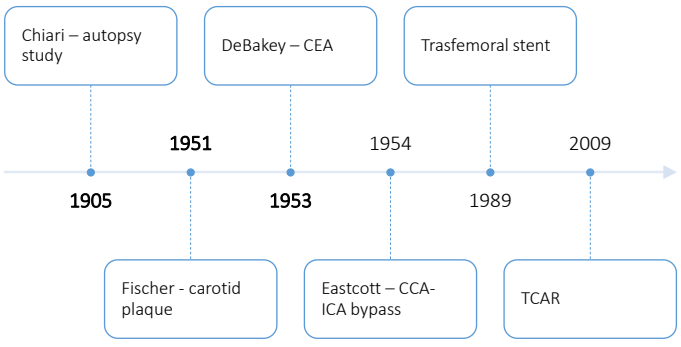
History



CARTER, Mr. Charles S.
Case No. 27474

OPERATIVE RECORD (Dictated and corrected by Dr. M. E. DeBakey)

Surgeon - M. E. DeBakey, M. D.
Date: August 7, 1953

Assistants - Drs. Cody, Brockman, Naaman

Preoperative Diagnosis - Atherosclerotic occlusive disease 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 thrombosis of internal carotid artery arising at origin of internal carotid artery and attached to well-localized atheromatous lesion producing severe stenosis at bifurcation of common carotid artery with patent external carotid artery which could be felt to pulsate by retrograde blood flow.

Procedure - Under general anesthesia, using Pentothal supplemented by ether and oxygen, the patient was prepped and draped to expose the left side of the neck. A longitudinal incision was made along the anterior border of the sternocleidomastoid muscle starting just below the angle of the jaw and extending downwards for about 9 cm. The incision was carried down by sharp and blunt dissection to expose the common carotid artery at the bifurcation which was freed from its sheath for a distance of about 4 cm. below the bifurcation. The internal and external carotid arteries were then similarly dissected free of surrounding tissue for about 3 cm. above the bifurcation. Umbilical tapes were then placed around the common carotid, internal carotid and external carotid arteries. Palpation revealed a weak pulse in the external carotid artery but none in the internal carotid artery or the common carotid artery just below the bifurcation. The common carotid artery at the bifurcation could not be collapsed between the thumb and finger and a firm mass could be felt at this level.

A longitudinal incision was then made in the internal carotid artery beginning about 2 cm. above its origin at the bifurcation and extending downward across the bifurcation into the common carotid artery for a distance of about 3 cm. Upon entering the lumen of the internal carotid artery a fresh thrombus was found completely occluding the lumen of the artery which arose and was adherent to an atheromatous lesion involving the common carotid artery at the bifurcation and virtually filling the lumen of this artery. The atheromatous lesion was firm, somewhat ulcerated and necrotic and having a yellowing to brownish color. It extended down below the bifurcation for about 2 cm. and immediately below it there was a partially organized and fresh clot filling much of the lumen of the common carotid artery.

Using a fine hemostat, the clot was easily separated from the intimal lining of the artery and carefully dislodged completely from the remaining upper portion of the internal carotid artery for a distance of about 5 cm. The clot was removed completely without fragmentation and it was noted that the distal end of the clot was smooth. Immediately following removal of the clot from the lumen of the

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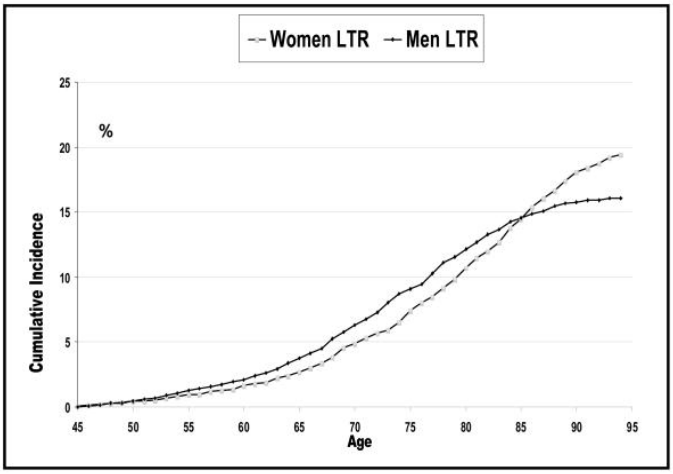
Background

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



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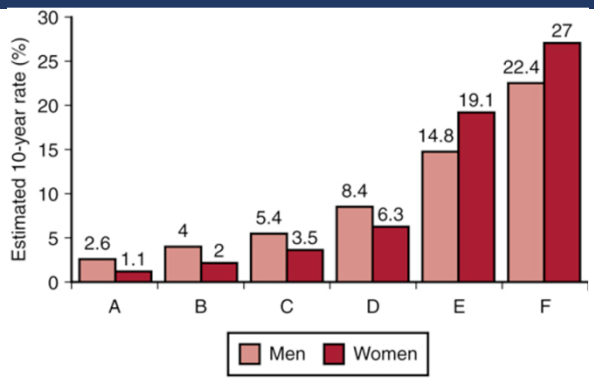
Risk Factors for Ischemic Stroke

- Sex
- Race
- Hypertension
- Family History
- Atrial fibrillation
- Cigarette smoking
- Hypercholesterolemia
- Diabetes
- Sedentary lifestyle



	A	B	C	D	E	F
Systolic BP	95–105	130–148	130–148	130–148	130–148	130–148
Diabetes	No	No	No	Yes	Yes	Yes
Cigarettes	No	No	No	Yes	Yes	Yes
Prior A Fib	No	No	No	No	Yes	Yes
Prior CVD	No	No	No	No	No	Yes

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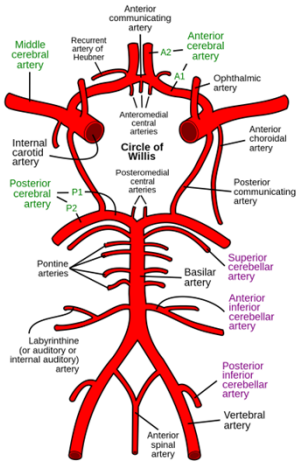
Pathophysiology of CAS and Ischemic Stroke

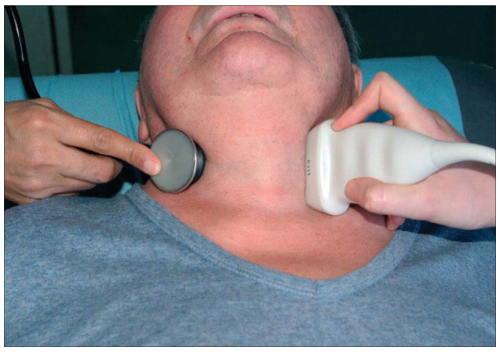
- 20% of ischemic strokes
- Embolization and hypoperfusion
- Hollenhorst reported on embolization to retinal vessels



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?



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Screening – Consensus statements

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.

AMERICAN COLLEGE of CARDIOLOGY
ACR American College of Radiology
SVS Society for Vascular Surgery

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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

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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

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Diagnostic Evaluation

- Once carotid artery stenosis has been identified it is important to determine the severity

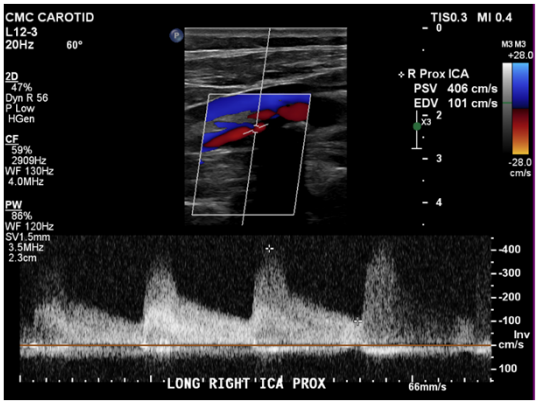
- Cerebral angiogram is the classic gold standard
- Asymptomatic: carotid ultrasound
- Symptomatic: CTA

Carotid Duplex Ultrasound

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

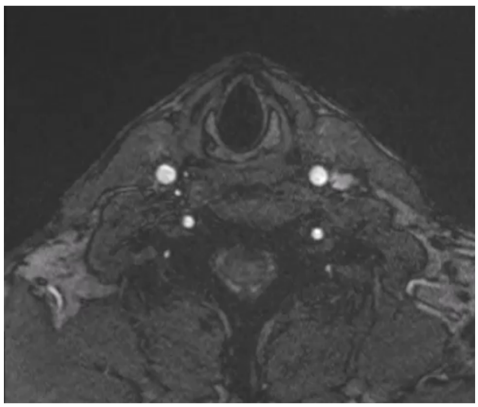
Classification	Stenosis
Mild	< 50%
Moderate	50-69%
Severe	> 70%

- Careful interpretation needed in the setting of contralateral occlusion



MRA

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



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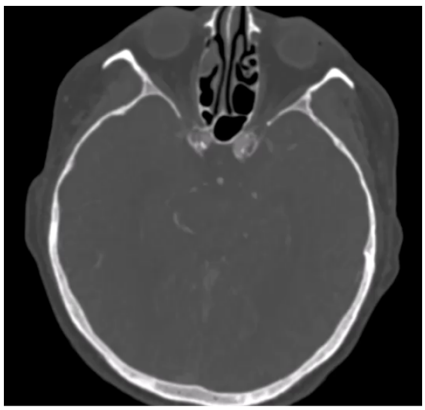
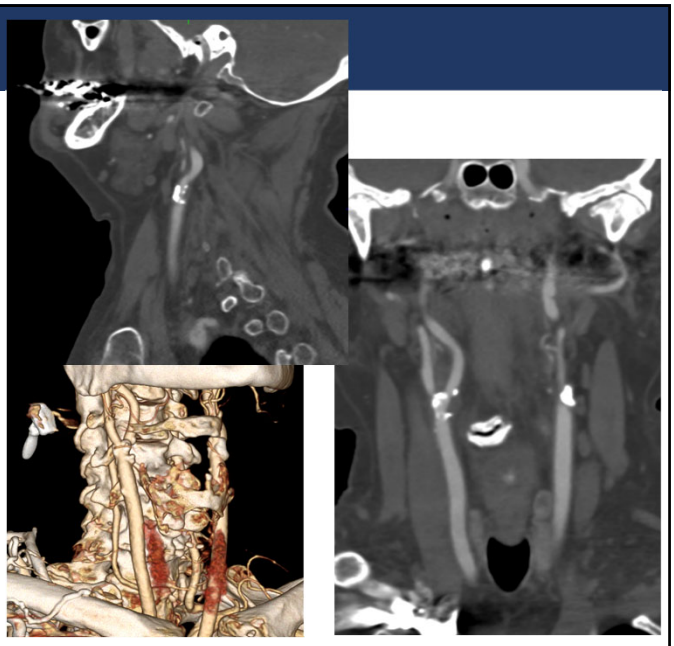
CTA

- Advantages: anatomic detail, rapid
- Disadvantages: contrast, radiation





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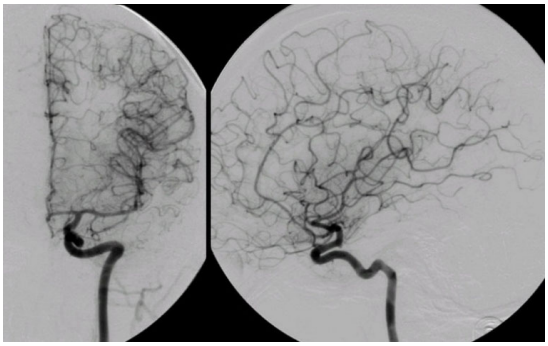
Catheter Based Cerebral Angiography

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



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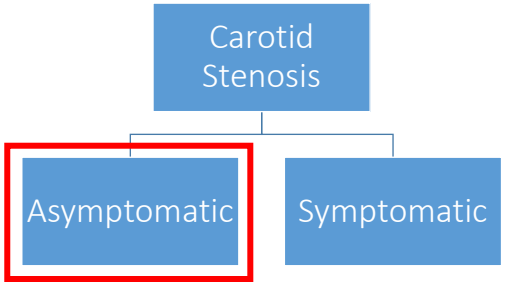
Management

Asymptomatic Disease



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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

Indication	At 3-5 months	At 6-8 months	At 9-12 months
Normal prior exam	Inappropriate		
Surveillance Frequency During First Year			
Plaque without significant stenosis	Inappropriate	Inappropriate	Inappropriate
Mild stenosis (<50%)	Inappropriate	Inappropriate	Inappropriate
Moderate stenosis (50-69%)	Inappropriate	Uncertain	Uncertain
Severe stenosis (70-99%)	Uncertain	Appropriate	Uncertain
Surveillance Frequence After First Year			
	Every 6 months	Every 12 months	Every ≥ 24 Months
Plaque without significant stenosis	Inappropriate	Inappropriate	inappropriate
Mild stenosis	Inappropriate	Uncertain	Uncertain
Moderate stenosis	Inappropriate	Appropriate	Uncertain
Severe stenosis	Appropriate	Appropriate	Uncertain

Who to revascularize?

- VA Trial (50-99%)
  - NEJM 1993
- Asymptomatic Carotid Atherosclerosis Study (ACAS) (60-99%)
  - JAMA 1995

	BMT	BMT+CEA	P
Ipsi-stroke or any peri-op stroke or death	11.0%	5.1%	p=0.004
Ipsi-TIA/stroke or any perio-op TIA/stroke/death	19.2%	8.2%	p<0.001

- 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%**

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

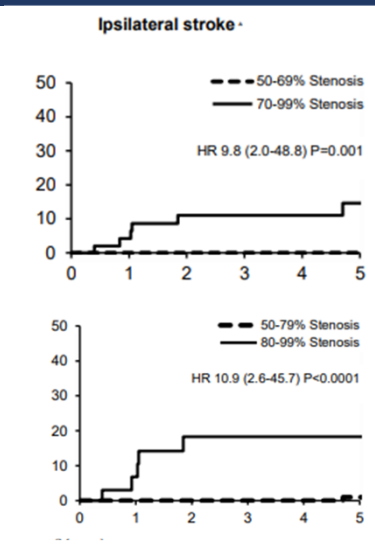
- JAMA 2022 by Robert W. Chang, et al
- 3737 patients (57% male)
- Mean follow-up of 4.1 years
- 133 ipsilateral strokes with mean annual stroke rate of 0.9%
- Kaplan-Meier estimate of ipsilateral stroke by 5 years was 4.7%

Should we wait for 80%?

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

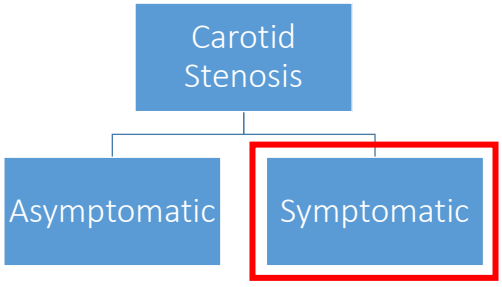
- 5-year risk of ipsilateral ischemic stroke
  - 70-99% 14.6% (6 of 53)
  - 50-69% none (0 of 154)
  - p<0.0001

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



Management

Symptomatic Disease



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

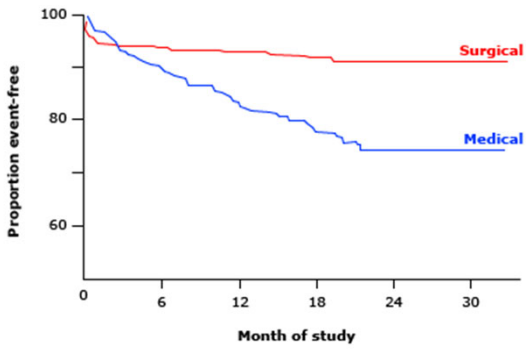
Who benefits?

Patient selection

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

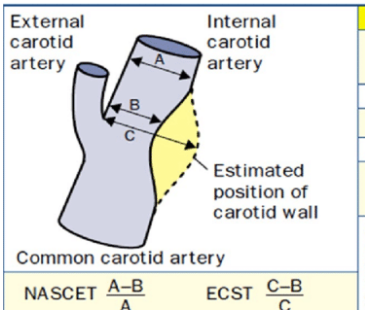
North American Symptomatic Carotid Endarterectomy Trial (NASCET)

Stenosis	CEA	BMT	p
< 50%	15%	19%	0.16
50-69%	16%	22%	0.045
70-99%	9%	26%	<0.001



European Carotid Surgery Trial (ECST)

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



NASCET	ECST
30	65
40	70
50	75
60	80
70	85
80	91
90	97

Approximate equivalent degrees of internal carotid artery stenosis used in NASCET and ESCT according to recent direct comparisons

Timing Carotid Revascularization

Timing of Revascularization – Wait 2 days

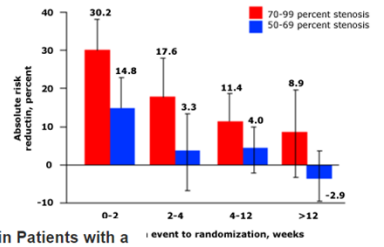
- We want to balance the risk of hemorrhagic conversion and recurrence of stroke
- Recommended to wait at least 2 days for a non-disabling stroke

- 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

Early carotid endarterectomy is associated with improved outcomes



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 *

	50%–69% Stenosis				70%–99% Stenosis		
ALL PATIENTS	ARR	NNT	Stroke/1000		ARR	NNT	Stroke/1000
<2 weeks	14.8%	7	148		23.0%	4	230
2–4 weeks	3.3%	30	33		15.9%	6	159
4–12 weeks	4.0%	25	40		7.9%	13	79
>12 weeks	–2.9%	nb	nb		7.4%	14	74

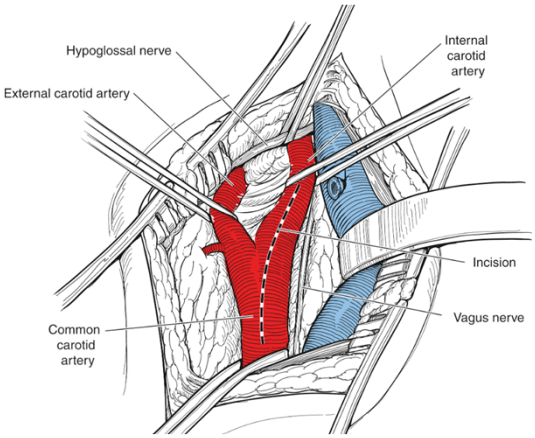
Timing of Revascularization

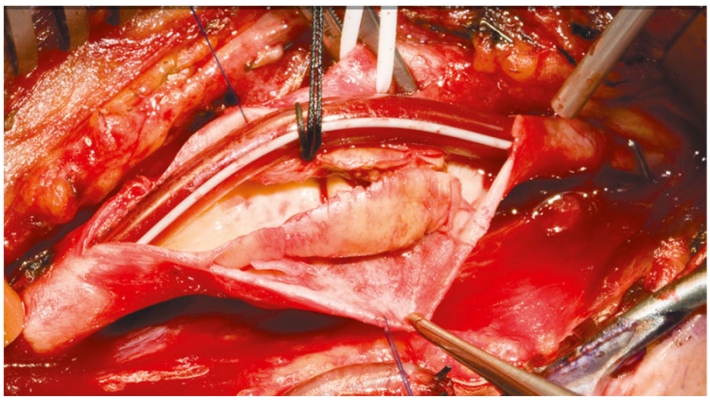
- Stroke in evolution
- Crescendo TIA

	Stroke and Death with CEA	<30% MCA territory volume
Stroke in Evolution	20.2%	2-8%
Crescendo TIA	11.4%	0-2%

Method of Revascularization

Carotid Endarterectomy





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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%

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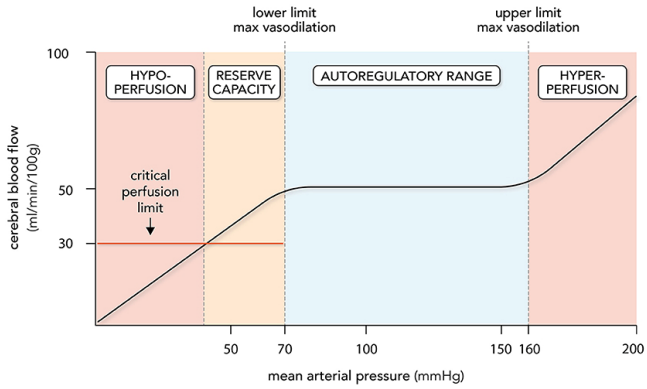
Cerebral Hyperperfusion Syndrome

- 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



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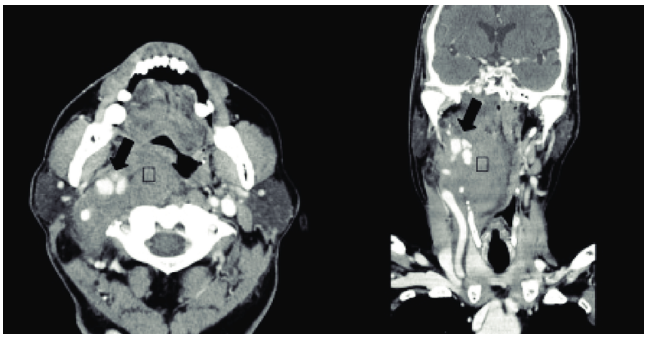
Hematoma

- 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



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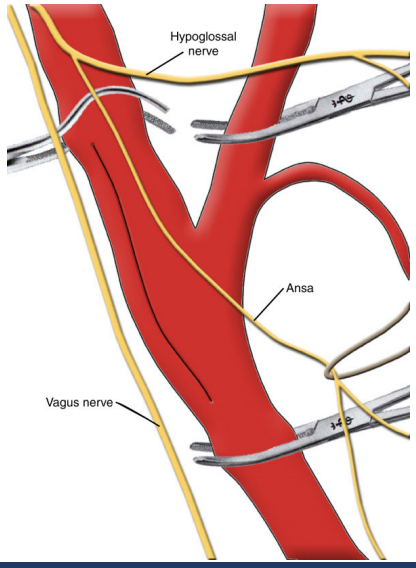
Cranial Nerve Injury

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



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Infection

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Restenosis

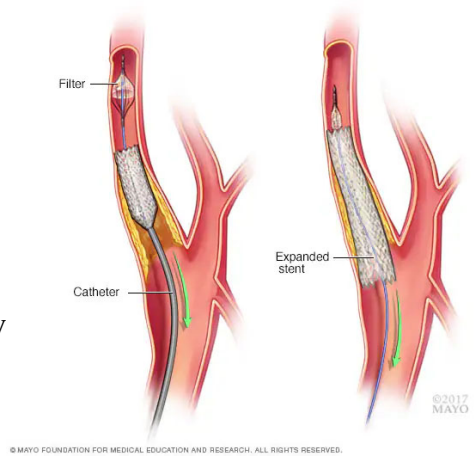
- Reported in 2-10% at 5 years
- Early (within 2-3 years) and Late
  - Early tends to be highly cellular and minimally ulcerated intimal hyperplasia (LOW risk of symptoms)
  - Late tends to be recurrence of disease
- Most are asymptomatic and found by follow-up carotid imaging
- Risk factors age <65,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

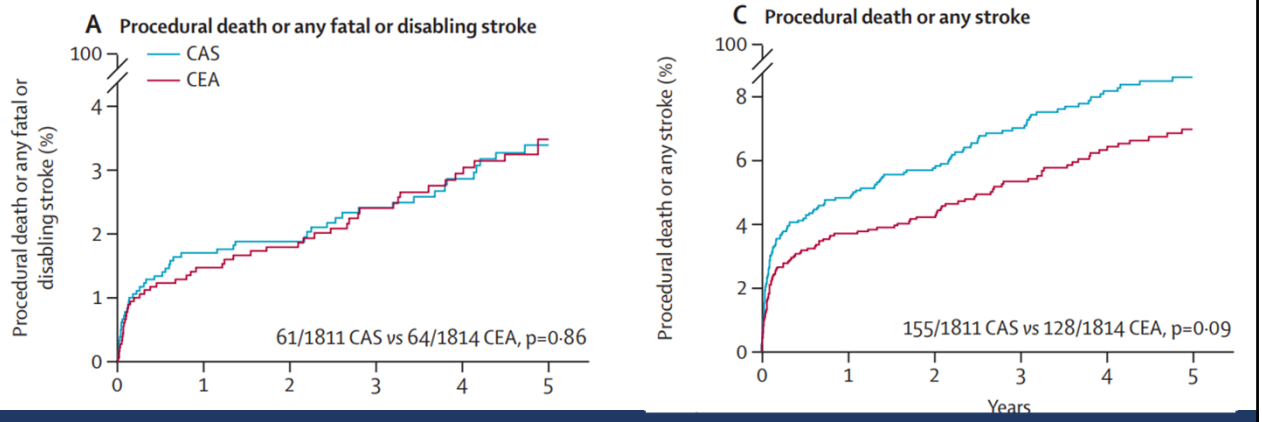
- 4 years composite
  - 7.2% vs 6.8%
- 10 years composite
  - 11.8% vs 9.9%

Periprocedural	CAS	CEA	95% CI / p
Composite	5.2%	4.5%	0.82-1.68
Death	0.7%	0.3%	p=0.18
Stroke	4.1%	2.3%	p=0.01
MI	1.1%	2.3%	p=0.03

ACST-2

- Published in Lancet in 2021

	CEA	CAS
Disabling stroke or death procedurally	1%	1%
Non-disabling procedural stroke	2%	2%



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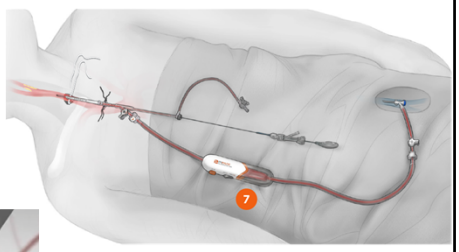
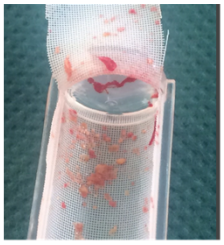
Transcarotid artery revascularization (TCAR)

- 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





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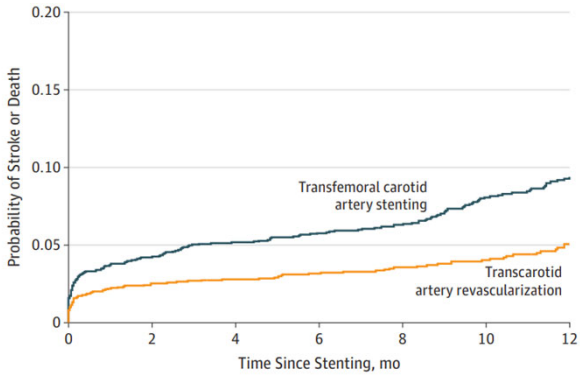
TCAR vs TF-CAS

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

	TCAR	TF-CAS
In-hospital Stroke or Death	1.6%	3.1%
Stroke	1.3%	2.4%
Death	0.4%	1.0%
MI	0.2%	0.3%
1-year ipsilateral stroke or death	5.1%	9.6%
Access site complication	1.3%	0.8%



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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%

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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

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