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Sentara Vascular Specialists

2022 MID-ATLANTIC CONFERENCE

10th ANNUAL CURRENT CONCEPTS IN

VASCULAR THERAPIES

Asymptomatic Critical Carotid Stenosis should always be treated surgically

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Sentara Vascular Specialists
EVMS Department of Surgery



Stroke Incidence

- 795,000 Strokes per year in U.S.
- 185,000 are recurrent
- 1/3 of all major strokes result in death.
- 1/3 lead to a major functional deficit; leading cause of long term disability.
- Estimated 8% of all strokes are thought to be secondary to carotid stenosis, and 3.5% to carotid occlusion.
- Annual cost to treat; \$70 billion expected to rise to \$138 billion by 2030.

CDC.Gov 2019



Embolic Stroke

• No accepted treatment options or preventive measures prior to the 1950's.



C Miller Fisher

Occlusion of the Internal Carotid Artery

Stroke 1951

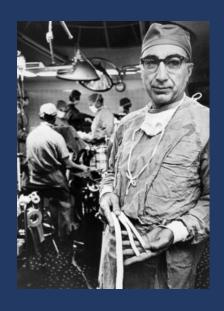
"One day surgeons may even devise a way to remove the offending plaque and thereby prevent stroke"

CDC.Gov 2019

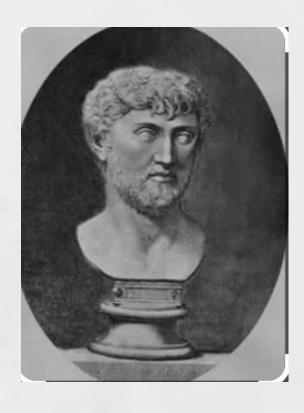


Carotid reconstruction

 DeBakey, 8/7/53, first successful CEA (53 yr old man with TIA)







"Act before disease has gained strength"

Publius Ovidium Naso Roman Poet



WE HAVE TO FIND THIS PLAQUE BEFORE IT FINDS OUR PATIENT'S BRAIN

CEA boom

- Rates of CEA rise dramatically through the 1980's.
 - Wide variation in training and surgical ability.
- Studies demonstrated high complication rates
 - 20% major morbidity.
 - Rand corp study suggests 30% inappropriate



Carotid Endarterectomy

- Henry J. M. Barnett, MD
- 20/20 Interview
- "Carotid endarterectomy is a procedure of no clinical value and should be legislated out of existence"

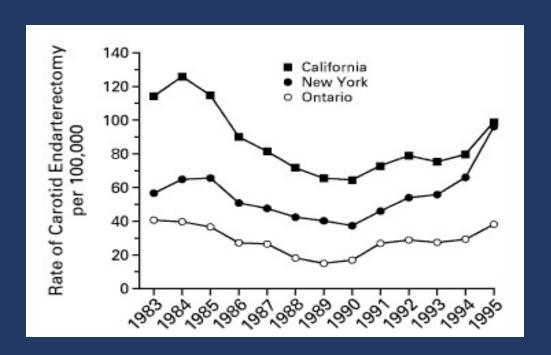


Asymptomatic Carotid disease

- ACAS (Asymptomatic Carotid Atherosclerosis Study)
 - North America
 - 1662 patients studied between 1987 -93
 - 5 year risk of ipsilateral stroke, perioperative stroke, or death
 - 5.1 % in the endarterectomy group
 - 11.0 % in the medically managed group
- ACST (Asymptomatic Carotid Surgery Trial)
 - European study with 3120 patients between 1993 2003
 - 5 year risk of stroke or perioperative death
 - 6.4 % in the endarterectomy group
 - 11.8 % in the medically managed group



CEA rates





Asymptomatic Carotid disease

What was the 'real benefit' associated with endarterectomy based on ACAS data?

- 19 CEA necessary to prevent 1 CVA.
- No other RCT for comparison



Revascularization in Asymptomatic Carotid Stenosis

- 130,000 CEAs in the US in 1995
- Medicare patients 2004-2006
 - 88% of carotid endarterectomies were for asymptomatic patients
 - 87% of carotid artery stenting procedures were for asymptomatic patients



Society recommendations for asymptomatic carotid stenosis

SVS

The committee recommends CEA as the first-line treatment for most symptomatic patients with stenosis of 50% to 99% and asymptomatic patients with stenosis of 60% to 99%. The perioperative risk of stroke and death in asymptomatic patients must be <3% to ensure benefit for the patient

ESVS

... the presence of one or more clinical and/or imaging features such as silent infarction on CT/MRI, stenosis progression, large plaque area, large juxta-luminal black area (JBA) on computerized plaque analysis, plaque echolucency, intra-plaque haemorrhage on MRI, impaired cerebral vascular reserve (CVR), and spontaneous embolisation on transcranial Doppler (TCD) monitoring, might be useful for selecting "higher-risk for stroke" patients for revascularisation



Society recommendations for asymptomatic carotid stenosis

Systematic Review of Guidelines for the Management of Asymptomatic and Symptomatic Carotid Stenosis

Anne L. Abbott , Kosmas I. Paraskevas, Stavros K. Kakkos, Jonathan Golledge, Hans-Henning Eckstein, Larry J. Diaz-Sandoval, Longxing Cao, Qiang Fu, Tissa Wijeratne, Thomas W. Leung, Miguel Montero-Baker, Byung-Chul Lee, Sabine Pircher, Marije Bosch, Martine Dennekamp and Peter Ringleb See fewer authors

Originally published 8 Oct 2015 | https://doi.org/10.1161/STROKEAHA.115.003390 | Stroke. 2015;46:3288–3301

Of 28 guidelines with asymptomatic carotid artery stenosis procedural recommendations, 24 (86%) endorsed CEA (recommended it should or may be provided) for ≈50% to 99% average-surgical-risk asymptomatic carotid artery stenosis, 17 (61%) endorsed CAS, 8 (29%) opposed CAS, and 1 (4%) endorsed medical treatment alone.



Currently, all asymptomatic stenosis patients should be treated medically: just look at the data!

Anne L. Abbott, MD, PhD, FRACP Knox Private Hospital, Melbourne, Australia

Two forms of revascularization intervention are offered in the name of reducing stroke risk associated with carotid arterial disease: procedural (carotid endarterectomy [CEA], trans-aortic carotid angioplasty/stenting [CAS]. and trans-carotid arterial revascularization [TCAR]), and non-procedural (medical intervention). Medical intervention consists of lifestyle changes and medication.1 Medical intervention is the gold standard by which all other interventions should be compared because it is noninvasive and of proven benefit in reducing risk for all arterial disease complications.



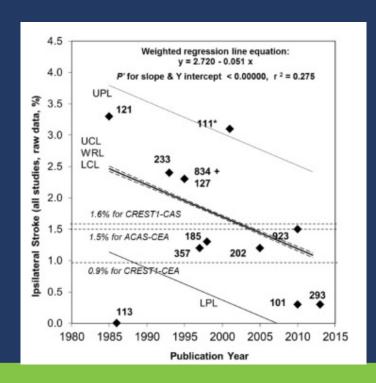
currently, all people with asymptomatic stenosis should be treated with medical intervention alone.¹ This is because reported ipsilateral stroke rates are so low with current standards of medical intervention Anne L Abbott, MD

Australian neurologist Melbourne

Prolific author, and recent winner of the Maddox award



Best Medical therapy



Abbott, et al JVS 2020



What is 'maximal medical therapy'?

- Hypertension SBP goal of 140 mmHg or less
- Dyslipidemia LDL less than 70 mg/dl with statin tx
- Diabetes Hgb A1c <7
- Obesity structured weight loss and BMI < 25
- Tobacco abstinence
- 'Lifestyle coaching' exercise, healthy eating habits



No Good Doing CEA or CAS on Those We Think May Benefit...

European Societies for Vascular Surgery & Cardiology

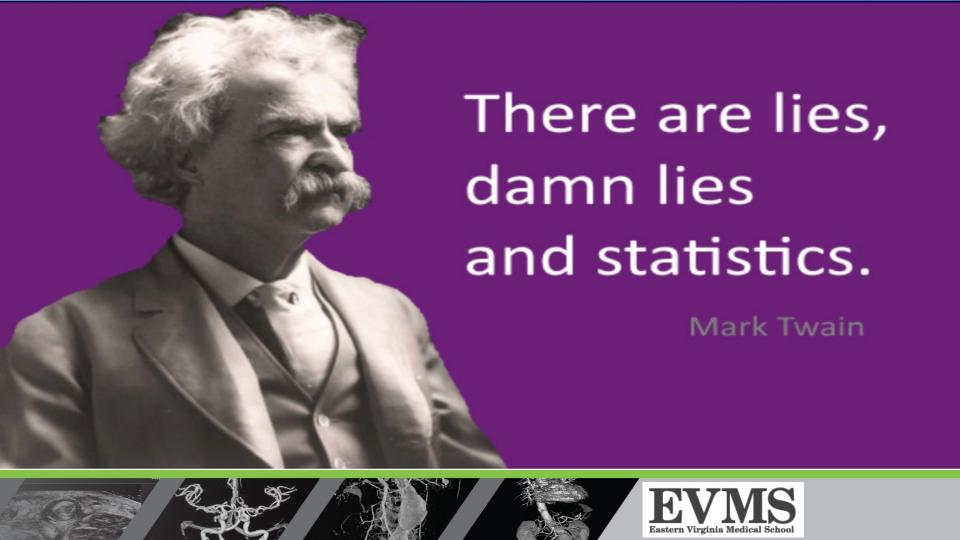
CEA (Class IIa) or CAS (Class IIb) endorsements for average CEA risk

50-99% ACS if ≥1 of these or other features:^

- Silent Infarct on CT
- Asymptomatic stenosis progression
- Large plaque area
- Juxtaluminal black areas on U/S
- Intra-plaque haemorrhage on MRI
- Impaired CVR
- 7. Plaque echolucency on U/S
- 8. Transcranial embolic signals +/- echolucency
- Contralateral TIA/stroke
- 10. Other (? 80-99% stenosis, younger patient etc)

^And if peri-procedural stroke/death rate <3%, patient life expectancy >5 years. EJVES, 2017





Results of CEA: Asx Stenosis

	Year	# Patients	% CVA/Death
ACAS ACST	1995 2004	724 1,348	2.3% 3.1%
		•	
CREST (Asx)	2011	1,196	1.4%
Vascular Surgeons			1.1%

Risk factor profile and anatomic features of previously asymptomatic patients presenting with carotid-related stroke

Derek Klarin, MD,^a Richard P. Cambria, MD,^b Emel A. Ergul, MS,^a Scott B. Silverman, MD,^c Virendra I. Patel, MD, MPH,^d Glenn M. LaMuraglia, MD,^a Mark F. Conrad, MD, MMSc,^a and W. Darrin Clouse, MD,^a Boston and Brighton, Mass; and New York, NY

- 1469 patients followed over 5 years with >50% ICA stenosis
- Stroke incidence 17%
- 5.2% with annual rate of progression
- Statistically significant risk factors for CVA
 - Rate of progression
 - DM
 - Degree of stenosis
 - HTN
 - Prior contralateral symptoms



Risk factor profile and anatomic features of previously asymptomatic patients presenting with carotid-related stroke

Derek Klarin, MD,^a Richard P. Cambria, MD,^b Emel A. Ergul, MS,^a Scott B. Silverman, MD,^c Virendra I. Patel, MD, MPH,^d Glenn M. LaMuraglia, MD,^a Mark F. Conrad, MD, MMSc,^a and W. Darrin Clouse, MD,^a Boston and Brighton, Mass; and New York, NY

- 3382 pts with CVA over 10 year period
- 7% of CVA associated with hemodynamically significant carotid disease
- ½ statin ½ asa
- 35% CVA occurred while patient taking both statin and asa



european journal of neurology the official journal of the european academy of neurology



High cardiovascular event rates in patients with asymptomatic carotid stenosis: the REACH registry*

F. T. Aichner, R. Topakian, M. J. Alberts, D. L. Bhatt, H.-P. Haring, M. D. Hill, G. Montalescot, S. Goto, E. Touzé, J.-L. Mas, P. G. Steg, J. Röther, for the REACH Registry Investigators

>30,000 patients – Compared ACS >70% with matched controls

■ TIA 3.5 versus 1.6%

■ Non-fatal CVA 2.6 versus 1.7%

■ Death/MI/CVA 6.0 versus 4.2%

"Prior cerebral ischemic event is the most powerful predictor of stroke."



Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis.

Dominic P J Howard, DPhil。Liam Gaziano, MSc。 Prof Peter M Rothwell, FMedSci 😕 🖂 on behalf of the Oxford Vascular Study

- Prospective, population based study, with meta-analysis of publications of ACS and CVA between 2002 – 17.
- 2178 pts with ACS that suffered a TIA or stroke
- Stroke risk increased with the degree of stenosis
 - 5yr stroke risk 18.3 with critical stenosis
 - "...the benefit of endarterectomy might be underestimated in patients with severe stenosis."
- 23 of 56 studies stratified results based on degree of stenosis –
 "...stroke risk was linearly associated with degree of ipsilateral stenosis."

Neurology, 2021



Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis.

Dominic P J Howard, DPhil • Liam Gaziano, MSc • Prof Peter M Rothwell, FMedSci $\stackrel{>}{\sim}$ $\stackrel{\square}{\simeq}$ • on behalf of the Oxford Vascular Study

"...the stroke risk being less than 5% after 5 years on contemporary medical therapy for patients with moderate stenosis, but approximately 15% in patients with severe stenosis. The strong association between the degree of asymptomatic carotid artery stenosis and ipsilateral stroke risk fits well with the proposed synergistic effect of flow reduction and embolisation in the pathogenesis of stroke distal to the carotid plaque."

Neurology, 2021



Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification

Andrew N. Nicolaides, MS, FRCS, PhD (Hon),* Stavros K. Kakkos, MD, MSc, PhD, DIC,* Efthyvoulos Kyriacou, BSc, PhD,* Maura Griffin, MSc, DIC, PhD,* Michael Saberai, MD, FRCS, PhD,* Dafydd, J. Thomas, MD, PhD,* Thomas Tegos, MD, PhD,* George Geroulakos, MD, PhD,* olicos Labropoulos, PhD, DIC, RVT,* Caroline I. Doré, BSc,* Tim P. Morris, MSc,* Ross Naylor, MD, FRCS,* an Anne L. Abbott, MB, BS, FRACP, PhD,* for the Asymptomatic Carotid Stenosis and Risk of Stroke (ACSES) Stauy Group, London una Lettester, United Kingdom; Limanol, Cypeus, Stony Brook, NT; and Melbourne, Australia

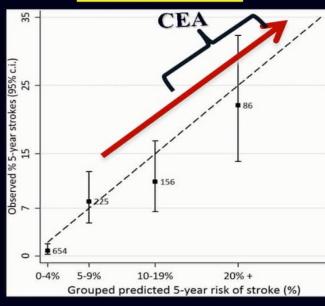
Patients: 1,121

50 -99% Stenosis

F/U: 6-96 (Mean, 48) Months

CORI: 130 Events

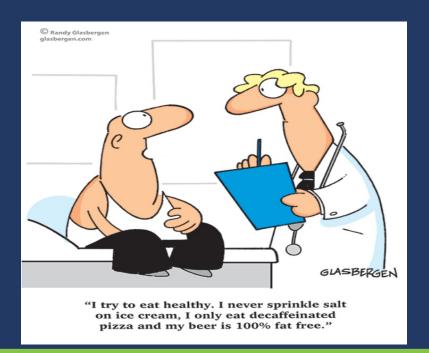
5-Year Stroke Risk Asx Patients



ACSRS

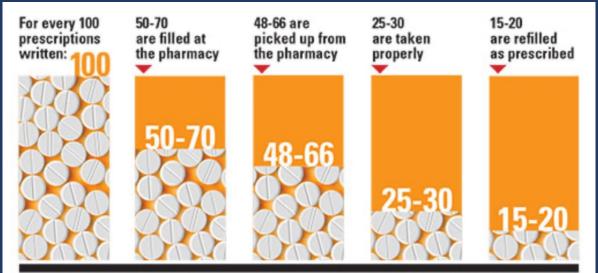
J Vasc Surg, 2010

Real world



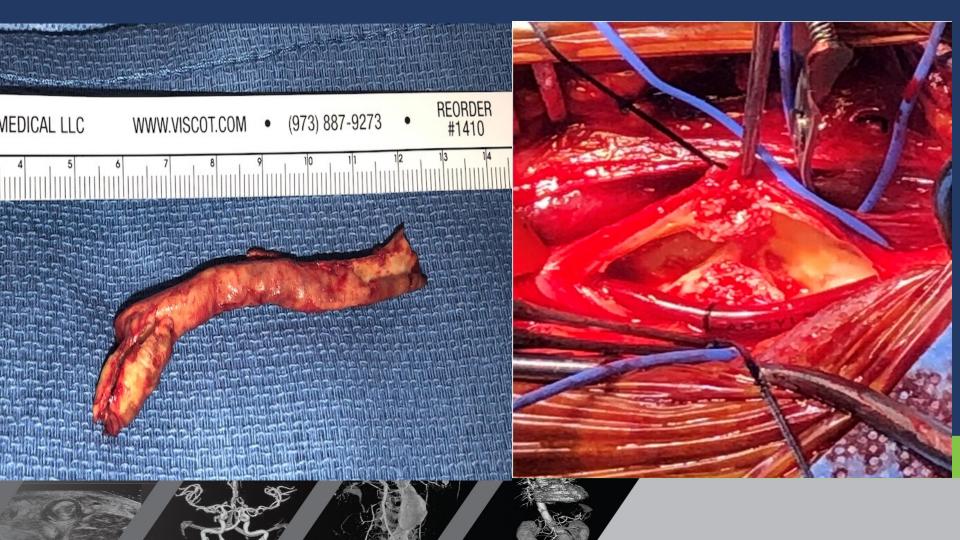


BMT - compliance



Source: National Association of Chain Drug Stores, Pharmacies: Improving Health, Reducing Costs, July 2010. Based on IMS health data.





How should we determine outcome?

- Is risk of stroke the only parameter that should be assessed?
- What are the sequelae of chronic cerebral hypoperfusion?
- Should we be looking at this in a broader sense?
- How to determine clinical improvement when outcomes are less clearly defined.



Non Stroke related benefits with restored perfusion

Asymptomatic carotid stenosis is associated with cognitive impairment

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Brajesh K Lal <sup>1</sup>, Moira C Dux <sup>2</sup>, Siddhartha Sikdar <sup>3</sup>, Carly Goldstein <sup>4</sup>, Amir A Khan <sup>5</sup>, John Yokemick <sup>6</sup>, Limin Zhao <sup>4</sup>
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50% of pts with CAS had impairment in 2/9 neuropsychiatric domains
 The remainder trended towards improvement

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CLINICAL RESEARCH STUDY | VOLUME 44, ISSUE 5, P1016-1022, NOVEMBER 01, 2006

The impact of carotid stenting on the hemodynamic parameters and cerebrovascular reactivity of the ipsilateral middle cerebral artery

Giorgos Sfyroeras, MD • Christos D. Karkos, MD, FRCS, PhD A Charalampos Liasidis, MD • ...

Athanasios S. Dimitriadis, MD, PhD • Konstantinos Kouskouras, MD, PhD •

Thomas S. Gerassimidis, MD, PhD • Show all authors
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Decreased vasomotor reactivity associated with increasing degree of stenosis
 Diminished cerebrovascular reserve improves with revascularization



RECOMMENDATIONS FOR ASX CAROTID STENOSIS

- HIGH GRADE LESIONS (80-99%)
- PROGRESSION OF DISEASE
- VULNERABLE PLAQUE
 - PLAQUE AREA >80
 - JUXTA-LUMINAL BLACK AREA > 8 cm²
- $_{\circ}$ CONTRALATERAL CVA or OCCLUSION (\downarrow CV RESERVE)
- MULTIPLE TCD "HITS"
- MULTIPLE ULCERATIONS



Conclusions

- Asymptomatic, critical carotid artery stenosis is associated with a 3 5% annual stroke risk.
- \circ Perioperative complication rates associated with CEA/TCAR are 1 2%.
- Indications for intervention in moderate CAS are less clear, and best medical therapy is an appropriate treatment option.
- Multiple factors, in addition to degree of stenosis, need to be taken into account before recommending repair.
- As treatment evolves, so do indications for intervention.



Thank you





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