Symptomatic Cervical Carotid Artery Stenosis

Objectives

- Stroke Mechanisms
- Evaluation
- Epidemiology
- Management
  - Medical Management
  - Carotid Endarterectomy (CEA)
  - Carotid Artery Stenting (CAS)
- Uncertainties

Cervical Carotid Stenosis

- ~10% ischemic stroke
- Carotid bifurcation, proximal cervical ICA

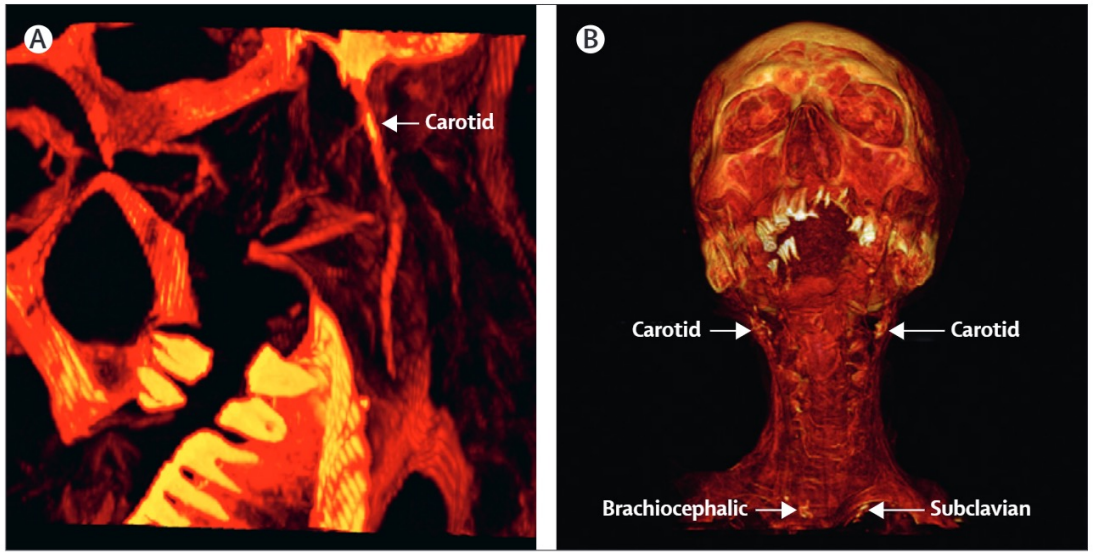
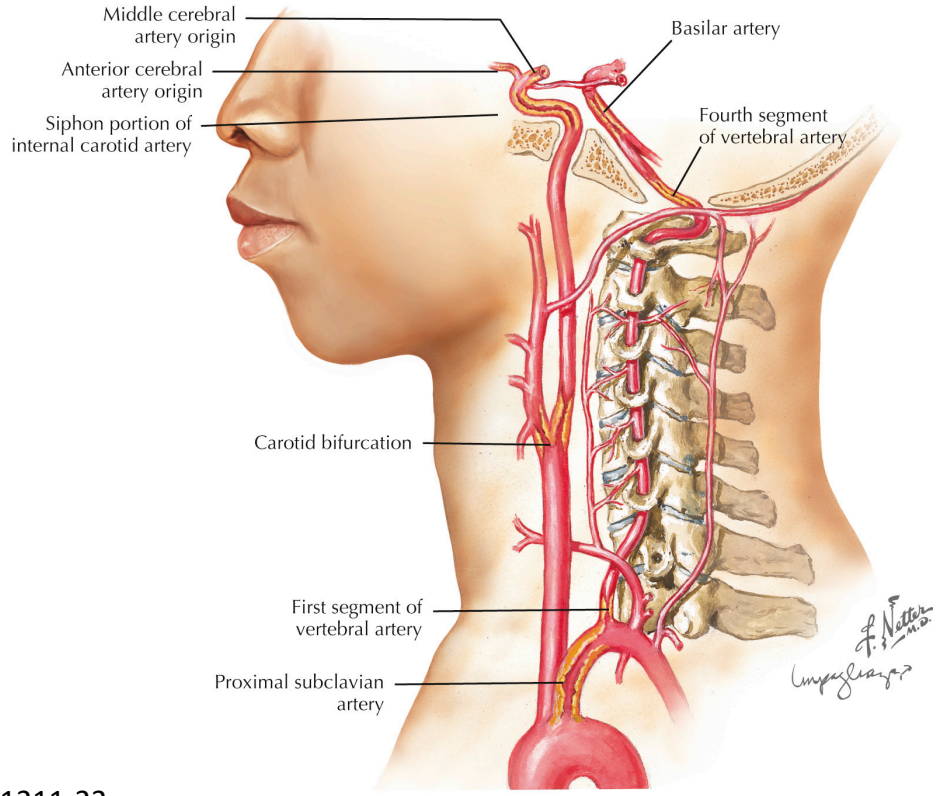


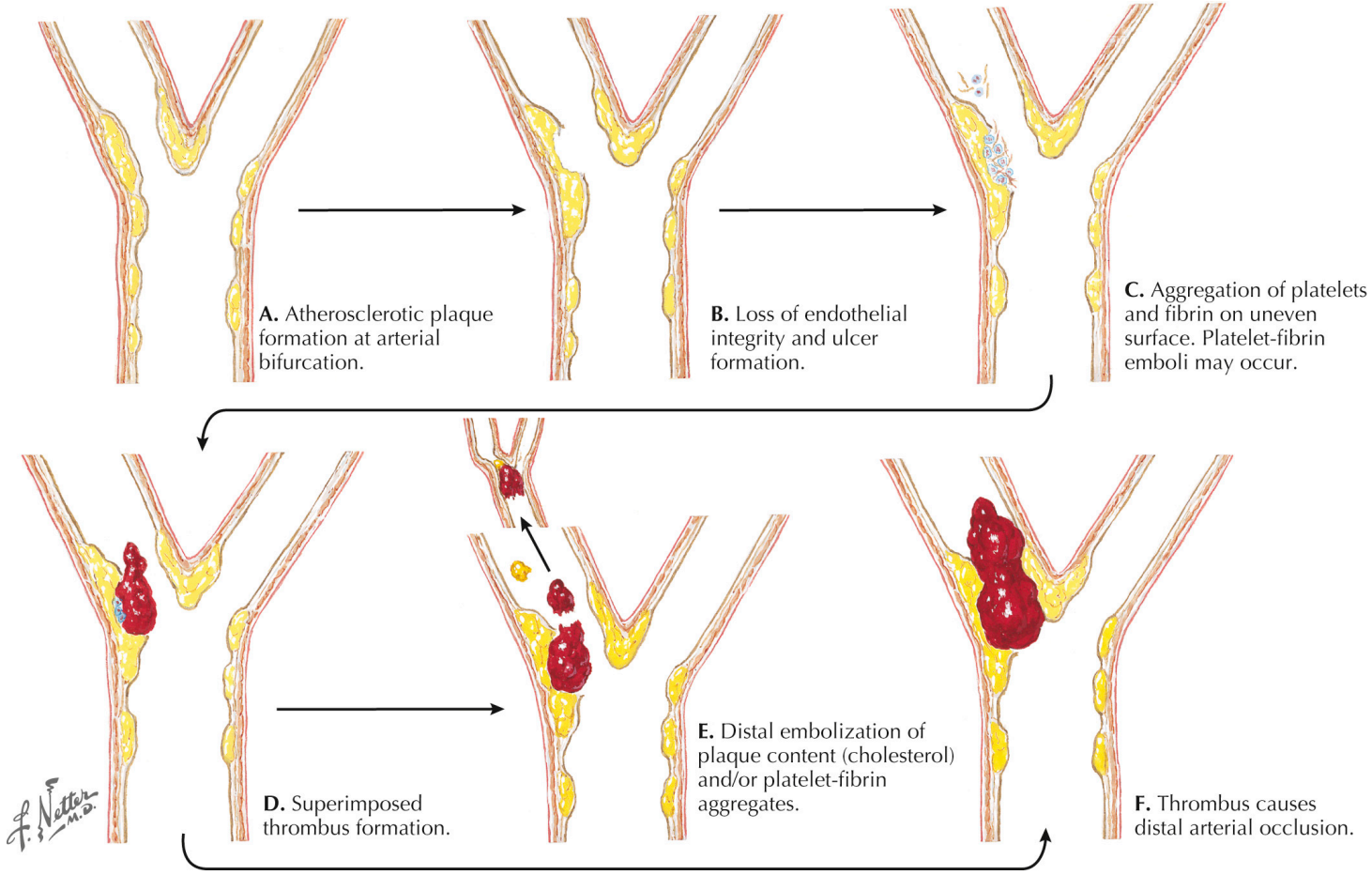
Figure 5: **Carotid disease**
Sagittal three-dimensional (3D) maximum projection rendered (A) and coronal 3D volume rendered (B) CT reconstruction showing carotid artery disease. (A) Carotid calcifications in the mummy of an Unangan woman (mummy 134) aged 25–29 years, who lived in the late 19th century CE and was found on Kagamil island in the Aleutian Islands. (B) Bilateral carotid, bilateral subclavian, and brachiocephalic calcification of Hatiay (mummy 23), a male Egyptian scribe aged 40–50 years, who lived during the New Kingdom (1570–1293 BCE) and was found near modern day Luxor. CE=common era. BCE=before common era.



Lancet. 2013 Apr 6;381(9873):1211-22.
Continuum (Minneap Minn). 2017 Feb;23(1, Cerebrovascular Disease):133-157.
Voetsch, Barbara, Netter's Neurology, 15, 169-189.

Stroke Mechanisms

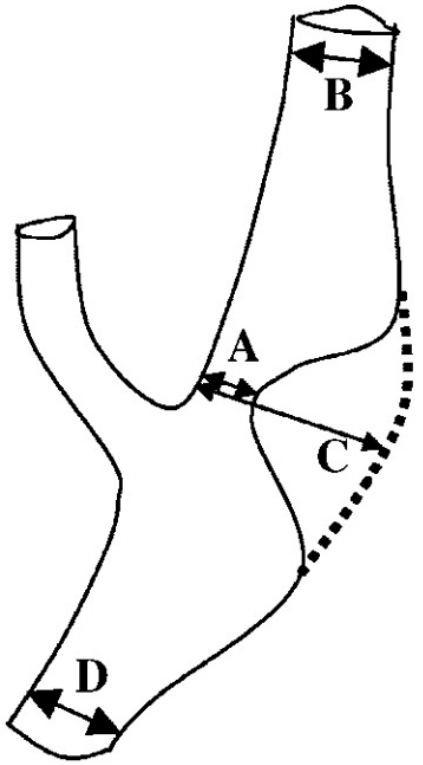
- Embolism
  - plaque content (cholesterol)
  - platelet-fibrin (+/- red blood cell) aggregates
- Hemodynamic infarction
- Total carotid occlusion



Voetsch, Barbara, Netter's Neurology, 15, 169-189.

Stenosis Severity

- Mild: <50%
- Moderate: 50-69%
- Severe: 70-99%
- Occluded (or near-occluded)



NASCET = (B-A)/B x 100 % stenosis

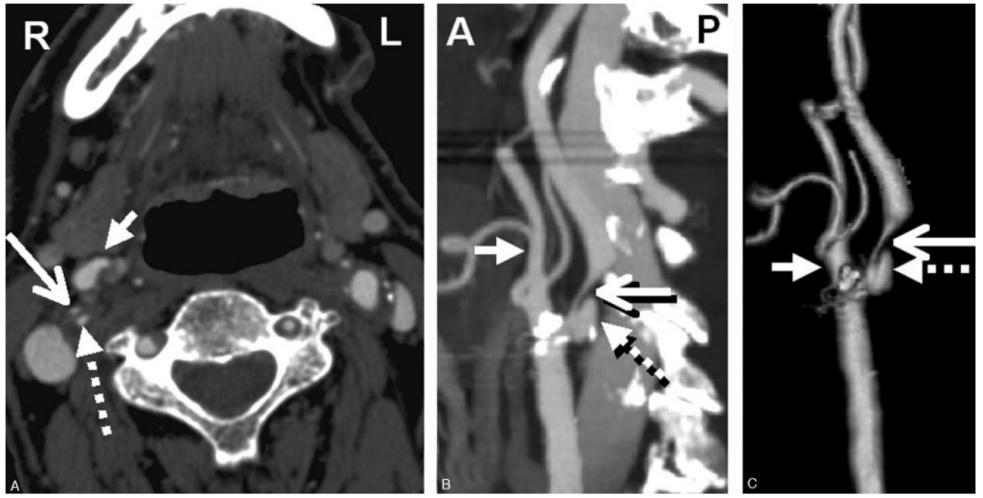
ECST = (C-A)/C x 100 % stenosis

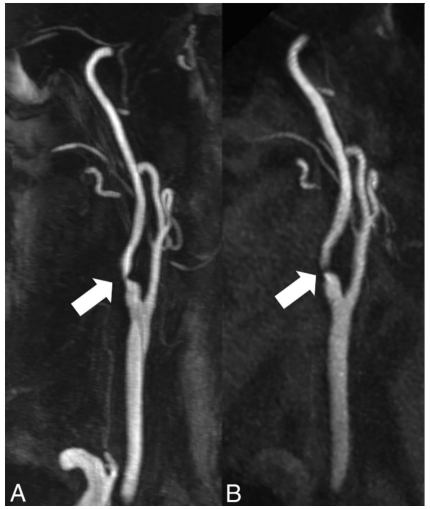
CC = (D-A)/D x 100 % stenosis

Figure 1. Diagram of an ICA stenosis illustrating different measurement methods. A, Luminal diameter at the site of maximal narrowing. B, Diameter of normal distal ICA beyond the bulb where the artery walls are parallel. C, Diameter of estimated original width of the ICA at the site of maximal narrowing. D, Diameter of normal CCA proximal to the bulb where artery walls are parallel.

Stroke. 2004 Sep;35(9):2083-8.

Evaluation





- CTA
  - calcification
  - surrounding bone + soft tissue
- CE-MRA > TOF-MRA
  - TOF-MRA
    - may over-estimate degree of stenosis
    - less accurate for moderate stenosis

	DUS	CTA	MRA	CEMRA
70–99% stenosis				
Sensitivity (95% CI)	0·89 (0·85–0·92	0·77 (0·68–0·84)	0·88 (0·82–0·92)	0·94 (0·88–0·97)
Specificity (95% CI)	0·84 (0·77–0·89)	0·95 (0·91–0·97)	0·84 (0·76–0·97)	0·93 (0·89–0·96)
50–69% stenosis				
Sensitivity (95% CI)	0·36 (0·25–0·49)	0·67 (0·30–0·90)	0·37 (0·26–0·49)	0·77 (0·59–0·89)
Specificity (95% CI)	0·91 (0·87–0·94)	0·79 (0·63–0·89)	0·91 (0·78–0·97)	0·97 (0·93–0·99)
0–49% stenosis or 100% occluded				
Sensitivity (95% CI)	0·83 (0·73–0·90)	0·81 (0·59–0·93)	0·81 (0·70–0·88)	0·96 (0·90–0·99)
Specificity (95% CI)	0·84 (0·62–0·95)	0·91 (0·74–0·98)	0·88 (0·76–0·95)	0·96 (0·90–0·99)

Table 3: Meta-analysis of sensitivity and specificity for all stenosis groups and imaging techniques

Lancet. 2006 May 6;367(9521):1503-12.
AJNR Am J Neuroradiol. 2006 Jan;27(1):13-9.
AJNR Am J Neuroradiol. 2019 Sep;40(9):1529-1537.

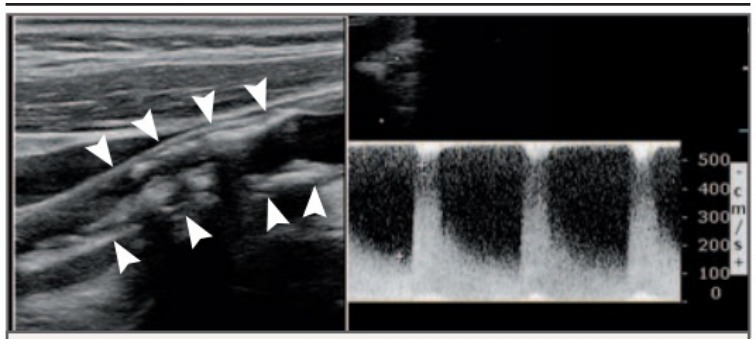


Figure 2. Duplex Ultrasonography of the Carotid Artery Showing Severe Carotid Stenosis.

- Duplex U/S
  - near-occlusion (small residual lumen) can be difficult to assess
  - may over-estimate degree of stenosis
    - contralateral high-grade stenosis or occlusion
  - less accurate for moderate stenosis
  - operator-dependent
- DSA
  - gold standard
  - invasive, stroke risk

	DUS	CTA	MRA	CEMRA
70–99% stenosis				
Sensitivity (95% CI)	0·89 (0·85–0·92	0·77 (0·68–0·84)	0·88 (0·82–0·92)	0·94 (0·88–0·97)
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50–69% stenosis				
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0–49% stenosis or 100% occluded				
Sensitivity (95% CI)	0·83 (0·73–0·90)	0·81 (0·59–0·93)	0·81 (0·70–0·88)	0·96 (0·90–0·99)
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Table 3: Meta-analysis of sensitivity and specificity for all stenosis groups and imaging techniques

Lancet. 2006 May 6;367(9521):1503-12.
N Engl J Med. 2013 Sep 19;369(12):1143-50.

- Screening → Non-invasive imaging most appropriate
  - CE-MRA ≥ CTA ≈ TOF-MRA ≈ CUS for high-grade stenosis
  - limited data and lower accuracy for moderate-grade stenosis
- Complete Occlusion
  - CTA
  - MRA + CUS

Table 1 Methodological characteristic-based comparison among the existing imaging modalities [68–71]

Diagnostic test	Methodology	Advantage	Limitations/drawbacks
Computed tomography angiography (CTA)	Use of high-dose X-rays to get a detailed picture of the vascular system and its functioning Patients may also have a dye injected to make it easier to spot blockages	The exam is quick 3D results Able to identify a wide variety of abnormalities	Risk associated with radiation exposure and contrast use (e.g. allergic reaction, contrast-induced nephropathy) Incidental findings may lead to unnecessary further tests Presence of vessel calcification leads to an inaccurate stenosis estimation Large area is needed to house the equipment
Magnetic resonance angiography (MRA)	Make use of large magnets and radio waves to take pictures of internal organs like heart and arteries	Does not involve exposure to ionizing radiation	Not safe for patients with implants that are not MRI-conditional Time consuming Not suitable for patient with claustrophobia Not widely available Contrast associated adverse reaction (e.g. nephrogenic systemic fibrosis in patients with kidney impairment)
Duplex ultrasound (DUS)	To check the blood flow to the brain for a probable plaque formation in the carotid artery	Reasonable tool in picking up carotid atherosclerosis	Require trained personnel to perform and interpret Reflect the presence of systemic atherosclerosis

Biomed Eng Online. 2019 May 28;18(1):66.

- Transcranial doppler ultrasound
  - adjunct to CUS
  - largely supplanted by CTA/MRA
  - high-intensity transient signal (HITS) or microembolic signals

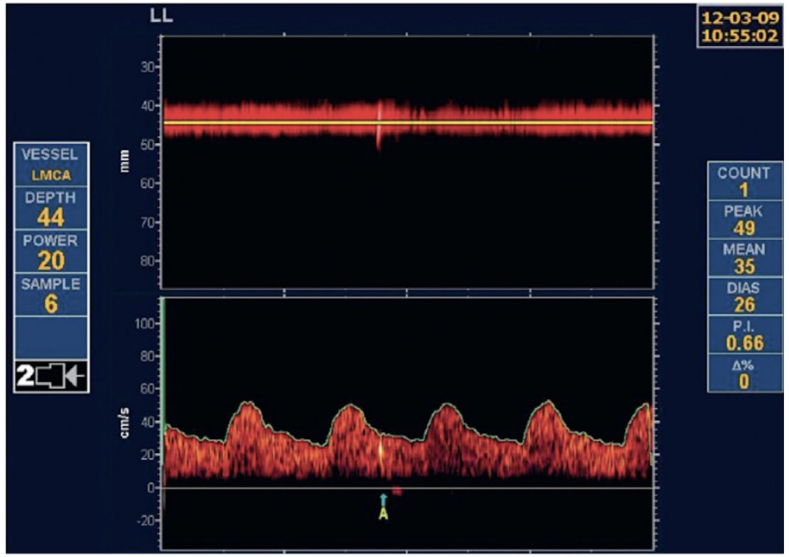


Fig. 1 – Microembolic signal on transcranial Doppler. Upper panel: M-mode recording; the arrow points to an image of a microembolus. Lower panel: the Doppler velocity envelope; the arrow (A) points to the high-intensity transit signal created by a microembolus. From Spence JD. Transcranial Doppler: uses in stroke prevention. *J Vasc Ultrasound* 2015;39:183–7 [21], reprinted with permission.

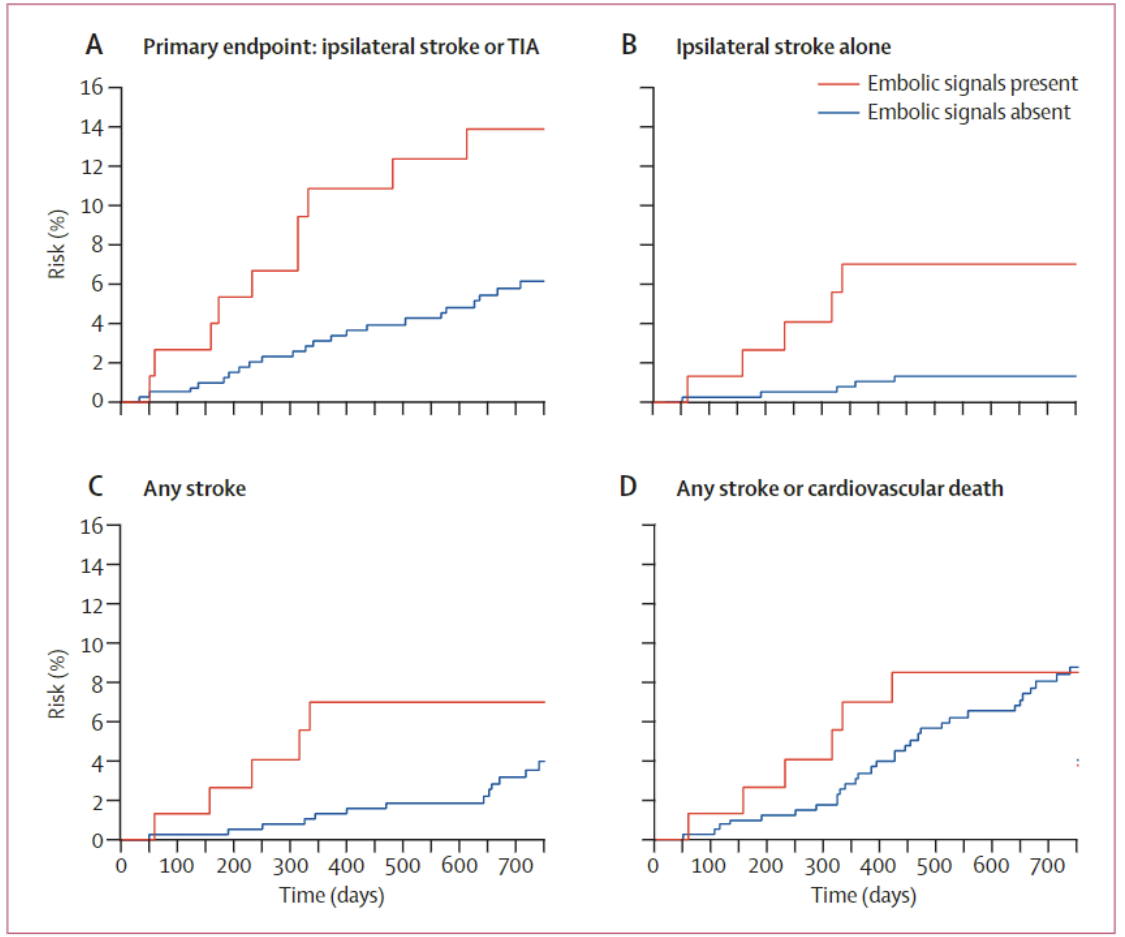
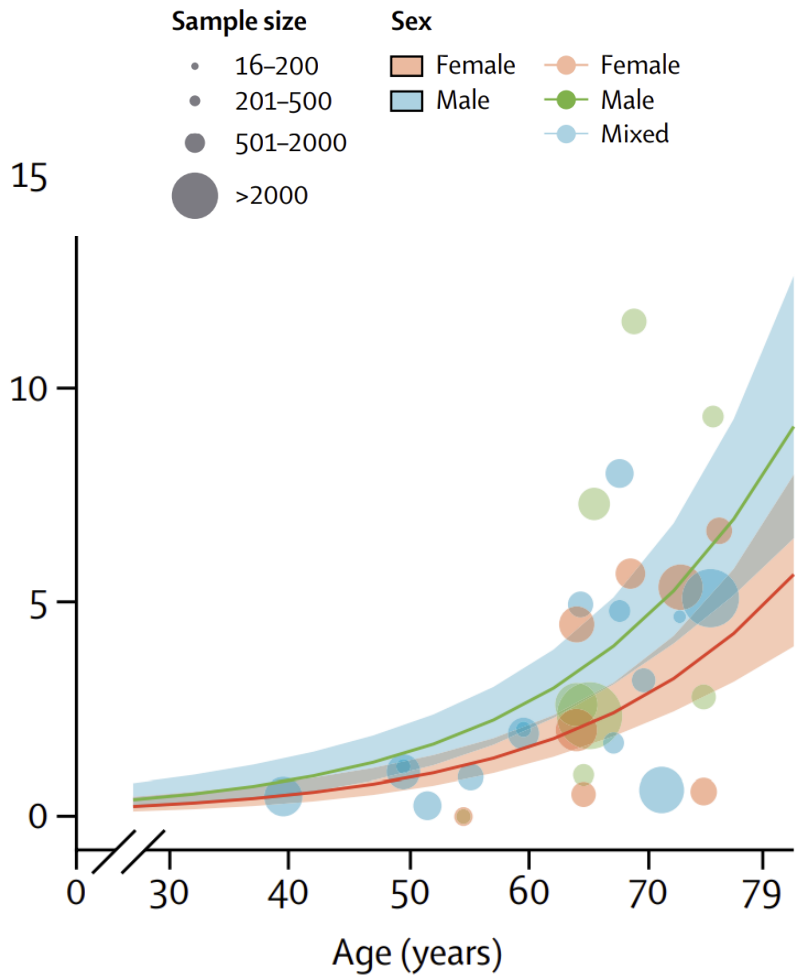


Figure 1: **Survival plots for the association between the presence of embolic signals and cumulative event rates for the analysis of whether embolic signals at baseline predict risk**
77 patients had embolic signals and 390 did not. TIA=transient ischaemic attack.

Lancet Neurol. 2010 Jul;9(7):663-71.
Semin Vasc Surg. 2017 Mar;30(1):62-66.

Moderate-Severe Carotid Stenosis



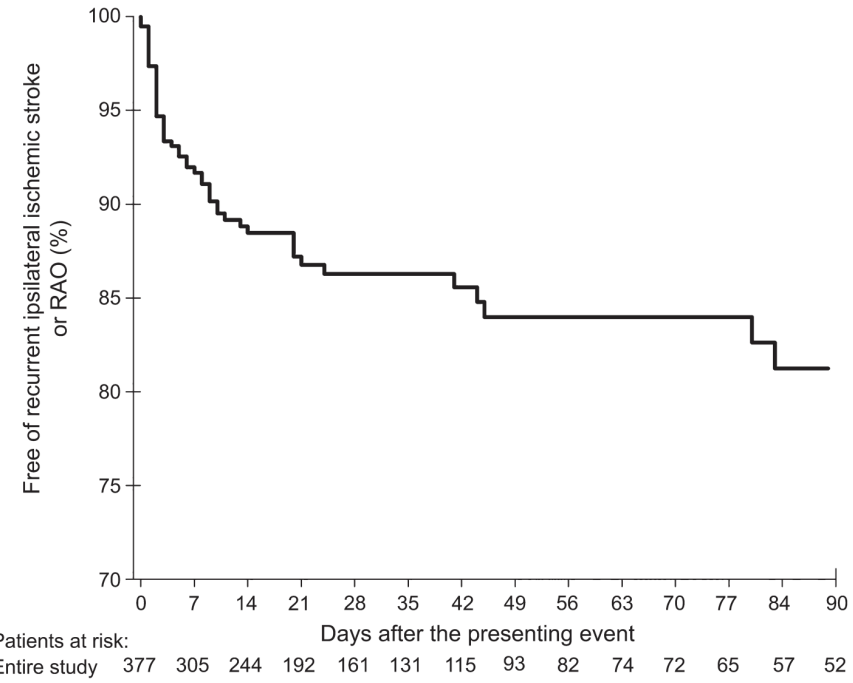
	Carotid stenosis	
	Men	Women
30–34 years	0·5% (0·3–1·0)	0·3% (0·2–0·6)
35–39 years	0·7% (0·4–1·2)	0·4% (0·2–0·7)
40–44 years	0·9% (0·6–1·5)	0·6% (0·4–0·9)
45–49 years	1·3% (0·8–1·9)	0·8% (0·5–1·1)
50–54 years	1·7% (1·2–2·4)	1·0% (0·7–1·4)
55–59 years	2·2% (1·7–3·0)	1·3% (1·0–1·8)
60–64 years	3·0% (2·3–3·9)	1·8% (1·4–2·4)
65–69 years	4·0% (3·1–5·1)	2·4% (1·9–3·1)
70–74 years	5·3% (4·0–6·8)	3·2% (2·4–4·2)
75–79 years	6·9% (5·2–9·3)	4·3% (3·1–5·8)
Overall (30–79 years) in 2020	1·8% (1·3–2·6)	1·2% (0·8–1·6)

Lancet Glob Health. 2020 May;8(5):e721-e729.

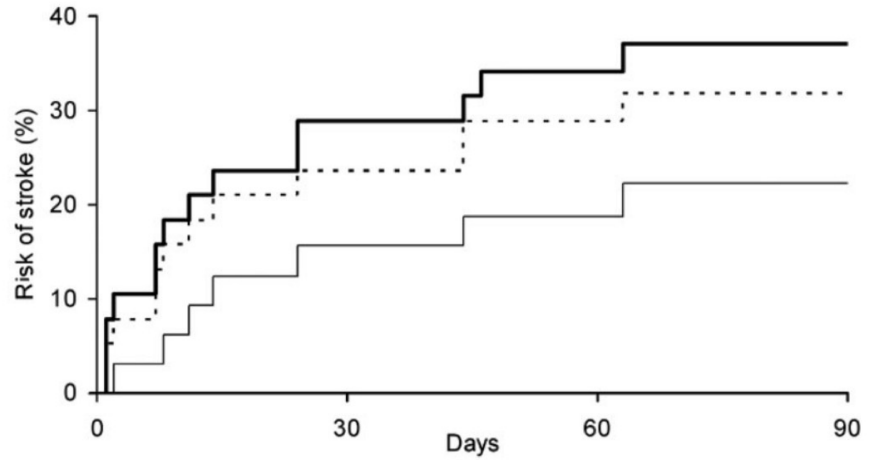
Symptomatic Carotid Stenosis

Infarction / transient ischemia attributable to significant ipsilateral carotid artery stenosis w/in 6 months

Figure 2 Kaplan-Meier analysis of the main outcomes



Kaplan-Meier analysis of the risk of recurrent ipsilateral ischemic stroke or retinal artery occlusion (RAO) within 90 days c the presenting event, prior to carotid endarterectomy (CEA)/carotid artery stenting (CAS). (CEA/CAS was used as censorin event.)



Number of patients				
All recurrent stroke	38	27	22	19
Recurrent stroke after seeking medical attention	38	29	24	21
Recurrent stroke after seeking medical attention excluding carotid occlusions	32	27	23	20

Neurology. 2005 Aug 9;65(3):371-5.
Neurology. 2016 Feb 9;86(6):498-504.

Model		
Risk factor	Hazard ratio (95% CI)	p value
Stenosis (per 10%)	1·18 (1·10–1·25)	<0·0001
Near occlusion	0·49 (0·19–1·24)	0·1309
Male sex	1·19 (0·81–1·75)	0·3687
Age (per 10 years)	1·12 (0·89–1·39)	0·3343
Time since last event (per 7 days)	0·96 (0·93–0·99)	0·0039
Presenting event		
Ocular	1·000	0·0067
Single transient ischaemic attack	1·41 (0·75–2·66)	
Multiple transient ischaemic attacks	2·05 (1·16–3·60)	
Minor stroke	1·82 (0·99–3·34)	
Major stroke	2·54 (1·48–4·35)	
Diabetes	1·35 (0·86–2·11)	0·1881
Previous myocardial infarction	1·57 (1·01–2·45)	0·0471
Peripheral vascular disease	1·18 (0·78–1·77)	0·4368
Treated hypertension	1·24 (0·88–1·75)	0·2137
Irregular/ulcerated plaque	2·03 (1·31–3·14)	0·0015

Table: Cox model for 5-year risk of ipsilateral ischaemic stroke on medical treatment in patients with recently symptomatic carotid stenosis derived from ECST

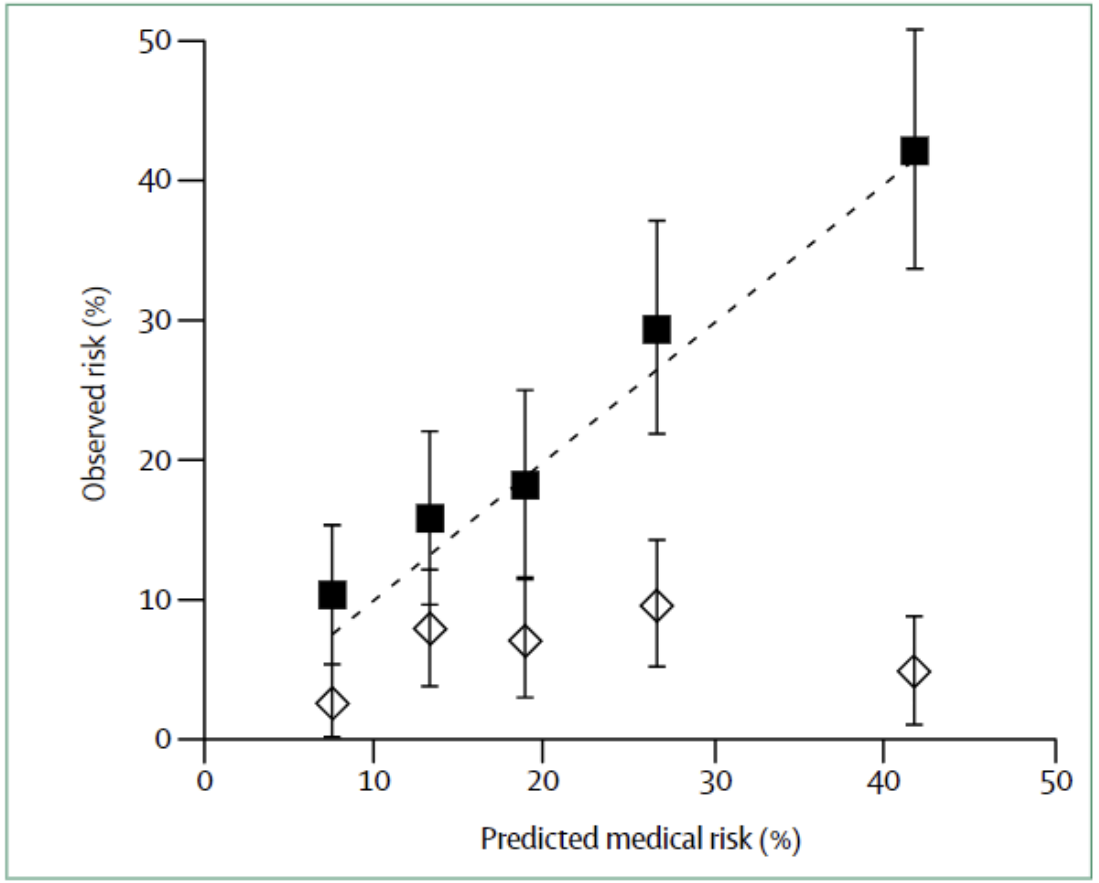


Figure 4: **Reliability of ECST prognostic model for 5 year risk of stroke on medical treatment in patients with 50–99% stenosis in NASCET (squares). Operative risk in patients randomised to surgery in NASCET is also stratified by predicted risk of stroke on medical treatment (diamonds)**

Error bars represent 95% CIs.

https://www.ndcn.ox.ac.uk/divisions/cpsd/carotid-stenosis-tool

Lancet. 2005 Jan 15-21;365(9455):256-65.

Management

- Medical management +/- carotid revascularization
- Advances in medical management
  - unknown if medical mgmt. would affect risk reduction conferred by revascularization

Stroke. 2021 May 24:STR0000000000000375.

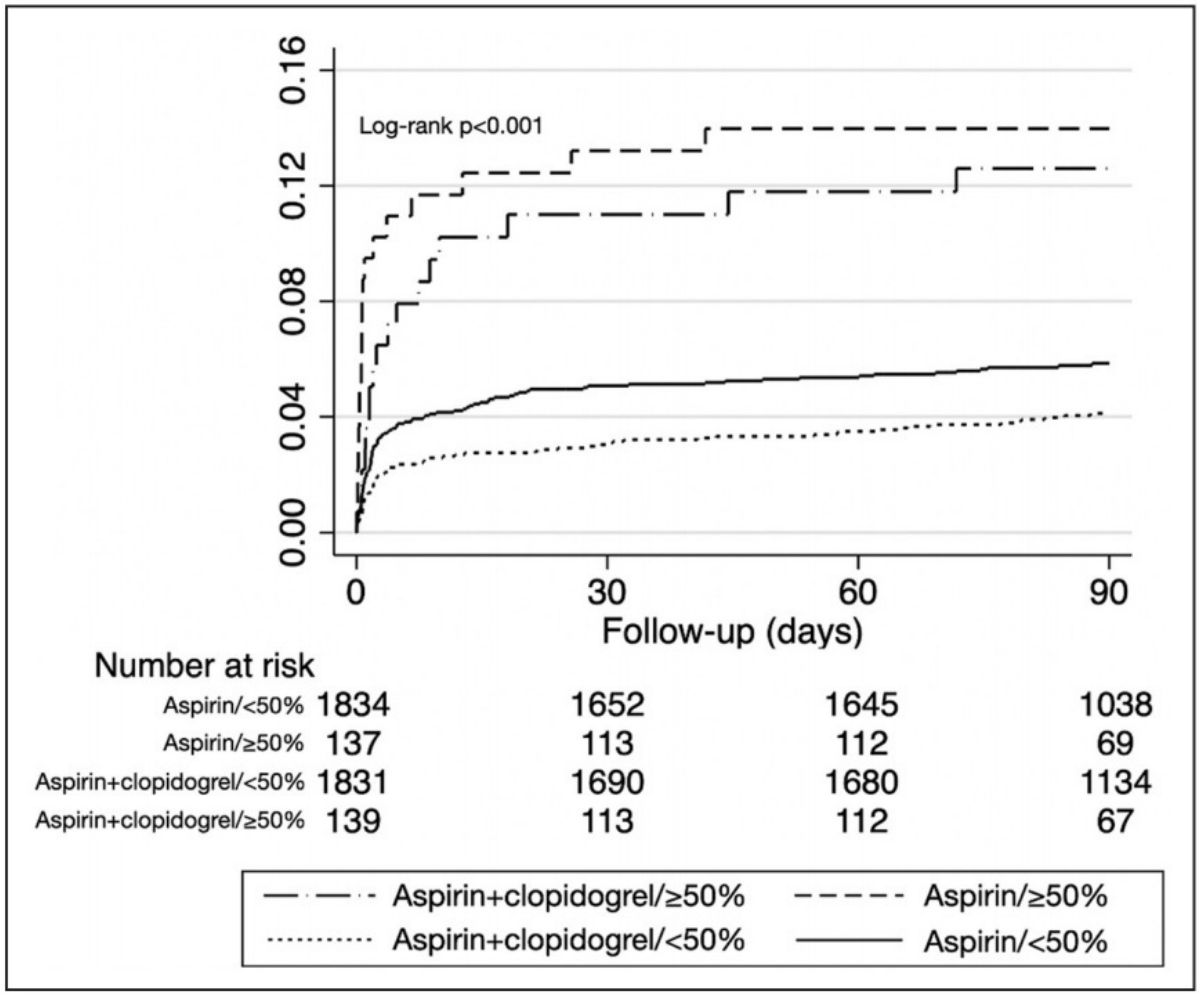
Recommendations for Extracranial Carotid Stenosis
Referenced studies that support recommendations are summarized in online Data Supplement 28.

COR	LOE	Recommendations
1	A	1. In patients with a TIA or nondisabling ischemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis, carotid endarterectomy (CEA) is recommended to reduce the risk of future stroke, provided that perioperative morbidity and mortality risk is estimated to be <6%.[369]
1	A	2. In patients with ischemic stroke or TIA and symptomatic extracranial carotid stenosis who are scheduled for carotid artery stenting (CAS) or CEA, procedures should be performed by operators with established periprocedural stroke and mortality rates of <6% to reduce the risk of surgical adverse events.[370]
1	A	3. In patients with carotid artery stenosis and a TIA or stroke, intensive medical therapy, with antiplatelet therapy, lipid-lowering therapy, and treatment of hypertension, is recommended to reduce stroke risk.[210]
1	B-R	4. In patients with recent TIA or ischemic stroke and ipsilateral moderate (50%–69%) carotid stenosis as documented by catheter-based imaging or noninvasive imaging, CEA is recommended to reduce the risk of future stroke, depending on patient-specific factors such as age, sex, and comorbidities, if the perioperative morbidity and mortality risk is estimated to be <6%.[369]

Intensive Medical Therapy

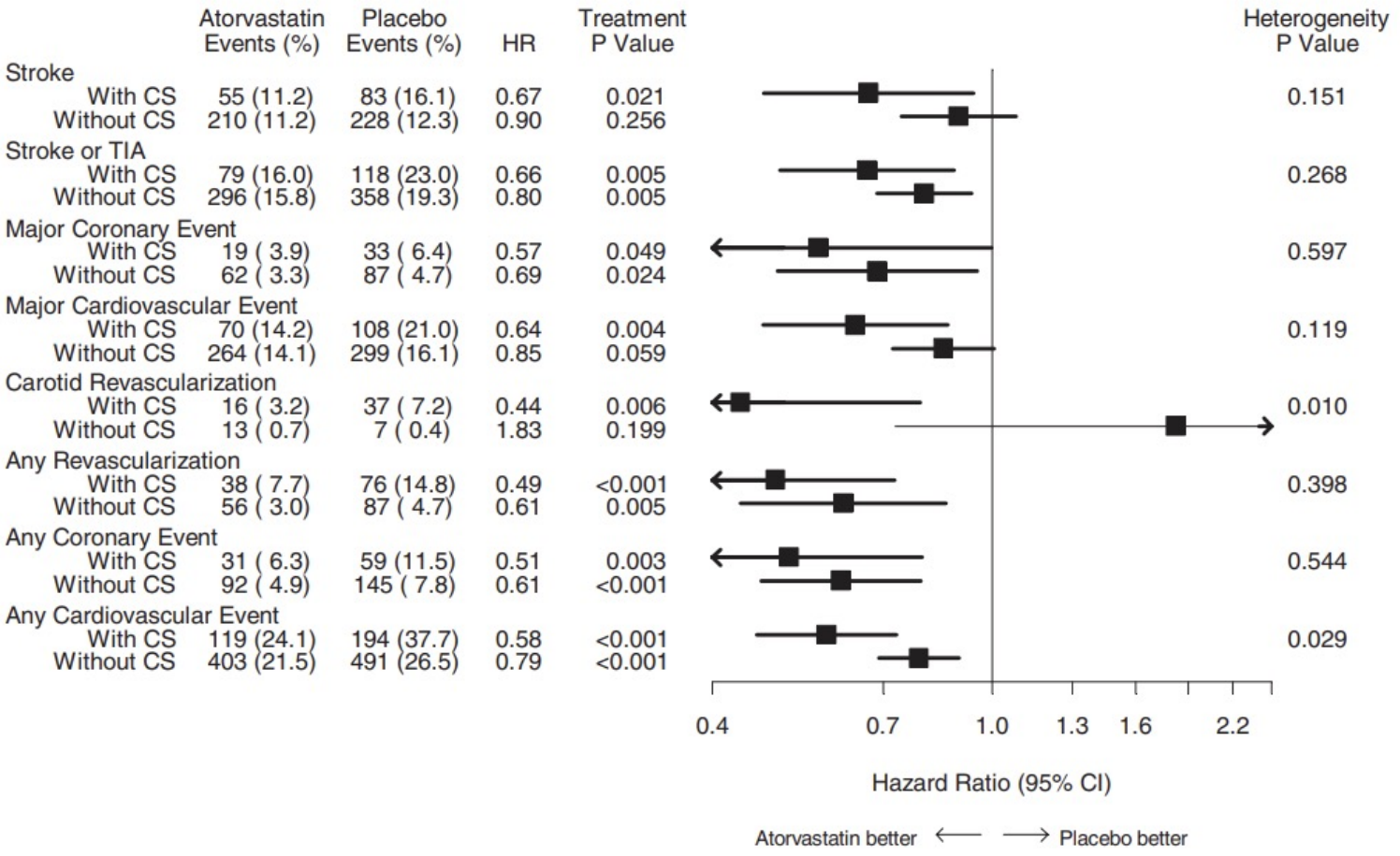
- Antiplatelet therapy
  - aspirin
  - clopidogrel
  - short-term aspirin + clopidogrel
    - minor ischemic stroke / high-risk TIA
    - treatment benefit ≈ in ≥50% & <50% carotid stenosis
    - TCD + HITS

End Point	Treatment Group		Relative Risk Reduction or Embolization Rate Reduction, % (95% CI)	*P*
	Dual Thgerapy	Monotherapy		
ITT analysis	n=51	n=56		
MES present at day 7, n (%)	21 (43.8)	40 (72.7)	39.8 (13.8, 58.0)	0.005
MES present at day 2, n (%)	28 (56.0)	40 (74.1)	24.4 (−1.2, 43.5)	0.065
MES frequency day 7, mean±SD	1.8±3.9	5.9±9.3	61.4 (31.6, 78.2)	0.001
MES frequency day 2, mean±SD	3.3±6.4	9.5±14.6	61.6 (34.9, 77.4)	<0.001



Circulation. 2005 May 3;111(17):2233-40.
Stroke. 2021 Jul;52(7):2414-2417.

- Hypertension
  - long-term target BP <130/80 mm Hg
  - gradual reduction
    - high-grade stenosis or occlusion
      * diuretic
- LDL-Cholesterol
  - target <70 mg/dL
  - statin therapy +/- ezetimibe
    - PCSK-9 inhibitor
- Hypertriglyceridemia
  - icosapent ethyl



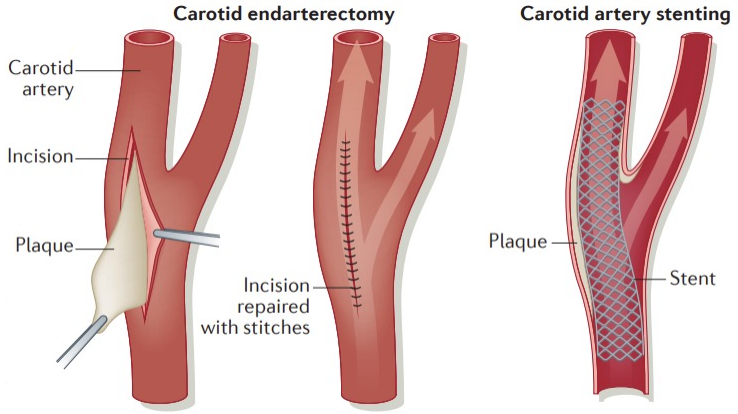
Stroke. 2008 Dec;39(12):3297-302.

- Diabetes
  - glycemic management → target HgA1c ≤ 7%
    - ≤6.5% (hypoglycemia)
  - glucose-lowering therapeutics that reduce vascular disease risk
    - glucagon-like protein 1 receptor agonists
    - thaizolidinediones
    - sodium-glucose cotrasporter 2 inhibitors
- Obstructive sleep apnea
  - positive airway pressure treatment (CPAP)

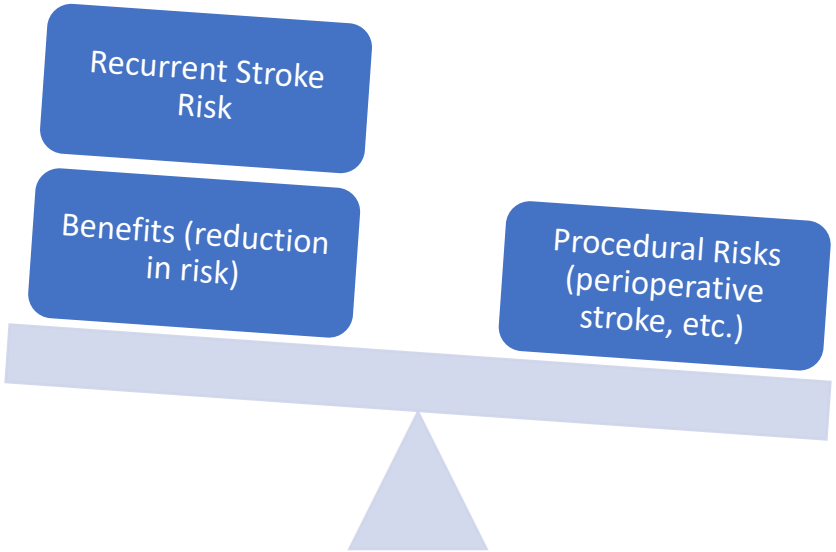
Measure	Intervention and Comments
Lifestyle modification	
For all patients	Show patients images of their plaques, compare the patient's plaque burden with that of healthy persons of the same age and sex, describe the risks associated with that degree of plaque burden and progression and the possibility of plaque regression.
Smoking cessation	Counseling, liberal nicotine replacement therapy, varenicline or bupropion (depending on history of depression or contraindications).
Mediterranean diet	Counseling, provision of a booklet summarizing advice and providing recipes and links to Internet sites; repeated at follow-up visits as necessary.
Obesity	Counseling on caloric restriction, referral to dietitian, bariatric surgery in refractory patients with severe obesity and diabetes mellitus or insulin resistance.
Exercise	Recommendations for moderate exercise at least 30 minutes per day, with advice tailored to the patient's disabilities, if any.
Blood pressure	Advice on how to reduce salt intake, limit alcohol intake, avoid licorice and decongestants.

Continuum (Minneap Minn). 2017 Feb;23(1, Cerebrovascular Disease):133-157.

Carotid Revascularization



- Benefits > Risks
  - high-grade > moderate-grade symptomatic carotid stenosis
  - men > women



Mayo Clin Proc. 2017 Jul;92(7):1144-1157.
Nat Rev Cardiol 13, 181 (2016).

- Risks > Benefits
  - <50% symptomatic carotid stenosis
  - carotid occlusion or near occlusion, severe infarction/disability

- Carotid Endarterectomy (CEA)
- Carotid Artery Stenting (CAS)
  - comorbidities
  - surgical risk
    - periop risk (stroke/death) <6%
  - anatomy of symptomatic artery

- Limited evidence → proximal CCA, tandem CCA/ICA stenosis

Timing of Revascularization

- evidence principally for CEA
  - pooled 2° analyses - NASCET/ECST, observational studies
  - nondisabling stroke / TIA

- most benefit → < 2 weeks
  - moderate stenosis, women → benefit less clear > 2 weeks
  - not very early / emergent (2 days)

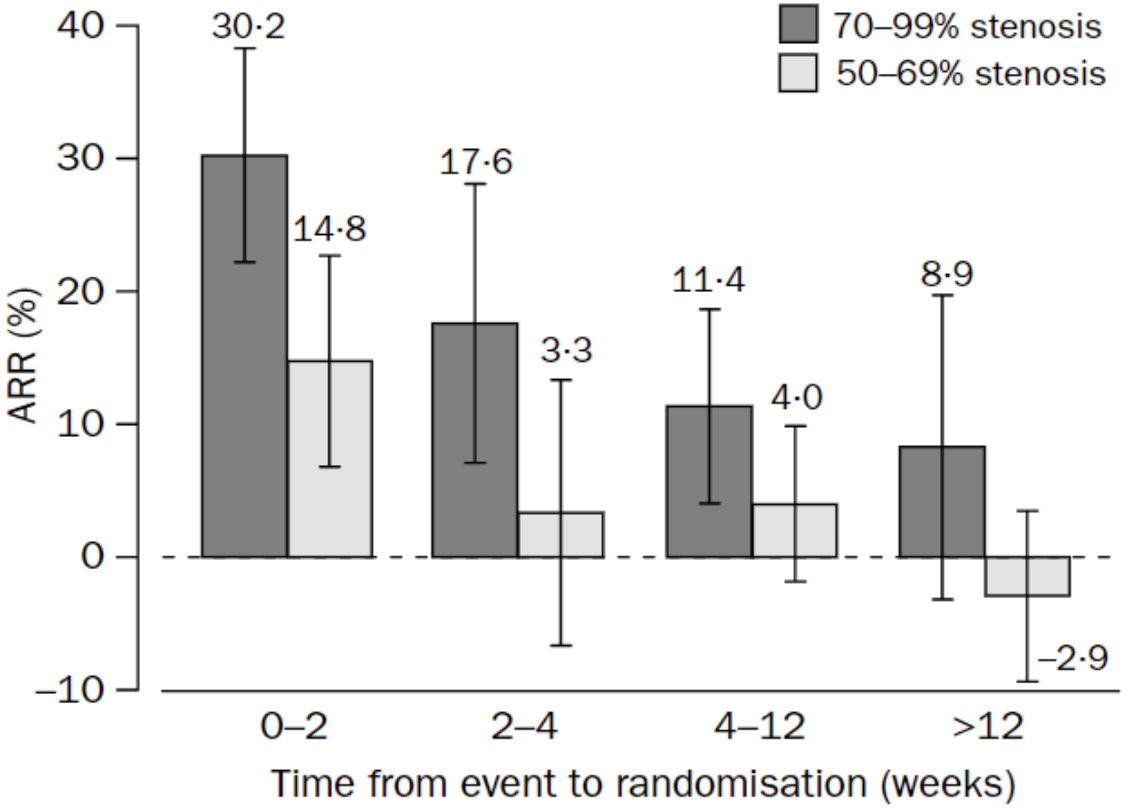


Figure 5: **Absolute reduction with surgery in the 5-year cumulative risk of ipsilateral carotid ischaemic stroke and any stroke or death within 30 days after trial surgery in patients with 50–69% stenosis and ⩾70% stenosis without near-occlusion stratified by the time from last symptomatic event to randomisation**

Lancet. 2004 Mar 20;363(9413):915-24.

Table. Outcomes Summary

	Perioperative Stroke % Proportion (95% CI)	Perioperative Stroke and Death % Proportion (95% CI)
CEA procedures		
CEA within 0–15 d		
All patients	3.36 (2.57–4.25)	3.80 (2.99–4.71)
TIA subgroup of patients	1.64 (0.72–2.94)	1.86 (0.82–3.31)
Stroke subgroup of patients	4.99 (3.55–6.61)	4.94 (3.44–6.70)
Excluding administrative studies	3.28 (2.63–3.99)	3.57 (2.85–4.37)
Excluding thrombolysis studies	3.29 (2.48–4.22)	3.77 (2.91–4.74)
CEA within 0–7 d		
All patients	3.25 (2.12–4.61)	3.61 (2.60–4.78)
TIA subgroup of patients	1.51 (0.47–3.10)	1.87 (0.58–3.86)
Stroke subgroup of patients	5.31 (2.74–8.67)	5.55 (2.79–9.19)
CEA within 0–48 h		
All patients	5.26 (2.80–8.43)	5.75 (3.73–8.17)
TIA subgroup of patients	2.74 (0.45–6.87)	2.78 (0.40–7.20)
Stroke subgroup of patients	7.95 (4.58–12.15)	8.44 (4.96–12.74)
CAS procedures		
CAS within 0–15 d		
All patients	4.76 (2.47–7.75)	6.92 (5.47–8.52)
TIA subgroup of patients	2.07 (0.17–6.02)	3.42 (0.68–8.13)
Stroke subgroup of patients	7.96 (2.31–16.58)	7.96 (2.31–16.58)
CAS within 0–7 d		
All patients	4.76 (2.45–7.80)	6.63 (4.25–9.49)
TIA subgroup of patients	1.93 (0.11–5.91)	3.31 (0.59–8.15)
Stroke subgroup of patients	7.94 (1.26–19.61)	7.94 (1.26–19.61)
CAS within 0–48 h		
All patients	2.07 (1.19–3.18)	5.43 (2.67–9.09)
TIA subgroup of patients	2.07 (0.17–6.02)	3.42 (0.68–8.13)
Stroke subgroup of patients	7.94 (1.26–19.61)	7.94 (1.26–19.61)
Studies on revascularization after thrombolysis within 15 d		
Patients after thrombolysis	3.87 (1.89–6.51)	3.87 (1.89–6.51)

CAS indicates carotid stenting; CEA, carotid endarterectomy; CI, confidence interval; and TIA, transient ischemic attack.

Stroke. 2004 Dec;35(12):2855-61.
Stroke. 2009 Oct;40(10):e564-72.
Stroke. 2015 Dec;46(12):3423-36.

Carotid Endarterectomy

- NASCET
- ECST
- VACS

→ pooled analyses demonstrate groups most likely to benefit

Neurology. 1995 Nov;45(11):1965-70.

Table 1. Comparison of symptomatic carotid endarterectomy trials

	NASCET	ECST	VACS
Design features			
Design	RCT	RCT "Uncertainty principle"	RCT
Qualifying symptoms	TIA Nondisabling stroke Amaurosis	TIA Nondisabling stroke Amaurosis/retinal infarction	TIA Nondisabling stroke Amaurosis
Pt. age	<79	—	—
Time	120 days	6 months	120 days
Exclusions	Incompetence Carotid occlusion Severe distal CVD <5 yr life expectancy Nonatherosclerotic CVD Cardioembolic source Prior ipsilateral CEA Major stroke Medical exclusions — — — —	— Carotid occlusion Severe distal CVD Poor general health — Cardioembolic source Prior ipsilateral CEA Major stroke Medical exclusions — — — —	— Carotid occlusion Severe distal CVD <3 yr life expectancy — Cardioembolic source Prior ipsilateral CEA Major stroke Medical exclusions Global ischemia Seizures Prior EC-IC bypass Incapacitating neurologic disease
% Stenosis	30-99% 70-99% reported	0-99% 0-29, 70-99% reported	50-99%
Measure*	Residual lumen/ normal lumen distal to stenosis	Residual lumen/ estimate of normal lumen at level of stenosis	Residual lumen/ normal lumen distal to stenosis
Co-Rx	ASA 1,300 mg	±ASA ? dose	ASA 325 mg
1° Outcomes	Stroke Death	Disabling stroke Fatal stroke Perioperative death	Stroke Death Crescendo TIA
Planned follow-up	30 days, then q 3 months × 1 year, then q 4 months	4 months, 12 months, then q 12 months	30 days, then q 3 months × 1 year, then q 6 months
Site characteristics and requirements			
Sites	50 centers, US and Canada	80 centers, 14 European countries	13 centers, VAMCs
Center qualifications	<6% 30 days stroke and death (50 consecutive CEAs over prior 2 yr)	—	>25 CEAs/yr over prior 3 yr <6% 30 days morbidity and mortality over the prior 3 yr
Surgeon qualifications	—	—	>10 CEAs/yr over prior 3 yr <6% 30 days morbidity and mortality over the prior 3 yr
Patient characteristics			
Patients			
Surgical	328	455	92
Medical	331	323	101
Male:Female	68%:32%	70%:30%	100%:0
Actual follow-up	Mean, 18 months 98%†	Mean, 2.7 yr 87%†	Mean, 1 yr 99%†
Age	65 (median)	62 (mean)	65 (mean)

NASCET North American Symptomatic Carotid Endarterectomy Trial.
ECST European Carotid Surgery Trial.
VACS VA Cooperative Study.
RCT Randomized controlled trial.
TIA Transient ischemic attack.
CVD Cerebrovascular disease.
CEA Carotid endarterectomy.
EC-IC Extracranial-intracranial.
Co-Rx Co-treatment.
ASA Aspirin.
VAMC Veterans Administration Medical Center.
* See text for explanation of measurement techniques.
† Percent of enrolled patients available for follow-up evaluation or those having a specified outcome event.

Moderate & Severe Carotid Stenosis

% Stenosis	Outcome	Relative Risk (95% CI) * 5-year cumulative	Absolute Risk Reduction	Number Needed to Treat
70-99% Stenosis	Ipsilateral ischemic stroke & operative stroke / death	0.47 (0.25 – 0.88)	**17%**	**6**
	Any stroke / operative death	0.53 (0.42 – 0.67)		
50-69% Stenosis	Ipsilateral ischemic stroke & operative stroke / death	0.84 (0.60 – 1.18)	**4.5%**	**22**
	Any stroke / operative death	0.77 (0.63 – 0.94)		

Lancet. 2003 Jan 11;361(9352):107-16.
Cochrane Database Syst Rev. 2017 Jun 7;6(6):CD001081.
Cochrane Database Syst Rev. 2020 Sep 12;9:CD001081.

Moderate Carotid Stenosis – Sex Differences

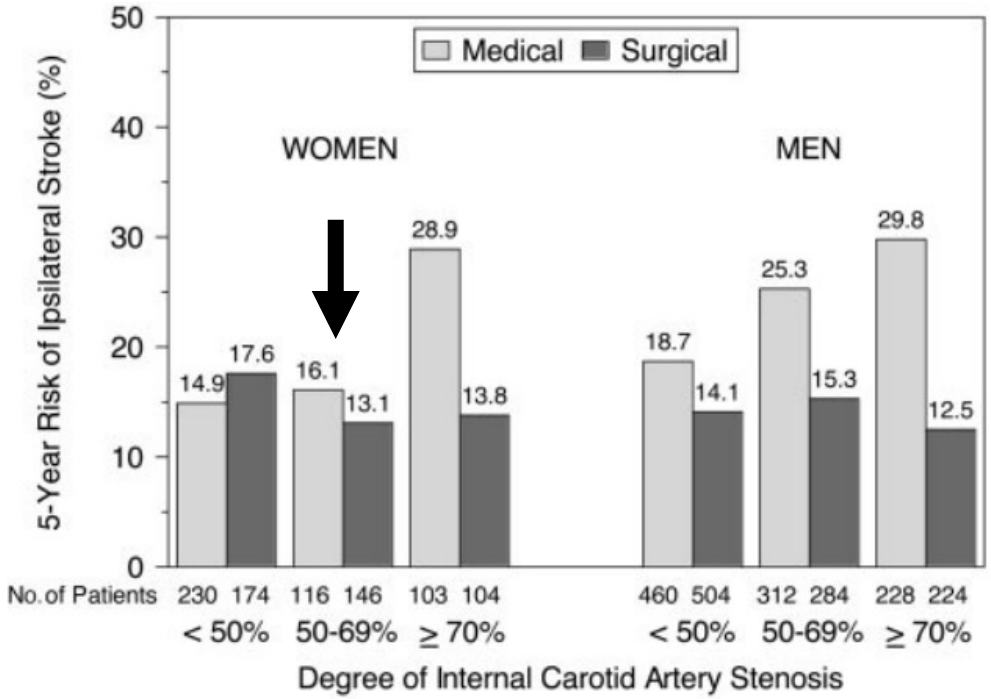
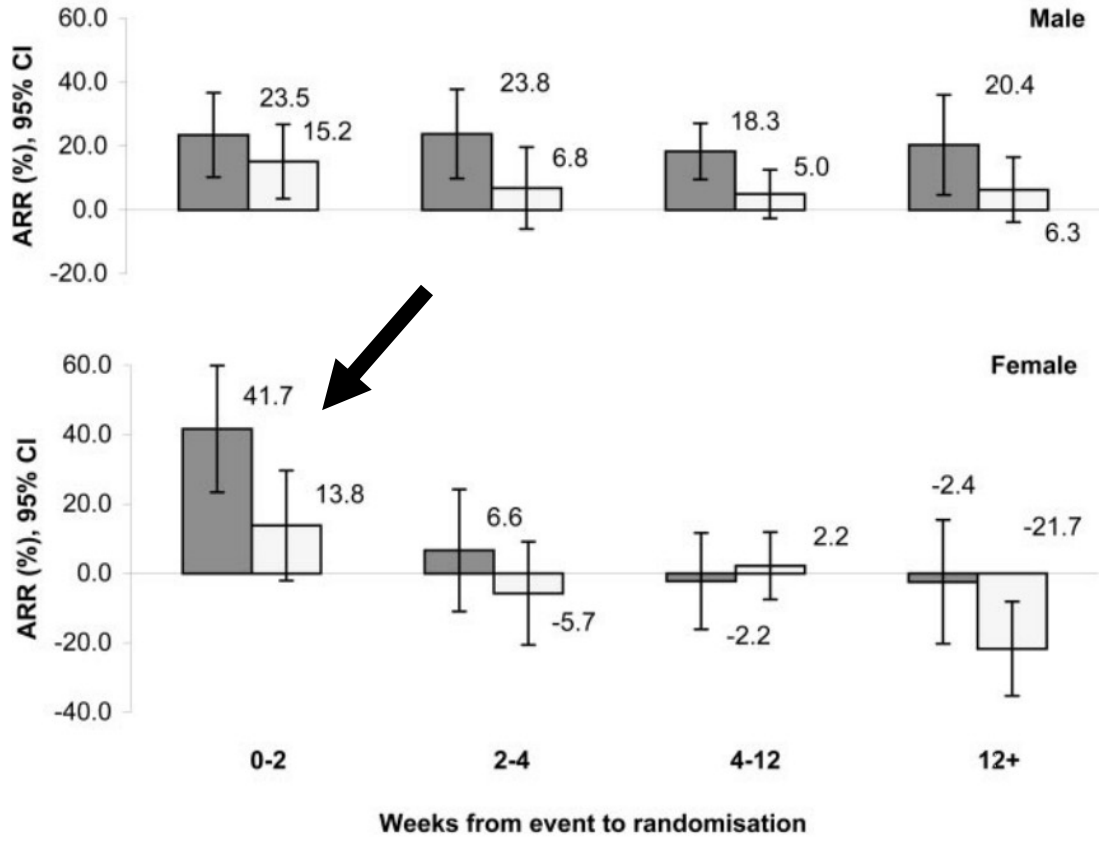


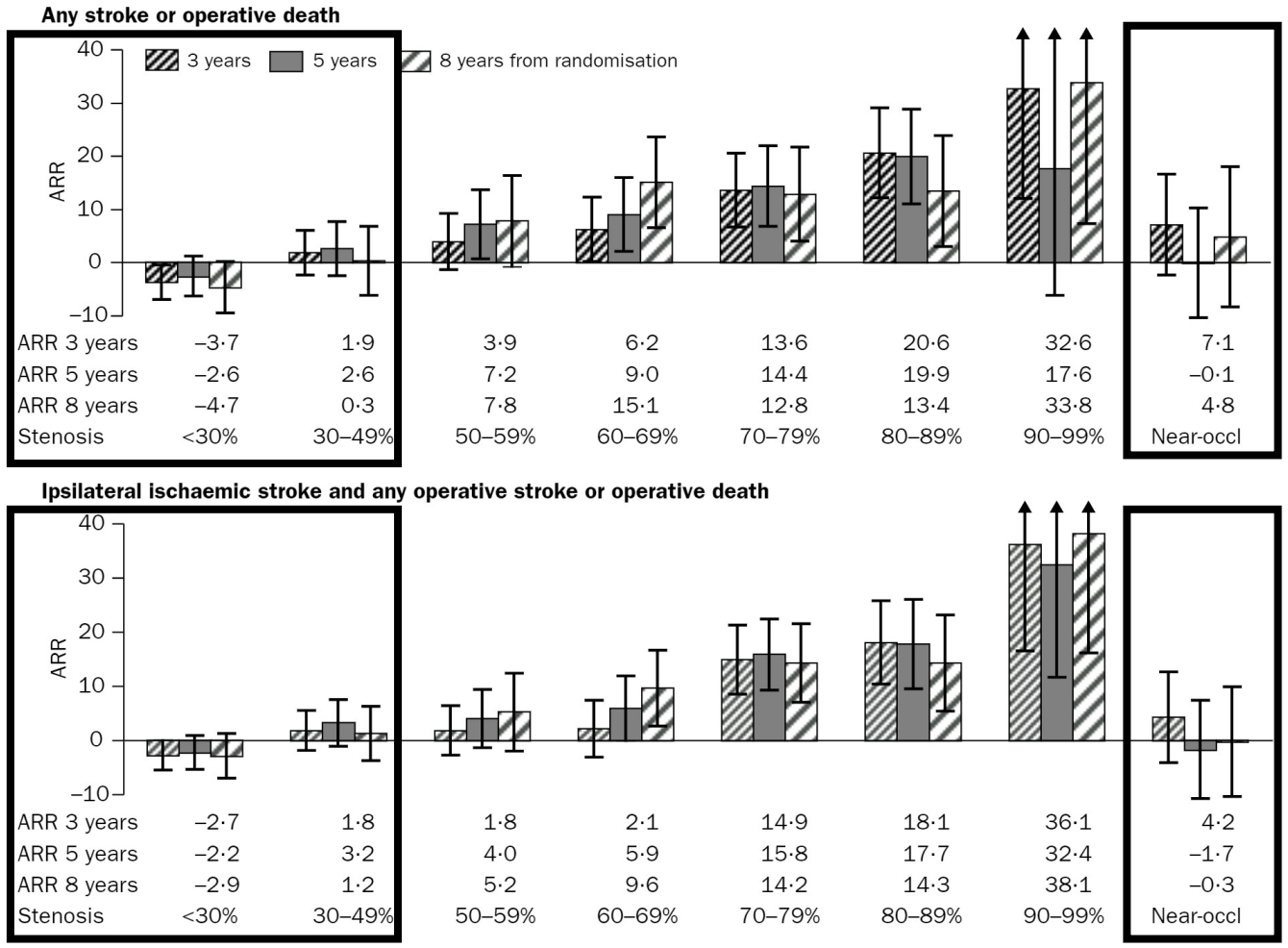
Figure 1. Kaplan–Meier 5-year risks of ipsilateral ischemic stroke for NASCET patients according to gender and degree of internal carotid artery stenosis in the medical and surgical groups. The number of patients at risk is shown below each bar. The Kaplan–Meier risk estimates are shown above the bars.



Stroke. 2004 Dec;35(12):2855-61.
Stroke. 2005 Jan;36(1):27-31.

Uncertain Benefit

- Mild (<50%) carotid stenosis
  - Harmful for <30% stenosis
- Near Occlusion
  - angiographic collapsed ICA distal to ICA stenosis + faster ECA filling & intracranial circulation filling from collateral vessels
- Total Occlusion



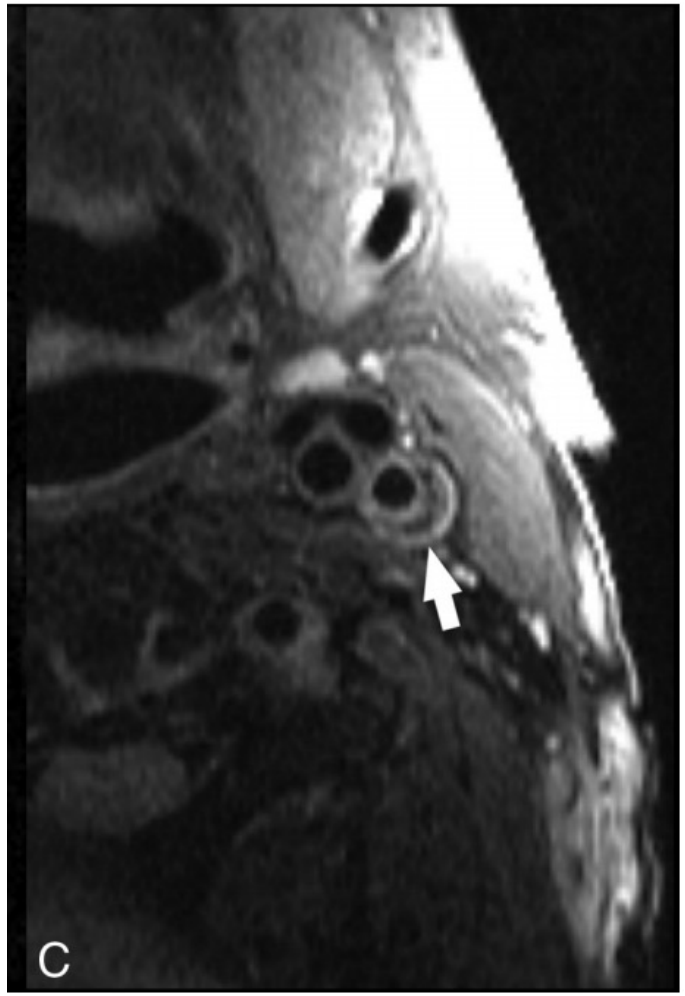
Lancet. 2003 Jan 11;361(9352):107-16.
Cochrane Database Syst Rev. 2020 Sep 12;9:CD001081.

Table 2. Features of Nonstenotic Plaques That Are Associated With Higher Risk of Stroke

Plaque Feature	Imaging Modality
Ulceration	MRI, CTA
Intraplaque hemorrhage	MRI[9,13–16,18,22]
Fibrous cap rupture	MRI,[10] ultrasound[11]
Plaque thickness*	MRI, CTA,[12] ultrasound[19]
Plaque echolucency	Ultrasound[11]
Lipid-rich core	MRI[18]

CTA indicates computed tomography angiography; and MRI, magnetic resonance imaging.

*Previous publications suggest a 3-mm cutoff for plaque thickness.[12]



AJNR Am J Neuroradiol. 2017 Apr;38(4):664-671.
AJNR Am J Neuroradiol. 2018 Feb;39(2):E9-E31.
Stroke. 2020 Apr;51(4):1321-1325

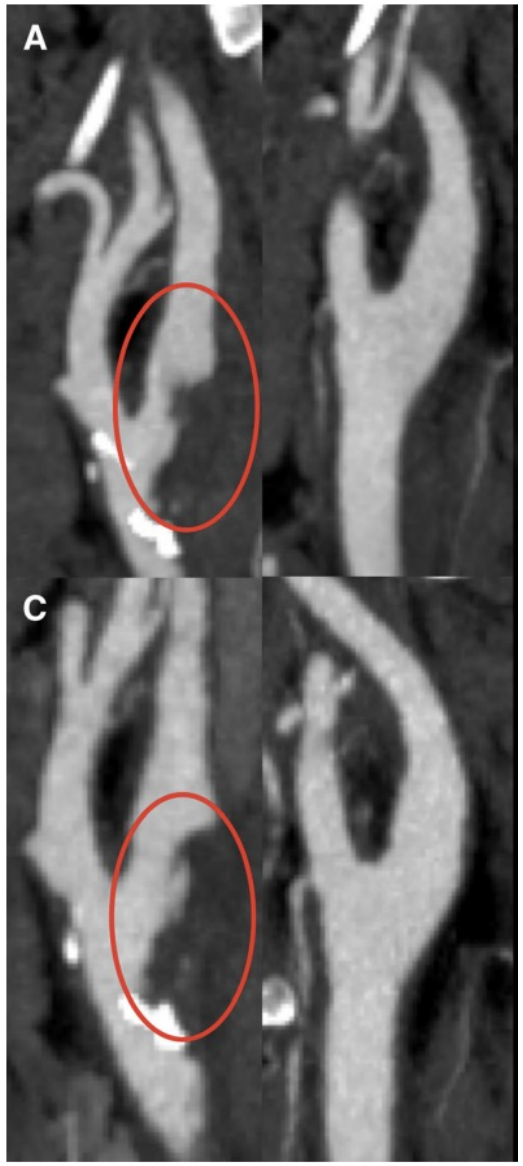
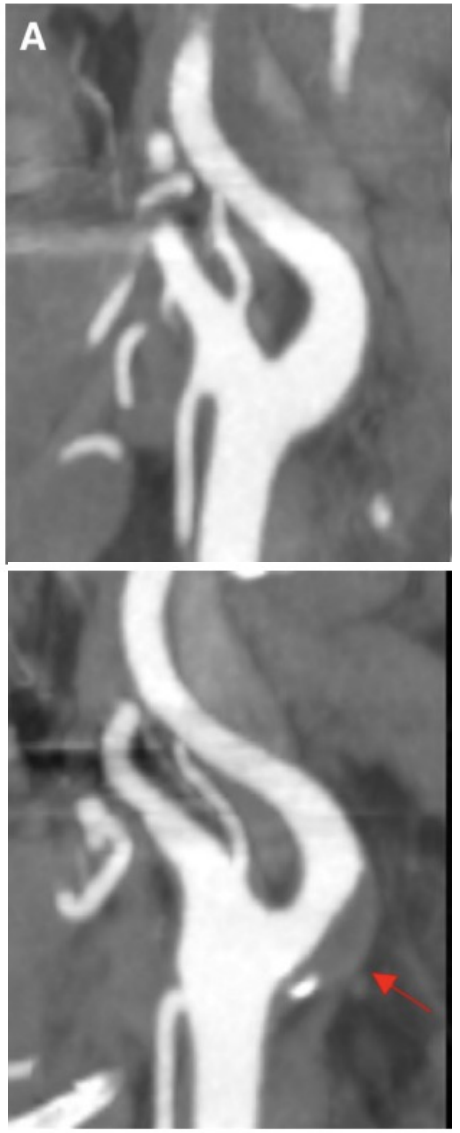


Table 3. Suggested Working Definition of SyNC

If no other stroke causes are present (ESUS based on current definition): all of the following	Definite SyNC
Nonstenotic (<50%) carotid plaque with high risk features* and changing morphology (on at least 2 exams at any time point, detected on ultrasound, DSA, CTA, or MRI)	
Imaging findings† consistent with recurrent embolic stroke(s) confined to the corresponding ICA territory§ (co-existing old and new strokes or new strokes on 2 exams)	
Absence of acute or chronic infarcts in other vascular territories	
If no other stroke causes are present (ESUS based on current definition): all of the following	Probable SyNC
Nonstenotic (<50%) carotid plaque with high-risk features* (detected on ultrasound, DSA, CTA, or MRI)	
Imaging findings† consistent with acute embolic stroke(s) confined to the corresponding ICA territory§	
Absence of acute or chronic infarcts in other vascular territories	
In presence of a potential cardiac cause: all of the following‡	
Nonstenotic (<50%) carotid plaque with high risk features* and changing morphology (on at least 2 exams at any time point, detected on ultrasound, DSA, CTA or MRI)	
Imaging finding† consistent with acute embolic stroke(s) confined to the corresponding ICA territory§	
Absence of acute or chronic infarcts in other vascular territories	
In presence of a potential cardiac cause: all of the following‡	
Nonstenotic (<50%) carotid plaque with high risk features* (detected on ultrasound, DSA, CTA, or MRI)	
Imaging findings† consistent with recurrent embolic stroke(s) confined to the corresponding ICA territory§ (coexisting old and new strokes or new strokes on 2 exams)	
Absence of acute or chronic infarcts in other vascular territories	
In presence of a potential cardiac cause: all of the following‡	Possible SyNC
Nonstenotic (<50%) carotid plaque with high-risk features* (detected on ultrasound, DSA, CTA, or MRI)	
Imaging findings† consistent with acute embolic stroke(s) confined to the corresponding ICA territory§	
Absence of acute or chronic infarcts in other vascular territories	



Stroke. 2020 Apr;51(4):1321-1325.

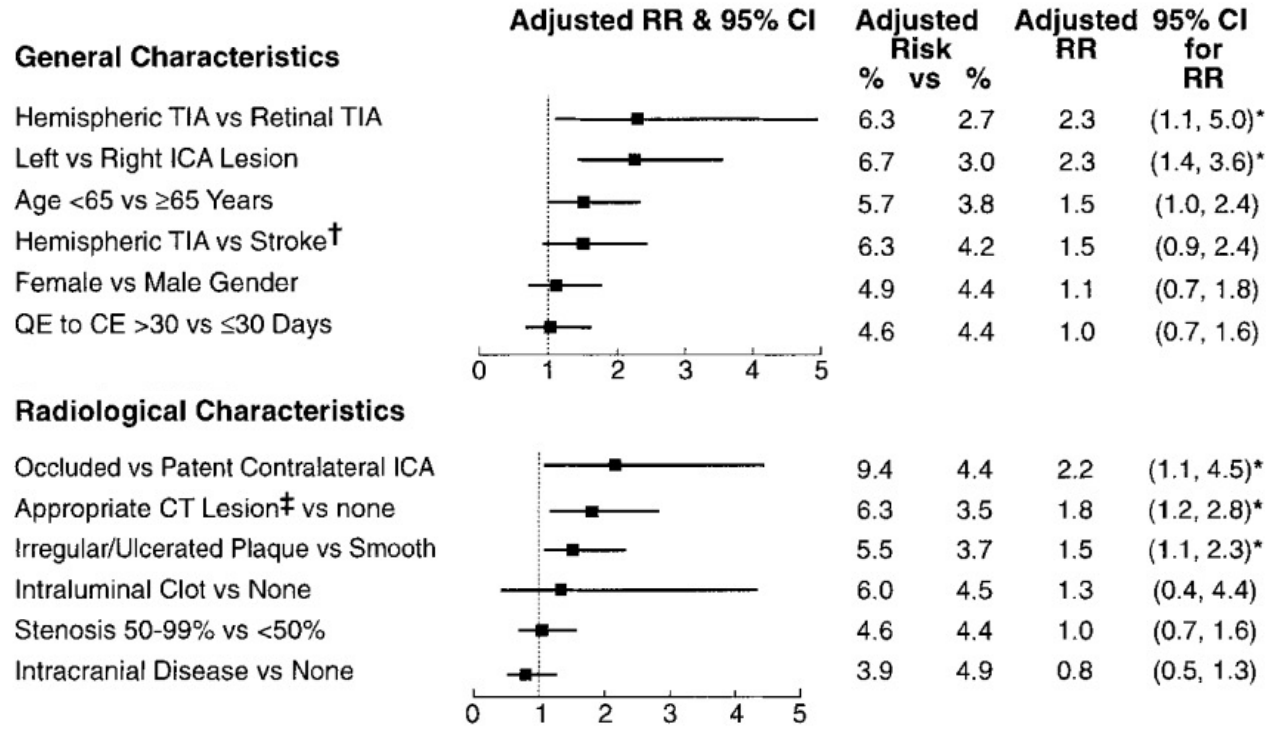
Additional Considerations

- Age > 75 years: ↑ benefit
- Retinal ischemia: ↓ risk
  (vs. hemispheric TIA)
- Increased surgical risk
  - contralateral high-grade stenosis or occlusion

TABLE 3. Adjusted Hazard Rates and Ratios From Final Cox Regression Model

Baseline Factor	Adjusted Hazard Rates %	%	Adjusted Hazard Ratio	*P*
Hx myocardial infarction or angina vs none	11.7	7.1	1.6*	0.007
Hx hypertension vs none	10.0	6.5	1.5†	0.04

*95% CI, 1.2–2.4.
†95% CI, 1.1–2.3.



J Neurosurg. 1995 Nov;83(5):778-82.
Stroke. 1999 Sep;30(9):1759-63.
Stroke. 1999 Sep;30(9):1751-8.
N Engl J Med. 2001 Oct 11;345(15):1084-90.
Lancet. 2004 Mar 20;363(9413):915-24.

Carotid Stenting

- CREST
- ICSS
- SPACE
- EVA-3S

- Periprocedural stroke/death → CAS > CEA
- Long-term (>120 days) stroke risk → CEA ≈ CAS

	All events (CEA, n=2361; CAS, n=2393)				Periprocedural events (within 120 days) (CEA, n=2361; CAS, n=2393)				Postprocedural events (after 120 days) (CEA, n=2168; CAS, n=2121)				
	Events	Risk at 5 years	Absolute risk difference at 5 years	Hazard ratio (CAS *vs* CEA)	Events	Risk at 120 days	Absolute risk difference at 120 days	Hazard ratio (CAS *vs* CEA)	Events	Risk at 5 years	Absolute risk difference at 5 years	Hazard ratio (CAS *vs* CEA)	Annual event rate per person-years
Any stroke or death within 120 days and ipsilateral stroke afterwards													
CEA	184 (7·8%)	8·3% (7·2 to 9·6)	3·0% (1·2 to 4·8)	1·45 (1·20 to 1·75)	129 (5·5%)	5·5% (4·7 to 6·5)	3·2% (1·7 to 4·7)	1·61 (1·29 to 2·01)	55 (2·5%)	3·1% (2·3 to 4·1)	0·1% (–1·2 to 1·3)	1·06 (0·73 to 1·54)	0·60% (0·46 to 0·79)
CAS	263 (11·0%)	11·4% (10·1 to 12·8)	..	..	206 (8·6%)	8·7% (7·6 to 9·9)	..	..	57 (2·7%)	3·2% (2·3 to 4·2)	..	..	0·64% (0·49 to 0·83)

Lancet Neurol. 2019 Apr;18(4):348-356.

- CAS → Periprocedural stroke/death risk ↑ w/ age
- MI, cranial nerve palsy risk → CAS < CEA
- CAS Favored
  - surgically inaccessible plaque
  - restenosis after CEA
  - radiation
  - cardiac disease, anatomy affecting surgical risk or access

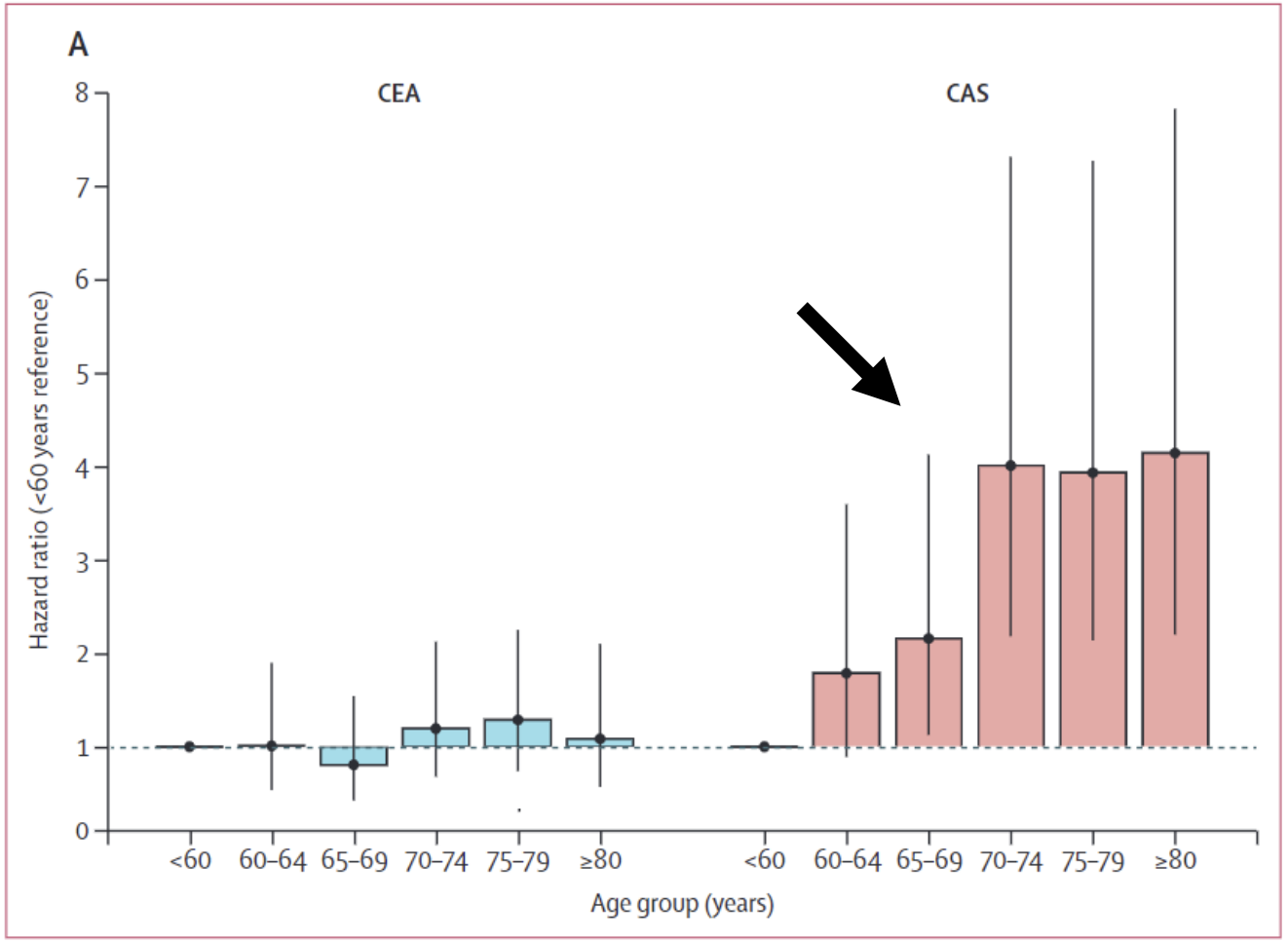
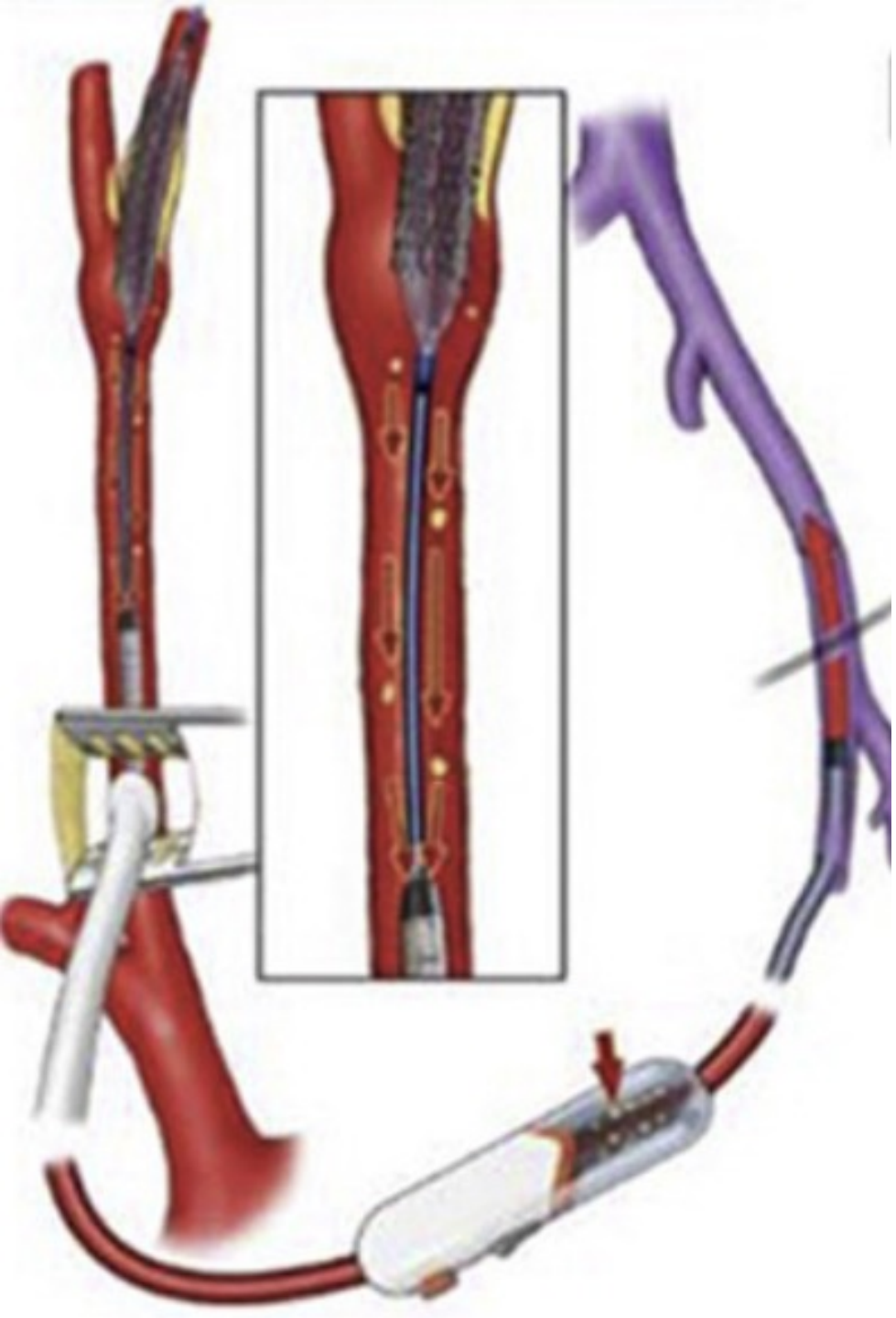


Figure 3: Adjusted hazard ratios for events in patients treated with CEA or CAS (relative to patients aged <60 years) during the periprocedural period (A) and post-procedural (B) period

Lancet. 2016 Mar 26;387(10025):1305-11.



Trans-Carotid Carotid Artery Revascularization

- Prospective, single-arm study & post-approval registry
  - ROADSTER, ROADSTER 2
- Observational studies
  - TCAR surveillance project

- Comparative evidence
  - TCAR vs CEA → no difference in stroke/death/MI
  - TCAR vs transfemoral CAS → lower risk of in-hospital stroke/death

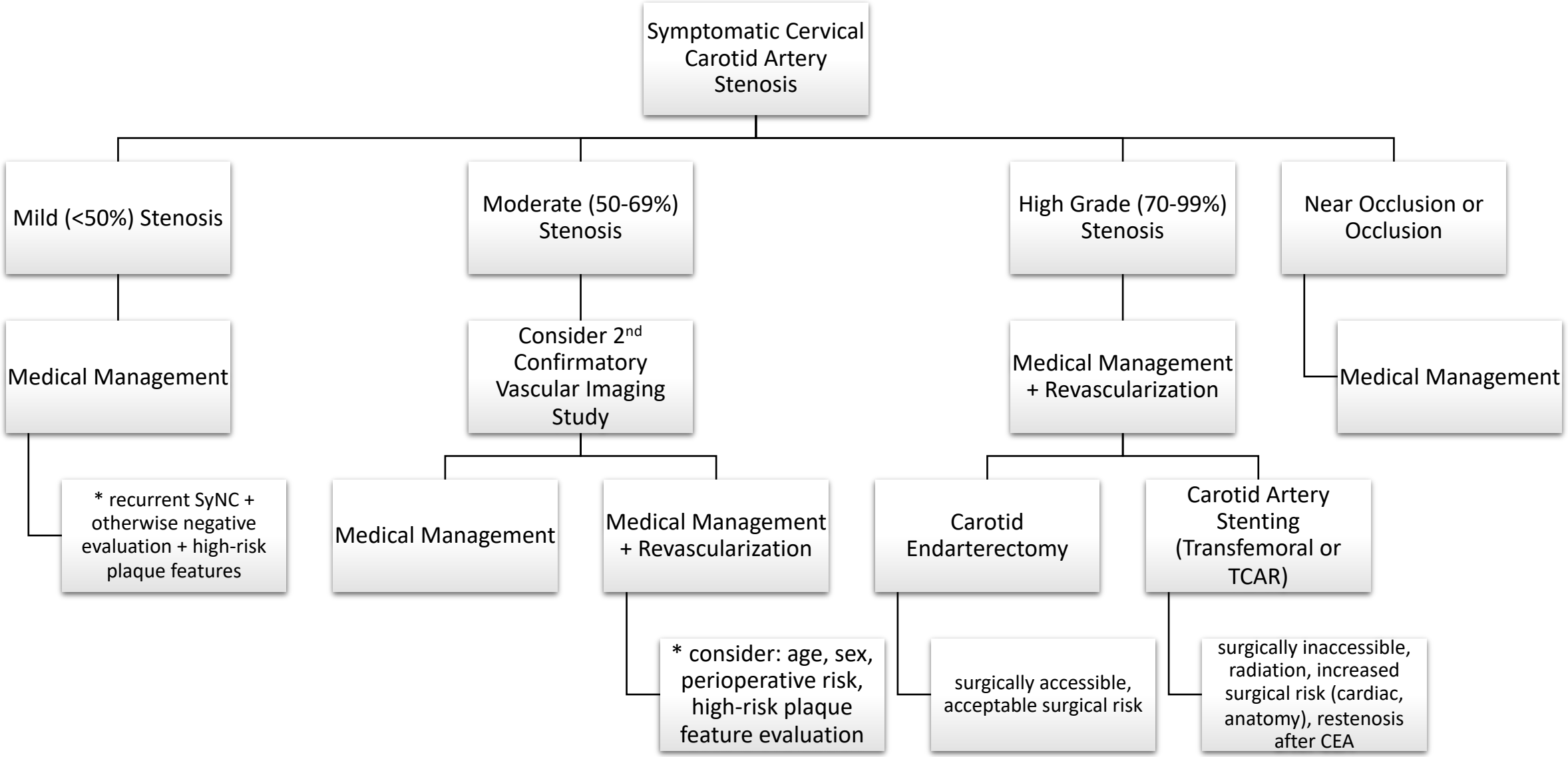
J Vasc Surg. 2019 Jul;70(1):123-129.
JAMA. 2019 Dec 17;322(23):2313-2322.
Stroke. 2020 Sep;51(9):2620-2629.
JAMA Netw Open. 2021 Feb 1;4(2):e2037885.

Uncertainties

- Benefits/Risks of revascularization w/ modern medical tx
  - TCAR
  - Elderly
  - SyNC
- Biomarkers
  - Carotid MRI
  - Serologic
- Sex differences in outcomes
- Novel atherosclerotic disease treatments & stroke risk
  - Anti-inflammatory drugs

Key Points

- ≥ 50% symptomatic carotid stenosis → ~10% ischemic stroke
- Non-invasive vascular imaging less accurate for moderate carotid stenosis
- Recurrent stroke risk highest early after symptomatic carotid stenosis
- Advances in medical management
- Revascularization most beneficial for symptomatic 70-99% carotid stenosis within 2 weeks of TIA/stroke
- CEA likely preferred over transfemoral CAS
  - TCAR risks lower



* Revascularization most appropriate if <6% risk of perioperative stroke/death, life expectancy >5 years

Questions?